universität wien

MASTERARBEIT / MASTER'S THESIS

Titel der Masterarbeit / Title of the Master's Thesis

„Dietary supplements and glycaemic control in patients with type 2 diabetes: a systematic review and meta-analysis“

verfasst von / submitted by

Melanie Lehner, BSc

angestrebter akademischer Grad / in partial fulfilment of the requirements for the degree of

Master of Science (MSc)

Wien, 2017 / Vienna 2017

Studienkennzahl lt. Studienblatt / degree programme code as it appears on the student record sheet:	A 066 838
Studienrichtung lt. Studienblatt / degree programme as it appears on the student record sheet:	Masterstudium Ernährungswissenschaften
Betreut von / Supervisor:	Dipl. oec. troph. Dr. Georg Hoffmann, Privatdoz.

Index

1 Acknowledgements

Firstly, I want to thank my supervisor, Dr. Georg Hoffmann, for his time, help and advice as I worked on my master's thesis. Secondly, I want to express my appreciation towards Kathi for always being there for me with an open ear not only during the process of writing my thesis, but throughout the whole duration of my master's degree. A big thanks goes out to my parents; without their love, financial and mental support the last five years of studying would not have been possible for me. I also want to thank my brother for his continued help as well as Karen and Mike for assisting me in proofreading this paper. Furthermore, I want to express my appreciation to the professors at the university of Vienna for making studying nutrition science almost always a pleasure for me. Finally, I want to thank my classmates from the university and all my friends for making the last five years one of the best times of my life that I'll always gladly look back at.

2 List of abbreviations

AA = amino acid

ABM = *Agaricus blazei* Murill

ADA = American Diabetes Association

AHA = American Heart Association

ALA = alpha-linolenic acid

BCAA = branched-chain amino acids

BMI = body mass index

CI = confidence interval

DAG = diacylglycerol

DALY = disability-adjusted life year

DHA = docosahexaenoic acid

DJC = Danzhijiangtang capsules

DPP-4 = dipeptidyl peptidase 4

EPA = eicosapentaenoic acid

EPA-E = eicosapentaenoic acid ethyl

FBG = fasting blood glucose

FPG = fasting plasma glucose

G. biloba = *Gingko biloba*

GLP-1 = Glucagon-like peptide 1

GLUT-4 = glucose transporter type 4

HbA1c = Glycated Haemoglobin

HDL = high-density lipoprotein

HOMA = homeostasis model assessment

IR = insulin resistance

M. charantia = *Momordica charantia*

MD = mean difference

min = minutes

MVM = multivitamin/mineral

N/A = not applicable

N. sativa = Nigella sativa

NIDDM = non-insulin-dependent diabetes mellitus

NNFTRI = National Nutrition and Food Technology Research Institute

OGTT = oral glucose tolerance test

OHA = oral hypoglycaemic agent

ONS = oral nutritional supplement

PA = physical activity

PPAR-δ = peroxisome proliferator activated receptor delta

RCT = randomized controlled trial

SD = standard deviation

SDI = socio-demographic index

SMD = standardized mean difference

T2DM = type 2 diabetes mellitus

TAG = triacylglycerol

UK = United Kingdom

US = United States

USA = United States of America

WHO = World Health Organization

YLD = years lived with disease/disability

YLL = years of life lost

3 List of figures

4 List of tables

5 Introduction

5.1 Definition and description of diabetes mellitus

The group of metabolic diseases that results from failures in insulin action, insulin secretion, or both is called diabetes. The known forms of diabetes are type 1 diabetes, type 2 diabetes, gestational diabetes mellitus and other specific forms of diabetes such as genetic defects of the β-cell or insulin action, endocrinopathies caused by excess quantities of hormones that antagonize insulin action, diseases of the exocrine pancreas, infections, chemical- or drug-induced diabetes, uncommon types of immune-mediated diabetes or other genetic syndroms that are sometimes related to diabetes. One of the types of diabetes not discussed in this paper, type 1 diabetes mellitus, is caused by the destruction of the β-cells and typically results in an absolute insulin deficiency. Type 2 diabetes, formerly also known as adult-onset diabetes or non-insulin-dependent diabetes mellitus (NIDDM), is characterized by an ineffectiveness of the body to use insulin (1). This type of diabetes accounts for approximately 90-95% of people suffering from diabetes. Unlike type 1 diabetic patients, type 2 diabetics, gestational diabetics and patients with other specific forms of diabetes do not need insulin to survive but may need it for glycaemic control. (2)

The chronic hyperglycaemia that occurs in a diabetic patient leads to long-term damage of organs like the blood vessels, eyes, kidneys, nerves, and the heart. Severity of type 2 diabetes can range from a predominant insulin resistance (IR) with a relative lack of insulin to a predominant failure in insulin secretion with IR. Type 2 diabetes mellitus (T2DM) often goes years without being diagnosed due to the gradual development of hyperglycaemia and the lack of classic symptoms in early stages when the diabetes is not severe enough. Insulin concentrations may even seem normal or increased in type 2 diabetics, but their higher blood sugar levels show a β-cell malfunction in these cases. A large percentage of type 2 diabetics suffer from adiposity. Generally, elderly, obese and people lacking physical exercise are at higher risk for developing diabetes. Diabetes is also more common in women with prior gestational diabetes and people with dyslipidemia and hypertension. (2)

According to the Global Burden of Disease 2016 Causes of Death Collaborators, diabetes takes the 10th place in the ranking of the 10 leading causes of total years of life lost (YLL) in Austria, while in the United States (US) and Germany, diabetes fortunately did not make it onto the list (3). When it comes to the ranking of the leading causes for years lived with disease/disability (YLD), diabetes makes for a scary 3rd place in the US, while it takes 8th place in the German ranking and is ranked 9th in Austria – making diabetes a lesser problem in Austria compared to many other Western European countries (4). In Austria, diabetes is the 10th leading cause of all-age disability-adjusted life years (DALYs), while in Germany it is the 8th leading cause and in the US, it even accounts for the 6th leading cause of all-age DALYs (5). Looking at the development over time, diabetes has gone from 23rd place in 1990 and 16th place in 2006 to being ranked 12th in 2016 in the list of the leading level 3 causes for total DALYs (5). Meanwhile, its place in the ranking of the 30 leading level 4 causes of YLDs has barely changed – going from a 9th place in 1990 and 2006 to an 8th place in 2016 (4). While in 1990, diabetes did not even make it onto the list of the 30 leading level 3 causes for total YLLs being ranked 32nd in the low socio-demographic index (SDI) group, it ranked 23rd in 2006 and 21st in 2016 (3). In the high SDI group, diabetes has risen from rank 13 in 1990 to rank 11 in 2006 and 2016 (3). The trends for YLL and especially DALYs are evidence to just how important good diabetes therapy options have become.

There are several ways to achieve glycaemic control and improve insulin resistance; however, restoration to a normal state is rather rare (2). These measures include diet, physical activity, weight reduction, oral glucose-lowering agents and/or subcutaneous insulin injections (6). Another option that is becoming more and more common is the use of supplements to help achieve glycaemic control. Supplements are becoming more popular now that everything is accessible easily on the internet and the web also allows a fast spread of information through bloggers and other forums that praise the efficacy of these supplements. The question that arises from this movement is: Do supplements really help? This systematic review and meta-analysis aims to examine the influence of supplements on glycaemic parameters in people suffering from

diabetes mellitus type 2. Until now, a review and meta-analysis of this scale that examines every supplement that has ever been used in an randomized controlled trial (RCT) has never been done before.

5.2 Classification of diabetes

Table 1 shows the diagnostic criteria for diabetes mellitus according to the World Health Organization (WHO) as well as the American Diabetes Association (ADA). Glycated haemoglobin (HbA1c) is a widely used standard biomarker to measure chronic glycaemia, reflecting average glucose levels from the last two to three months (2).

Table 1: Diagnostic criteria for diabetes mellitus [modified after (2)]

	mg/dL	mmol/L	%	Note
Glycated Haemoglobin	N/A	N/A	≥6.5	Tests should be performed in a laboratory using methods that are National Glycohemoglobin Standardization Program certified and standardized to the Diabetes Control and Complications Trial assay.
Fasting plasma glucose	≥126	≥7.0	N/A	Fasting = no caloric intake for ≥8 hours
2-h plasma glucose in an 75-h OGTT	≥200	≥11.1	N/A	Tests should be performed according to WHO regulations (75g anhydrous sugar dissolved in water)
Random plasma glucose	≥200	≥11.1	N/A	In patients exhibiting classic symptoms of hyperglycaemia or a hyperglycaemic crisis

N/A = not applicable, WHO = World Health Organization

5.3 Prevalence of diabetes mellitus

The prevalence of diabetes in individuals aged >18 years worldwide was 8.5% in 2014 compared to 4.7% in 1980 while the total count of diabetics went from 108 million people in 1980 to 422 million people in 2014 (7). Prediction models report an estimated number of 592 million diabetics in the year 2035 (8). In 2004, the number of people suffering from diabetes mellitus was 220.5 million with the Western Pacific being ranked 1st as the region with the most diabetics with a total of 56 million people (9). However, the fastest rise of diabetes prevalence has been taking place in middle- and low-income countries (7).

Figures 1 and 2 show the global prevalence of adults with a fasting blood glucose ≥7.0 mmol/L or on medication for raised blood glucose in 2014 separated in male and female populations.

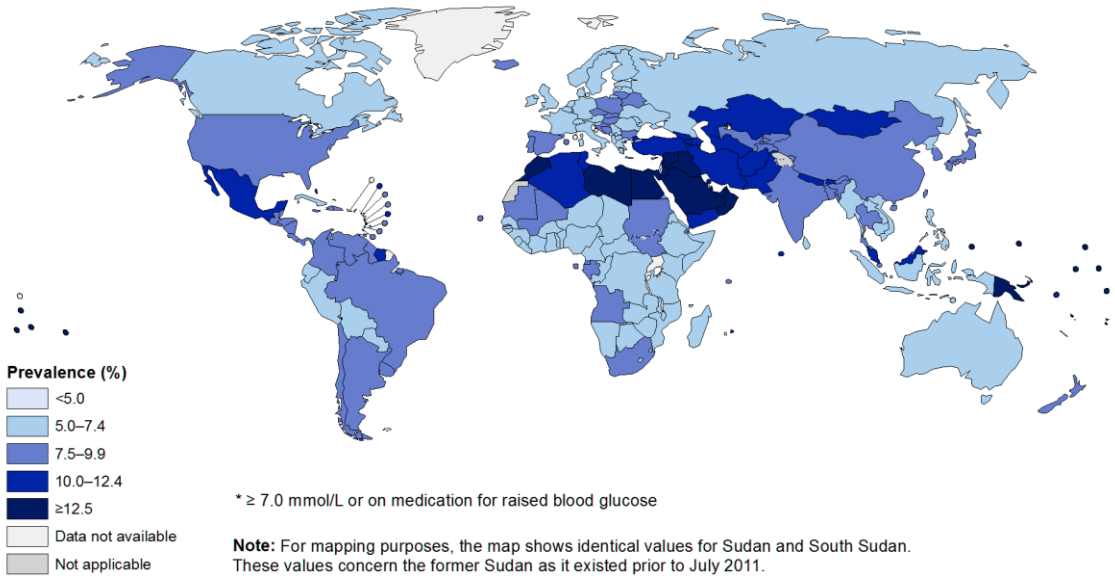

Figure 1: Global prevalence of elevated fasting blood sugar* in men aged ≥18 years in 2014 (age standardized estimate) [modified after (10)]

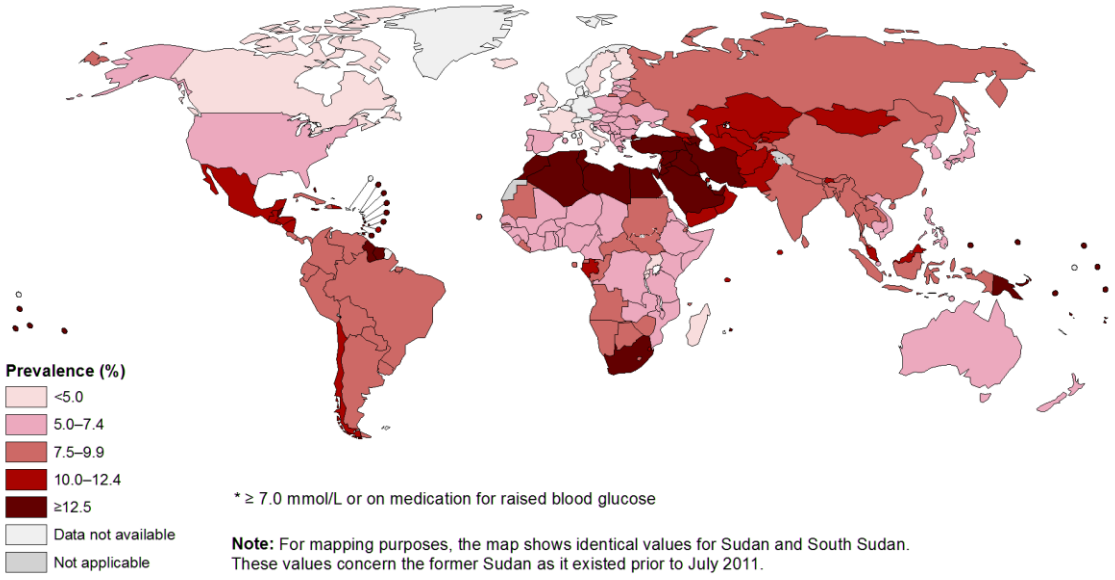

Figure 2: Global prevalence of elevated fasting blood sugar* in women aged ≥18 years in 2014 (age standardized estimate) [modified after (10)]

5.4 Use of supplements for glycaemic control in different countries

While non-antioxidant as well as antioxidant micronutrients are supposed to have an influence on the development and the complications of type 2 diabetes, especially micronutrients and vitamins with an antioxidant function play an important role since the complications and consequences of the disease arise from an imbalance between the formation of free radicals and their control by natural antioxidants (11, 12).

Diabetes cost the US-American healthcare system 245 billion dollars in 2012 and this sum is expected to grow as the number of diagnosed individuals increases (13). However, the efficacy of antidiabetic medication of 41% is low (14, 15) and a stable blood sugar control for more than 8 years is lacking (16). The use of metformin is associated with side effects like gastrointestinal discomfort and a potential toxicity and adverse events during sulfonylurea treatment include weight gain, hypoglycaemia and cardiovascular damage (17). Additionally, pioglitazone treatment goes along with an elevated risk of edema, bladder cancer and distal bone fractures in postmenopausal women (16). Hence, more and more patients try to manage their diabetes with alternative medicine and supplements. The use of supplements is a huge market with US-American citizens spending 12.8 billion dollars out-of-pocket on natural product supplements in 2012 (18). This is about 24% of their out-of-pocket expenditures on prescription drugs (18). Since the family income in American households has increased, out-of-pocket purchases of supplements and other complementary approaches have gone up significantly (18).

Although health claims about nutritional supplements are prohibited in Austria, Austrians spend about 100 million euros annually on supplements. Magnesium supplements appear to be the most popular. However, two thirds of these magnesium supplements contain amounts of magensium way above the daily requirement. This can lead to vomiting, diarrhea, insomnia, irritations of the skin and could damage the liver and kidneys. In addition, the wrong combinations of supplements could interfere with their absorption. (19)

According to the 2016 forsa-survey in Germany, two thirds of the 1001 participants consumed at least one nutritional supplement in the 6-month period before the survey. The majority of consumers, as well as, about 50% of the total number of survey-participants believe in a health benefit through the use of supplements. While young adults under the age of 29 are more likely to use supplementation, level of education had no influence on the likelihood of supplement use. However, a higher level of education leads to a greater belief in the efficacy. Overall, 51% of the people believed in the efficacy of supplements while 38% of them also said that they hardly feel informed about the risks of nutritional supplementation. (20)

Surveys like these are an indication for how important it is to perform reviews and meta-analyses like this one to clarify the current situation and state of knowledge on supplements.

6 Hypothesis

H0: In RCTs, the use of supplements (vitamin C, vitamin D, vitamin E, vitamin C + E, vitamin B6, folate + vitamin B6 and 12, calcium + vitamin D, vitamin E + alpha-lipoic acid, alpha-lipoic-acid, linoleic acid, fish oil, EPA, EPA + DHA, n-3 fatty acids + low-dose aspirin, amino acids (AAs), magnesium, zinc, selenium, chromium, cinnamon, probiotics, synbiotics, prebiotics, flaxseed, zinc + flaxseed oil, garlic, coenyzme Q10, antioxidant supplements, resveratrol, Pancreas Tonic, sucralose, pistachios, yeast, the mushroom *Agaricus blazei* Murill (ABM), tea extract, silymarin, Pycnogenol, soy, cranberry extract, anthocyanin, DAG, Caiapo, diabetes-specific oral nutritional supplements (ONS), DBCare, ginger, *M. charantia*, Nigella sativa (N. sativa), whortleberry, Korean red ginseng (Panax ginseng) rootlets, *Gingko biloba (G. biloba)* L. leaves dry extract, berberine, Danzhijiangtang capsules (DJC, a traditional Chinese medicine), minerals + vitamins, zinc + vitamins + minerals, magnesium + zinc, melatonin + zinc) in T2DM patients has no influence on glycaemic outcomes (HbA1c, glucose, insulin, HOMA-IR [homeostasis model assessment-estimated insulin resistance], HOMA-beta, QUICKI, adiponectin, C-peptide, 2-h 75 g OGTT glucose).

H1: In RCTs, the use of supplements (vitamin C, vitamin D, vitamin E, vitamin C + E, vitamin B6, folate + vitamin B6 and 12, calcium + vitamin D, vitamin E + alpha-lipoic acid, alpha-lipoic-acid, linoleic acid, fish oil, EPA, EPA + DHA, n-3 fatty acids + low-dose aspirin, AAs, magnesium, zinc, selenium, chromium, cinnamon, probiotics, synbiotics, prebiotics, flaxseed, zinc + flaxseed oil, garlic, coenyzme Q10, antioxidant supplements, resveratrol, Pancreas Tonic, sucralose, pistachios, yeast, ABM, tea extract, silymarin, Pycnogenol, soy, cranberry extract, anthocyanin, DAG, Caiapo, diabetes-specific ONS, DBCare, ginger, *M. charantia*, N. sativa, whortleberry, Korean red ginseng (Panax ginseng) rootlets, *G. biloba* L. leaves dry extract, berberine, DJC, minerals + vitamins, zinc + vitamins + minerals, magnesium + zinc, melatonin + zinc) in T2DM patients has an influence on glycaemic outcomes (HbA1c, glucose, insulin, HOMA-IR, HOMA-beta, QUICKI, adiponectin, C-peptide, 2-h 75 g OGTT glucose).

7 Methods

7.1 Data sources and searches

The preliminary registration number of the present systematic review and meta-analysis within the PROSPERO database „International prospective register of systematic reviews“ is 76434.

A literature search was performed in the online databases PubMed (from 1966), Web of Science (from 1899) and the Cochrane Trial Register until May 2017. PubMed was searched using the search terms: (supplement*[tiab] OR vitamin*[tiab] OR multimineral*[tiab] OR cholecalciferol[tiab] OR ergocalciferol[tiab] OR ascorbic acid[tiab] OR antioxidant*[tiab] OR protein[tiab] OR amino acid*[tiab] OR micronutrient*[tiab] OR calcium[tiab] OR magnesium[tiab] OR potassium[tiab] OR selenium[tiab] OR iron[tiab] OR zinc[tiab] OR omega 3[tiab] OR fatty acid*[tiab] OR fiber[tiab] OR fibre[tiab] OR beta carotene[tiab] OR folic acid[tiab] OR niacin[tiab] OR thiamine[tiab] OR riboflavin[tiab] OR eicosapentaenoic acid[tiab] OR docosahexaenoic acid[tiab] OR linolenic acid[tiab] OR olive oil[tiab] OR inulin[tiab] OR psyllium[tiab] OR cellulose[tiab] OR copper[tiab] OR iodine[tiab] OR prebiotics[tiab] OR probiotics[tiab] OR synbiotics[tiab]) AND (diabetes[MeSH]) AND (Hemoglobin A, Glycosylated[tiab] OR insulin[tiab] OR fasting serum glucose[tiab] OR fasting plasma glucose[tiab] OR fasting glucose[tiab] OR glucose tolerance[tiab] OR hemoglobin A1c[tiab] OR glycated hemoglobin[tiab]) NOT (Case-Control Studies[MeSH] OR Cohort Studies[MeSH] OR case-control[tiab] OR cohort[tiab] OR case-report[tiab] OR adolescents[All Fields] OR children[All Fields] OR gestational[tiab] OR pregnant[tiab] OR pregnancy[tiab]) NOT (rats[tiab] OR monkeys[tiab] OR primates[tiab] OR rabbits[tiab] OR cats[tiab] OR dogs[tiab] OR mice[tiab] OR pigs[tiab] OR cows[tiab]) AND ((Randomized Controlled Trial[ptyp] OR Clinical Trial[ptyp]) AND humans[MeSH Terms] AND adult[MeSH Terms]), while Web of Science was searched using the terms: TS=(supplement*[tiab] OR vitamin*[tiab] OR multimineral*[tiab] OR cholecalciferol[tiab] OR ergocalciferol[tiab] OR ascorbic acid[tiab] OR antioxidant*[tiab] OR protein[tiab] OR amino acid*[tiab] OR micronutrient*[tiab] OR calcium[tiab] OR magnesium[tiab] OR potassium[tiab] OR selenium[tiab] OR iron[tiab] OR

zinc[tiab] OR omega 3[tiab] OR fatty acid*[tiab] OR fiber[tiab] OR fibre[tiab] OR beta carotene[tiab] OR folic acid[tiab] OR niacin[tiab] OR thiamine[tiab] OR riboflavin[tiab] OR eicosapentaenoic acid[tiab] OR docosahexaenoic acid[tiab] OR linolenic acid[tiab] OR olive oil[tiab] OR inulin OR psyllium OR cellulose OR copper[OR iodine OR prebiotics OR probiotics OR synbiotics) AND TS=(diabetes) AND TS=(Hemoglobin A, Glycosylated OR insulin OR fasting serum glucose OR fasting plasma glucose OR fasting glucose OR glucose tolerance OR hemoglobin A1c OR glycated hemoglobin) and the Cochrane Trials Register was searched using: (supplement*(tiab) OR vitamin*(tiab) OR multimineral*(tiab) OR cholecalciferol(tiab) OR ergocalciferol(tiab) OR ascorbic acid(tiab) OR antioxidant*(tiab) OR protein(tiab) OR amino acid*(tiab) OR micronutrient*(tiab) OR calcium(tiab) OR magnesium(tiab) OR potassium(tiab) OR selenium(tiab) OR iron(tiab) OR zinc(tiab) OR omega 3(tiab) OR fatty acid*(tiab) OR fiber(tiab) OR fibre(tiab) OR beta carotene(tiab) OR folic acid(tiab) OR niacin(tiab) OR thiamine(tiab) OR riboflavin(tiab) OR eicosapentaenoic acid(tiab) OR docosahexaenoic acid(tiab) OR linolenic acid(tiab) OR olive oil(tiab) OR inulin OR psyllium OR cellulose OR copper OR iodine OR prebiotics OR probiotics OR synbiotics) AND diabetes. The languages were restricted to English, German and Dutch.

Additionally, reviews and meta-analyses found through the database search were screened manually for further eligible studies. The authors were contacted for trials that could not be accessed online.

7.2 Eligibility criteria

Studies were included if they met the following criteria: 1) RCT design including crossover design; 2) humans only; 3) adults only (≥ 18 years); 4) a minimum intervention duration of 12 weeks; 5) patients with established type 2 diabetes mellitus; and 6) the assessment of glycaemic control as outcome parameter. Included in the meta-analysis was the supplementation with: vitamin C, vitamin D, vitamin E, vitamin C + E, vitamin B6, folate + vitamin B6 and 12, calcium + vitamin D, vitamin E + alpha-lipoic acid, alpha-lipoic-acid, linoleic acid, fish oil, EPA, EPA + DHA, n-3 fatty acids + low-dose aspirin, AAs, magnesium, zinc,

selenium, chromium, cinnamon, probiotics, synbiotics, prebiotics, flaxseed, zinc + flaxseed oil, garlic, coenyzme Q10, antioxidant supplements, resveratrol, Pancreas Tonic, sucralose, pistachios, yeast, ABM, tea extract, silymarin, Pycnogenol, soy, cranberry extract, anthocyanin, diacylglycerol, Caiapo, diabetes-specific ONS, DBCare, ginger, *M. charantia*, N. sativa, whortleberry, Korean red ginseng (Panax ginseng) rootlets, *G. biloba* L. leaves dry extract, berberine, DJC, minerals + vitamins, zinc + vitamins + minerals, magnesium + zinc, melatonin + zinc.

7.3 Exclusion criteria

Studies about gestational diabetes mellitues, type 1 diabetes mellitus and prediabetes were excluded.

7.4 Data extraction

First, the titles and abstracts of all retrieved records were screened. Full texts of records that passed the title and abstract screening were retrieved and examined based on the eligibility and exclusion criteria mentioned above.

7.5 Statistical analysis

The Review Manager 5.3 (Nordic Cochrane Center, Copenhagen) was used to perform the statistical analysis. Standard pairwise meta-analyses of all studies that intervened with the same supplement were performed. The pooled effects of the interventions were examined as mean differences (MD). In a random-effects model, either the post-intervention means ± standard deviations (SD) or the changes from baselines values ± standard deviation of intervention and control group were compared. If data was given as mean ± standard errors or mean and 95% confidence interval (CI), the standard error was converted into SD using SD=SE×√N. The confidence interval was converted using SD=[(√N)×(upper limit-lower limit)÷[tinv(1-0.95;N-1)*2]. The outcomes are depicted as forest plots. Funnel plots were used for those cases where there were at least five trials using the same supplement to examine one of the nine outcome parameters. Funnel plots are used in meta-analyses to identify possible publication bias. In a

scatterplot, the therapy effect on the x-axis is plotted against the SD on the y-axis. A symmetric form indicates a balanced trial publication. Results from bigger studies should be more precise and therefore closer to the mean formed by all study results.

8 Results

Figure 3 illustrates the process from the 2831 hits in the three databases PUBMED, Web of Science and the Cochrane Trial Register and the 13 studies handpicked from reviews and meta-analyses to the 122 trials that were included in the systematic review and the 105 trials included in the meta-analysis in form of a flow chart.

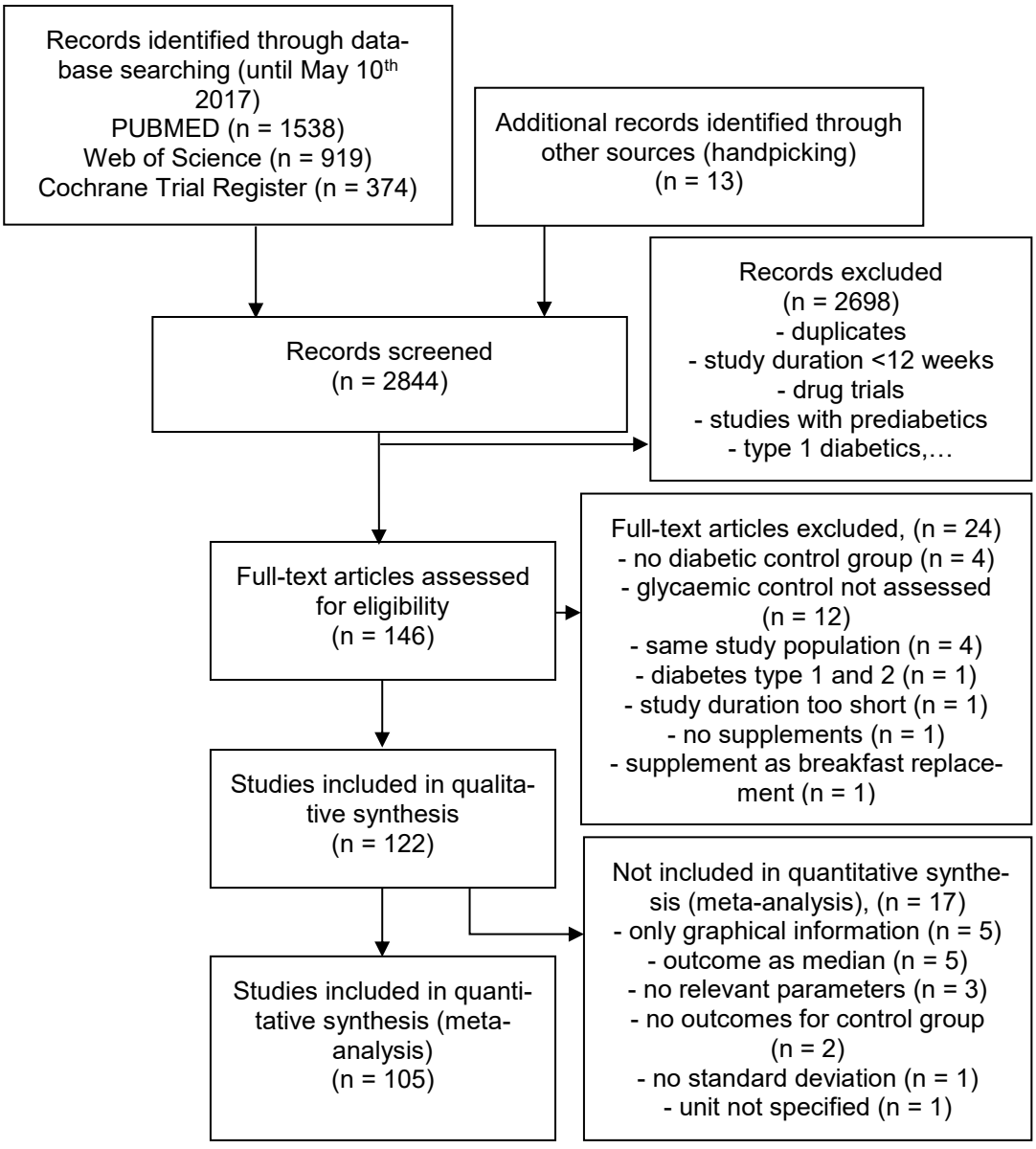

Figure 3: Flow diagram

Table 2 shows the general study characteristics of the 122 studies included in this review.

Table 2: General study characteristics of the included trials

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
Akbari Fakhrabadi et al. (21)	2014	Iran	RCT	N/A	"Supported by a collaboration of the faculty of Health and Yazd Diabetes Research Center of Shahid Sadoughi University of Medical Sciences as an MSc dissertation"	12 weeks	N/A	70 T2DM patients aged 35-65 years with neuropathic signs	31.25% male in the intervention, 20% male in the placebo group	56.7±6.4 in the intervention, 54.8±6.7 in the placebo group	28.7±4.1 in the intervention, 29.6±3.1 in the placebo group	N/A	9 in the intervention, 9 in the placebo group were taking oral hypoglycaemic agents (OHAs), 44 patients took insulin	1853.5±115.9 kcal/d in the intervention, 1835.4±120.8kcal in the placebo group at week 0, 1723±105.0kcal in the intervention, 1805±110.0kcal in the placebo group at week 12; 88.2±30.2 Mets/week in the intervention, 85.2±27.2 in the placebo group at week 0, 87.5±29.8 in the intervention, 85.9±25.9 in the placebo group at week 12
Akilen et al. (22)	2010	UK (United Kingdom)	RCT	N/A	Supported by Thames Valley University UK; "Jeffrey Kelson Diabetes and Endocrine	12 weeks	N/A	58 T2D patients (HbA1c > 7%)	25 men, 33 women	54.9±9.8	33.36±4.20 in the cinnamon, 32.13±8.30 in the placebo	90% in the cinnamon group never smoked, 7%	80% in the cinnamon, 71% in the placebo group	2 lifestyle and diet advice sessions

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
					Centre, Central Middlesex Hospital London; Brent NHS London; Department of Dietetics, Brent National Health Services, London; Research and Development Office, Brent National Health Services, London and Holland and Barrett Ltd, UK"						group at baseline; 32.30±3.87 in the cinnamon, 31.94±7.76 in the placebo group post-intervention	used to smoke, 3% smoke daily; 93% in the placebo group never smoked, 0% used to smoke, 7% smoke daily	took metformin, 7% in the cinnamon, 8% in the placebo group took sulfonylureas, 13% in the cinnamon, 11% in the placebo group took both	as standard care; no changes in usual PA levels throughout the study
Al-Maroof et al. (23)	2006	Iraq	RCT	N/A	N/A	3 months	N/A	101 T2DM patients	N/A	54.6±9.2	28.6±4.2	N/A	OHAs	N/A
Anderson et al. (24)	1997	China	RCT	N/A	The Diabetes Action Foundation partially funded this study with grants	4 months	N/A	180 T2DM patients, otherwise free of disease, aged 35-65 years (FBG: 7.2-15.5 mmol/L, 2-h blood sugar: 9.4-16.7 mmol/L, HbA1c 8.0-12.0%)	17 women/ 33 men in group 0, 20 women/ 33 men in group 3.85, 26 women/ 26 men in group 19.2	55.5±1.2 total in group 0, 55.7±1.2 in group 3.85, 54.6±1.4 in group 19.2; 56.4±1.8 for women in group 0, 53.8±1.8 in group 3.85, 54.1±2.3 in group 19.2; 55.1±1.5 for men in group 0, 56.8±1.7 in group 3.85, 55.2±1.8	24.8±0.5 total for group 0, 25.0±0.5 for group 3.85, 24.8±0.4 for group 19.2; 25.8±1.1 for women in group 0, 25.0±0.9 in group 3.85, 25.0±0.6 in group 19.2; 24.3±0.5 for men in group 0, 25.0±0.5 in group 3.85, 24.6±0.6 in group 19.2	N/A	92 patients took sulfonylurea (glibenclamide, glinclazid, glipizide), 69 took phenformin, 38 took traditional Chinese medicines, 22 took no agents, 9 took insulin; several took >1 agent	Patients were encouraged not to change their usual diet and exercise.

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
										in group 19.2				
Anderson et al. (25)	2001	Tunisia	RCT	N/A	Partially supported "by grants from the Diabetes Action Foundation, Washington, DC, and Labcatal Pharmaceutical, Montrouge Cedex, France"	6 months	N/A	110 Tunisian adults aged <65 years with diabetes for ≥ 5 years (HbA1c >7.5%, fasting sugar >8 mmol/L), 60 healthy controls as reference group for plasma thiobarbituric acid reactive substances	N/A	51.5±1.62 in the zinc, 52.0±1.58 in the chromium, 53.8±1.88 in the zinc/chromium, 55.5±1.43 in the placebo group	28.9±0.15 in the zinc, 29.5±0.16 in the chromium, 28.6±0.16 in the zinc/chromium, 29.6±0.15 in the placebo group	N/A	N/A	N/A
Aro et al. (26)	1981	Finland	RCT	N/A	"Supported by the Nutrition Research Foundation of Finnish Sugar Co. Ltd." A. Aro received "a research grant from the State Medical Research Council of Finland"	crossover: 3 months, 3 months	N/A	11 T2DM patients aged 39-69 years with a mean duration of T2DM of 6.5 years (1-15 year range), 2 ≥20% overweight patients	only men	53	N/A	N/A	2 on diet therapy alone, 7 on 10-15 mg glibenclamide therapy per day	N/A
Ashraf et al. (27)	2011	Pakistan	RCT	N/A	N/A	24 weeks	N/A	60 recently diagnosed T2DM patients aged 25-70 years with FBG <126 mg/dL	17 men/13 women in the intervention, 16 men/14 women	40±5.04 in the intervention, 35±4.58 in the placebo group	N/A	N/A	Drugs other than the metformin used in the trial were prohibited.	Subjects were encouraged to maintain nutritional plan, PA, and lifestyle as

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
									in the placebo group					constant as possible during the study.
Barchetta et al. (28)	2016	Italy	RCT	N/A	"Research grants from the Sapienza University Ateneo Scientific Research and the Italian Minister of University and Research"	24 weeks	N/A	65 non-alcoholic fatty liver disease patients with T2DM aged 25-70 years; 92% sub-optimal serum 25(OH)D levels (<75 nmol/L); 67% hypovitaminosis D (<50nmol/L)	70% men in intervention, 60% in placebo group	58.7±9.9	29.3±4.4 in intervention, 30.8±4.5 in placebo group	N/A	16% insulin treatment in the intervention, 18% in the placebo group	N/A
Barre et al. (29)	2008	Canada	RCT	N/A	"Cape Breton University Research Assistance Programme and Summer Stipend Research Assistance grants for operating funds, Canadian Institutes for Health Research institutional grant (to Cape Breton University) for operating funds, Canada Foundation for Innovation and Nova Scotia Health Research Foundation for equipment grants"	3 month lead-in, 3 month treatment	N/A	40 T2DM patients aged ≥18 years	10 men/8 women in the flaxseed oil, 8 men/6 women in the safflower oil group	59.5±1.7 in the flaxseed oil, 60.7±2.9 in the safflower oil group	32.4±0.9 in the flaxseed oil, 30.3±0.7 in the safflower oil group at visit 1, 32.3±1.0 in the flaxseed oil, 30.3±0.8 in the safflower oil group at visit 2	N/A	No insulin therapy	no physical training program, consistent diet during study period
Bonsu et al. (30)	2012	Canada	RCT	N/A	N/A	12 weeks	N/A	36 subjects aged >40 years diagnosed with T2DM	58% men in the experimental,	64.0±5.8 in the experimental, 66.0±11.2	31.0±4.5 in the experimental, 29.7±4.3 in	N/A	N/A	Subjects were motivated not to change usual diet

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
								within the previous 10 years	50% in the control group	in the control group	the control group			and exercise patterns (lifestyle was not monitored)
Boshtam et al. (31)	2005	Iran	RCT	N/A	"Grant from the Academy of Medical Science of Iran"	27 weeks	N/A	100 T2DM patients aged 20-60 years without complications	N/A	54.5±7.3 in the placebo, 52.8±8.8 in the treated group	24.2±3.6 in the placebo, 25.0±3.6 in the treated group	nonsmokers	Glibenclamid, 2 patients (1 in every group) additionally took metformin	N/A
Breslavsky et al. (32)	2013	Israel	RCT	N/A	N/A	12 months	N/A	47 T2DM patients	11 men/13 women in the vitamin D, 11 men/12 women in the placebo group	66.8±9.2 in the vitamin D, 65.8±9.7 in the placebo group	27.9±5.2 in the vitamin D, 30.6±5.1 in the placebo group	25% current smokers in the vitamin D, 13% in the placebo group	62.5% in the vitamin D, 34.8% in the placebo group took metphormin, 33.3% in the vitamin D, 13.0% in the placebo group took sulfonilurea, 20.8% in the vitamin D, 17.4% in the placebo group took repaglinide, 8.3% in the vitamin D, 13% in the placebo group took DDP-4 inhibitors; 58.3% in the vitamin D, 43.5% in the placebo group received insulin treatment	N/A

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
Cheng et al. (33)	2010	Taiwan	RCT	N/A	National Science Council in Taiwan	12 weeks	N/A	28 subjects with T2DM for ≥ 1 year with stable medication	52.9% men in the rice bran, 36.4% in the placebo group	58.9±10.4 in the rice bran, 57.7±5.7 in the placebo group	25.0±2.2 in the rice bran, 25.6±2.1 in the placebo group	N/A	In the rice bran group, 4 used metformin, 5 glibenclamide, 4 gliclazide and 4 glipizide; in the placebo group, 3 used metformin, 3 glibenclamide, 3 gliclazide and 2 glipizide.	Counseled to maintain usual diet and exercise patterns
Cruz et al. (34)	2008	Mexico	RCT	N/A	"Supported by the Coordinación de Investigación en Salud, Instituto Mexicano del Seguro Social, Mexico"	3 months	N/A	74 subjects with T2DM, BMI ≤30 kg/m²	58% women in the placebo, 50% in the glycine group	59.5±9.6 in the placebo, 57.5±9.8 in the glycine group	28.9±3.7 in the placebo, 28.5±3.6 in the glycine group at baseline; 28.9±3.8 in the placebo, 28.3±3.5 in the glycine group at 3 months	N/A	30.5% treated with glybenclamide in the placebo, 23.7% in the glycine group; 19.4% with metformin in the placebo, 13.1% in the glycine group; 27.7% with glybenclamide + metformin in the placebo, 18.4% in the glycine group	Everyone maintained individual dietary habits.
Dakhale et al. (35)	2011	India	RCT	N/A	N/A	12 weeks	N/A	70 T2DM patients aged 30-60 years with FBG 126-250 mg/dL	15 men/18 women in group A, 13 men/20 women in group B	48.33±1.39 in group A, 45.88±1.42 in group B	N/A	no heavy smokers	metformin	Normal dietary habits while reducing vitamin C-rich food

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
Dans et al. (36)	2007	Philip-pines	RCT	N/A	Herbcare Corp.	3 months	N/A	40 T2DM patients (re-cently diag-nosed or poorly con-trolled) aged ≥18 years with HbA1c of 7-9%	7 men in the Char-antia, 8 in the placebo group	58.70±9.81 in the Char-antia, 59.76±10.04 in the placebo group	26.37±4.75 in the Charantia, 26.00±3.94 in the placebo group	N/A	OHAs	N/A
de Oliveira et al. (37)	2011	Brazil	RCT	N/A	"Supported by the Sao Paulo State Funding Agency, Bra-zil (grant 2004/04108-1)"	16 weeks	N/A	102 patients with T2DM aged 38-75	61.5% male in the li-poic acid, 72.0% in the vitamin E, 68% in the vitamin E+lipoic acid, 57.7% in the placebo group, 64.7% total	9.8% aged 39-49, 26.5% aged 50-59, 47.1% aged 60-69, 16.6% aged ≥70	9.8% BMI<25, 58.8% BMI 25-30, 31.4% BMI>30	Smokers who smoked >10 cigarettes per day were ex-cluded; 11.5% smokers in the lipoic acid, 12% in the vit-amin E, 12% in the vitamin E + lipoic acid, 7.7% in the placebo group	N/A	Patients were counseled to main-tain their usual diet.
Derosa et al. (38)	2011	Italy	RCT	N/A	N/A	12 months	N/A	258 sub-jects aged ≥18 of with uncontrolled T2DM (HbA1c > 8.0%)	62 men/64 women in the orlistat, 65 men/67 women in the orlistat+ L-car-nitine group	53±6 in the orlistat, 51±4 in the orlistat+L-carnitine group	33.1±2.9 at baseline, 32.5±2.3 at 3 months, 31.6±1.8 at 6 months, 30.8±1.5 at 9 months, 29.8±1.2 at 12 months in the orlistat; 32.9±2.8 at baseline, 31.9±2.0 at 3	21 male/25 female smok-ers at base-line, 21 male/24 fe-male at 3 months, 20 male/23 fe-male at 6 months, 20 male/23 fe-male at 9 months, 20	Treatment with various OHAs or insu-lin	Diet with close to -600 kcal/d based on American Heart As-sociation (AHA) rec-ommenda-tions (50% carbohy-drates, 30% fat,

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
											months, 30.7±1.6 at 6 months, 30.1±1.4 at 9 months, 29.0±1.3 at 12 months in the orlistat+L-carnitine group	male/22 female at 12 months in the orlistat group; 20 male/23 female at baseline, 20 male/21 female at 3 months, 19 male/20 female at 6 months, 19 male/19 female at 9 months, 18 male/19 female at 12 months in the orlistat+L-carnitine group		6% saturated, 20% proteins, maximum cholesterol: 300 mg/d, fiber: 35 g/d), no vitamin or mineral preparations throughout study/were motivated to raise PA by cycling or "walking briskly for 20-30min 3-5x/week"
Derosa et al. (39)	2010	Italy	RCT	N/A	University of Pavia	12 months	N/A	254 subjects aged ≥18 with uncontrolled T2DM (HbA1c >8.0%)	63 men/62 women at baseline, 61 men/58 women at 3 months, 59 men/57 women at 6 months, 58 men/54 women at 9	54±5 in the sibutramine plus L-carnitine, 51±4 in the sibutramine group	33.4±3.2 at baseline, 33.0±3.0 at 3 months, 32.2±2.7 at 6 months, 30.9±2.1 at 9 months, 30.3±1.9 at 12 months in the sibutramine; 33.9±3.5 at baseline, 32.6±2.9 at 3 months, 32.1±2.6 at 6 months,	22 male and 19 female smokers in the sibutramine plus L-carnitine group, 24 male and 18 female smokers in the sibutramine group	Treatment with various OHAs or insulin	Diet with close to --600 kcal/d based on American Heart Association (AHA) recommendations (50% carbohydrates, 30% fat, 6% saturated, 20% proteins, maximum

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
									months, 56 men/54 women at 12 months in the sibutramine group; 65 men/64 women at baseline, 63 men/61 women at 3 months, 61 men/59 women at 6 months, 59 men/56 women at 9 months, 57 men/56 women at 12 months in the intervention group		30.8±2.0 at 9 months, 30.1±1.8 at 12 months in the sibutramine+L-carnitine group			cholesterol: 300 mg/d, fiber: 35 g/d), no vitamin or mineral preparations throughout study/were motivated to raise PA by cycling or "walking briskly for 20-30min 3-5x/week"
Derosa et al. (40)	2003	Italy	RCT	N/A	N/A	4 week wash-out, 6 month treatment	N/A	94 subjects with hypercholesterolemia and	52.2% men in the L-carnitine,	52±6 in the L-carnitine, 50±7 in	27.3±2.5 in the L-carnitine, 26.8±2.2 in	N/A	No use of hypolipidemic medication	Therapeutic diabetes mellitus diet, advised to

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
								newly diagnosed T2DM	47.9% in the placebo group	the placebo group	the placebo group			cycle aerobically for ≥ 30 min (minutes) 3-4x/week
Derosa et al. (41)	2016	Italy	RCT	N/A	Costs to publish in open access covered by Difass International Società a responsabilità limitata	3 months	N/A	105 Caucasian overweight (25 ≤BMI< 30 kg/m²) T2DM patients aged 18-75 years (HbA1c >7.0%)	26 men/28 women in the intervention, 25 men/26 women in the placebo group at baseline; 25 men/28 women in the intervention, 24 men/25 women in the placebo group at 3 months	52.2±7.9 in the intervention, 53.1±8.3 in the placebo group	28.4±2.5 in the intervention, 28.1±2.2 in the placebo group at baseline; 28.3±2.4 in the intervention, 28.3±2.4 in the placebo group at 3 months	12 male/10 female smokers in the intervention, 13 male/12 female smokers in the placebo group at baseline; 11 male/10 female smokers, 13 male/12 female smokers in the placebo group at 3 months	N/A	Energy-controlled diet based on AHA recommendations
De Valk et al. (42)	1998	Netherlands	RCT	N/A	N/A	3 months	N/A	50 moderately controlled T2DM patients aged <80 years (age at clinical onset of T2DM >40 years, ade-	16 males/9 females in the supplementation, 12 males/13 females in the	63.0±8.2 in the supplementation, 62.0±7.3 in the control group	28.7 (26.7-30.9) in the supplementation, 27.1 (25.4-28.9) in the control group	N/A	adequate control with oral agents before study entry; “patients were asked not to alter their insulin regimen or co-medication”	Subjects were asked to maintain their usual dietary habits.

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
								quate control with oral agents during the 1st year and/or presence of endogenous insulin production, and ≥ 6 months insulin usage)	control group					
Eftekhari et al. (43)	2011	Iran	RCT	N/A	Shiraz University of Medical Sciences: grant number 88-4617	12 weeks	N/A	70 subjects with T2DM aged 30-75 years	35 men, 35 women	53.8±8.9 in the treatment, 52.4±7.8 in the control group	28.3±4.4 in the treatment, 27.0±4.8 in the control group	N/A	Metformin, glybenclamide	1728±455 kcal in the treatment, 1664±454 kcal in the control group, 65.6±7.3% carbohydrates in the treatment, 63.8±4.3% in the control group, 15.3±4.3% protein in the treatment, 14.6±3.3% in the control group, 18.8±4.4% fat in the treatment, 21.2±4.3% in the control group
Eibl et al. (44)	1995	Austria	RCT	N/A	N/A	3 months	N/A	40 T2DM patients (HbA1c	47 men/40 women	63±8 in the verum,	27.5±3.2 in the verum,	N/A	OHAs: sulfonylurea, metformin	Treatment with diet and OHAs

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
								<8%) with hypomagnesemia, 30 healthy subjects as control group	in the verum, 53 men/60 women in the placebo group	54±1.5 in the placebo group	29.3±5 in the placebo group			
Elwakeel et al. (45)	2015	Egypt	RCT	N/A	Not funded externally, except for the support of Al-Azhar University	6 months	N/A	40 T2DM patients with chronic periodontitis	20 males, 20 females	40.05±9	23.52±0.83 in the experimental, 23.38±0.9 in the control group	Smokers or former smokers were excluded	OHAs	Therapy with PA + diet
Eriksson et al. (46)	1995	Finland	RCT	N/A	N/A	crossover: 90 day run-in, 90 day treatment, 4 week wash-out, 90 day treatment	N/A	27 T2DM patients with a duration of 10 ± 1 years	N/A	61±2	28.9±0.8	N/A	N/A	"weight maintaining diet": 55% carbohydrates, 15% protein, ≤30% fat
Faghihi et al. (47)	2014	Iran	RCT	N/A	Tehran University of Medical Sciences: grant number 7709-33-03-87	3 months	N/A	60 T2DM patients aged 18-70 years	16 males/17 females in the selenium, 18 males/9 females in the placebo group	53.54±7.52 in the selenium, 55.76±7.77 in the placebo group	28.31±3.63 in the selenium, 27.89±4.35 in the placebo group	N/A	27% used metformin in the selenium group, 6% sulfonylurea, 36% metformin + sulfonylurea, 6% metformin + pioglitazone, 18% metformin, sulfonylurea + acarbose and 6% metformin, sulfonylurea + pioglitazone; 11% used metformin in the placebo	Patients should maintain their usual dietary patterns and PA.

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
													group, 4% sulfonylurea, 48% metformin + sulfonylurea, 22% metformin, sulfonylurea + acarbose and 15% metformin, sulfonylurea + pioglitazone	
Fang et al. (48)	2013	China	RCT	N/A	N/A	12 weeks	N/A	62 subjects "with newly diagnosed T2DM subclinical vascular lesions"	7 men/14 women in the control, 16 men/15 women in the intervention group	53.67±9.32 in the control, 51.90±10.13 in the treatment group	N/A	N/A	Acarbose, pioglitazone hydrochloride, Metformin hydrochloride, gliclazide sustained release and repaglinide tablets	Dietary control and regular PA for all study participants
Farvid et al. (49)	2005	Iran	RCT	N/A	"Grant from Research Undersecretary of Tehran University of Medical Sciences"	3 months	N/A	77 T2DM patients (≥ 1 year) aged 30-69 years with a bias towards non-macroalbuminuric and non-hypertensive patients (excretion of albumin in urin >300mg/g creatinine)	9 men/10 women in group P, 8 men/10 women in group M, 9 men/11 women in group V, 9 men/10 women in group MV	50±9 in the placebo, 52±8 in magnesium + zinc, 50±9 in the vitamin, 50±9 in the mineral + vitamin group	27.4±3.7 in the placebo, 27.7±4.7 in magnesium + zinc, 27.5±4.7 in the vitamin, 29.2±4.0 in the mineral + vitamin group	3 smokers in the placebo, 2 in magnesium + zinc, 3 in the vitamin, 2 in the mineral + vitamin group	4 treated with diet only, the rest with metformin and/or sulfonylurea	4 patients treated with diet only

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
Feinglos et al. (50)	2013	USA	RCT	N/A	N/A	"20-week study period (8 weeks baseline, 12 weeks treatment)"	N/A	37 T2DM patients (34 Caucasian) aged 36-80 years (clinical diagnosis ≥ 1 year before study), diet-controlled and/or by oral sulfonylurea, HbA1c: 6-10%	75% male in the placebo, 67% in the psyllium 3.4g, 64% in psyllium 6.8g group	56.5±9.99 in the placebo, 61.8±9.39 in the psyllium 3.4g, 64.8±8.42 in the psyllium 6.8g group	N/A	N/A	75% in the placebo, 87% in the 3.4 g psyllium, 79% in the 6.8 g psyllium group used sulfonylurea	"restricted diet for all 20 weeks of the study"
Fenercioglu et al. (51)	2010	Turkey	RCT	N/A	"Supported by Yeditepe University and Com Ilac Chemistry Industry and Trade Company"	3 months	N/A	114 T2DM patients aged 40-65 years without complications	22 men/34 women in the intervention, 21 men/37 women in the control group	53.51±6.82 in the study, 53.91±7.16 in the control group	31.37±4.98 in the study, 30.29±6.28 in the control group	non-smokers	Metformin, ascarbose	standard diet (1500 kcal) "rich in vegetables, 3 servings of fruits", max. 3 slices of bread/d, aerobic PA regimen of 150 min/week
Firouzi et al. (52)	2016	Malaysia	RCT	N/A	"Universiti Putra Malaysia and research grant of B-Crobes Laboratory Sdn. Bhd"	12 weeks	N/A	136 T2DM patients (for ≥ 6 months) aged 30-70 years, HbA1c: 6.5-12%, FBG <15 mmol/L, BMI: 18.5-40 kg/m²	34 males in the placebo, 31 in the probiotics group; 34 females in the	54.2±8.3 in the placebo, 52.9±9.2 in the probiotics group	29.3±5.3 in the placebo, 29.2±5.6 in the probiotics group	N/A	stable drug dose for ≥ 3 months prior to study, 1.5% from the placebo, 8.8% from the probiotic group on diet treatment alone	total PA score (MET_min/week): 1989±1869 in the placebo, 1784±2100 in the probiotics group; sedentary activity

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
									placebo, 37 in the probiotics group					(hours/day): 5.5±3.0 in the placebo, 6.2±3.3 in the probiotics group
Foster et al. (53)	2014	Australia	RCT	N/A	Medical Advances Without Animals Trust & Sydnovate	12 weeks	N/A	48 postmenopausal women with T2DM	only women	65.0±7.8	28.6±5.1	smokers were excluded	Insulin users were excluded.	N/A
Ginter et al. (54)	1978	Czechoslovakia	RCT	N/A	N/A	12 months	N/A	"48 permanently hypercholesterolemic outpatients", mostly obese with stable maturity-onset T2DM	29 men, 19 women	50-60	N/A	N/A	no insulin, oral diabetic agents or drugs influencing lipid metabolism	Diet for diabetics
Goh et al. (55)	2014	Singapore	RCT	N/A	"Supported by the National Medical Research Council"	2 week placebo run-in, 12 week treatment	N/A	10 Chinese T2DM patients aged 40-69 years (HbA1c: 7.1–12.0%), on stable OHAs for 3 months	only men	56.3±6.0 total, 56.8±5.3 in the placebo, 55.8±7.3 in the resveratrol group	26.9±5.8 total, 24.4±3.6 in the placebo, 29.4±6.8 in the resveratrol group	30% current smokers total, 20% in the plaebo, 10% in the resveratrol group	50% in the placebo, 40% in the resveratrol group used any metformin, 40% in the placebo, 50% in the resveratrol group used any sulfonylurea, 10% in the resveratrol group used any glitazone	total daily PA: 397118±149214 counts at baseline, 43.2±105.2% at week 12
Grotz et al. (56)	2003	USA	RCT	N/A	"Supported by McNeil Specialty Products Company and Tate &	6 weeks screening, 13	4 weeks	136 subjects aged 31-70 years	67% men in	58.0±1.05 in the placebo,	31.6±0.91 in the placebo, 31.6±0.69 in	N/A	diabetes management with insulin or	Subjects should maintain a

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
					Lyle Specialty Sweeteners"	weeks test phase		with T2DM for ≥1 year (HbA1c ≤10%), generally healthy	the placebo, 63% in the sucralose group	57.2±1.03 in the sucralose group	the sucralose group; 30.1±5.2 for men in the placebo, 31.0±5.5 for men in the sucralose, 24.9±10.1 for women in the placebo, 32.7±5.8 for women in the sucralose group		OHAs, not both (~50% of the patients used OHAs including biguanides and different sulfonylureas)	diet of ~14% protein, 30-36% fat, 48-55% carbohydrate.
Gualano et al. (57)	2011	Brazil	RCT	in+J54	"Support from Conselho Nacional de Desenvolvimento Científico e Tecnológico"	12 weeks	N/A	28 patients aged >45 years prediagnosed with T2DM, and physically inactive for ≥ 1 year with a BMI of ≥ 30 kg/m²	8 females/5 males in the creatine, 8 females/4 males in the placebo group	57.5±5 in the creatine, 56.4±8.23 in the placebo group	≥30	N/A	13 in the creatine/12 in the placebo group took metformin, 7 in the creatine/6 in the placebo group took sulfonylurea, 2 in the creatine/2 in the placebo group took beta-blockers, 3 in the creatine/3 in the placebo group took ACE inhibitors, 13 in the creatine/12 in the placebo group took angiotensin receptor antagonists, 4 in the creatine/4 in the placebo group took thiazide, 11 in	"exercise training"

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
													the creatine/10 in the placebo group took statins, 2 in the creatine/2 in the placebo group took fibrates	
Guimaraes et al. (58)	2013	Brazil	RCT	N/A	Supleforma Compounding Pharmacy	90 days	90 days	56 overweight T2DM patients aged 30-60 years	9 females/4 males in the placebo, 10 females/3 males in the 50µg, 11 females/5 males in the 200µg group	50.47±1.17 in the placebo, 50.75±1.80 in the 50µg, 51.35±1.62 in the 200µg group	29.99±1.31 in the placebo, 31.66±1.31 in the 50µg, 33.10±1.18 in the 200µg group	N/A	main drugs: oral antidiabetic medication like sulfonylurea or biguanide and antihypertensives	2617.54±819.66 MET/week in the placebo, 2848.58±830.18 in the 50µg, 2727.07±758.85 in the 200µg at baseline, 174.31±946.11 change in the placebo, 1618.67±833.42 in the 50µg, -1018.33±734.32 in the 200µg group after 90 days; 1653.82 kcal/day total energy intake in the placebo, 1439.38±1

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
														91.54 in the 50µg, 1428.24±179.60 in the 200µg at baseline, -126.81±230.54 change in the placebo, -96.81±201.72 in the 50µg, 20.90±182.91 in the 200µg group after 90 days
Gullestad et al. (59)	1994	Norway	RCT	N/A	N/A	4 months	N/A	56 NIDDM patients (≥ 1 year)	N/A	64±8	25.4±3.7 in the magnesium, 25.3±4.1 in the placebo group	N/A	19 treated with OHAs, 24 with insulin	11 subjectsmal on diet only
Gunasekara et al. (60)	2011	Sri Lanka	RCT	N/A	International Atomic Energy Agency	4 months	N/A	96 patients with adult-onset T2DM for ≥ 2 years	12 men/17 women in group A, 11 men/20 women in group B, 10 men/26 women in group C	54.1±6.0 in the zinc+multivitamin/mineral (MVM), 51.2±6.0 in the MVM, 54.8±8.0 in the control group	23.89±3.5 in the zinc+ MVM, 24.64±4.0 in the MVM, 23.71±4.1 in the control group	N/A	Sulfonylurea (glibenclamide, glipizide, gliclazide, tobutamide), metformin or a combination of both, no insulin preparations	N/A

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
Hosseinzadeh et al. (61)	2013	Iran	RCT	N/A	Grant number 10428 "from Research Undersecretary of Tehran University of Medical Sciences"	12 weeks	N/A	89 T2DM patients (≥ 2 years) aged 35-55 years	21 male, 63 female	46.3±6.1	30.0±4.4 in the brewer's yeast, 29.9±4.7 in the placebo group at baseline; 29.8±4.4 in the brewer's yeast, 30.1±4.6 in the placebo group at 12 weeks	N/A	not taking insulin, counseled to maintain drugs throughout the study	Counseled to maintain diet and PA patterns throughout the study
Hosseinzadeh-Attar et al. (62)	2015	Iran	RCT	N/A	Support from the Tehran University of Medical Sciences (grant number 17100)	12 weeks	N/A	64 T2DM patients aged 20-60 years; BMI 25-35kg/m²	15 women/ 18 men in the placebo, 12 women/ 19 men in the intervention group	47.1±8.3 in the placebo, 45.2±7.6 in the intervention group	29.47±3.24 in the placebo, 29.52±2.8 in the intervention group at baseline; 29.52±3.9 in the placebo, 29.11±3.07 in the intervention group at end-of-trial	smokers were excluded	Metformin, glibenclamide	patients were encouraged to work out regularly
Hove et al. (63)	2015	Denmark	RCT	N/A	"Steno Diabetes Center A/S, Novo Nordisk A/S and Christian Hansen A/S"	12 weeks	N/A	41 T2DM patients aged 40-70 years (duration >1 year), HbA1c: 6.0-10.0%	Males only	58.5±7.7 in the Cardi04 yogurt, 60.6±5.2 in the placebo group	29.2±3.8 in the Cardi04, 27.7±3.3 in the placebo group at baseline; 29.2±3.8 in the Cardi04, 27.7±3.2 in the placebo group at end-of-trial	N/A	Only diet or glucose-lowering drugs: metformin, sulfonylurea, no insulin treatment	Diet or glucose-lowering drugs
Hsia et al. (64)	2004	USA	RCT	N/A	Partially supported by Grant number DK54047 from the National Institute of	1 month placebo run-in, 3	N/A	47 T2DM patients (≥ 1 year before study	4 males/9 females in the	47.4±7.0 in the placebo, 47.6±11.5	34.8±9.7 in the placebo, 31.4±5.7 in the pancreas	N/A	5 in the placebo, 5 in the pancreas tonic group, 8	Therapy "with diet and lifestyle"

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
					Diabetes and Digestive and Kidney Diseases, National Institutes of Health	month treatment		entry), treatment with stable dose of OHAs, "or a stable dietary and lifestyle regimen without pharmacotherapy, for at least 3 months"	placebo, 6 males/17 females in the pancreas tonic group, 11 male/16 female dropouts	in the pancreas tonic, 51.1±7.6 in the dropout group	tonic, 31.7±6.7 in the dropout group		in the dropouts treated with sulfonylurea, 1 in the placebo, 4 in the pancreas tonic group, 3 in the dropouts treated with metformin, 6 in the placebo, 9 in the pancreas tonic group9 in the dropouts treated with combination of both	
Hsu et al. (65)	2007	Taiwan	RCT	N/A	Grants from the Taipei Hospital and Eng Chiao Bio-Technology Co. Ltd in Taiwan	12 weeks	N/A	72 Chinese subjects aged 20-75 years that have had T2DM for >1 year	14 men/15 women in the intervention, 13 men/18 women in the placebo group	57.0±9.4 in the intervention, 56.4±12.0 in the placebo group	25.6±3.0 in the intervention, 27.7±5.7 in the placebo group after 12 week treatment	N/A	gliclazide or metformin for >6 months before study entry	Subjects should maintain an isocaloric diet and previous dietary patterns throughout the study.
Hsu et al. (66)	2011	Taiwan	RCT	N/A	National Science Council, Taiwan, Grant number 96-2320-B-192-001	16 weeks	N/A	80 Chinese T2DM patients (≥ 1 year) aged 20-65 years, BMI >25 kg/m²	12 men/23 women in the intervention, 12 men/21 women in the placebo group	50.5±9.2 in the intervention, 52.2±9.1 in the placebo group	30.3±4.3 in the intervention, 29.2±3.6 in the placebo group at baseline; 30.2±4.3 in the intervention, 29.2±3.3 in the placebo group after 16 weeks	N/A	Patients were asked to maintain a stable dose of prescribed hypoglycaemic drugs except for when hypoglycaemia occurs.	Patients should maintain an isocaloric diet and previous dietary patterns throughout the study.

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
Huseini et al. (67)	2006	Iran	RCT	N/A	"Grant sponsor: Endocrinology and Metabolism Research Center, Tehran University of Medical Sciences Tehran Iran; grant number: R507/2003"	4 months	N/A	51 T2DM patients aged 40-65 years with FBG <250 mg/dL	14 men/11 women in the silymarin, 5 men/21 women in the placebo group	53.0±6.6 in the silymarin, 54.1±6.0 in the placebo group	N/A	N/A	Metformin, glibenclamide	T2DM-management not exclusively by diet
Hussain et al. (68)	2007	Iraq	RCT	N/A	Luna Co., Egypt	120 days	N/A	59 T2DM patients (≥ 5 years) aged 35-58 years, poor glycaemic control	30 men, 29 women	49.2±4.8	31.66±0.47 in group A, 30.91±0.32 in group B, 31.04±0.32 in group C pre-treatment; 28.95±0.35 in group A, 30.68±0.28 in group B, 30.84±0.28 in group C post-treatment	N/A	previously controlled by diet + 10 mg glibenclamide /d	Controlled by diet
Hussain et al. (69)	2006	Iraq	RCT	N/A	Supported by the College of Pharmacy, University of Baghdad and the Specialized Center for Diabetes and Endocrinology in Baghdad, Iraq	90 days	N/A	46 T2DM aged 40-64 years (disease duration: 4.2±3.1 years), a healthy control of 17 subjects	25 men, 21 women	49.1±6.0	N/A	N/A	2550 mg metformin/day	all patients controlled by diet
Jafari et al. (70)	2016	Iran	RCT	N/A	"Vice Chancellor for Research, Isfahan University of Medical Sciences, Isfahan, Iran"	3 weeks run-in, 12 weeks intervention	N/A	59 post-menopausal women with T2DM	only women	57.8±5.5 in the fortified yogurt, 56.8±5.7 in the	28.00±0.82 in the fortified yogurt, 29.30±0.72 in the plain yogurt group	N/A	66.6% metformin in the FY group, 65.5% in PY group, 10% glitazone in FY group, 10.4% in PY	"weight-maintenance diet according to ADA

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
										plain yogurt group			group, 23.3% oral agent combination in FY group, 24.1% in PY group	Association guidelines"
Jayagopal et al. (71)	2002	UK	RCT	N/A	N/A	crossover: 12 week treatment, 2 week wash-out, 12 week treatment	N/A	32 postmenopausal T2DM patiens (controlled by diet)	only women	62.5±6.77	32.2±5.0	N/A	N/A	advice from a registered dietitian before randomization, patients were counseled to not alter their diabetes diet and level of PA during the study
Jorde et al. (72)	2009	Norway	RCT	N/A	"Grant from the Norwegian Diabetes Association"	6 months	N/A	36 subjects aged 21-75 years with T2DM	9 men/7 women in the vitamin D, 9 men/7 women in the placebo group	57.7±9.7 in the vitamin D, 54.8±5.9 in the placebo group	32.8±6.8 in the vitamin D group, 31.3±6.3 in the placebo group at baseline	25% current smokers in the vitamin D, 18.8% in the placebo group	metformin and bed-time insulin	N/A
Kaatabi et al. (73)	2015	Saudi Arabia	RCT	N/A	University of Dammam, from its own budget; not funded externally	12 months	N/A	114 T2DM patients aged 18-60 years	30 men/27 women in the control, 33 men/24 women in the	46.12±0.85 in the control, 46.82±1.14 in the N. sativa group	31.83±0.52 in the control, 30.48±0.53 in the N. sativa group	Subjects should not smoke.	Standard OHAs: 98 took sulfonylureas and metformin, 16 only metformin	N/A

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
									N. sativa group					
Kajanachumpol et al. (74)	1995	Thailand	RCT	N/A	"Grant from the Diabetes Association of Thailand"	12 weeks treatment	6 weeks	25 diabetics aged 60-80 years	24 women, 1 man	67.7±6.13 in the placebo (60-81), 64.1±6.1 in the zinc group (60-70)	N/A	N/A	10 drug therapies in the placebo, 4 in the zinc group, 3 insulin therapies in the placebo, 8 in the zinc group	Subjects were counseled to control glucose with diet + insulin or drugs combined.
Kampmann et al. (75)	2014	Denmark	RCT	N/A	"FOOD Study Group/Ministry of Food, Agriculture and Fisheris & Ministry of Family & Consumer Affairs, Denmark"	12 weeks	N/A	16 T2DM patients aged ≥18 years with hypovitaminosis D	6 men/1 women in the vitamin D, 2 men/6 women in the placebo group	61.6±4.4 in the vitamin D, 57±4.5 in the placebo group	35.3±2.9 in the vitamin D, 32.4±2.0 in the placebo group at baseline	N/A	Metformin and/or insulin	Patients were asked to maintain diet throughout the study.
Kleefstra et al. (76)	2006	Netherlands	RCT	N/A	N/A	6 months	N/A	53 T2DM patients aged <75 years with HbA1c ≥8% (men: creatinine ≤150 µmol/L, women: ≤120 µmol/L), ≥50 mol/min creatinine clearance and alanine aminotransferase ≤90 units/L	59% male in the placebo, 29% in the 500µg, 33% in the 1000µg group	62±7.5 in the placebo, 60±8.8 in the 500µg, 59±6.4 in the 1000µg group	34±4.3 in the placebo, 35±7.2 in the 500µg, 33±4.2 in the 1000µg group	N/A	daily insulin usage (≥50 units)	Subjects should not change diet or anything about their lifestyles.
Krul-Poel et al. (77)	2015	Netherlands	RCT	SUNNY Trial	No external funds	6 months	24 weeks	275 adult T2DM pa-	68% male in	67±8 in the vitamin D,	28.7±4.6 in the vitamin D, 28.5±4.5 in	14% current smokers in the vitamin D,	Metformin, sulfonylurea derivates	Treatment with life-

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
								tients without insulin treatment	the vitamin D, 62% male in the placebo group	67±9 in the placebo group	the placebo group at baseline; 29.0±4.6 in the vitamin D, 28.6±4.6 in the placebo group at end-of-trial	14% in the placebo group		style advice before study entry.
Lasaite et al. (78)	2014	Lithuania	RCT	N/A	"European Social Fund Agency, Lithuania according to the 'Human Resource Development Action Program', project number VP1-3.1-SMM-06-V-01-003"	18 months	N/A	56 patients with T2DM	37.5% men	57±9.8 in the *G. biloba*, 57.2±8.4 in the green tea, 56.8±11.9 in the placebo group	N/A	7.1% current, 14.3% former smokers	18.2% oral medicament therapy, 52.7% insulin, 29.1% oral medicaments + insulin	N/A
Lee et al. (79)	2008	Taiwan	RCT	N/A	"Grants from the Taichung Veterans General Hospital and Providence University, Taichung, Taiwan"	12 weeks	N/A	30 T2DM patients (diagnosis after 30 years of age) aged 50-75 years	9 men/6 women in the cranberry, 7 men/8 women in the placebo group	65±2 in the cranberry, 66±2 in the placebo group	26.2±0.7 in the cranberry, 25.9±1.0 in the placebo group	Subjects who smoked in the previous year were excluded	regular oral glucose-lowering drugs	N/A
Leenders et al. (80)	2011	Netherlands	RCT	N/A	N/A	6 months	N/A	60 elderly men with T2DM	only men	71±1 in the placebo, 71±1 in the leucine group	27.2±0.6 in the placebo, 27.4±0.6 in the leucine group	N/A	21 treated with metformin + sulfonylurea derivatives and/or thiazolidinediones, 28 with metformin, 5 with sulfonylurea	6 treated with diet recommendation alone
Levin et al. (81)	1981	USA	RCT	N/A	N/A	4 months	N/A	18 diabetic men aged 43-71 years	N/A	55.5±3.6 in the pxridoxine-	N/A	N/A	12 treated with insulin, 4 with oral hypoglycaemic	2 treated with diet only

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
								with symptomatic peripheral neuropathy		treated, 56.7±3.2 in the placebo-treated group			drugs, 2 with diet only	
Li et al. (82)	2015	China	RCT	N/A	"Guangdong Province Universities and the Colleges Funded Scheme (2011), and Guangzhou City Science and Technology Project (12C22061588)"	24 weeks	N/A	58 T2DM patients aged 56-67 years	17 men/12 women in the placebo, 17 men/12 women in the anthocyanin group	57.6±3.4 in the placebo, 58.1±2.3 in the anthocyanin group	23.9±3.5 in the placebo, 24.2±3.1 in the anthocyanin group	N/A	N/A	Patients should not change their usual lifestyle, dietary pattern and drugs.
Li et al. (83)	2008	China	RCT	N/A	Kao Corporation in Tokyo, Japan	14 days lead-in, 120 days treatment	N/A	127 T2DM patients aged 40-65 years	36 females/24 males in the DAG, 29 females/23 males in the TAG group	54.1±6.7 in the DAG, 53.9±6.0 in the TAG group	23.1±2.9 at day 0, 22.8±2.9 at day 60, 22.7±2.9 at day 120 in the DAG; 23.8±3.4 at day 0, 23.6±3.3 at day 60, 23.6±3.4 at day 120 in the TAG group	N/A	All except for 4 in the DAG and 4 in the TAG group used antidiabetic medications before the study: 32% glipizide, 25% acarbose, 21% insulin or protamine zinc insulin, 22% other antidiabetic medications (metformin, gliquidone, repaglinide)	PA should be the same throughout the study (should maintain usual PA)
Liu et al. (84)	2014	Taiwan	RCT	N/A	National Science Council, Taiwan: Grant number 101-2320-B-010-075	16 weeks	N/A	92 T2DM patients aged 20-65 years with	14 males/25 females	55.0±6.6 in the intervention,	26.2±4.2 in the intervention, 26.4±4.6	N/A	53.8% in the intervention, 60.5% in the placebo group	Patients should maintain

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
								lipid abnormalities	in the intervention, 18 males/20 females in the placebo group	53.5±7.0 in the placebo group	in the placebo group		used oral antidiabetes medication (35.9% sulfonylurea in the intervention, 24.2% in the placebo group, 43.6% biguanides in the intervention, 44.7% in the placebo group, 12.8% thiazolidinediones in the intervention, 5.3% in the placebo group, 2.6% α glucosidase inhibitors in the intervention, 5.3% in the placebo group, 10.3% dipeptidyl peptidase 4 (DPP-4) inhibitors in the intervention, 5.3% in the placebo group, 2.6% meglitinide in the intervention group, 35.9% in the intervention, 26.3% in the placebo group used a combination)	an isocaloric diet and their dietary patterns throughout the study.

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
Ludvik et al. (85)	2008	Germany	RCT	N/A	Partially sponsored by Dr Osami Aki of Fuji Sangyo (Japan)	5 months	N/A	61 T2DM patients	14 men/13 women in the Caiapo, 18 men/16 women in the placebo group	57.2±1.8 in the Caiapo, 61.1±1.5 in the placebo group	31.1±0.7 at baseline, 30.7±0.7 at the final visit in the Caiapo; 29.9±0.6 at baseline, 29.7±0.6 at the final visit in the placebo group	N/A	Treatment with diet alone	Treatment with diet alone, stable level of PA during the study
MacKenzie et al. (86)	2007	USA	RCT	N/A	"Grant from the Hitchcock Foundation (Lebanon, NH)"	3 months	N/A	49 T2DM patients (diagnosis ≥ 6 months' duration), HbA1c: 6.5-9.5% within these months	N/A	68.5±9.8 in the placebo, 60.6±9.9 in the intervention 375mg, 67.1±11.1 in the intervention 750mg group	30.7±5.2 in the placebo, 34.4±8.1 in the tea extract 375mg, 23.8±11.7 in the tea extract 750mg group	N/A	No insulin treatment	N/A
Magnoni et al. (87)	2008	Netherlands	RCT	N/A	"Sponsorship: Numico Research, Wagingen, The Netherlands"	12 weeks	N/A	40 patients diagnosed with T2DM for ≥ 6 months, aged >18 years, HbA1c: 6.5-8.5%	33.3% men total, 36.8% in the intervention, 30.0% in the control group	57.5±1.5 total, 55.7±2.1 in the intervention, 59.3±2.0 in the control group	32.2±0.9 total, 32.4±1.3 in the intervention, 32.1±1.2 in the control group	N/A	On controlled stabilized anti-diabetic medication for ≥ 1 month: metformin and/or sulfonylureas	Diabetic diet
Malaguarnera et al. (88)	2009	Italy	RCT	N/A	"Grant from the Ministero dell'Universita ` e Ricerca Scientifica e Tecnologica"	4 week placebo wash-out, 12 week treatment	N/A	81 T2DM patients aged 20-70 years (diagnosed ≤6 months) with hypercholesterolemia	28 men/12 women in the placebo, 30 men/11 women	48±11 in the placebo 49±13 in the L-carnitine group	27.4±1.8 in the placebo, 27.5±1.8 in the L-carnitine group	24 smokers/6 nonsmokers in the placebo, 34 smokers/7 nonsmokers in the L-carnitine group	N/A	Instructions from dietician "on dietary intake recording procedures as part of a

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
									in the L-carnitine group					behavior-modification program at each visit; resulting food diaries were later used for counseling."
Manzella et al. (89)	2001	Italy	RCT	N/A	"Supported by the Second University of Naples (Fondi Ateneo 1997)"	4 months	N/A	50 T2DM patients with cardiac autonomic neuropathy	N/A	65.1±3.9 in the placebo, 64.3±4.7 in the intervention group at baseline; 65.1±3.9 in the placebo, 64.3±4.7 in the intervention group at end of study	26.4±3.9 in the placebo, 26.2±4.3 in the vitamin E group at baseline; 26.4±3.9 in the placebo, 26.2±4.3 in the vitamin E group at end of study	nonsmokers	Metabolism sufficiently controlled by OHAs	N/A
Martin et al. (90)	2006	USA	RCT	N/A	"Grants R55 DK060126 and R01 DK060126 awarded to W.T.C. and M01RR00109"	4 week wash-out, 12 week treatment, 24 week treatment	N/A	37 T2DM patients aged 25-75 years (diagnosed ≥ 6 months prior to study); 125 ≤ FPG <170 mg/dL at the screening	17 males, 8 females	59.7±8	30±0.8	N/A	"glipizide gastrointestinal therapeutic system 5 mg/day"	On dietary treatment alone before study or on low dose of OHAs for ≥ 2 months
Mashavi et al. (91)	2008	Israel	RCT	N/A	N/A	4 months	N/A	60 T2DM patients	15 men/13 women	61.7±6.5 in the intervention, 30.6±5.3	31.8±5.1 in the intervention, 30.6±5.3	21% current smokers in	Therapy with ≥ 1500 mg metformin	N/A

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
									in the intervention, 13 men/16 women in the placebo group	tervention, 60.1±6.0 in the placebo group	in the placebo group	the intervention, 14% in the placebo group		
Mason et al. (92)	2016	Australia	RCT	N/A	Centre for Physical Activity & Nutrition Research	crossover: 4 month treatment, 1 month wash-out, 4 month treatment	N/A	35-70 year old subjects with stable blood sugar control: 6.5% < HbA1c <10.0%	12 men, 1 woman	57.9±2.5	30.5±0.8	only non-smokers	11 on metformin, 5 on sulfonylureas, 5 on DPP-4 inhibitors	Regular intensive PA prohibited; 1 person on diet-treatment only
Mayr et al. (93)	2016	Germany	RCT	N/A	Fresenius Kabi in Bad Homburg, Germany	12 weeks	N/A	40 T2DM patients >40 years old; (HbA1c 6.5-8.5%), who need nutritional support because of an involuntary weight loss: ≥5% over the previous 3 months or ≥10% over half a year	12 male/8 female in intervention, 8 male/12 female in control group	79.9 intervention; 82.0 control	24.0 in intervention, 22.0 in control group	N/A	Sulfonylureas or metformin	normal diet
McManus et al. (94)	1996	Canada	RCT	N/A	"Canadian Dairy Bureau and the Natural Sciences and Engineering Research Committee"	3 month run-in; crossover: 3 month treatment, 3 month treatment	N/A	11 T2DM patients, 81.5±4.2kg	3 men, 8 women	61.8±2.9	28.0±1.2 at baseline, 27.8±1.1 in the placebo, 27.9±1.03 in the linseed oil, 27.5±1.02 in the fish oil group	N/A	4 on oral sulfonylureas.	Subjects were advised "to maintain an isocaloric diet."

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
Mehrdadi et al. (95)	2017	Iran	RCT	N/A	"Tehran University of Medical Sciences & Health Services grant 26400"	12 weeks	N/A	64 patients aged 30-60 years with T2DM (duration >2 years) and BMI >25 and <35	57.1% male total, 50% male in the placebo, 65.4% in the Q10 group	47±8 total, 48±8 in the placebo, 46±7in the Q10 group	29.31±3.26 in the placebo, 29.68±2.92 in the Q10 group at baseline, 29.28±3.86 in the placebo, 29.21±3.25 in the Q10 group at end-of-trial	nonsmokers	1 in the placebo, 2 in the Q10 group took glybenglamid, 12 in the placebo, 13 in the Q10 group took metformin, 17 in the placebo, 11 in the Q10 group took both; patients under treatment with insulin were not recruited	Habitual dietary patterns and PA throughout the study period
Mirfeizi et al. (96)	2015	Iran	RCT	N/A	"Research grant from the Vice Chancellor of Research, Islamic Azad University, Karaj Branch: Grant number: 1/73295)"	90 days	N/A	105 T2DM patients aged 30-65 years; HbA1c >7% and FBG ≥140mg/dL	11.1% men in the cinnamon, 30% men in the whortleberry, 24.4% men in the placebo group	52±13 in the cinnamon, 55±10 in the whortleberry, 54±12 in the placebo group	28.36±3.27 in the cinnamon, 28.64±3.72 in the whortleberry, 29.94±4.45 in the placebo group	smokers were excluded	Biguanides, sulfonylurea derivatives, thiazolidines	Insulin treatment with specific PA and dietary regimens were exclusion criteria.
Mitra and Bhattacharya (97)	2006	India	RCT	N/A	Arunava Mitra of Crompton Greaves Ltd.	10 years	N/A	310 rural Indian people without liver, thyroid or kidney disease	263 men, 47 women	48±4.56	24.5±3.29	N/A	no lipid lowering, antidiabetic or antihypertensive agents	normal rural diet (70-80% carbohydrates, 10-20% proteins, 10% fat
Mobini et al. (98)	2017	Sweden	RCT	N/A	"BioGaia, the Swedish Research Council, the	12 weeks	N/A	46 abdominal obese	4 females/11 males	65±5 in the placebo,	30.7±4.0 in the placebo, 30.6±4.5 in	2 smokers in the placebo, 2	The anti-hyperglycaemic	N/A

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
					Swedish Diabetes Association, and ALF grants from the Sahlgrenska University Hospital"			T2DM patients(diagnosis >6 months before study) aged 50-75 (waist >80 cm for women; >94 cm for men); HbA1c 6.7%-10.4%	in the placebo, 3 females/12 males in the *L. reuteri* low, 3 females/11 males in the L. *reuteri* high group	66±6 in the L. *reuteri* low, 64±6 in the L. *reuteri* high group	the L. *reuteri* low, 32.3±3.4 in the L. *reuteri* high group at week 0; 30.8±4.2 in the placebo, 30.9±4.7 in the L. *reuteri* low, 32.1±3.5 in the L. *reuteri* high group at week 12	in the L. *reuteri* low, 2 in the L. *reuteri* high group	treatment included insulin, 11 in the placebo, 14 in the *L. reuteri* low, 10 in the *L. reuteri* high group took metformin, 4 in the placebo, 4 in the *L. reuteri* low, 2 in the *L. reuteri* high group used sulfonylurea/glinides, 1 in the *L. reuteri* low, 2 in the *L. reuteri* high group used GLP-1 agonists, 1 in the placebo, 1 in the *L. reuteri* low group used DPP-4 inhibitors	
Morgan et al. (99)	1995	USA	RCT	N/A	Pharmacaps, Incorporated in Elizabethtown, New Jersey	12 weeks	N/A	40 NIDDM patients with hyperlipidemia	18 males/22 females total, 4 men/6 women in the 9g fish oil, 6 men/4 women in the 18g fish oil, 4	53.9±7.0 total, 55.2±6.2 in the 9g fish oil, 53.4±8.8 in the 18g fish oil, 52.2±6.2 in the 9g corn oil, 54.6±7.1 in the 18g corn oil group	N/A	N/A	9 in the 9g fish oil, 7 in the 18g fish oil, 3 in the 9g corn oil, 3 in the 18g corn oil group were on insulin, 1 in the 9g fish oil, 1 in the 18g fish oil, 6 in the 9g corn oil, 6 in the 18g corn oil group were	4 treated with diet only

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
									men/6 women in the 9g corn oil, 4 men/6 women in the 18g corn oil group				on oral agents, 2 in the 18g fish oil, 1 in the 9g corn oil, 1 in the 18g corn oil group were on diet only	
Navarrete-Cortes et al. (100)	2014	Mexico	RCT	N/A	"Partially supported by the Programa de Fomento a la Investigación"	crossover: 3 month treatment, 3 month wash-out, 3 month treatment	2x 3 months	98 normomagnesemic patients aged 30-65 years with T2DM	36% male	52.84±8.42	30.55±5.72	smokers were excluded	55.3% used glibenclamide + metformin, 23.2% metformin, 10.7% glibenclamide, 7.2% glibenclamide + acarbose or acarbose alone, 3.6% diet + exercise	3.6% treated with diet + PA
Niemi et al. (101)	1988	Finland	RCT	N/A	"Financially supported by the Research Foundation of Finnish Sugar Co. Ltd. And the Orion Corporation Research Foundation"	crossover: 12 week treatment, 4 week washout, 12 week treatment	N/A	22 T2DM patients aged 40-76 years (poorly controlled)	16 women, 6 men	mean: 63	mean: 27	N/A	19 on OHAs, 3 on diet therapy only.	3 on diet control therapy alone; subjects should maintain their usual dietary pattern throughout the study
Nikooyeh et al. (102)	2014	Iran	RCT	N/A	National Nutrition and Food Technology Research Institute	2 week run-in, 12 week treatment	12 weeks	90 T2DM patients aged 30-50 years	55 women, 35 men	30-50 years	N/A	N/A	N/A	N/A
Nikooyeh	2011	Iran	RCT	N/A	Support from the National Nutrition and	2 week run-in, 12	N/A	90 diabetic patients	55 females,	50.7±6.1 total,	29.9±4.7 in the plain,	N/A	N/A	2 weeks (run-in) of

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
et al. (103)					Food Technology Research Institute	week treatment		aged 30-60 years with a FBG ≥ 126 mg/dL at the 1st visit	35 males	50.8±6.6 in the plain, 51.4±5.4 in the vitamin D-fortified, 49.9±6.2 in the vitamin D + calcium-fortified yogurt drink group	29.2±4.4 in the vitamin D-fortified, 29.1±5.5 in the vitamin D + calcium-fortified yogurt drink group at baseline; 30.0±4.7 in the plain, 28.3±4.4 in the vitamin D-fortified, 28.6±5.5 in the vitamin D + calcium-fortified yogurt drink group at end-of-trial			weight-maintenance diet for diabetics based on ADA recommendations, afterwards "equivalent amounts of dairy products were replaced by 2 servings of the yogurt drink"
Norris et al. (104)	2009	USA	RCT	N/A	Partially supported "by the National Center for Research Resources (UL1RR025755) and the Clinical Research Center at the Ohio State University (grant M01-RR00034) from the National Institutes of Health, the Caroline S Kennedy Endowment; An unrestricted monetary gift by Cognis (Monheim, Germany, and Cincinnati", Ohio)	crossover: 16 week treatment, 4 week wash-out, 16 week treatment	N/A	55 obese postmenopausal T2DM patients aged ≥70 years (HbA1c ≥6.5% and ≤14%)	only women	60.1±7.3 in the safflower oil to linoleic acid, 59.4±7.3 in the linoleic acid to safflower oil group, 59.7±7.3 total	36.3±6.1 in the safflower oil to linoleic acid, 37.1±7.2 in the linoleic acid to safflower oil group, 36.6±6.5 total	N/A	32 patients used sulfonylureas, 31 used biguanides, 19 used thiazolidinediones, 1 used an incretin mimetic, 1 used a alpha-glucosidase inhibitor, 8 used a combination therapy	safflower oil group: 1746±75 kcal at baseline, -154±92 kcal delta to week 16 in diet period 1; 158±5 Met.eq at baseline, 9±8 delta to week 16 in diet period 1; conjugated linoleic acid group: 1925±96 kcal at

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
														baseline, -395±126 delta to week 16 in diet period 1; 161± 7 Met.eq at baseline, -2± 10 delta to week 16 in diet period 1
Ogawa et al. (105)	2013	Japan	RCT	N/A	"A 21st Century Center of Excellence Program Special Research Grant" and "a research grant for cardiovascular research"	3 months	N/A	30 subjects on a liquid diet with T2DM	6 men/20 women total, 2 men/11 women in the CZ1.5, 4 men/9 women in the DIMS group	80.4±8.3 total, 81.2±7.6 in the CZ1.5, 79.5±8.6 in the DIMS group	20.1±3.6 total, 20.4±3.6 in the CZ1.5, 19.9±4.0 in the DIMS group at baseline; 20.3±3.6 in the CZ1.5, 20.1±4.0 in the DIMS group at end-of-trial	N/A	N/A	bedridden patients on liquid diet through tube
Pan et al. (106)	2007	China	RCT	N/A	Grants from the Major Project of Knowledge Innovation Program of the Chinese Academy of Sciences (KSCX1-YX-02), the Science and Technology Commission of Shanghai Municipality (04DZ14007), Knowledge Innovation Program of the Chinese Academy of Sciences (KSCX2-225), and the Ministry of Science and Technology of China (973	crossover: 12 week treatment, 8 week wash-out, 12 week treatment	32 weeks	73 patients aged 50-79 years with T2DM and a slight hypercholesterolemia	36.8% male total, 41.2% male in group A, 32.4% male in group B	63,.2±7.4, 64.4±7.1 in group A, 63.0±7.8 in group B	25.1±3.3 total; 25.0±3.3 at baseline, 25.2±3.3 at 12 weeks in group A; 25.1±3.3 at baseline, 25.2±3.5 at 12 weeks in group B	N/A	no exogenous insulin to control glucose	1911±329 kcal/day at week 0, 1858±365 kcal at week 12 in the intervention, 1840±327 kcal at week 0, 1866±321 kcal at week 12 in the placebo group;

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
					Program 2006CB503900)									32±6% fat at week 0, 31±7% at week 12 in the intervention, 31±6% at week 0, 31±6% at week 12 in the placebo group; 17±3% protein at week 0, 18±3% at week 12 in the intervention, 17±3% at week 0, 17±3% at week 12 in the placebo group; 88.0±32.7 MET-hours/week at week 0, 92.3±37.7 at week 12 in the intervention, 89.4±32.4 at week 0, 87.6±35.4 at week 12 in the

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
														placebo group
Paolisso et al. (107)	1995	Italy	RCT	N/A	N/A	crossover: 4 week follow-up, 4 month treatment, 30 day wash-out, 4 month treatment	4 weeks	40 aged, mildly overweight T2DM patients (mean duration 8.1±0.3 years) with normal arterial blood pressure, without micro- or macroangiopathy, normal kidney function ("microalbuminuria <20 μg/24 hours and plasma creatinine levels <100 μmol/L")	19 males, 21 females	72±0.5	27.7±0.3 at baseline, 27.6±0.8 in the placebo, 27.8±0.7 in the vitamin C group	N/A	23 on glibenclamide, 17 on glipizide	weight-maintaining food intake (≥250 g carbohydrates per day)
Paolisso et al. (108)	1993	Italy	RCT	N/A	N/A	crossover: 4 week prestudy period, 3 month treatment, 30 day wash-out, 3 month treatment	8 months	25 mildly overweight T2DM patients (mean duration: 8.4±0.3 years), without micro- or macroangiopathy, normal kidney function, HbA1c 7.8±0.3%	N/A	71.3±0.8	27.4±0.3 at baseline, 27.3±0.5 at the end of placebo, 27.3±0.4 at the end of vitamin E administration	N/A	13 on glipizide, 6 on tolbutamide, 6 on glyburide	weight-maintaining food intake (≥250 g carbohydrates, 14.1±0.6 mg vitamin E per day)

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
Parham et al. (109)	2014	Iran	RCT	N/A	N/A	crosso-ver: 2 week run-in, 12 week treatment, 8 week wash-out, 12 week treatment	N/A	48 T2DM patients (>1 year)	26.1% male in group A, 23.8% male in group B	53±10 in group A, 50±11 in group B	32.16±6.58 in group A, 30.24±4.03 in group B	N/A	Therapy with OHAs	Subjects should not change previous dietary habits and PA through-out the study.
Peder-sen et al. (110)	2016	UK	RCT	N/A	European Foundation for the Study of Dia-betes clinical research grant; “supported by the National Institute for Health Research Clinical Research Network: Kent, Surrey and Sussex”	12 weeks	N/A	29 T2DM patients aged 42-65 years (well-controlled diabetes)	only men	56.7±1.6 in the prebiotic, 58.1±1.7 in the pla-cebo group at baseline	28.0±1.1 at baseline, 28.2±1.1 at end-of-trial in the prebiotic; 28.4±0.9 at baseline, 28.5±1.4 at end-of-trial in the placebo group	N/A	7 in the prebi-otic, 3 in the placebo group on metformin, 3 in the prebi-otic, 2 in the placebo group on metformin + gliclazide, 1 in the prebi-otic, 2 in the placebo group on metformin + sitagliptin, 1 in the prebi-otic on met-formin + gliclazide + sitagliptin, 1 in the prebiotic on metformin + sitagliptin + thiazoli-dzinedione, 1 in the prebi-otic, 1 in the placebo group on sitagliptin + gliclazide, 1 in the placebo group on gliclazide	Subjects should maintain their life-style through-out the study, 6 subjects in the pla-cebo group on diet/PA treatment.

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
Pick et al. (111)	1996	Canada	RCT	N/A	Y. Mlkki, Exavena Oy/Inc in Espoo, Finland; Northern Alberta Institute of Technology and Patient Support Center, University of Alberta Hospitals; Clinical Investigation Unit, University of Alberta Hospitals; Quaker Oats Company of Canada Ltd in Peterborough, Ontario	crossover: 12 weeks treatment, 12 weeks treatment	N/A	8 NIDDM patients, BMI <35, HbA1c: <10%, plasma cholesterol: <7 mmol/L, plasma triglycerides: <5 mmol/L²	Men only	46±1	27.6±0.2	N/A	Lipid-lowering drugs prohibited, diabetes management with diet or OHAs	diabetes management with diet or OHAs
Racek et al. (112)	2006	Czech Republic	RCT	N/A	N/A	12 weeks	N/A	36 patients aged >18 years with clinically diagnosed T2DM	2 men/15 women in the placebo, 7 men/12 women in the chromium group	61.8 in the placebo, 60.8 in the chromium, 61.3 total	35.16 in the placebo, 33.59 in the chromium group, 34.33 total	N/A	3 used sulfonylurea derivates, 3 biguanides, 1 sulfonylurea and biguanides	Patients were counseled not to change their usual diet and PA habits throughout the study period.
Rodriguez-Moran et al. (113)	2003	Mexico	RCT	N/A	“Grants from the Consejo Nacional de Ciencia y Tecnologı´a de Me ´xico (FOSIVILLA 20000402008) and the Fondode Fomentoala Investigacion of the Mexican Social Security Institute (FP 2001/354)”	16 weeks	N/A	80 T2DM patients with decreased magnesium levels in the serum (≤0.74 mmol/L)	N/A	59.7±8.3 in the magnesium chloride, 54.1±9. in the control group	27.6±9.1 in the magnesium chloride, 28.6±4.2 in the control group at baseline; 27.7±9.6 in the magnesium chloride, 28.9±4.7 in the control group at end-of-trial	N/A	Therapy with glibenclamide	Counseled to consume >50% carbohydrates, <10% saturated fat, 20% mono- and polyunsaturated fat, ~1g protein/kg ideal body weight/d in the 3 months

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
														before the study; counseled to exercise for 30 min ≥ 3x/week
Rotman-Pikielny et al. (114)	2014	Israel	RCT	N/A	Dhanvantary Herbochem Pvt Ltd. Inc., Mira Road Thane, Maharashtra, India; Ace Continental Exports Inc. in London	12 weeks	1 week	35 T2DM patients (inadequately controlled in spite of OHA therapy) aged ≥18 years	44% male in the DBCare, 71% male in the placebo group	61.8±7.1 in the DBCare, 60.6±8.4 in the placebo group	27.1±4.3 in the DBCare, 29.8±4.0 in the placebo group	N/A	94.4% in the DBCare, 94.1% in the placebo group on metformin	N/A
Roussel et al. (115)	2003	Tunisia	RCT	N/A	Partially supported by grants from the Diabetes Action Foundation in Washington, DC, and Labcatal Pharmaceutical, Montrouge Cedex in France	6 months	N/A	56 Tunasian T2DM (≥ 5 years) patients aged 48-63 years (HbA1c: >7.5%, fasting glucose: >8 mmol/L), 60 healthy controls as reference for plasma TBARS	N/A	51.5±1.62 in the zinc, 55.5±1.43 in the placebo group	28.9±0.15 in the zinc, 29.6±0.15 in the placebo group	N/A	N/A	N/A
Rytter et al. (116)	2010	Sweden	RCT	N/A	Financially supported by Semper AB and Procordia AB	12 weeks treatment, 8 weeks wash-out	N/A	47 T2DM patients aged 40-75 years, HbA1c < 10% and BMI < 35 kg/m²	22 females, 18 males	61.9±7.2	28.3±3.8	6 smokers, 34 non-smokers	Diet-controlled or therapy with diet + OHAs	Patients should keep dietary habits and PA level stable throughout the test period.

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
Ryu et al. (117)	2014	Korea	RCT	N/A	Grant O.H.R, 2010 from the Korean Diabetes Association + support from the Daewoong Pharmaceutical Company and Handok pharmaceuticals Co., Ltd.	24 weeks	N/A	158 subjects aged 30-69 years with T2DM: stabilized glycaemic control (HbA1c <8.5%), vitamin D: < 20 ng/mL	57% male in the placebo, 43% male in the vitamin D group	55.9±8.1 in the placebo, 54.8±7.6 in the vitamin D group	25.6±3.6 in the placebo, 25.0±3.3 in the vitamin D group	N/A	N/A	47.1% in the placebo, 52.9% in the vitamin D group worked out regularly.
Sarbolouki et al. (118)	2013	Iran	RCT	N/A	Tehran University of Medical Sciences (Iran)	3 months	N/A	67 overweight patients aged 35-55 years with T2DM (defined as subject on OHAs or with a FPG concentration > 7.0 mmol/L)	13 men/22 women in the control; 13 men/19 women in the intervention group	45.3±3.93 in the control, 45.03±4.88 in the intervention group	27.80±1.65 in the control, 27.9±1.73 in the intervention group	nonsmokers	16% on sulfonylureas, 8% on biguanides, 76% on biguanides + sulfonylureas	Counseled not to change dietary patterns or PA level
Scroggie et al. (119)	2003	USA	RCT	N/A	Support from the Surgeon General's Office of the US Air Force (protocol SG0-FWH20000097)	90 days	N/A	38 subjects with “confirmed diagnosis of T2DM” (stable HbA1c that varied < 0.2% for ≥ 2 successional measurements ≥ 90 days apart from each other)	12 males/10 females in the glucosamine, 6 males/6 females in the placebo group	68.6 in the glucosamine, 70.7 in the placebo group	N/A	N/A	Therapy with a stable amount of oral antihyperglycaemic drugs or strict control through diet	Therapy with a stable amount of oral antihyperglycaemic drugs or strict control through diet
Shab-Bidar et al. (120)	2015	Iran	RCT	N/A	National Nutrition and Food Technology Research Institute (grant number 035360), Tehran University of	12 weeks	N/A	60 T2DM patients aged 30-60 years; FPG >7mmol/L	14 male/15 female in the control;	51.3±7.7 in the control; 54.1±8.0	28.6±4.2 in the control, 28.2±4.6 in the intervention group at	N/A	N/A	N/A

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
					Medical Sciences (grant number 10533), Iran National Science Foundation (grant number 8800420)				17 male/14 female in the intervention group	in the intervention group	baseline; 28.8±4.1 in the control group, 27.8±4.5 in the intervention group at end-of-trial			
Shab-Bidar et al. (121)	2011	Iran	RCT	N/A	National Nutrition and Food Technology Research Institute. Tehran University of Medical Sciences, Iran National Science Foundation	2 week run-in, 12 weeks treatment	12 weeks	100 T2DM patients aged 29-67 years	19 men/31 women in the placebo, 24 males/26 females in the intervention group	52.4±8.4 in the placebo, 52.6±6.3 in the intervention group	30.0±4.2 in the placebo, 28.6±4.0 in the intervention group at baseline; 30.2±4.3 in the placebo, 28.4±4.0 in the intervention group at end-of-trial	2% in the plain doogh, 10% in the vitamin D-fortified doogh group	OHAs: metformin, glibenclamid, glitazone	No treatments reducing weight
Shidfar et al. (122)	2015	Iran	RCT	N/A	No funding declared	3 months	N/A	50 subects with T2DM aged 20-60-year without insulin treatment	N/A	45.2±7.64 in the ginger, 47.1±8.31 in the placebo group	29.5±2.8 in the ginger, 29.2±3.1 in the placebo group at week 0, 29.6±2.1 in the ginger, 29.6±2.8 in the placebo group at week 12	nonsmokers	Glibenclamide, metformin or both	45.5% light PA in the ginger, 43.4% in the placebo at week 0, 22.7% moderate PA in the ginger, 34.7% in the placebo group at week 0, 31.8% vigorous PA in the ginger, 21.7% in

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
														the placebo group at week 0, 50% light activity in the ginger, 47.3% in the placebo group at week 12, 31.8% moderate PA in the ginger, 31.5% in the placebo group at week 12, 18.1% vigorous activity in the ginger, 21.1% in the placebo group at week 12
Shimizu et al. (123)	1995	Japan	RCT	N/A	N/A	12 months	N/A	54 patients with NIDDM without abnormal levels of blood urea nitrogen and creatinine in the serum	12 men/4 women in the control, 10 men/19 women in the eicosapentaenoic acid ethyl	58.6±1.8 in the control, 66.3±2.5 in the EPA-E treated group	22.8±1.2 in the control, 23.9±1.0 in the EPA-E treated group	N/A	1 in the control group treated with diet alone, 8 with sulfonylurea, 7 with insulin; 2 in the EPA-E treated group treated with diet alone, 17 with sulfonylurea, 10 with insulin	1 in the control group, 2 in the EPA-E treated group treated with diet alone

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
									(EPA-E) treated group					
Solerte et al. (124)	2004	Italy	RCT	N/A	Partial support by a grant from the University of Pavia in Italy	crossover: 2 week run-in, 16 week treatment, 2 week washout, 16 week treatment	34 weeks	34 T2DM patients aged 65-83 years (HbA1c >7%, diagnosis 5-15 years before trial), BMI 18-23 kg/m²	N/A	65-85 years	between 18-23	N/A	25 on OHAs (9 on metformin, 8 on metformin combined with glibenclamide, 5 on repaglinide combined with metformin, 3 on glimepiride), 9 on insulin	N/A
Solerte et al. (125)	2008	Italy	RCT	N/A	University of Pavia in Italy	crossover: 2 week run-in, 16 week treatment, 2 week washout, 16 weeks treatment, 26 weeks maintenance treatment period	60 weeks	34 T2DM patients aged 65-85 years (HbA1c >7%)	N/A	65-83 years	between 19-23	N/A	Insulin or OHAs	N/A
Strobel et al. (126)	2014	Germany	RCT	N/A	Grant based on EU framework 7 project program (Natural Immune Modulation for Intervention in Type 1 Diabetes, grant agreement number 241447)	6 months	N/A	86 T2DM patients aged 18-80 years (no vitamin D supplementation for ≥ 3 months before the beginning of the study)	24 men in the verum, 24 in the placebo group	median age of 61 (36-78) in the verum, 60 (30-78) in the placebo group	30.5 in the verum, 31.1 in the placebo group	N/A	Exclusion of subjects on glycosides, glucocorticoids, bisphosphonates, orbenzodiazepines, calcimimetics, and phenytoin; subjects	N/A

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
													where treatment with one of these was planned	
Tajabadi-Ebrahimi et al. (127)	2017	Iran	RCT	N/A	The Vice-chancellor for Research, Kashan University of Medical Science, and Iran provided a grant.	12 weeks	N/A	60 overweight T2DM patients aged 40-85 years suffering from coronary heart disease	N/A	64.0±11.7 in placebo; 64.2±12.0 in synbiotic group	29.6±4.6 in placebo, 32.2±6.0 in synbiotic group at baseline, 29.7±4.7 in placebo, 32.2±6.1 in synbiotic group at end-of-trial	N/A	N/A	Patients were asked not to change habitual dietary patterns and PA level.
Taylor et al. (128)	2010	Canada	RCT	N/A	"Flax Council of Canada and the Canada Manitoba Agri-food Research Development Initiative"	12 weeks	N/A	34 T2DM patients aged 35-65 years	17 males/17 females	52.4±1.5	32.4±1.0	N/A	no antihyperglycaemic drugs	1974±129 kcal in the control, 1879±113 kcal in the flaxseed, 1819±128 kcal in the flaxseed oil group at baseline, 2052±95 kcal in the control, 1997±83 kcal in the flaxseed, 2293±92 kcal in the flaxseed oil group during treatment
Turpeinen et al. (129)	2000	Finland	RCT	ALCAR	"Grants from the University of Kuopio, Kuopio University	1 year	N/A	19 T2DM patients	N/A	56±5 in the placebo,	N/A	N/A	N/A	N/A

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
					Hospital, and Hoffman La Roche Ltd., Basel, Switzerland"; "from the Council for Health Research, Academy of Finland (to Dr. Matti I. J. Uusitupa)"; "from the North Savo Cultural Foundation and the Aarne and Aili Turunen Foundation (to Dr. Anu K. Turpeinen)"					57±2 in the acetyl-L-carnitine group				
Tütüncü et al. (130)	1998	Turkey	RCT	N/A	N/A	6 months	N/A	21 T2DM patients suffering from peripheral neuropathy	1 men/9 women in the placebo, 2 men/9 women in the vitamin E group	59.3±9.8 in the placebo, 57.2±13.0 in the vitamin E group	26.7±5.2 in the placebo, 28.1±6.1 in the vitamin E group	N/A	Therapy with OHAs or only diet	Therapy with OHAs or only diet
Uusitupa et al. (131)	1984	Finland	RCT	N/A	N/A	crossover: 18 weeks 1st treatment, 18 weeks 2nd treatment, 18 weeks 1st treatment	N/A	19 T2DM patients (mean FBG concentration at study entry: 9.7±0.9 mmol/L)	18 females, 1 male	62±1.8	N/A	N/A	13 on antihypertensive medication, no change in treatments during the study	Only therapy by diet
Vaisman et al. (132)	2006	Israel	RCT	N/A	N/A	3 months	N/A	26 NIDDM patients (uncontrolled): high HbA1c levels + 2-h postprandial sugar >200mg% as indicators	N/A	65.4±10.7 in the fructose, 59.5±9.1 in the control group	29.5±3.9 in the fructose, 30.5±5.2 in the control group	N/A	Metformin, sulfonylurea, avandia; therapy with insulin mixtard for 1 person in each group	Patients should maintain their diet habits and PA throughout the study.

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
von Hurst et al. (133)	2010	New Zealand	RCT	N/A	"New Zealand Lottery Board (Lottery Health Grant) and New Zealand Department of Internal Affairs"	6 months	N/A	114 insulin resistent, vitamin D deficient South Asian women aged 23-68 years with a fasting serum sugar <7.2 mmol/L in Auckland	only women	41.8±10.1 in the vitamin D, 41.5±9.1 in the placebo group	27.5±5.0 in the vitamin D, 27.4±3.7 in the placebo group	N/A	Medication for diabetes was exclusion criterion	N/A
Vuksan et al. (134)	2008	Canada	RCT	N/A	"Grant from the Korean Ministry of Agriculture and Forestry and National Agricultural Cooperative Federation"	crossover: 4 week run-in, 12 week treatment, 4-6 week washout, 12 week treatment	N/A	19 T2DM (>6 months, well-controlled) patients aged 18-65 years without manifest complications; not pregnant; metabolically stable with a HbA1c level of 6.0-8.5% and a FPG level of 6.4-8.5 mmol/L)	11 males, 8 females	64±2	28.9±1.4	N/A	no insulin, herbs, supplement use, 5 on diet alone, 3 on sulfonylurea + diet, 3 on metformin + diet, 5 on sulfonylurea/metformin + diet, 1 on sulfonylurea/metformin/rosiglitazone + diet, 1 on sulfonylurea/rosiglitazone + diet, 1 on acarbose + diet)	diet according to the Canadian Diabetes Association nutrition guidelines
Wainstein et al. (135)	2011	Israel	RCT	N/A	N/A	2 week run-in, 12 week treatment, 4 week washout	18 weeks	59 T2DM patients (for ≥ 3 months) aged ≥30 years, HbA1c: 6.5-10.5%	51.7% women in the cinnamon, 30% in the placebo group	61.7±6.3 in the cinnamon, 64.4±15.4 in the placebo group	29.8±4.3 in the cinnamon, 30.9±6.9 in the placebo group	2 smokers in the cinnamon, 4 in the placebo group	Sulfonylurea and/or metformin + lifestyle therapy	PA: ~2.6 hours/week; sulfonylurea and/or metformin + lifestyle therapy

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
Watts et al. (136)	2002	Australia	RCT	N/A	"Research grants from Diabetes Australia, The National Health and Medical Research Council of Australia and The Medical Research Foundation, Royal Perth Hospital"	12 weeks	N/A	40 T2DM patients aged <75 years, BMI <40 kg/m² with dyslipidaemia (fasting serum triglycerides >1.8 mmol/L or HDL cholesterol <1.0 mmol/L with total cholesterol <6.5 mmol/L and total cholesterol:HDL ratio >4); 18 healthy controls to compare vascular function	13 males/2 females in the placebo, 18 males/2 females in the intervention group	54.1±10.4 in the placebo, 52.7±6.2 in the intervention group	31.3±5.4 in the placebo, 29.9±3.3 in the intervention group	Smokers were excluded	Insulin treatment was exclusion criterion.	N/A
Wolffenbuttel et al. (137)	1992	Netherlands	RCT	N/A	N/A	crossover: 3 months, 3 months	N/A	12 T2DM patients (time since onset: 11 years) without liver or kidney disease	6 males, 6 females	62±10	25.8±3.5	N/A	Treatment with OHAs, 11 on sulfonylurea; no corticosteroids	3267-9345 kJ/d total energy intake
Yin et al. (138)	2008	China	RCT	N/A	Financially supported by Xinhua Hospital; partial support from the National Institutes of Health grant (P50 AT02776-020002)	3 months	N/A	84 T2DM patients aged 25-75 years, HbA1c >7.0% or FBG >7.0 mmol/L	49 women, 35 men	aged 25-75 years	>22 kg/m²	N/A	1 group received metformin as control group.	Only diet therapy for 2 months before assignment to groups
Yiu et al. (139)	2013	China	RCT	N/A	No support by commercial funds	12 weeks	N/A	100 T2DM patients	54% male in	65.8±7.3 in the	25.8±4.3 in the treatment,	30% ever smokers in	20% in the treatment,	Patients should not

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
								with suboptimal vitamin D level (< 30 ng/mL)	the treatment, 46% male in the placebo group	treatment, 64.9±8.9 in the placebo group	25.1±3.4 in the placebo group	the treatment, 26% in the placebo group	28% in the placebo group on insulin, 82% in the treatment, 80% in the placebo group on biguanides, 60% in the treatment, 38% in the placebo group on sulfonylureas, 4% in the treatment group on alpha-glucosidase inhibitor, 2% in the treatment, 2% in the placebo group on thiazolidinediones, 6% in the treatment group on DPP-4 inhibitors	to change dietary habits and lifestyle during the supplementation period.
Zhang et al. (140)	2008	China	RCT	N/A	Grant 2006 CB 503904 from 973 Project, 04DZ19502 from the Shanghai Committee for Science and Technology, 30700383 and 30725037 from the National Natural Science Foundation of China, Y0204 and E03007 from the Shanghai Education Commission	2 week run-in, 3 month treatment	3 months	116 newly diagnosed (based on the WHO) T2DM patients aged 25-70 years with dyslipidemia, BMI: 19-40 kg/m²	30 men/28 women in the berberine, 31 men/21 women in the placebo group	51±9 in the berberine group at baseline, 51±10 at end-of-trial	25.2±3.1 at baseline, 24.3±3.2 at end-of-trial in the berberine; 25.9±3.8 at baseline, 25.4±3.6 at end-of-trial in the placebo group	14 current smokers in the berberine, 20 in the placebo group	Patients using or having used diabetes medication were excluded.	PA and diet instructions in the 2 weeks run-in period

Author	Year	Country	Study design	RCT name	Funding source	Study duration	Follow-Up	Study population	Sex	Age	BMI	Current/ Ex-smokers	Medication	Exercise/ diet
Zheng et al. (141)	2015	China	RCT	N/A	"National Natural Science Foundation of China (81273054); PhD Programs Foundation of Ministry of Education of China (20120101110107); National Program on Key Basic Research Project of China (973 Program: 2011CB504002); National High-Tech R&D Program of China (863 Program, N20080753)"	14 days run-in, 120 days treatment	N/A	127 T2DM patients aged 40-65 years	40.8% men in the normal weight, 44.4% in the overweight group	53±6 in the normal weight, 53.4±7.3 in the overweight group	21.7±1.9 in the normal weight, 27.2±1.4 in the overweight group	N/A	Metformin, acarbose, glipizide, repaglinide, gliquidon, "insulin or protamine zinc insulin"	Patients were asked not to alter their normal PA and diet throughout the study.
Zibadi et al. (142)	2008	USA	RCT	N/A	Horphag Research provided a research grant.	12 weeks	N/A	48 T2DM patients aged 40-75 years with mild to moderate hypertension	14 men/10 women in the placebo, 13 men/11 women in the pycnogenol group	58.4±11.5 in the placebo, 61.3±9.1 in the pycnogenol group	N/A	N/A	Angiotensin-converting enzyme inhibitors to treat hypertension; insulin treatment was exclusion criterion.	N/A

ADA = American Diabetes Association, AHA = American Heart Association, BMI = body mass index, DAG = diacylglycerol, DPP-4 = dipeptidyl peptidase 4, EPA-E = eicosapentaenoic acid ethyl, FBG = fasting blood glucose, FPG = fasting plasma glucose, *G. biloba* = *Gingko biloba*, GLP-1 = Glucagon-like peptide 1, HbA1c = Glycated Haemoglobin, HDL = high-density lipoprotein, *M. charantia* = *Momordica charantia*, min = minutes, MVM = multivitamin/mineral, N/A = not applicable, N. sativa = Nigella sativa, NIDDM = non-insulin-dependent diabetes mellitus, NNFTRI = National Nutrition and Food Technology Research Institute, OGTT = oral glucose tolerance test, OHA = oral hypoglycaemic agent, PA = physical activity, RCT = randomized controlled trial, T2DM = type 2 diabetes mellitus, TAG = triacylglycerol, UK = United Kingdom, USA = United States of America
CZ1.5, DIMS = liquid diets

Table 3 shows the treatment arms and number of participants at randomization as well as at time of analysis in the 122 trials of the systematic review. For a clearer arrangement, this table has been separated into three parts. Five columns for four treatment arms in the beginning, a part with 16 columns and 15 treatment arms for the study by Mitra and Bhattacharya, and another part with five colums, four treatment arms for the remaining studies.

Table 3: Description of control and intervention arms and number of participants according to the different arms of the included trials

Author	Arm 1: Dose, n at randomization/n at analysis	Arm 2: Dose, n at randomization/n at analysis	Arm 3: Dose, n at randomization/n at analysis	Arm 4: Dose, n at randomization/n at analysis
Akbari Fakhrabadi et al. (21)	200 mg Coenzyme Q10/d, 37/32	Placebo: microcrystalline cellulose, 37/30	N/A	N/A
Akilen et al. (22)	2 g cinnamon/day (4 x 500 mg), 30/30	2 g placebo: starch-filled (4 x 500 mg), 28/28	N/A	N/A
Al-Maroof et al. (23)	Oral zinc sulfate (30 mg elemental zinc/cap daily), 50/43	Placebo, 51/43	N/A	N/A
Anderson et al. (24)	Indistinguishable placebo tablets, 60/N/A	100 µg (1.92 µmol) chromium in the form of chromium picolinate 2x/day, 60/N/A	500µg (9.6 µmol) chromium 2x/day, 60/N/A	N/A
Anderson et al. (25)	30 mg/d zinc in the form of zinc gluconate, 27/27	400 µg/d chromium in the form of chromium pidolate, 27/27	Combination of zinc and chromium, 27/27	Placebo, 29/29
Aro et al. (26)	21 g guar gum, 11 crossover subjects/9 crossover subjects	Placebo: wheat flour, 11 crossover subjects/9 crossover subjects	N/A	N/A
Ashraf et al. (27)	Capsule Garlic 300 mg 3x/day + Metformin 500 mg 2x/day, 30/27	Placebo + Metformin 500 mg 2x/day, 30/27	N/A	N/A
Barchetta et al. (28)	2000 IU cholecalciferol/day, 29/26	Placebo, 36/29	N/A	N/A
Barre et al. (29)	Flaxseed oil containing 60 mg ALA/kg body weight/day, 18/18	Placebo: safflower oil, 14/14	N/A	N/A
Bonsu et al. (30)	Fiber supplement: inulin (10 g), 18/12	Placebo: xylitol (10 g), 18/14	N/A	N/A
Boshtam et al. (31)	200 IU/day vitamin E capsules, 50/50	Placebo, 50/50	N/A	N/A
Breslavsky et al. (32)	1000 U vitamin D/day, 24/24	Placebo: microcrystalline cellulose, 23/23	N/A	N/A
Cheng et al. (33)	“Stabilized rize bran” (20 g), 17/17	Placebo: milled rice, 11/11	N/A	N/A
Cruz et al. (34)	5 g glycine/d, 38/38	5 g placebo/d, 36/36	N/A	N/A
Dakhale et al. (35)	Vitamin C + metformin: each 500 mg 2x/day, 35/33	Placebo + metformin (500 mg 2x/day), 35/33	N/A	N/A
Dans et al. (36)	2 *M. charantia* tablets 3x/day, 20/20	2 placebo tablets 3x/day, 20/20	N/A	N/A
de Oliveira et al. (37)	LA: 600 mg, 26/26	Alpha-tocopherol: 800 mg, 25/25	Alpha-tocopherol (800 mg) + LA (600 mg), 25/25	Placebo, 26/26
Derosa et al. (38)	120 mg Orlistat 3x/day + L-carnitine 2 g 1x/day, 132/132	120 mg Orlistat 3x/day, 126/126	N/A	N/A
Derosa et al. (39)	10 mg Sibutramine + 2 g L-carnitine, 129/113	10 mg Sibutramine, 125/110	N/A	N/A
Derosa et al. (40)	1 g L-carnitine 2x/day, 46/46	Placebo, 48/48	N/A	N/A
Derosa et al. (41)	Alpha-lipoic acid (600 mg), L-carnosin (165 mg), zinc (7.5 mg), B-vitamins; 54/51	Placebo: 1x/day, 51/49	N/A	N/A

De Valk et al. (42)	Magnesium: 15 mmol, 25/18	Placebo, 25/16	N/A	N/A
Eftekhari et al. (43)	2 tablets calcitriol/day: 0.25 µg 1,25-dihydroxy cholecalciferol/tablet, 35/35	Placebo, 35/35	N/A	N/A
Eibl et al. (44)	30 mmol magnesium citrate/day, 20/18	Placebo, 20/20	N/A	N/A
Elwakeel et al. (45)	n-3 fatty acids + low-dose aspirin, 20/20	Placebo: coconut oil + lactose, 20/20	N/A	N/A
Eriksson et al. (46)	2g ascorbic acid/day, N/A/27 crossover subjects	600 mg magnesium/day, N/A/27 crossover subjects	N/A	N/A
Faghihi et al. (47)	200 µg selenium, 33/33	Placebo, 27/27	N/A	N/A
Fang et al. (48)	DJCs (1.8 g effective extract in every tablet, 5 tablets, 3x/day) + to routine western medicine, 31/31	routine western medicine, 31/31	N/A	N/A
Farvid et al. (49)	200 mg magnesium + 30 mg zinc, N/A/16	Vitamin C (200 mg) + vitamin E (100 IU), N/A/18	minerals plus vitamins, N/A/17	Placebo: lactose, N/A/18
Feinglos et al. (50)	Placebo 2x/day, 8/8	3.4 g psyllium 2x/day, 15/15	6.8 g psyllium 2x/day, 14/14	N/A
Fenercioglu et al. (51)	“Polyphenol-rich antioxidant supplement” with pomegranate extract, green tea extract, ascorbic acid; 56/56	Placebo: 5% polyvinylpyrrolidone, 3% sodium starch glycolate, 1% magnesium stearate, 91% microcrystalline cellulose; 58/58	N/A	N/A
Firouzi et al. (52)	Probiotics: “3 x 10^10 dose of 6 viable microbial cell preparation strains”, 68/68 by intention to treat, 53 per protocol	Placebo, 68/68 by intention to treat, 48 per protocol	N/A	N/A
Foster et al. (53)	40 mg/d zinc + 2 g/d flaxseed oil, N/A/23	Placebo, N/A/20	N/A	N/A
Ginter et al. (54)	500 mg ascorbic acid/day, 35/35	Placebo, 13/13	N/A	N/A
Goh et al. (55)	Resveratrol: 3g, 5/5	Placebo, 5/5	N/A	N/A
Grotz et al. (56)	Placebo: cellulose, 69/68	667 mg sucralose in tablets, 67/65	N/A	N/A
Gualano et al. (57)	5 g/day creatine, 14/13	Placebo, 14/12	N/A	N/A
Guimaraes et al. (58)	NC0: placebo, 15/13	NC50: 50 µg chromium in the form of chromium nicotinate, 18/13	NC200: 200 µg chromium in the form of chromium nicotinate, 23/16	N/A
Gullestad et al. (59)	15 mmol magnesium-lactate-citrate capsules/day, 25/N/A	Placebo, 29/N/A	N/A	N/A
Gunasekara et al. (60)	Zinc + MVM: 22 mg/day oral zinc sulfate + multivitamin/mineral preparation, 29/28	MVM: multivitamin/mineral preparation without zinc, 31/31	Placebo, 36/32	N/A
Hosseinzadeh et al. (61)	Brewer's yeast (6 300mg capsules/day, 1800 mg total), 45/42	Placebo (6 300mg capsules/day), 44/42	N/A	N/A
Hosseinzadeh-Attar et al. (62)	200 mg Coenzyme Q10/d, 31/31	Placebo: maize starch, 33/33	N/A	N/A
Hove et al. (63)	Cardi04 yogurt: milk fermented with *L. helveticus* (300 mL), 23/23	Placebo yogurt: milk that has been artificially acidified (300 mL), 18/18	N/A	N/A
Hsia et al. (64)	Pancreas Tonic (2 tablets 3x/day), 31/23	Placebo (2 tablets 3x/day), 16/13	N/A	N/A
Hsu et al. (65)	Extract of ABM (500 mg/tablet), 36/29	Placebo (cellulose): 1500 mg, 36/31	N/A	N/A

Hsu et al. (66)	Green tea extract (decaffeinated): 1500 mg, 40/35	Placebo: microcrystalline cellulose, 40/33	N/A	N/A
Huseini et al. (67)	200 mg silymarin 3x/day, 25/25	Placebo capsules 3x/day, 26/26	N/A	N/A
Hussain et al. (68)	Silymarin (200 mg/d) in addition to glibenclamide (10 mg/day), 18/18	Placebo (200 mg/d) in addition to glibenclamide (10 mg/day), 20/20	10 mg/day glibenclamide alone, 21/21	N/A
Hussain et al. (69)	placebo + 2550 mg metformin/day, 15/15	10 mg melatonin + 50 mg zinc acetate as single daily doses + 2550 mg metformin/day, 18/18	10 mg melatonin + 50 mg zinc acetate as single daily doses, 13/13	N/A
Jafari et al. (70)	"Vitamin d-fortified low fat yogurt": 2000 IU vitamin D in 100g, 32/30	"Plain low fat yogurt", 32/29	N/A	N/A
Jayagopal et al. (71)	30 g/d soy protein, 132 mg/d isoflavones, 32 crossover subjects/32 crossover subjects	Placebo: 30 g/d cellulose, 32 crossover subjects/32 crossover subjects	N/A	N/A
Jorde et al. (72)	40,000 IU cholecalciferol/week, 20/16	Placebo, 16/16	N/A	N/A
Kaatabi et al. (73)	Placebo: 260 mg activated charcoal tablets, 57/48	N. sativa: 500 mg, 57/48	N/A	N/A
Kajanachumpol et al. (74)	1 zinc tablet/day after breakfast (50 mg zinc sulfate), 12/12	Placebo: 1 tablet/day after breakfast, 13/13	N/A	N/A
Kampmann et al. (75)	Colecalciferol: 280µg/day for 2, 150µg/day for 10 weeks, 8/7	Placebo, 8/8	N/A	N/A
Kleefstra et al. (76)	Placebo, 19/17	500 µg chromium/day in the form of chromium picolinate, 17/14	1000 µg chromium/day in the form of chromium picolinate, 17/15	N/A
Krul-Poel et al. (77)	50,000 IU Vitamin D3/month, 136/129	50,000 IU placebo/month, 138/132	N/A	N/A
Lasaite et al. (78)	*"G. biloba* L. leaves dry extract", 25/25	"Green tea dry extract", 17/17	Placebo, 14/14	N/A
Lee et al. (79)	3 cranberry extract tablets/day (500 mg powder/tablet), 15/15	Placebo every day, 15/15	N/A	N/A
Leenders et al. (80)	L-Leucine: 2.5 g, 30/29	Placebo: wheat flour, 30/28	N/A	N/A
Levin et al. (81)	Vitamin B6 (pyrodoxine hydrochloride 50 mg 3x/day), 9/9	Indistinguishable placebo capsules, 9/9	N/A	N/A
Li et al. (82)	Anthocyanins: 160mg 2x/day, 29/29	Placebo: pullulan + maltodextrin, 29/29	N/A	N/A
Li et al. (83)	DAG: 25 g/d, 66/60	TAG: 25 g/d, 61/52	N/A	N/A
Liu et al. (84)	Green tea extract: 500 mg, 46/39	Placebo: cellulose, 46/38	N/A	N/A
Ludvik et al. (85)	4 g Caiapo/day, 27/27	Placebo, 34/34	N/A	N/A
MacKenzie et al. (86)	Placebo: 0 mg tea extract, 18/16	Single tablet: 375 mg tea extract (150 mg green tea catechins + 75 mg black tea theaflavins), 17/16	Double tablet: 750 mg tea extract (300 mg green tea catechins + 150 mg black tea theaflavins), 19/17	N/A
Magnoni et al. (87)	"Diabetes-specific ONS" Diasip: 2 x 200 mL, 20/19	Standard ONS, 20/20	N/A	N/A
Malaguarnera et al. (88)	L-carnitine 1x/day, 41/41	Placebo, 40/40	N/A	N/A
Manzella et al. (89)	600 mg/d vitamin E, 25/25	Placebo: sodium citrate, 25/25	N/A	N/A

Martin et al. (90)	Sulfonylurea + placebo, 12/11	Sulfonylurea + chromium in the form of chromium picolinate (1000 µg), 17/14	N/A	N/A
Mashavi et al. (91)	1000 mcg folate, 400 mcg vitamin B12, 10 mg vitamin B6; N/A/28	Placebo, N/A/29	N/A	N/A
Mason et al. (92)	Ascorbic acid: 2 x 500 mg/day, 13 crossover subjects/13 crossover subjects	Placebo: "560 mg gelatine, 8 mg calcium carbonate, vegetable magnesium stearate and vegetable cellulose"; 13 crossover subjects/13 crossover subjects	N/A	N/A
Mayr et al. (93)	"Diabetes-specific ONS": 2 x 200 mL, 20/20	Standard ONS (isocaloric): 1.5kcal/mL, 20/20	N/A	N/A
McManus et al. (94)	Placebo: olive oil (35 mg 18:1 fatty acids/kg body weight/day), 11 crossover subjects	Linseed oil: 35 mg 18:3n-3/kg body weight/day, 11 crossover subjects	Fish oil: 35 mg 20:5n-3 + 22:6n-3/kg body weight/day, 11 crossover subjects	N/A
Mehrdadi et al. (95)	200 mg Coenzyme Q10, 32/26	Placebo: maize starch, 32/30	N/A	N/A
Mirfeizi et al. (96)	1000 mg cinnamon/d; 30/30	1000mg whortleberry/d; 30/30	Placebo: 1000 mg starch/d; 45/45	N/A

Author	Arm 1: Dose, n at randomization/n at analysis	Arm 2: Dose, n at randomization/n at analysis	Arm 3: Dose, n at randomization/n at analysis	Arm 4: Dose, n at randomization/n at analysis	Arm 5: Dose, n at randomization/n at analysis	Arm 6: Dose, n at randomization/n at analysis	Arm 7: Dose, n at randomization/n at analysis	Arm 8: Dose, n at randomization/n at analysis	Arm 9: Dose, n at randomization/n at analysis	Arm 10: Dose, n at randomization/n at analysis	Arm 11: Dose, n at randomization/n at analysis	Arm 12: Dose, n at randomization/n at analysis	Arm 13: Dose, n at randomization/n at analysis	Arm 14: Dose, n at randomization/n at analysis	Arm 15: Dose, n at randomization/n at analysis
Mitra and Bhattacharya (97)	30 mL sesame oil, 15 mL flax oil, 15 g soybean; 20/N/A	30 mL coconut oil, 150 g rice containing retrograded starch, 10 g psyllium husk, 25 g fenugreek; 20/N/A	15 mL flax oil, 30 mL sunflower oil, 25 g fenugreek; 20/N/A	30 mL coconut oil, 10 g psyllium husk, 25 g fenugreek; 20/N/A	30 mL sunflower oil, 15 g soybean, 25 g fenugreek, 3 capsules fish oil; 20/N/A	30 mL sesame oil, 15 g soybean, 25 g fenugreek, 3 capsules fish oil; 20/N/A	30 mL sesame oil, 25 g flax gum, 15 g soybean, 3 capsules fish oil; 20/N/A	30 mL sesame oil, 15 mL flax oil, 25 g fenugreek; 20/N/A	30 mL sesame oil, 10 g psyllium husk, 15 mL flax oil, 20/N/A	30 mL sunflower oil, 15 g soybean, 25 g/day flax gum; 20/N/A	30 mL sunflower oil, 15 g soybean, 25 g fenugreek; 20/N/A	15 mL flax oil, 30 mL sesame oil, 150 g rice containing retrograde starch, 15 g soybean; 20/N/A	30 mL sunflower oil, 25 g flax gum, 15 mL flax oil, 15 g soybean; 20/N/A	30 mL sesame oil, 25 g flax gum, 15 mL flax oil, 15 g soybean; 20/N/A	control: rural diet; 30/N/A

Author	Arm 1: Dose, n at randomization/n at analysis	Arm 2: Dose, n at randomization/n at analysis	Arm 3: Dose, n at randomization/n at analysis	Arm 4: Dose, n at randomization/n at analysis
Mobini et al. (98)	Placebo: slightly sweet powder, 15/15	Low dose *L.reuteri* DSM 17938: 10^8 colony-forming units/day, 16/15	High dose *L.reuteri* DSM 17938: 10^10 colony-forming units, 15/14	N/A
Morgan et al. (99)	Fish oil: 9 g, 10/10	Fish oil: 18 g, 10/10	Corn oil: 9 g, 10/10	Corn oil: 18 g, 10/10
Navarrete-Cortes et al. (100)	Magnesium lactate: 360 mg elemental magnesium, 50/30	Placebo: "microcrystalline cellulose, croscarmellose sodium, povidone and magnesium stearate"; 48/26	N/A	N/A
Niemi et al. (101)	microcrystalline cellulose: 3x/day with meals (first 5 g/d, raised to 15 g/d in the first 2 weeks of the treatment phases), 20 crossover subjects included in analysis	guar gum: 3x/day with meals (first 5 g/d, raised to 15 g/d in the first 2 weeks of the treatment phases), 18 crossover subjects included in analysis	N/A	N/A

Nikooyeh et al. (102)	2x 250-mL bottles of “plain doogh”: calcium (150 mg)/bottle, 30/30	2x 250-mL bottles of “vitamin D-fortified doogh”: calcium (150 mg) + vitamin D (500 IU) per bottle, 30/30	2x 250-mL bottles of “calcium-vitamin D-fortified doogh”: calcium (250 mg) + vitamin D (500 IU) per bottle, 30/30	N/A
Nikooyeh et al. (103)	2x 250-mL bottles of “plain doogh”: calcium (150 mg)/bottle, 30/30	2x 250-mL bottles of “vitamin D-fortified doogh”: calcium (150 mg) + vitamin D (500 IU) per bottle, 30/30	2x 250-mL bottles of “calcium-vitamin D-fortified doogh”: calcium (250 mg) + vitamin D (500 IU) per bottle, 30/30	N/A
Norris et al. (104)	control: safflower oil (8 g oil/d), 33/27	Linoleic acid: 8 g oil/day, 22/16	N/A	N/A
Ogawa et al. (105)	EPA (25 mg/100kcal)/DHA (17 mg/100kcal)-rich liquid diet, 15/13	Liquid diet with a lack in EPA/DHA, 15/13	N/A	N/A
Pan et al. (106)	Lignan tablets derived from flaxseed: 360 mg/d, 37 started with lignan/34	Placebo: 3 tablets/d (98% rice flour), 36 started with placebo/34	N/A	N/A
Paolisso et al. (107)	Placebo: sodium citrate, 40 crossover subjects	0.5 g vitamin C 2x/day, 40 crossover subjects	N/A	N/A
Paolisso et al. (108)	Placebo: sodium citrate, 13 started with placebo/13	900 mg vitamin E/day, 12 started with vitamin E/12	N/A	N/A
Parham et al. (109)	50 g pistachios/day, 24 started with pistachios/23	No pistachios in diet + PA, 24 started with placebo/21	N/A	N/A
Pedersen et al. (110)	5.5 g prebiotic supplement/day: galacto-ligosaccharide mixture, 16/14	5.5 g placebo supplement/day: maltodextrin, 16/15	N/A	N/A
Pick et al. (111)	“Oat bran concentrate bread”, 8/8	“Control white bread”, 8/8	N/A	N/A
Racek et al. (112)	400 µg chromium/d in the form of chromium-enriched yeast, 19/19	Placebo, 17/17	N/A	N/A
Rodriguez-Moran et al. (113)	50 mL magnesium chloride solution: 50 g magnesium chloride/1000 mL solution, 40/32	Placebo, 40/31	N/A	N/A
Rotman-Pikielny et al. (114)	DBCare: 11 herbal ingredients, 18/17	Placebo: lactose (0.5 g), 17/15	N/A	N/A
Roussel et al. (115)	30 mg zinc/d in the form of zinc gluconate, 27/27	Placebo: “stearate of magnesium, 6 mg, silicon dioxide, 6 mg, cornstarch 28 mg and lactose, 200 mg”, 29/29	N/A	N/A
Rytter et al. (116)	8 antioxidant tablets, N/A/13	16 antioxidant tablets, N/A/14	8 placebo tablets: paraffin oil, N/A/13	N/A
Ryu et al. (117)	Placebo: 100 mg elemental calcium 2x/day, 79/64	Vitamin D: 1000 IU cholecalciferol/day in combination with 100 mg elemental calcium 2x/day, 79/65	N/A	N/A
Sarbolouki et al. (118)	Purified EPA: 2 g/day, 32/32	Placebo: Corn oil (2 g/day), 35/35	N/A	N/A
Scroggie et al. (119)	Glucosamine tablets: glucosamine hydrochloride, low-molecular-weight sodium chondroitin sulfate, manganese, ascorbic acid, 26/22	Placebo: cellulose, 12/12	N/A	N/A
Shab-Bidar et al. (120)	“Plain doogh”: calcium (170 mg per 250mL); 29/29	“Vitamin D3-fortified doogh”: calcium (170 mg) + vitamin D3 (12.5 µg) per 250mL; 31/31	N/A	N/A
Shab-Bidar et al. (121)	“Plain yogurt drink”: calcium (170 mg), 50/50	“Vitamin D3-fortified yogurt drink”: calcium (170 mg) + vitamin D3 (500 IU) per 250mL, 50/50	N/A	N/A

Shidfar et al. (122)	3 g ginger (powdered), 25/22	Placebo: lactose, 25/23	N/A	N/A
Shimizu et al. (123)	Tablet with 300 mg purified EPA-E 3x/day, 29/N/A	Controls not treated with EPA, 16/N/A	N/A	N/A
Solerte et al. (124)	AA supplements: 449 kcal/d as snacks of 8 g AA, 18/18	Placebo, 16/16	N/A	N/A
Solerte et al. (125)	AA supplements: 70.6 kcal/d as snacks of 8 g AA, 18/18	Placebo, 16/16	N/A	N/A
Strobel et al. (126)	Vitamin D: Vigantol oil: 1904 IU, 43/39	Placebo oil: medium chain triglycerides, 43/33	N/A	N/A
Tajabadi-Ebrahimi et al. (127)	800 mg inuslin + 2 × 10^9 Lactobacillus acidophilus + 2 × 10^9 Lactobacillus casei + 2 × 10^9 colony-forming units/g Bifidobacterium bifidum, 30/30	Placebo: starch, 30/30	N/A	N/A
Taylor et al. (128)	Bakery product with no flax, 9/9	Bakery product with milled flaxseed (13.32 g/d), 13/13	Bakery product with flaxseed oil (13 g/d), 12/12	N/A
Turpeinen et al. (129)	Acetyl-L-carnitine: 1500 mg, N/A/13	Placebo, N/A/6	N/A	N/A
Tütüncü et al. (130)	Vitamin E: 900 mg, 11/11	Placebo: same composition except for DL-alpha-to-copheryl acetate, 10/10	N/A	N/A
Uusitupa et al. (131)	Guar gum (granulated): 6 weeks 2.5 g 3x/day, 6 weeks 5 g 3x/day, 6 weeks 7 g 3x/day; 10/8 started with intervention	Placebo: wheat flour (granulated), 9/9 started with placebo	N/A	N/A
Vaisman et al. (132)	Fructose 2x/day: 7.5 g, N/A/12	Maltodextrin 3x/day: 7.5 g, N/A/13	N/A	N/A
von Hurst et al. (133)	Vitamin D3: 4000 IU = 100 μg, N/A/42	Placebo tablets, N/A/39	N/A	N/A
Vuksan et al. (134)	Korean red ginseng (Panax ginseng) rootlets: 3 times 2g in 500 mg tablets, 39 crossover subjects/19 crossover subjects	Placebo (500 mg tablets), 39 crossover subjects/19 crossover subjects	N/A	N/A
Wainstein et al. (135)	1200 mg cinnamon/day, 29/29	Placebo: microcrystalline cellulose (400 mg), 30/30	N/A	N/A
Watts et al. (136)	200 mg coenzyme Q10: 2 50 mg tablets 2x/day, N/A/20	Placebo, N/A/15	N/A	N/A
Wolffenbuttel et al. (137)	guar bread: 11.2 g/d (75 g guar/kg flour), 12/12	control: whole grain bread, 12/12	N/A	N/A
Yin et al. (138)	Berberine (500 mg) 3x/day, 18/15	Metformin (500 mg) 3x/day, 18/16	N/A	N/A
Yiu et al. (139)	5000 IU vitamin D/day, 50/50	Placebo: microcrystalline cellulose (300 mg), 50/50	N/A	N/A
Zhang et al. (140)	1 g berberine per day, 59/58	Placebo, 57/52	N/A	N/A
Zheng et al. (141)	25 mL DAG/day, 66/66	25 mLTAG/day, 61/61	N/A	N/A
Zibadi et al. (142)	125 mg in form of a Pycnogenol pill every day, 24/24	Placebo, 24/24	N/A	N/A

AA = amino acid, ABM = Agaricus blazei Murill, DAG = diacylglycerol, DHA = docosahexaenoic acid, DJC = Danzhijiangtang capsules, EPA = eicosapentaenoic acid, *G. biloba* = *Gingko biloba*, *M. charantia* = *Momordica charantia*, N/A = not applicable, N. sativa = Nigella sativa, ONS = oral nutritional supplement, PA = physical activity, TAG = triacylglycerol

Table 4 shows the different trials' side effects.

Table 4: Side effects reported in the included trials

Author	Arm 1	Arm 2	Arm 3	Arm 4
Akbari Fakhrabadi et al. (21)	N/A	N/A	N/A	N/A
Akilen et al. (22)	None	1 slight gastric upset for a couple of days	N/A	N/A
Al-Maroof et al. (23)	N/A	N/A	N/A	N/A
Anderson et al. (24)	N/A	N/A	N/A	N/A
Anderson et al. (25)	No adverse events	No adverse events	No adverse events	N/A
Aro et al. (26)	Flatulence, 2 dropouts due to abdominal discomfort and meteorism	N/A	N/A	N/A
Ashraf et al. (27)	N/A	N/A	N/A	N/A
Barchetta et al. (28)	No major side effects	No major side effects	N/A	N/A
Barre et al. (29)	N/A	N/A	N/A	N/A
Bonsu et al. (30)	N/A	N/A	N/A	N/A
Boshtam et al. (31)	N/A	N/A	N/A	N/A
Breslavsky et al. (32)	N/A	N/A	N/A	N/A
Cheng et al. (33)	N/A	N/A	N/A	N/A
Cruz et al. (34)	N/A	N/A	N/A	N/A
Dakhale et al. (35)	No severe adverse effect documented	No severe adverse effect documented	N/A	N/A
Dans et al. (36)	1 epigastric pain + diarrhea, 2 diarrhea, 1 gastroenteritis, 1 cholecystolithiasis (did not appear attributed to medication ingestion), 1 chest pain, 1 urinary incontinence, 1 fever	1 diarrhea	N/A	N/A
de Oliveira et al. (37)	N/A	N/A	N/A	N/A
Derosa et al. (38)	15 malaise, 13 oily evacuation, 10 elevated defecation, 6 fecal urgency, 4 flatulence, 1 constipation, 1 abdominal pain	11 malaise, 8 oily evacuation, 6 elevated defecation, 4 fecal urgency, 3 flatulence, 1 constipation, 1 abdominal pain	N/A	N/A
Derosa et al. (39)	3 headache, 2 constipation, 2 insomnia, 3 dry mouth, 1 increased blood pressure, 1 increased heart rate, 2 malaise, 2 palpitation	4 headache, 2 constipation, 3 insomnia, 1 dry mouth, 2 increased blood pressure, 2 increased heart rate, 1 malaise	N/A	N/A
Derosa et al. (40)	No medication-related adverse effects documented	N/A	N/A	N/A
Derosa et al. (41)	None documented.	None documented.	N/A	N/A
De Valk et al. (42)	None documented.	None documented.	N/A	N/A

Eftekhari et al. (43)	N/A	N/A	N/A	N/A
Eibl et al. (44)	1 nausea after 2 months., 10 diarrhea after 1 month, 7 diarrhea after 2 months, 4 diarrhea after 3 months, 3 meteorism after 1 month, 2 meteorism after 2 months, 2 meteorism after 3 months, 4 gastric pain after 1 month, 2 gastric pain after 2 months, 2 gastric pain after 3 months, 2 improvement of cardiac pain after 3 months	1 nausea after 1 month, 1 nausea after 2 months, 4 diarrhea after 1 month, 2 diarrhea after 2 months, 2 diarrhea after 3 months, 1 tiredness after 2 months, 1 meteorism after 1 month, 1 meteorism after 3 months, 2 gastric pain after 1 month, 1 gastric pain after 2 months, 1 gastric pain after 3 months	N/A	N/A
Elwakeel et al. (45)	13 (“nausea, abdominal upsets, irritating fish-scented halitosis”; did not stop supplementation though)	N/A	N/A	N/A
Eriksson et al. (46)	N/A	N/A	N/A	N/A
Faghihi et al. (47)	Adverse events on glucose homeostasis	N/A	N/A	N/A
Fang et al. (48)	N/A	N/A	N/A	N/A
Farvid et al. (49)	2 withdrawals during the 1st week of study due to adverse events.			
Feinglos et al. (50)	N/A	N/A	N/A	N/A
Fenercioglu et al. (51)	N/A	N/A	N/A	N/A
Firouzi et al. (52)	Some minor gastric disturbances, 2 unexpected events (sexual impotency, carbuncle) observed - unlikely because of supplementation	Some minor gastric disturbances	N/A	N/A
Foster et al. (53)	N/A	N/A	N/A	N/A
Ginter et al. (54)	N/A	N/A	N/A	N/A
Goh et al. (55)	3 (slight asymptomatic increase in alanine transaminase, slight hypoglycaemia and diarrhea, slight cellulitis)	1 (slight cellulitis)	N/A	N/A
Grotz et al. (56)	No discontinuations due to adverse effects.	No discontinuations due to adverse effects, no adverse effects reported as probably or definitely attributed to sucralose supplementation	N/A	N/A
Gualano et al. (57)	No serious adverse effects; diarrhea, nausea, cramps in a few subjects	Diarrhea, nausea, cramps in a few subjects	N/A	N/A
Guimaraes et al. (58)	N/A	N/A	N/A	N/A
Gullestad et al. (59)	N/A	N/A	N/A	N/A
Gunasekara et al. (60)	N/A	N/A	N/A	N/A
Hosseinzadeh et al. (61)	N/A	N/A	N/A	N/A
Hosseinzadeh-Attar et al. (62)	N/A	N/A	N/A	N/A
Hove et al. (63)	Adverse events noted at every visit.	Adverse events noted at every visit.	N/A	N/A

Hsia et al. (64)	6 (5 adverse effects total: migraine +itchy eyes, sore throat, 1 exacerbation of back + leg pain, 1 slight hypoglycaemia; 2 adverse effects throughout run-in: gastrointestinal advserse effects due to use of metformin + “flushing sensation in the face”)	5 (7 adverse effects total: “nightmares, dizzy spells, abdominal pain, flank pain, insomnia, leg numbness, weakness on exertion”; 2 adverse effects throughout run-in: ear pain and headache)	N/A	N/A
Hsu et al. (65)	3 hypoglycaemia-like symptoms, 2 itching skin	1 hypoglycaemia-like symptoms, 1 skin allergy + papules, 1 feeling of fullness and nausea	N/A	N/A
Hsu et al. (66)	1 hypoglycaemic symptoms, 2 slight constipation, 2 abdominal discomfort	1 slight constipation, 1 abdominal discomfort	N/A	N/A
Huseini et al. (67)	None documented.	N/A	N/A	N/A
Hussain et al. (68)	N/A	N/A	N/A	N/A
Hussain et al. (69)	N/A	N/A	N/A	N/A
Jafari et al. (70)	N/A	N/A	N/A	N/A
Jayagopal et al. (71)	Mostly gastrointestinal, similar during both supplementation periods, 2 development of heartburn, 6 complaints about feeling bloated, 1 myocardial infarction	Mostly gastrointestinal, similar during both supplementation periods, 1 development of heartburn, 6 complaints about feeling bloated, 1 self-limiting ulcers in the mouth	N/A	N/A
Jorde et al. (72)	N/A	N/A	N/A	N/A
Kaatabi et al. (73)	None documented.	None documented.	N/A	N/A
Kajanachumpol et al. (74)	N/A	N/A	N/A	N/A
Kampmann et al. (75)	None	3 (diarrhea, transient cerebral ischemia, hypoglycaemia)	N/A	N/A
Kleefstra et al. (76)	N/A	N/A	2 discontinuations of study medication because of adverse events: 1 complaint “of frequent watery stools, weakness, dizziness, nausea, and headaches”; 1 complained of “vertigo with nausea and vomiting”	N/A
Krul-Poel et al. (77)	1 (urolithiasis, excluded at month 3)	N/A	N/A	N/A
Lasaite et al. (78)	N/A	N/A	N/A	N/A
Lee et al. (79)	N/A	N/A	N/A	N/A
Leenders et al. (80)	No negative ones	N/A	N/A	N/A
Levin et al. (81)	N/A	N/A	N/A	N/A
Li et al. (82)	No reports of adverse effects.	No reports of adverse effects.	N/A	N/A
Li et al. (83)	No adverse effects monitored.	N/A	N/A	N/A
Liu et al. (84)	No serious adverse events	No serious adverse events	N/A	N/A

Ludvik et al. (85)	96 adverse events	120 adverse events	N/A	N/A
MacKenzie et al. (86)	Tablets too big to swallow	Withdrawal due to excessive sweat after intake of single dose	Withdrawal due to systemic rash	N/A
Magnoni et al. (87)	34 gastrointestinal related adverse effects (15 suffered from belching and bloating), 5 not gastrointestinal related adverse effects, 2 dropouts because of adverse effects (gastrointestinal related)	27 gastrointestinal related adverse effects (8 suffered from belching and bloating), 5 not gastrointestinal related adverse effects, 1 dropout because of adverse effects (gastrointestinal related and dyspnoe/paleness)	N/A	N/A
Malaguarnera et al. (88)	2 nausea, 2 slight headache, 2 abdominal pain	1 diarrhea, 1 nausea, 1 headache	N/A	N/A
Manzella et al. (89)	N/A	N/A	N/A	N/A
Martin et al. (90)	N/A	N/A	N/A	N/A
Mashavi et al. (91)	N/A	N/A	N/A	N/A
Mason et al. (92)	1 (“minor gastrointestinal discomfort during the first 1-2 weeks”, did not withdraw)	N/A	N/A	N/A
Mayr et al. (93)	No adverse effects documented	No adverse effects documented	N/A	N/A
McManus et al. (94)	N/A	Therapy not related to adverse events on blood sugar homeostasis	N/A	N/A
Mehrdadi et al. (95)	N/A	N/A	N/A	N/A
Mirfeizi et al. (96)	N/A	N/A	N/A	N/A
Mitra and Bhattacharya (97)	N/A for all 15 treatment arms			
Mobini et al. (98)	7 gastrointestinal symptoms, 5 hypoglycaemia, 4 infection, 2 headache, 2 musculoskeletal symptoms	8 gastrointestinal symptoms, 6 infection, 4 headache, 3 hypoglycaemia, 2 musculoskeletal symptoms	8 gastrointestinal symptoms, 6 infection, 4 hypoglycaemia, 4 musculoskeletal symptoms, 3 headache,	N/A
Morgan et al. (99)	N/A	N/A	N/A	N/A
Navarrete-Cortes et al. (100)	None documented.	None documented.	N/A	N/A
Niemi et al. (101)	N/A	N/A	N/A	N/A
Nikooyeh et al. (102)	No adverse event following treatment	No adverse event following treatment	No adverse event following treatment	N/A
Nikooyeh et al. (103)	N/A	N/A	N/A	N/A
Norris et al. (104)	Different adverse effects during the study, no difference between treatments	Different adverse effects during the study, no difference between treatments	N/A	N/A
Ogawa et al. (105)	N/A	N/A	N/A	N/A
Pan et al. (106)	Mostly gastrointestinal (23% diarrhea, 32% flatulence, 4% nausea)	Mostly gastrointestinal (23% diarrhea, 32% flatulence, 4% nausea)	N/A	N/A

Paolisso et al. (107)	No dropouts because of adverse events.	N/A	N/A	N/A
Paolisso et al. (108)	N/A	No adverse events monitored.	N/A	N/A
Parham et al. (109)	N/A	N/A	N/A	N/A
Pedersen et al. (110)	No adverse ones documented	No adverse ones documented	N/A	N/A
Pick et al. (111)	Minor ones documented: initial flatulence (decreased over time)	N/A	N/A	N/A
Racek et al. (112)	No adverse events, no dropouts due to adverse events	No dropouts due to adverse events	N/A	N/A
Rodriguez-Moran et al. (113)	No severe adverse effects; most common (37.5%): mild “abdominal and unspecific bone pain” throughout the 1st month, 2 mild diarrhea	No severe adverse effects; 1 mild diarrhea	N/A	N/A
Rotman-Pikielny et al. (114)	5 patients (total quantity of side effects: 7; 7 hypoglycaemic events, 1 raised amount of hypoglycaemic drugs, 2 reduced amount of hypoglycaemic drugs, 1 flatulence, 1 diarrhea, 1 abdominal pain	4 patients (total quantity of side effects: 6; 1 hypoglycaemic event, 1 raised amount of hypoglycaemic drugs, 1 reduced amount of hypoglycaemic drugs, 2 flatulence, 1 nausea, 1 diarrhea)	N/A	N/A
Roussel et al. (115)	No observed adverse events	N/A	N/A	N/A
Rytter et al. (116)	N/A	N/A	N/A	N/A
Ryu et al. (117)	N/A	N/A	N/A	N/A
Sarbolouki et al. (118)	N/A	N/A	N/A	N/A
Scroggie et al. (119)	1 withdrawal due to a possible adverse event caused by supplementation: excessive flatus	N/A	N/A	N/A
Shab-Bidar et al. (120)	N/A	N/A	N/A	N/A
Shab-Bidar et al. (121)	N/A	N/A	N/A	N/A
Shidfar et al. (122)	N/A	N/A	N/A	N/A
Shimizu et al. (123)	None monitored.	N/A	N/A	N/A
Solerte et al. (124)	None	None	N/A	N/A
Solerte et al. (125)	No adverse events seen whilst active intervention.	No adverse events seen whilst active intervention.	N/A	N/A
Strobel et al. (126)	N/A	N/A	N/A	N/A
Tajabadi-Ebrahimi et al. (127)	N/A	N/A	N/A	N/A
Taylor et al. (128)	N/A	N/A	N/A	N/A
Turpeinen et al. (129)	N/A	N/A	N/A	N/A
Tütüncü et al. (130)	N/A	N/A	N/A	N/A

Uusitupa et al. (143)	N/A	N/A	N/A	N/A
Vaisman et al. (132)	N/A	N/A	N/A	N/A
von Hurst et al. (133)	No adverse events monitored in serum calcium results, 2 had constipation and headaches		N/A	N/A
Vuksan et al. (134)	1 dropout due to adverse event	2 dropouts due to adverse event	N/A	N/A
Wainstein et al. (135)	N/A	N/A	N/A	N/A
Watts et al. (136)	N/A	N/A	N/A	N/A
Wolffenbuttel et al. (137)	Faster satiation, increased flatulence in some subjects	N/A	N/A	N/A
Yin et al. (138)	6 diarrhea, 4 constipation, 11 flatulence, 2 abdominal pain		N/A	N/A
Yiu et al. (139)	No significant ones documented.	No significant ones documented.	N/A	N/A
Zhang et al. (140)	No severe adverse effects	No severe adverse effects	N/A	N/A
Zheng et al. (141)	N/A	N/A	N/A	N/A
Zibadi et al. (142)	No adverse effects documented	1 withdrawal because of an unwanted side effect	N/A	N/A

DAG = diacylglycerol

8.1 HbA1c

Figure 4 shows that the decrease in HbA1c was significantly more pronounced following prebiotic supplementation compared to their respective control groups: MD -0.38% [95% CI -0.60, -0.16], P = 0.0006.

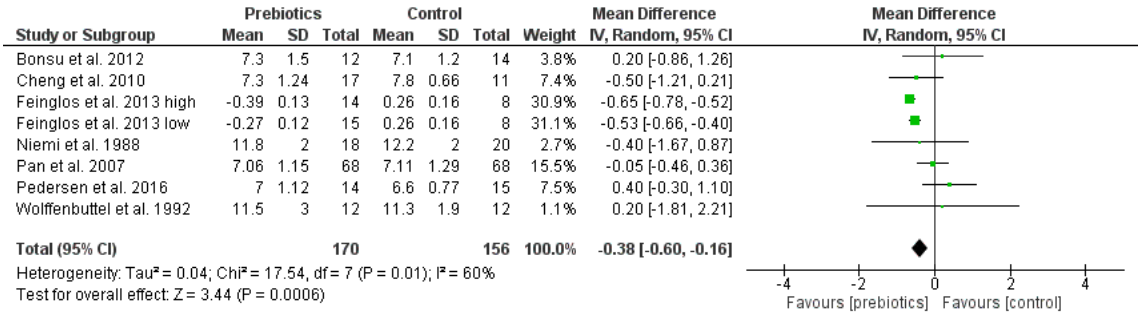

Figure 4: Forest plot showing aggregated weighted MD including 95% CI for HbA1c after prebiotic supplementation vs. control.
The squares represent the point estimates of the intervention effect, the horizontal lines represent the corresponding 95% CI. The dimension of the squares indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MDs with 95% CI for all randomized trials. CI = confidence interval, HbA1c = Glycated Haemoglobin, I² = heterogeneity, MD = mean difference, SD = standard deviation, high = high dose of psyllium, low = low dose of psyllium

Compared to their respective control groups, decrease in HbA1c was significantly more distinct following AA supplementation: MD -0.36% [95% CI -0.67, -0.05], P = 0.02 (Figure 5). A sensitivity analysis showed a non-significant decrease in HbA1c after exclusion of all data on L-canitine: MD -0.34 [95% CI -0.91,0.24], P = 0.25

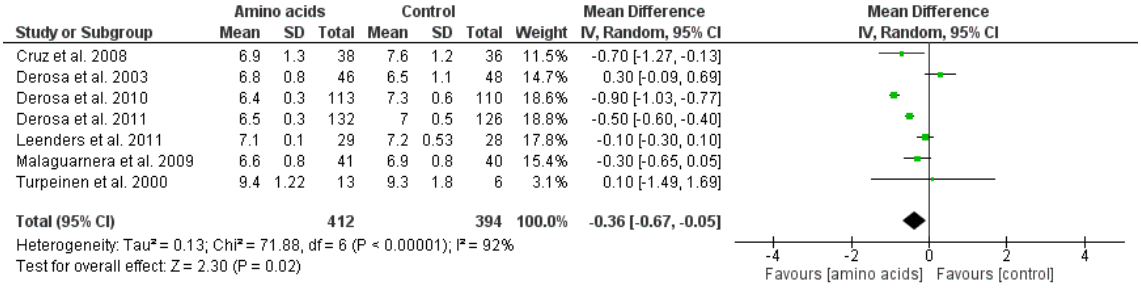

Figure 5: Forest plot showing aggregated weighted MD including 95% CI for HbA1c after AA supplementation vs. control.
The squares represent the point estimates of the intervention effect, the horizontal lines represent the corresponding 95% CI. The dimension of the squares indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MDs with 95% CI for all randomized trials. AA = amino acid, CI = confidence interval, HbA1c = Glycated Haemoglobin, I² = heterogeneity, MD = mean difference, SD = standard deviation

Decrease in HbA1c was significantly more pronounced following vitamin E supplementation compared to their respective control groups: MD -0.56% [95% CI -0.83, -0.29], P < 0.0001 (Figure 6).

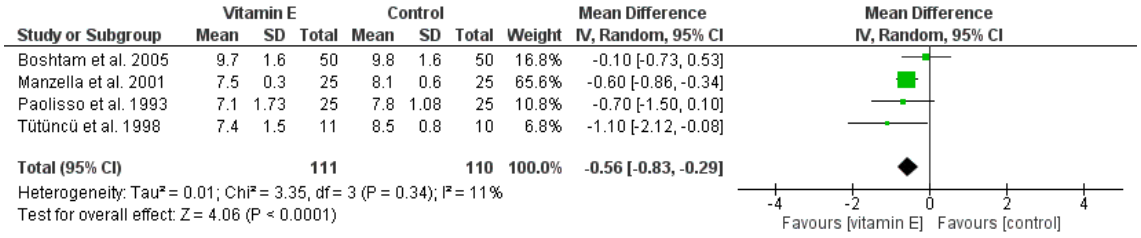

Figure 6: Forest plot showing aggregated weighted MD including 95% CI for HbA1c after vitamin E supplementation vs. control.
The squares represent the point estimates of the intervention effect, the horizontal lines represent the corresponding 95% CI. The dimension of the squares indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MDs with 95% CI for all randomized trials. CI = confidence interval, HbA1c = Glycated Haemoglobin, I² = heterogeneity, MD = mean difference, SD = standard deviation

Figure 7 shows that compared to their respective control groups, decrease in HbA1c was significantly more distinct following flaxseed supplementation: MD -0.54% [95% CI -0.95, -0.12], P = 0.01.

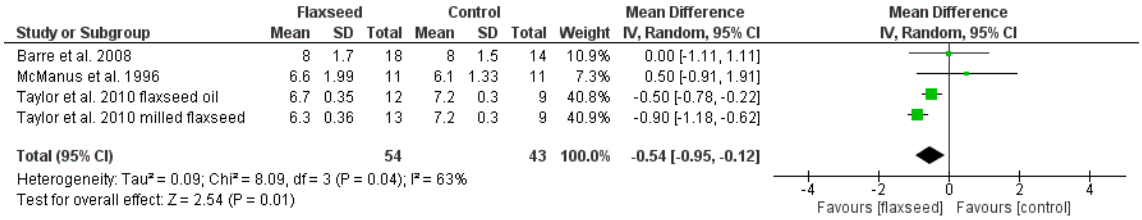

Figure 7: Forest plot showing aggregated weighted MD including 95% CI for HbA1c after flaxseed supplementation vs. control.
The squares represent the point estimates of the intervention effect, the horizontal lines represent the corresponding 95% CI. The dimension of the squares indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MDs with 95% CI for all randomized trials. CI = confidence interval, HbA1c = Glycated Haemoglobin, I² = heterogeneity, MD = mean difference, SD = standard deviation

Figure 8 shows that the decrease in HbA1c was significantly more pronounced following the supplementation of berberine compared to their respective control groups: MD -0.66% [95% CI -1.00, -0.33], P = 0.0001.

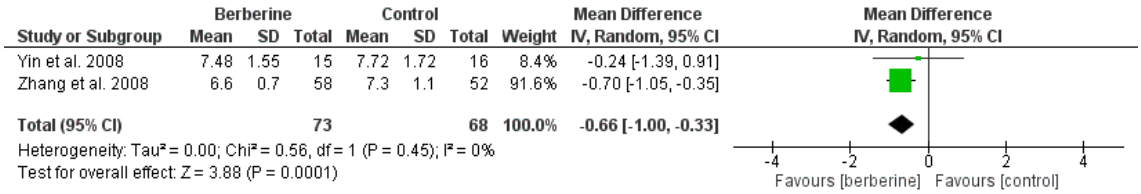

Figure 8: Forest plot showing aggregated weighted MD including 95% CI for HbA1c after berberine supplementation vs. control.
The squares represent the point estimates of the intervention effect, the horizontal lines represent the corresponding 95% CI. The dimension of the squares indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MDs with 95% CI for all randomized trials. CI = confidence interval, HbA1c = Glycated Haemoglobin, I² = heterogeneity, MD = mean difference, SD = standard deviation

Compared to their respective control groups, decrease in HbA1c was significantly more distinct following the supplementation of silymarin: MD -1.92% [95% CI -3.32, -0.51], P = 0.007 (Figure 9).

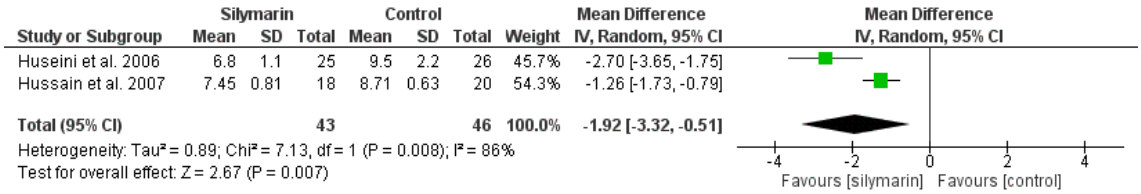

Figure 9: Forest plot showing aggregated weighted MD including 95% CI for HbA1c after silymarin supplementation vs. control.
The squares represent the point estimates of the intervention effect, the horizontal lines represent the corresponding 95% CI. The dimension of the squares indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MDs with 95% CI for all randomized trials. CI = confidence interval, HbA1c = Glycated Haemoglobin, I² = heterogeneity, MD = mean difference, SD = standard deviation

Decrease in HbA1c was significantly more pronounced following the supplementation of zinc, vitamins and minerals compared to the control group: MD -0.68% [95% CI -1.32, -0.04], P = 0.04 (Figure 10).

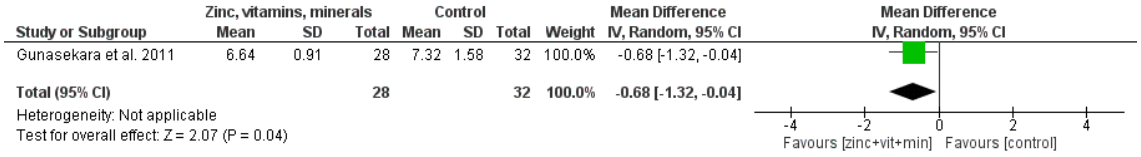

Figure 10: Forest plot showing the aggregated weighted MD including 95% CI for HbA1c after zinc, vitamin and mineral supplementation vs. control.
The square represents the point estimates of the intervention effect, the horizontal line represents the corresponding 95% CI. The dimension of the square indicates the weight of the study

within the meta-analysis. The diamond summarizes the pooled MD with 95% CI for all randomized trials. CI = confidence interval, HbA1c = Glycated Haemoglobin, I² = heterogeneity, MD = mean difference, SD = standard deviation

Figure 11 shows that compared to the control group, decrease in HbA1c was significantly more distinct following the supplementation of melatonin and zinc: MD -2.09% [95% CI -3.26, -0.92], P = 0.0004.

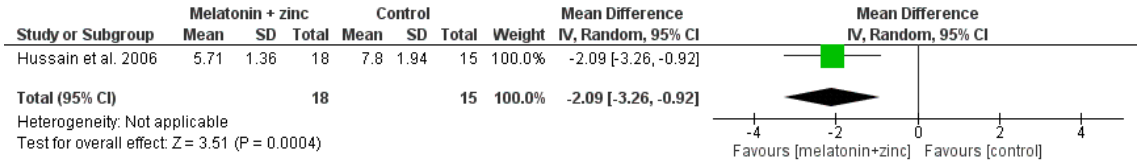

Figure 11: Forest plot showing the aggregated weighted MD including 95% CI for HbA1c after melatonin and zinc supplementation vs. control.
The square represents the point estimates of the intervention effect, the horizontal line represents the corresponding 95% CI. The dimension of the square indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MD with 95% CI for all randomized trials. CI = confidence interval, HbA1c = Glycated Haemoglobin, I² = heterogeneity, MD = mean difference, SD = standard deviation

Compared to the control group, decrease in HbA1c was significantly more distinct following calcium and vitamin D supplementation: MD -1.40% [95% CI -2.08, -0.72], P < 0.0001 (Figure 12).

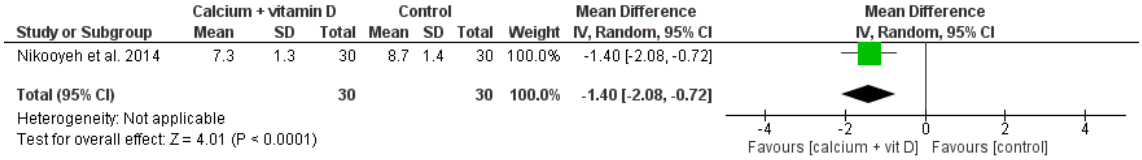

Figure 12: Forest plot showing the aggregated weighted MD including 95% CI for HbA1c after calcium and vitamin D supplementation vs. control.
The square represents the point estimates of the intervention effect, the horizontal line represents the corresponding 95% CI. The dimension of the square indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MD with 95% CI for all randomized trials. CI = confidence interval, HbA1c = Glycated Haemoglobin, I² = heterogeneity, MD = mean difference, SD = standard deviation

Decrease in HbA1c was significantly more pronounced following alpha-lipoic acid supplementation compared to the control group: MD -0.50% [95% CI -0.62, -0.38], P < 0.00001 (Figure 13).

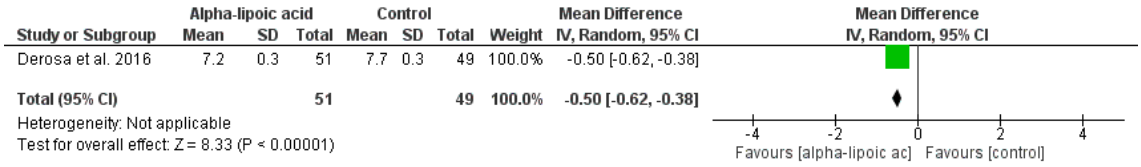

Figure 13: Forest plot showing the aggregated weighted MD including 95% CI for HbA1c after alpha-lipoic acid supplementation vs. control.
The square represents the point estimates of the intervention effect, the horizontal line represents the corresponding 95% CI. The dimension of the square indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MD with 95% CI for all randomized trials. CI = confidence interval, HbA1c = Glycated Haemoglobin, I² = heterogeneity, MD = mean difference, SD = standard deviation

Figure 14 shows that compared to the control group, decrease in HbA1c was significantly more distinct following pistachio supplementation: MD -0.40% [95% CI -0.64, -0.16], P = 0.001.

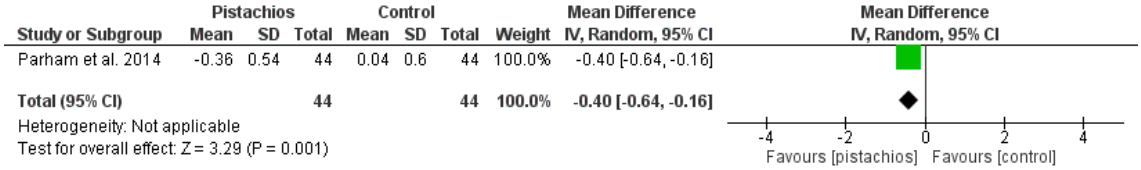

Figure 14: Forest plot showing the aggregated weighted MD including 95% CI for HbA1c after pistachio supplementation vs. control.
The square represents the point estimates of the intervention effect, the horizontal line represents the corresponding 95% CI. The dimension of the square indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MD with 95% CI for all randomized trials. CI = confidence interval, HbA1c = Glycated Haemoglobin, I² = heterogeneity, MD = mean difference, SD = standard deviation

Figure 15 shows that the decrease in HbA1c was significantly more pronounced following the supplementation of Pycnogenol compared to the control group: MD -0.90% [95% CI -1.78, -0.02], P = 0.04.

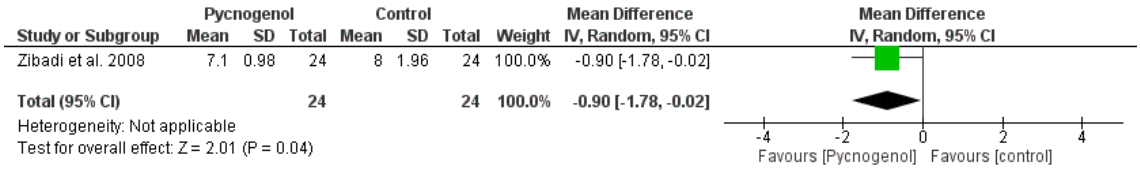

Figure 15: Forest plot showing the aggregated weighted MD including 95% CI for HbA1c after Pycnogenol supplementation vs. control.
The square represents the point estimates of the intervention effect, the horizontal line represents the corresponding 95% CI. The dimension of the square indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MD with 95% CI for all randomized trials. CI = confidence interval, HbA1c = Glycated Haemoglobin, I² = heterogeneity, MD = mean difference, SD = standard deviation

Figure 16 shows that the increase in HbA1c was significantly more pronounced following zinc supplementation compared to the control group: MD 0.60% [95% CI 0.05, 1.15], P = 0.03.

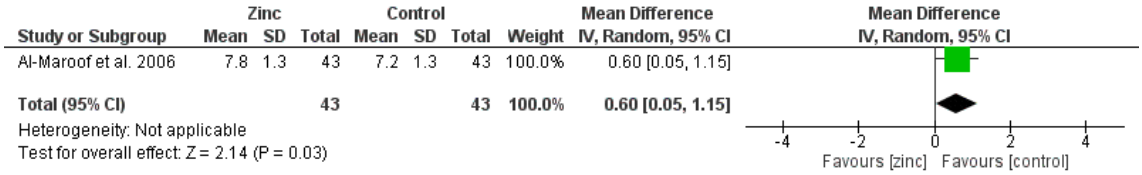

Figure 16: Forest plot showing the aggregated weighted MD including 95% CI for HbA1c after zinc supplementation vs. control.
The square represents the point estimates of the intervention effect, the horizontal line represents the corresponding 95% CI. The dimension of the square indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MD with 95% CI for all randomized trials. CI = confidence interval, HbA1c = Glycated Haemoglobin, I^2 = heterogeneity, MD = mean difference, SD = standard deviation

Compared to the control group, the increase in HbA1c was significantly more distinct following the supplementation of a diabetes specific ONS: MD 1.85% [95% CI 1.02, 2.68], P < 0.0001 (Figure 17).

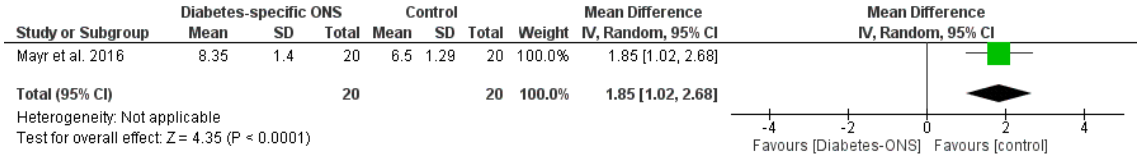

Figure 17: Forest plot showing the aggregated weighted MD including 95% CI for HbA1c after a diabetes-specific ONS vs. control.
The square represents the point estimates of the intervention effect, the horizontal line represents the corresponding 95% CI. The dimension of the square indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MD with 95% CI for all randomized trials. CI = confidence interval, HbA1c = Glycated Haemoglobin, I^2 = heterogeneity, MD = mean difference, SD = standard deviation

Figure 18 shows that supplementation of ginger was close to having a significant influence on the change in HbA1c compared to the control group: MD -0.70% [95% CI -1.45, 0.05], P = 0.07.

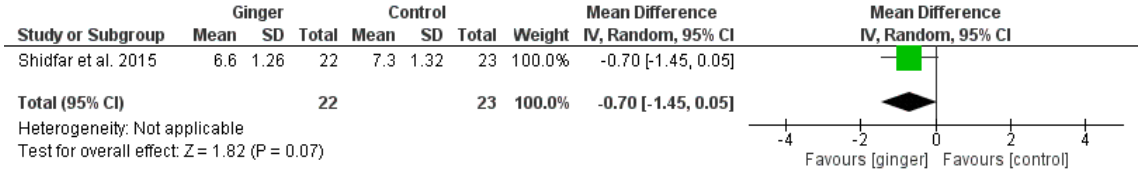

Figure 18: Forest plot showing the aggregated weighted MD including 95% CI for HbA1c after ginger vs. control.
The square represents the point estimates of the intervention effect, the horizontal line represents the corresponding 95% CI. The dimension of the square indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MD with 95% CI for all randomized trials. CI = confidence interval, HbA1c = Glycated Haemoglobin, I^2 = heterogeneity, MD = mean difference, SD = standard deviation

8.2 Glucose

Figure 19 shows that the decrease in glucose was significantly more pronounced following prebiotic supplementation compared to their respective control groups: MD -0.83 mmol/L [95% CI -1.55, -0.10], P = 0.03.

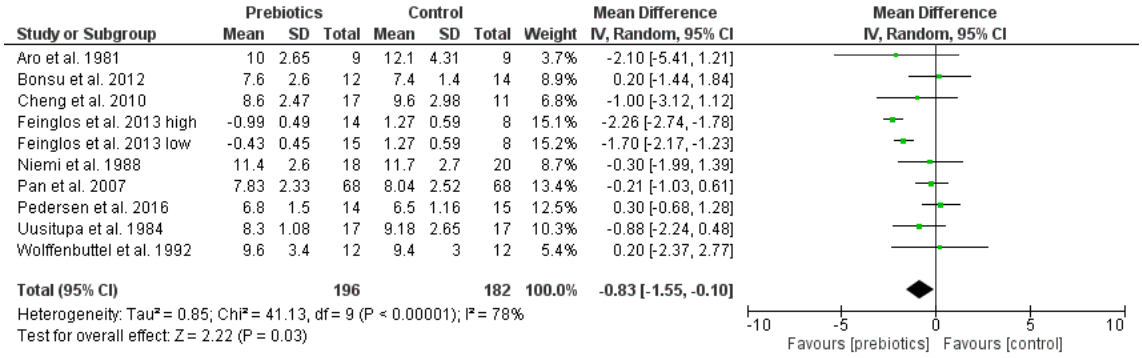

Figure 19: Forest plot showing the aggregated weighted MD including 95% CI for glucose after prebiotic supplementation vs. control.
The squares represent the point estimates of the intervention effect, the horizontal lines represent the corresponding 95% CI. The dimension of the squares indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MDs with 95% CI for all randomized trials. CI = confidence interval, I^2 = heterogeneity, MD = mean difference, SD = standard deviation, high = high dose of psyllium, low = low dose of psyllium

Compared to their respective control groups, decrease in glucose was significantly more distinct following AA supplementation: MD -0.40 mmol/L [95% CI -0.48, -0.32], P < 0.00001 (Figure 20). A sensitivity analysis showed a non-significant decrease in glucose after exclusion of all data on L-canitine: MD -0.24 [95% CI -0.83, 0.34], P = 0.42

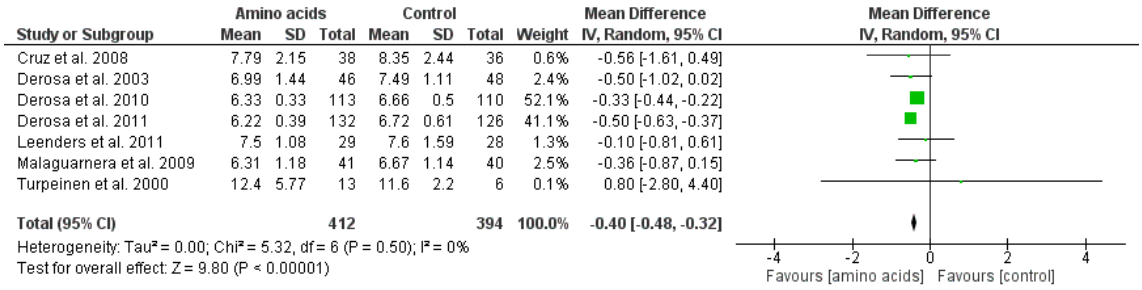

Figure 20: Forest plot showing the aggregated weighted MD including 95% CI for glucose after AA supplementation vs. control.
The squares represent the point estimates of the intervention effect, the horizontal lines represent the corresponding 95% CI. The dimension of the squares indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MDs with 95% CI for all randomized trials. AA = amino acid, CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation

Decrease in glucose was significantly more pronounced following vitamin C supplementation compared to their respective control groups: MD -0.65 mmol/L [95% CI -1.07, -0.23], P = 0.003 (Figure 21).

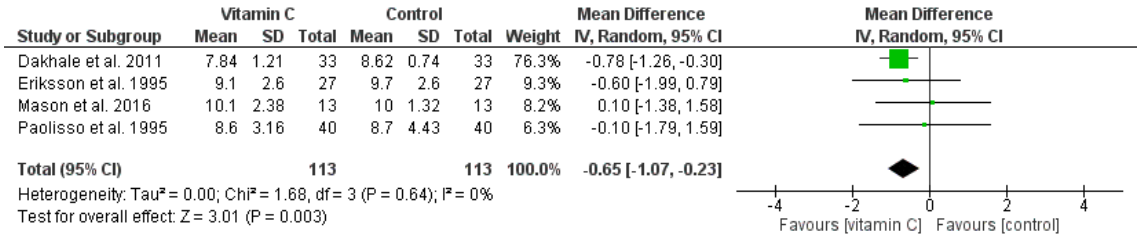

Figure 21: Forest plot showing the aggregated weighted MD including 95% CI for glucose after vitamin C supplementation vs. control.
The squares represent the point estimates of the intervention effect, the horizontal lines represent the corresponding 95% CI. The dimension of the squares indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MDs with 95% CI for all randomized trials. CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation

Figure 22 shows that compared to their respective control groups, decrease in glucose was significantly more distinct following flaxseed supplementation: MD -0.98 mmol/L [95% CI -1.18, -0.79], P < 0.00001.

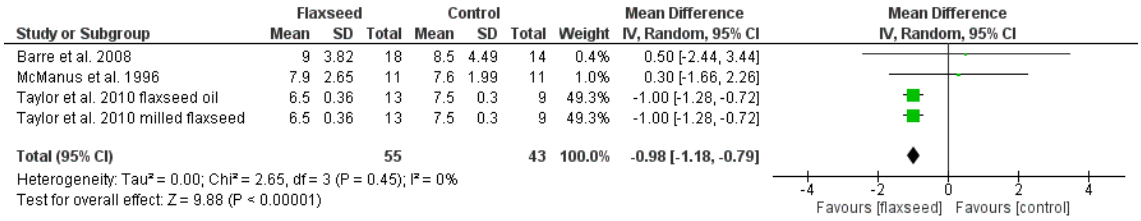

Figure 22: Forest plot showing the aggregated weighted MD including 95% CI for glucose after flaxseed supplementation vs. control.
The squares represent the point estimates of the intervention effect, the horizontal lines represent the corresponding 95% CI. The dimension of the squares indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MDs with 95% CI for all randomized trials. CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation

Figure 23 shows that the decrease in glucose was significantly more pronounced following the supplementation of probiotics compared to their respective control groups: MD -0.85 mmol/L [95% CI -1.50, -0.21], P = 0.010.

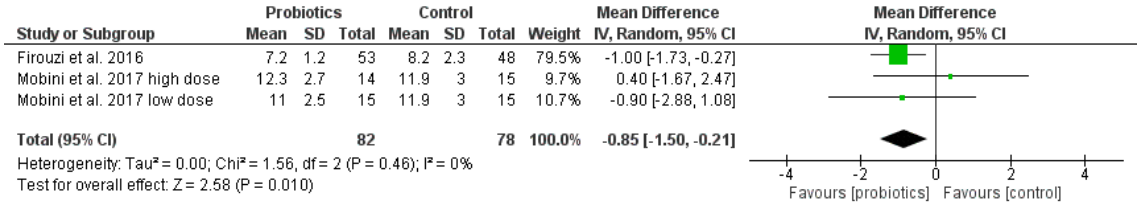

Figure 23: Forest plot showing the aggregated weighted MD including 95% CI for glucose after probiotic supplementation vs. control.
The squares represent the point estimates of the intervention effect, the horizontal lines represent the corresponding 95% CI. The dimension of the squares indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MDs with 95% CI for all randomized trials. CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation, high = high dose *L. reuteri*, low = low dose *L. reuteri*

Compared to their respective control groups, decrease in glucose was significantly more distinct following the supplementation of DAG: MD -0.74 mmol/L [95% CI -1.39, -0.09], P = 0.03 (Figure 24).

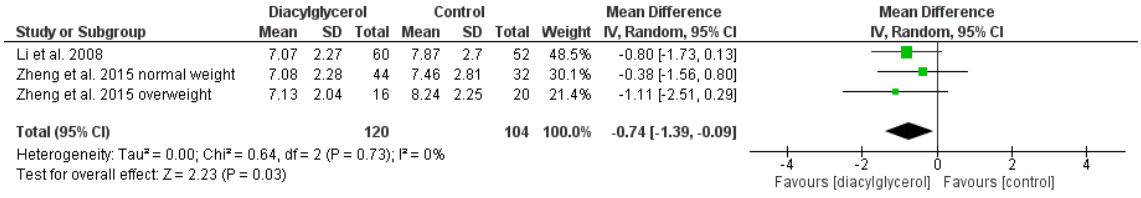

Figure 24: Forest plot showing the aggregated weighted MD including 95% CI for glucose after DAG supplementation vs. control.

The squares represent the point estimates of the intervention effect, the horizontal lines represent the corresponding 95% CI. The dimension of the squares indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MDs with 95% CI for all randomized trials. CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation, normal weight = normal weight subjects, overweight = overweight subjects

Decrease in glucose was significantly more pronounced following the supplementation of berberine compared to their respective control groups: MD -0.76 mmol/L [95% CI -1.24, -0.29], P = 0.002 (Figure 25).

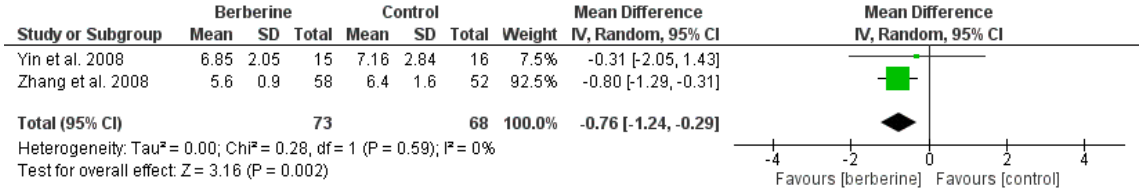

Figure 25: Forest plot showing the aggregated weighted MD including 95% CI for glucose after berberine supplementation vs. control.
The squares represent the point estimates of the intervention effect, the horizontal lines represent the corresponding 95% CI. The dimension of the squares indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MDs with 95% CI for all randomized trials. CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation

Figure 26 shows that compared to their respective control groups, decrease in glucose was significantly more distinct following the supplementation of silymarin: MD -2.11 mmol/L [95% CI -3.69, -0.53], P = 0.0009.

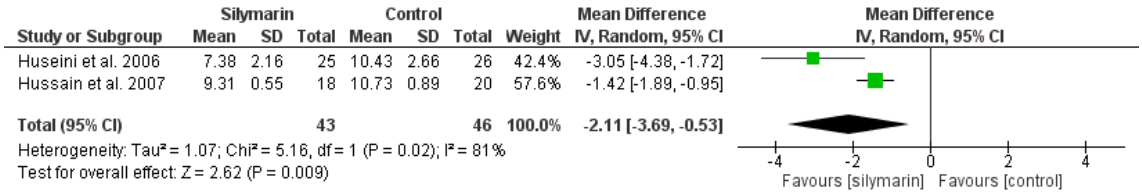

Figure 26: Forest plot showing the aggregated weighted MD including 95% CI for glucose after silymarin supplementation vs. control.
The squares represent the point estimates of the intervention effect, the horizontal lines represent the corresponding 95% CI. The dimension of the squares indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MDs with 95% CI for all randomized trials. CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation

Compared to the control group, decrease in glucose was significantly more distinct following pistachio supplementation: MD -0.89 mmol/L [95% CI -1.45, -0.33], P = 0.002 (Figure 27).

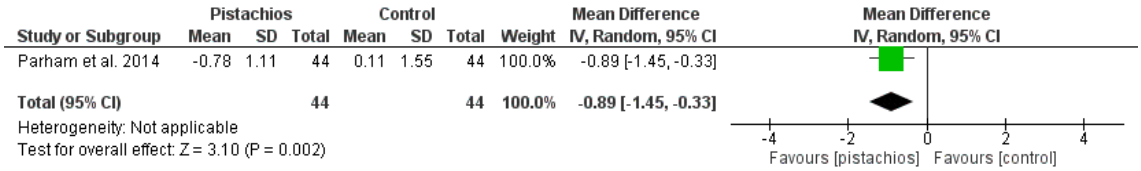

Figure 27: Forest plot showing the aggregated weighted MD including 95% CI for glucose after pistachio supplementation vs. control.
The square represents the point estimates of the intervention effect, the horizontal line represents the corresponding 95% CI. The dimension of the square indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MD with 95% CI for all randomized trials. CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation

Decrease in glucose was significantly more pronounced following Caiapo supplementation compared to the control group: MD -0.73 mmol/L [95% CI -1.43, -0.03], P = 0.04 (Figure 28).

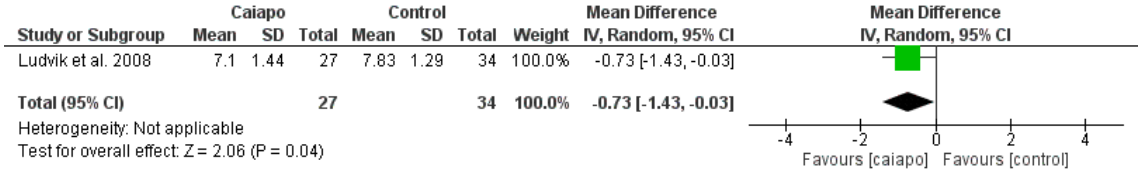

Figure 28: Forest plot showing the aggregated weighted MD including 95% CI for glucose after Caiapo supplementation vs. control.
The square represents the point estimates of the intervention effect, the horizontal line represents the corresponding 95% CI. The dimension of the square indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MD with 95% CI for all randomized trials. CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation

Figure 29 shows that compared to the control group, decrease in glucose was significantly more distinct following Pycnogenol supplementation: MD -1.98 mmol/L [95% CI -3.59, -0.37], P = 0.02.

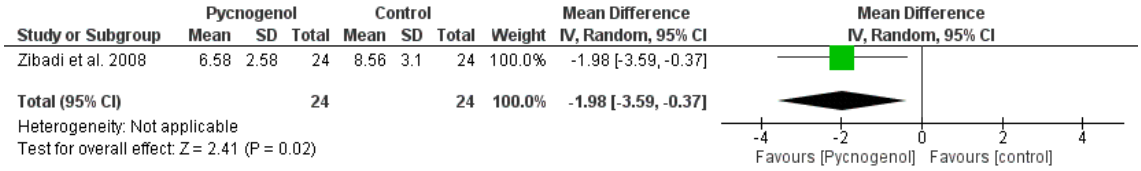

Figure 29: Forest plot showing the aggregated weighted MD including 95% CI for glucose after Pycnogenol supplementation vs. control.
The square represents the point estimates of the intervention effect, the horizontal line represents the corresponding 95% CI. The dimension of the square indicates the weight of the study

within the meta-analysis. The diamond summarizes the pooled MD with 95% CI for all randomized trials. CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation

Supplementation of calcium and vitamin D was close to having a significant impact on the change in glucose compared to the control group: MD -1.60 mmol/L [95% CI -3.23, 0.03], P = 0.05 (Figure 30).

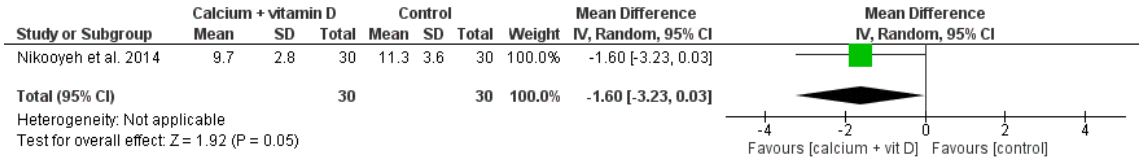

Figure 30: Forest plot showing the aggregated weighted MD including 95% CI for glucose after calcium and vitamin D supplementation vs. control.
The square represents the point estimates of the intervention effect, the horizontal line represents the corresponding 95% CI. The dimension of the square indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MD with 95% CI for all randomized trials. CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation

Figure 31 shows that supplementation of linoleic acid was close to having a significant influence on the increase of glucose compared to the control group: MD 1.33 mmol/L [95% CI -0.06, 2.72], P = 0.06.

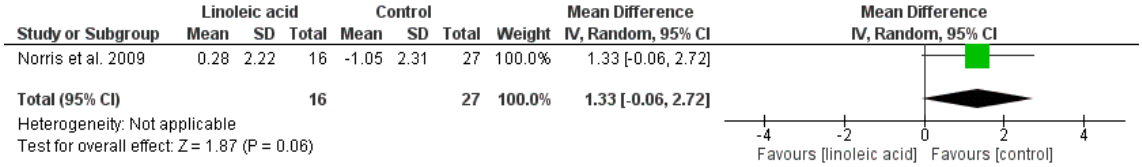

Figure 31: Forest plot showing the aggregated weighted MD including 95% CI for glucose after linoleic acid supplementation vs. control.
The square represents the point estimates of the intervention effect, the horizontal line represents the corresponding 95% CI. The dimension of the square indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MD with 95% CI for all randomized trials. CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation

8.3 Insulin

Changes in insulin levels were significantly more prominent in the intervention groups treated with vitamin C compared to the respective control groups: MD -2.66 µU/mL [95% CI -4.51, -0.82], P = 0.005 (Figure 32).

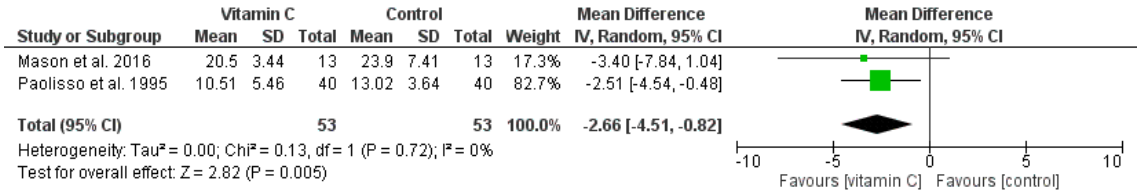

Figure 32: Forest plot showing the aggregated weighted MD including 95% CI for insulin after vitamin C supplementation vs. control.
The squares represent the point estimates of the intervention effect, the horizontal lines represent the corresponding 95% CI. The dimension of the squares indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MDs with 95% CI for all randomized trials. CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation

The change in insulin level was significantly stronger in the intervention group treated with probiotics compared to the control group: MD -3.40 µU/mL [95% CI -5.86, -0.94], P = 0.007 (Figure 33).

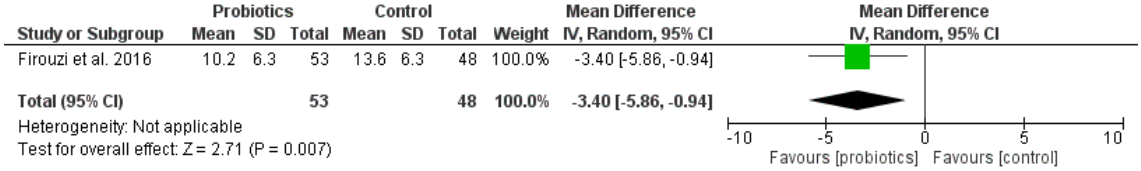

Figure 33: Forest plot showing the aggregated weighted MD including 95% CI for insulin after probiotic supplementation vs. control.
The square represents the point estimates of the intervention effect, the horizontal line represents the corresponding 95% CI. The dimension of the square indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MD with 95% CI for all randomized trials. CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation

The change in insulin level was significantly more prominent in the intervention group treated with calcium and vitamin D compared to the control group: MD -4.40 µU/mL [95% CI -6.66, -2.14], P = 0.0001 (Figure 34).

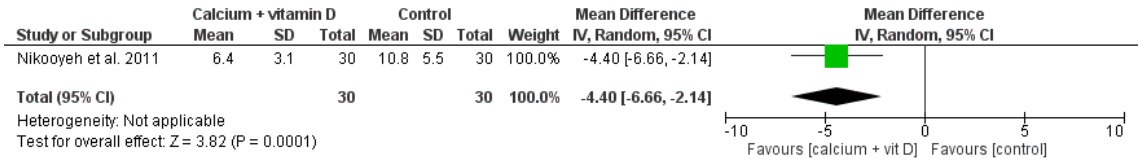

Figure 34: Forest plot showing the aggregated weighted MD including 95% CI for insulin after calcium and vitamin D supplementation vs. control.
The square represents the point estimates of the intervention effect, the horizontal line represents the corresponding 95% CI. The dimension of the square indicates the weight of the study

within the meta-analysis. The diamond summarizes the pooled MD with 95% CI for all randomized trials. CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation

The change in insulin level was significantly stronger in the intervention group treated with ginger compared to the control group: MD -2.01 µU/mL [95% CI -3.90, -0.12], P = 0.04 (Figure 35).

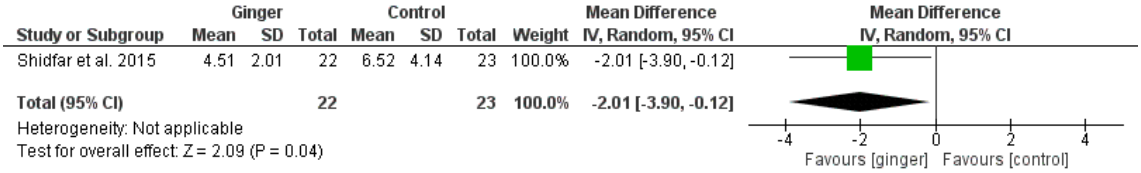

Figure 35: Forest plot showing the aggregated weighted MD including 95% CI for insulin after ginger supplementation vs. control.
The square represents the point estimates of the intervention effect, the horizontal line represents the corresponding 95% CI. The dimension of the square indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MD with 95% CI for all randomized trials. CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation

The change in insulin level was significantly more prominent in the intervention group treated with ABM compared to the control group: MD -5.70 UI/L [95% CI -8.97, -2.43], P = 0.0006 (Figure 36).

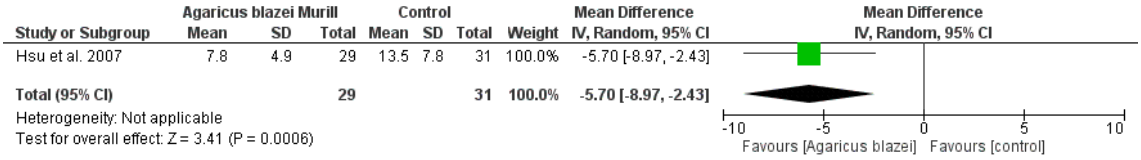

Figure 36: Forest plot showing the aggregated weighted MD including 95% CI for insulin after ABM supplementation vs. control.
The square represents the point estimates of the intervention effect, the horizontal line represents the corresponding 95% CI. The dimension of the square indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MD with 95% CI for all randomized trials. ABM = *Agaricus blazei* Murill, CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation

Figure 37 shows that the change in insulin level was significantly stronger in the intervention group treated with the DJC compared to the control group: MD -1.10 µU/mL [95% CI -2.01, -0.19], P = 0.02.

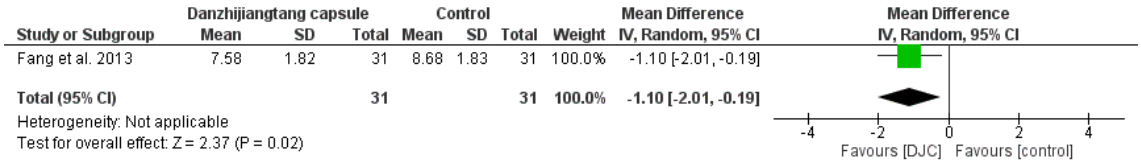

Figure 37: Forest plot showing the aggregated weighted MD including 95% CI for insulin after DJC supplementation vs. control.
The square represents the point estimates of the intervention effect, the horizontal line represents the corresponding 95% CI. The dimension of the square indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MD with 95% CI for all randomized trials. CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation

The increase in insulin level was significantly stronger in the intervention groups treated with zinc, vitamins and minerals compared to the control group: MD 8.96 µmol/L [95% CI 0.99, 16.93], P = 0.03 (Figure 38).

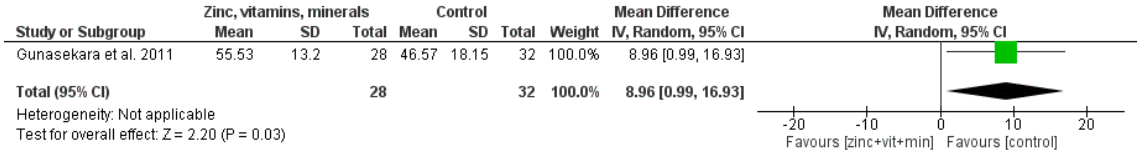

Figure 38: Forest plot showing the aggregated weighted MD including 95% CI for insulin after zinc, vitamin and mineral supplementation vs. control.
The square represents the point estimates of the intervention effect, the horizontal line represents the corresponding 95% CI. The dimension of the square indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MD with 95% CI for all randomized trials. CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation

Supplementation of vitamin D was close to having a significant influence on the changes in insulin levels compared to their respective control groups: MD -3.65 µU/mL [95% CI -7.49, 0.20], P = 0.06 (Figure 39).

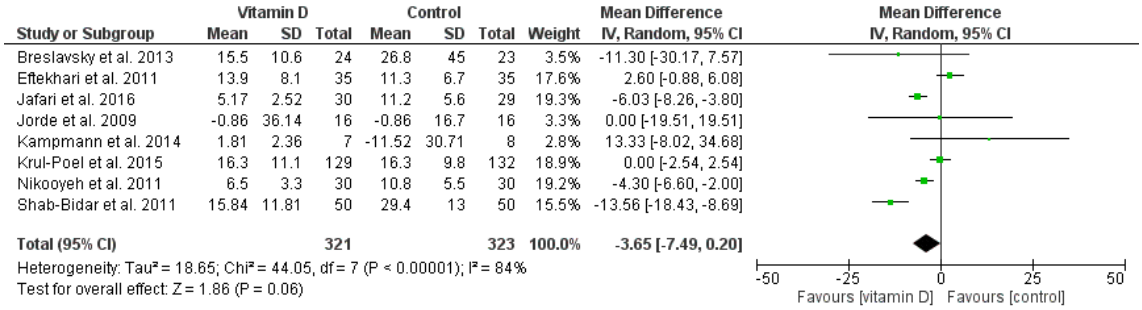

Figure 39: Forest plot showing the aggregated weighted MD including 95% CI for insulin after vitamin D supplementation vs. control.

The squares represent the point estimates of the intervention effect, the horizontal lines represent the corresponding 95% CI. The dimension of the squares indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MDs with 95% CI for all randomized trials. CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation

Figure 40 shows that supplementation of synbiotics was close to having a significant impact on the changes in insulin levels compared to their respective control groups: MD -4.30 µIU/mL [95% CI -8.94, 0.34], P = 0.07.

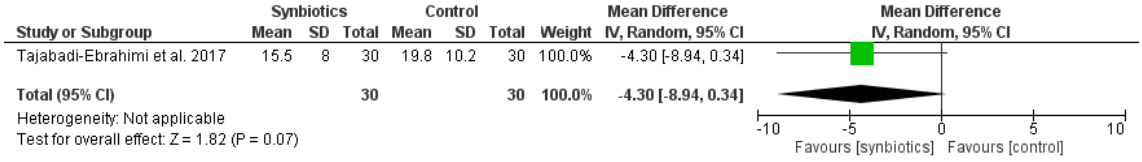

Figure 40: Forest plot showing the aggregated weighted MD including 95% CI for insulin after synbiotic supplementation vs. control.
The squares represent the point estimates of the intervention effect, the horizontal lines represent the corresponding 95% CI. The dimension of the squares indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MDs with 95% CI for all randomized trials. CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation

Supplementation of DAG was close to having a significant impact on the changes in insulin levels compared to their respective control groups: MD -6.43 µU/mL [95% CI -13.51, 0.64], P = 0.07 (Figure 41).

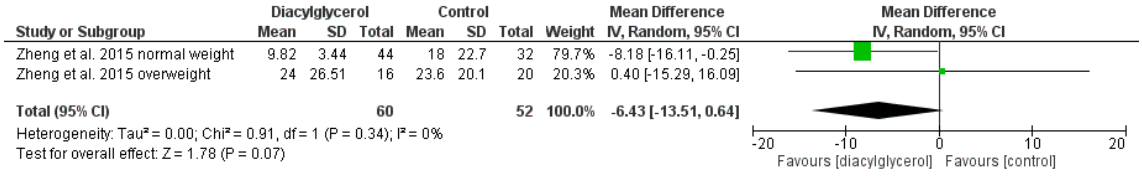

Figure 41: Forest plot showing the aggregated weighted MD including 95% CI for insulin after DAG supplementation vs. control.
The squares represent the point estimates of the intervention effect, the horizontal lines represent the corresponding 95% CI. The dimension of the squares indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MDs with 95% CI for all randomized trials. CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation, normal weight = normal weight subjects, overweight = overweight subjects

8.4 HOMA-IR

Changes in HOMA-IR were significantly more prominent in the intervention groups treated with AAs compared to the respective control groups: MD -0.65 [95% CI -1.11, -0.20], P = 0.005 (Figure 42). A sensitivity analysis showed a non-significant change in HOMA-IR after exclusion of all data on L-canitine: MD -0.40 [95% CI -1.44, 0.64], P = 0.45

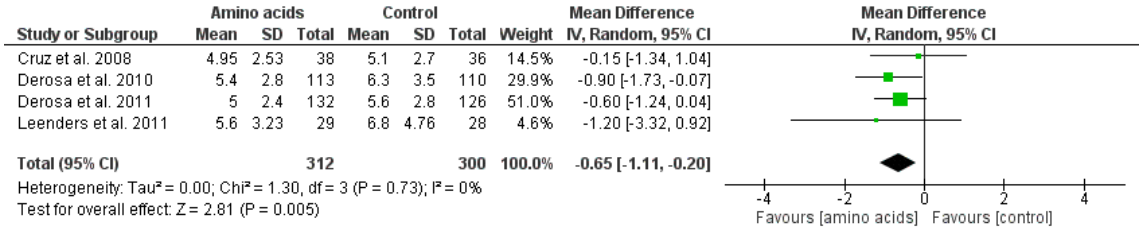

Figure 42: Forest plot showing the aggregated weighted MD including 95% CI for HOMA-IR after AA supplementation vs. control.
The squares represent the point estimates of the intervention effect, the horizontal lines represent the corresponding 95% CI. The dimension of the squares indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MDs with 95% CI for all randomized trials. AA = amino acid, CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation

The changes in HOMA-IR were significantly stronger in the intervention groups treated with vitamin E compared to the respective control groups: MD -0.55 [95% CI -0.65, -0.45], P < 0.00001 (Figure 43).

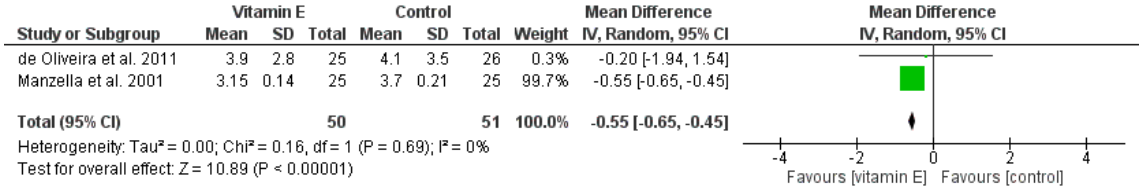

Figure 43: Forest plot showing the aggregated weighted MD including 95% CI for HOMA-IR after vitamin E supplementation vs. control.
The squares represent the point estimates of the intervention effect, the horizontal lines represent the corresponding 95% CI. The dimension of the squares indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MDs with 95% CI for all randomized trials. CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation

The change in HOMA-IR was significantly more prominent in the intervention group treated with probiotics compared to the control group: MD -2.00 [95% CI -2.90, -1.10], P < 0.0001 (Figure 44).

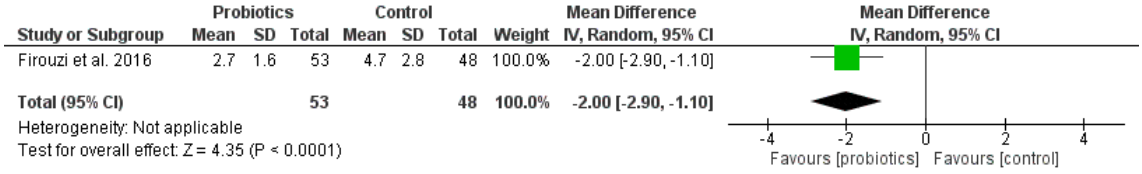

Figure 44: Forest plot showing the aggregated weighted MD including 95% CI for HOMA-IR after probiotic supplementation vs. control.
The square represents the point estimates of the intervention effect, the horizontal line represents the corresponding 95% CI. The dimension of the square indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MD with 95% CI for all randomized trials. CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation

The change in HOMA-IR was significantly stronger in the intervention group treated with calcium and vitamin D compared to the control group: MD -2.50 [95% CI -3.93, -1.07], P = 0.0006 (Figure 45).

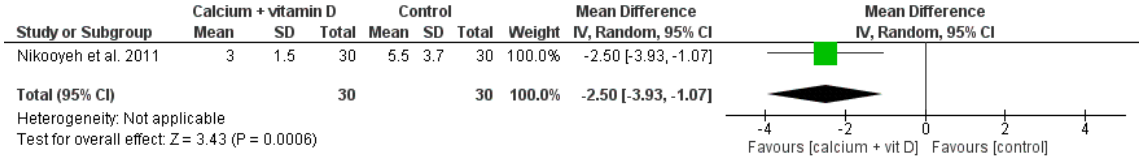

Figure 45: Forest plot showing the aggregated weighted MD including 95% CI for HOMA-IR after calcium and vitamin D supplementation vs. control.
The square represents the point estimates of the intervention effect, the horizontal line represents the corresponding 95% CI. The dimension of the square indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MD with 95% CI for all randomized trials. CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation

The change in HOMA-IR was significantly more prominent in the intervention group treated with magnesium compared to the control group: MD -1.20 [95% CI -1.80, -0.60], P < 0.0001 (Figure 46).

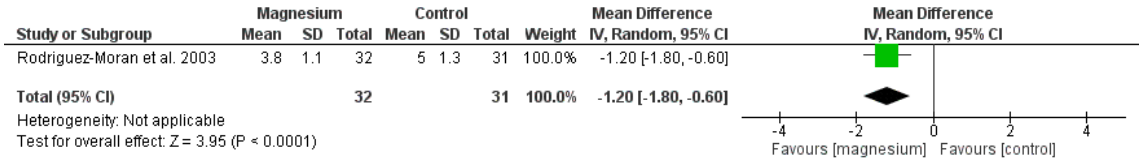

Figure 46: Forest plot showing the aggregated weighted MD including 95% CI for HOMA-IR after magnesium supplementation vs. control.
The square represents the point estimates of the intervention effect, the horizontal line represents the corresponding 95% CI. The dimension of the square indicates the weight of the study

within the meta-analysis. The diamond summarizes the pooled MD with 95% CI for all randomized trials. CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation

The change in HOMA-IR was significantly stronger in the intervention group treated with EPA compared to the control group: MD -1.00 [95% CI -1.88, -0.12], P = 0.03 (Figure 47).

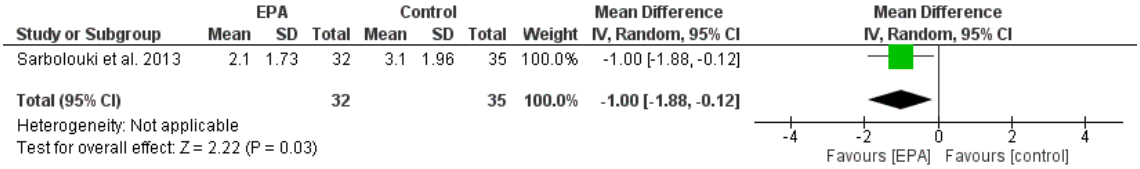

Figure 47: Forest plot showing the aggregated weighted MD including 95% CI for HOMA-IR after EPA supplementation vs. control.
The square represents the point estimates of the intervention effect, the horizontal line represents the corresponding 95% CI. The dimension of the square indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MD with 95% CI for all randomized trials. CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation

The change in HOMA-IR was significantly more prominent in the intervention group treated with ABM compared to the control group: MD -3.00 [95% CI -5.76, -0.24], P = 0.03 (Figure 48).

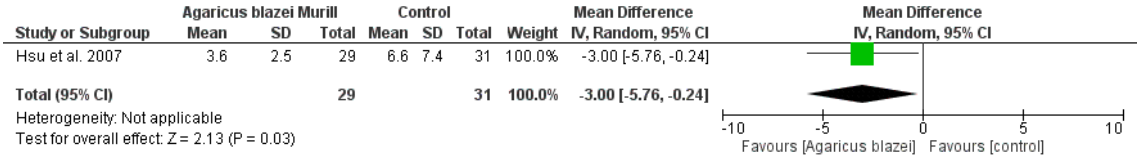

Figure 48: Forest plot showing the aggregated weighted MD including 95% CI for HOMA-IR after ABM supplementation vs. control.
The square represents the point estimates of the intervention effect, the horizontal line represents the corresponding 95% CI. The dimension of the square indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MD with 95% CI for all randomized trials. ABM = *Agaricus blazei* Murill, CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation

The change in HOMA-IR was significantly stronger in the intervention group treated with N. sativa compared to the control group: MD -22.50 [95% CI -22.96, -22.04], P < 0.00001 (Figure 49).

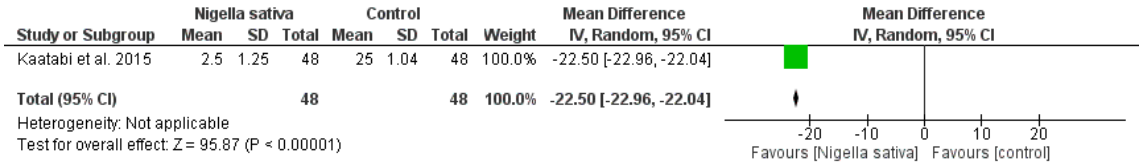

Figure 49: Forest plot showing the aggregated weighted MD including 95% CI for HOMA-IR after N. sativa supplementation vs. control.
The square represents the point estimates of the intervention effect, the horizontal line represents the corresponding 95% CI. The dimension of the square indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MD with 95% CI for all randomized trials. CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation

Supplementation of berberine was close to having a significant influence on the change in HOMA-IR compared to the control group: MD -0.85 [95% CI -1.74, 0.04], P = 0.06 (Figure 50).

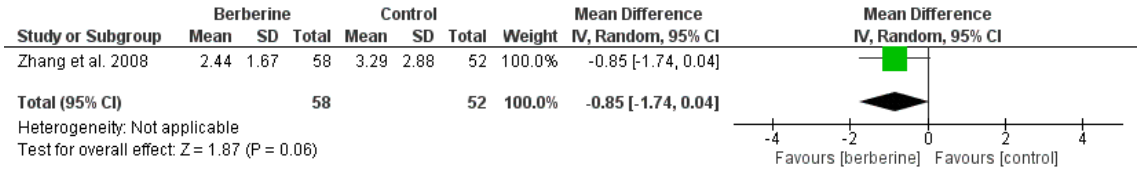

Figure 50: Forest plot showing the aggregated weighted MD including 95% CI for HOMA-IR after berberine supplementation vs. control.
The square represents the point estimates of the intervention effect, the horizontal line represents the corresponding 95% CI. The dimension of the square indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MD with 95% CI for all randomized trials. CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation

8.5 HOMA-beta

The change in HOMA-beta was significantly more prominent in the intervention group treated with synbiotics compared to the control group: MD -24.00 [95% CI -43.28, -4.72], P = 0.01 (Figure 51).

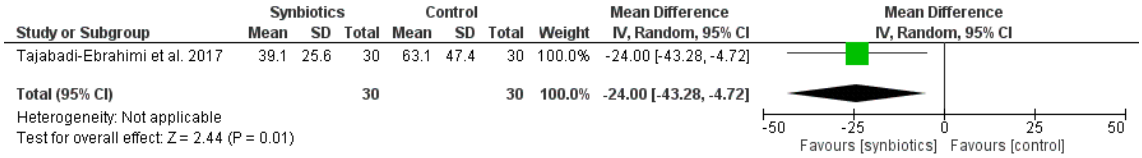

Figure 51: Forest plot showing the aggregated weighted MD including 95% CI for HOMA-beta after synbiotic supplementation vs. control.
The square represents the point estimates of the intervention effect, the horizontal line represents the corresponding 95% CI. The dimension of the square indicates the weight of the study

within the meta-analysis. The diamond summarizes the pooled MD with 95% CI for all randomized trials. CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation

8.6 QUICKI

Figure 52 shows that the increase in QUICKI was significantly more pronounced following yeast supplementation compared to the control group: MD 0.02 [95% CI 0.01, 0.03], P = 0.0010.

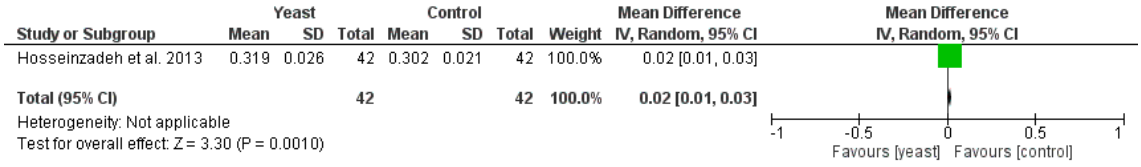

Figure 52: Forest plot showing the aggregated weighted MD including 95% CI for QUICKI after yeast supplementation vs. control.
The square represents the point estimates of the intervention effect, the horizontal line represents the corresponding 95% CI. The dimension of the square indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MD with 95% CI for all randomized trials. CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation

Supplementation of probiotics was close to having a significant influence on the change in QUICKI compared to the control group: MD 0.02 [95% CI 0.00, 0.04], P = 0.01 (Figure 53).

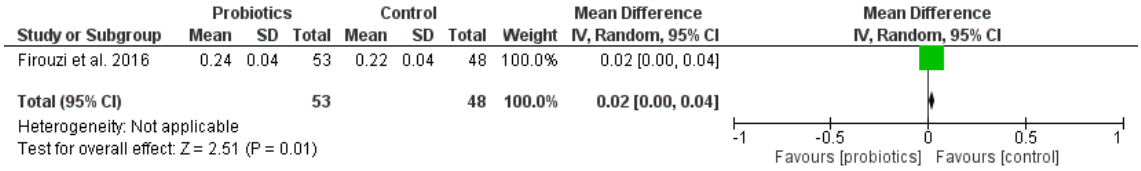

Figure 53: Forest plot showing the aggregated weighted MD including 95% CI for QUICKI after probiotic supplementation vs. control.
The square represents the point estimates of the intervention effect, the horizontal line represents the corresponding 95% CI. The dimension of the square indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MD with 95% CI for all randomized trials. CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation

8.7 Adiponectin

Figure 54 shows that the decrease in adiponectin was significantly more pronounced following AA supplementation compared to the control group: MD -1.00 µg/mL [95% CI -1.46, -0.54], P < 0.0001.

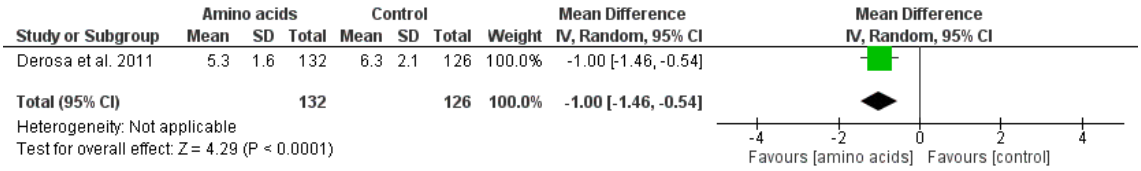

Figure 54: Forest plot showing the aggregated weighted MD including 95% CI for adiponectin after AA supplementation vs. control.
The square represents the point estimates of the intervention effect, the horizontal line represents the corresponding 95% CI. The dimension of the square indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MD with 95% CI for all randomized trials. AA = amino acid, CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation

Compared to the control group, decrease in adiponectin was significantly more distinct following Caiapo supplementation: MD -3.10 µg/mL [95% CI -4.99, -1.21], P = 0.001 (Figure 55).

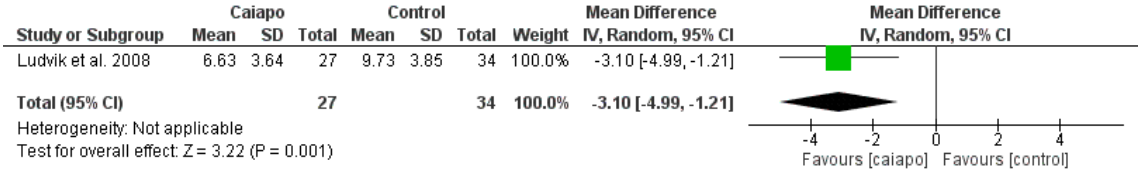

Figure 55: Forest plot showing the aggregated weighted MD including 95% CI for adiponectin after Caiapo supplementation vs. control.
The square represents the point estimates of the intervention effect, the horizontal line represents the corresponding 95% CI. The dimension of the square indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MD with 95% CI for all randomized trials. CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation

8.8 C-Peptide

Increase in C-Peptide was significantly more pronounced following melatonin and zinc supplementation compared to the control group: MD 0.38 ng/mL [95% CI 0.04, 0.72], P = 0.03 (Figure 56).

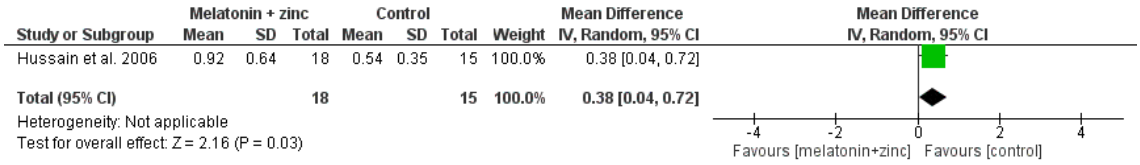

Figure 56: Forest plot showing the aggregated weighted MD including 95% CI for C-Peptide after melatonin and zinc supplementation vs. control.
The square represents the point estimates of the intervention effect, the horizontal line represents the corresponding 95% CI. The dimension of the square indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MD with 95% CI for all randomized trials. CI = confidence interval, I² = heterogeneity, MD = mean difference, SD = standard deviation

8.9 2-h 75 g OGTT glucose

Decrease in 2-h 75 g OGTT glucose was significantly more pronounced following berberine supplementation compared to the control group: MD -2.10 mmol/L [95% CI -3.15, -1.05], P < 0.0001 (Figure 57).

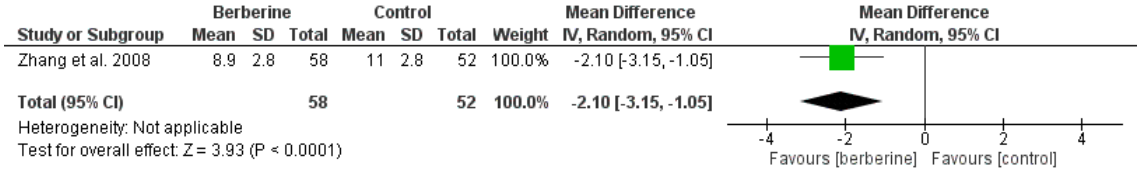

Figure 57: Forest plot showing the aggregated weighted MD including 95% CI for 2-h 75 g OGTT glucose after berberine supplementation vs. control.
The square represents the point estimates of the intervention effect, the horizontal line represents the corresponding 95% CI. The dimension of the square indicates the weight of the study within the meta-analysis. The diamond summarizes the pooled MD with 95% CI for all randomized trials. CI = confidence interval, I² = heterogeneity, MD = mean difference, OGTT = OGTT = oral glucose tolerance test, SD = standard deviation

8.10 Heterogeneity

50% was used as a threshold for heterogeneity in this meta-analysis. Hence, while heterogeneity was not important for the use of vitamin E (11%) or berberine (0%) to lower HbA1c, amino acids (0%), vitamin C (0%), flaxseed (0%), probiotics (0%), DAG (0%) or berberine (0%) to reduce glucose, vitamin C (0%) or DAG (0%) to change insulin levels and amino acids (0%) or vitamin E (0%) to change HOMA-IR, heterogeneity was found for the use of prebiotics (60%), flaxseed (63%), amino acids (92%) or silymarin (86%) to decrease HbA1c, the use of prebiotics (78%), amino acids (60%) or silymarin (81%) to reduce glucose and the use of vitamin D (84%) to change insulin levels.

8.11 Publication bias

Merely the funnel plot for vitamin E supplementation and glucose levels shows only low to middle asymmetry (Figure 66), suggesting a low to moderate likelihood of a publication bias. For all other funnel plots (Figure 58-65, 67-70), high asymmetry can be seen, indicating a higher likelihood of a publication bias. Hence, a publication bias as an influencing factor in this meta-analysis can not be ruled out completely.

8.11.1 HbA1c

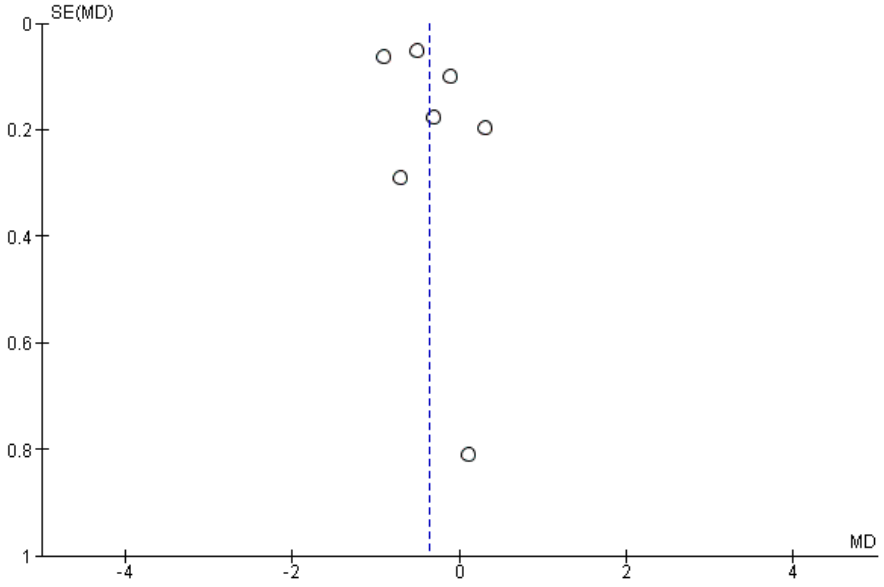

Figure 58: Funnel plot depicting the study precision for AA supplementation and HbA1c given as SE of MD against the MD effect estimated with 95 % CIs.
SE = standard error, MD = mean difference, CI = confidence interval

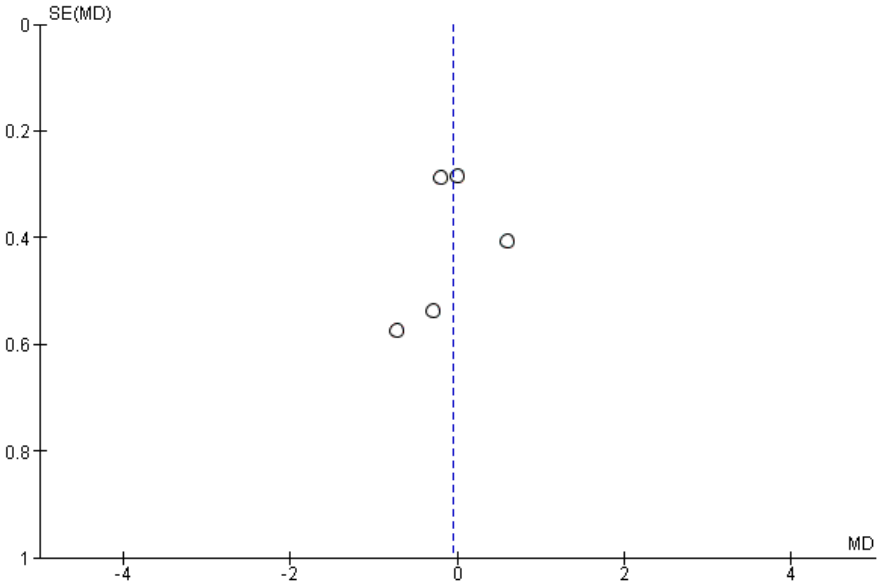

Figure 59: Funnel plot depicting the study precision for chromium supplementation and HbA1c given as SE of MD against the MD effect estimated with 95 % CIs.
SE = standard error, MD = mean difference, CI = confidence interval

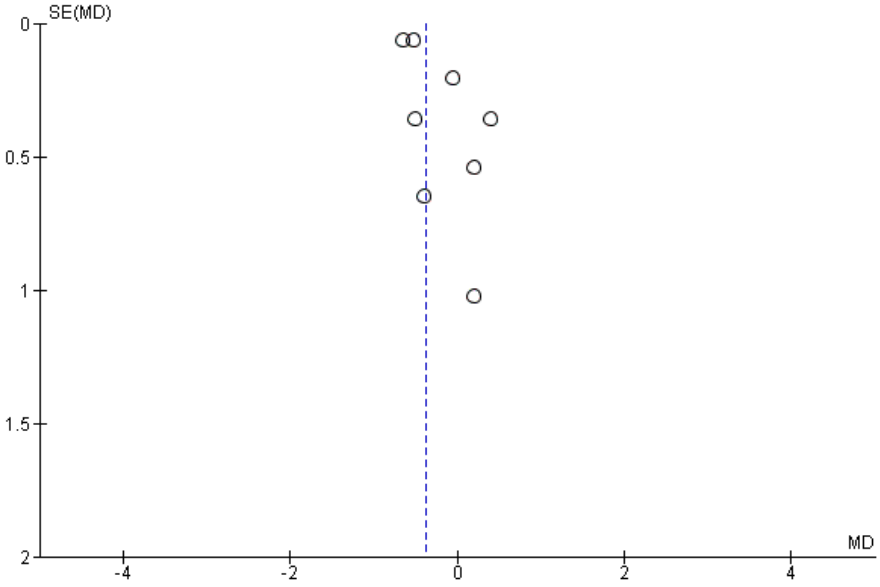

Figure 60: Funnel plot depicting the study precision for prebiotic supplementation and HbA1c given as SE of MD against the MD effect estimated with 95 % CIs.
SE = standard error, MD = mean difference, CI = confidence interval

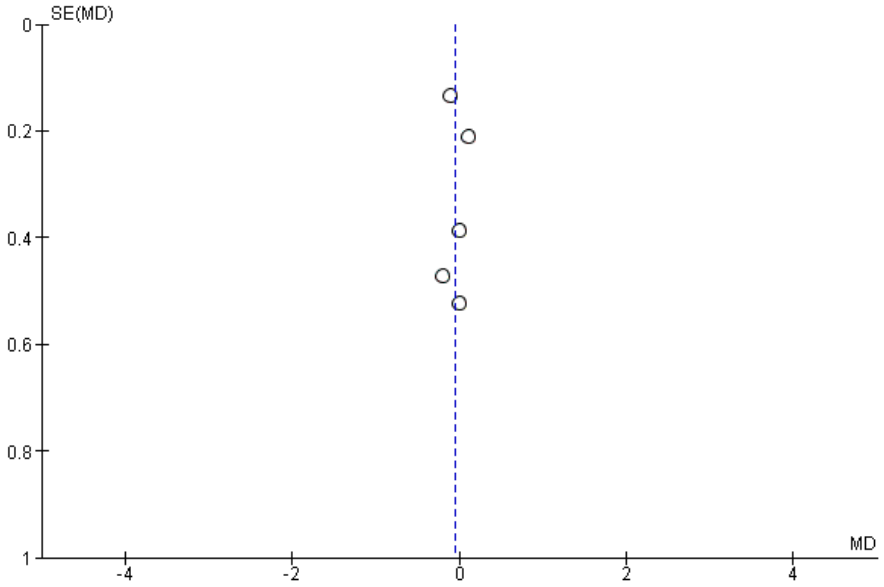

Figure 61: Funnel plot depicting the study precision for tea extract supplementation and HbA1c given as SE of MD against the MD effect estimated with 95 % CIs.
SE = standard error, MD = mean difference, CI = confidence interval

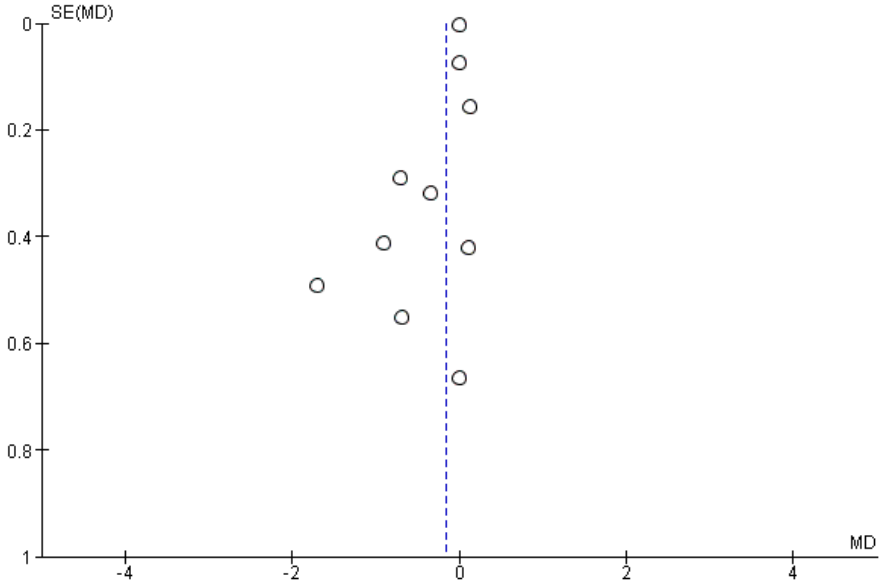

Figure 62: Funnel plot depicting the study precision for vitamin D supplementation and HbA1c given as SE of MD against the MD effect estimated with 95 % CIs.
SE = standard error, MD = mean difference, CI = confidence interval

8.11.2 Glucose

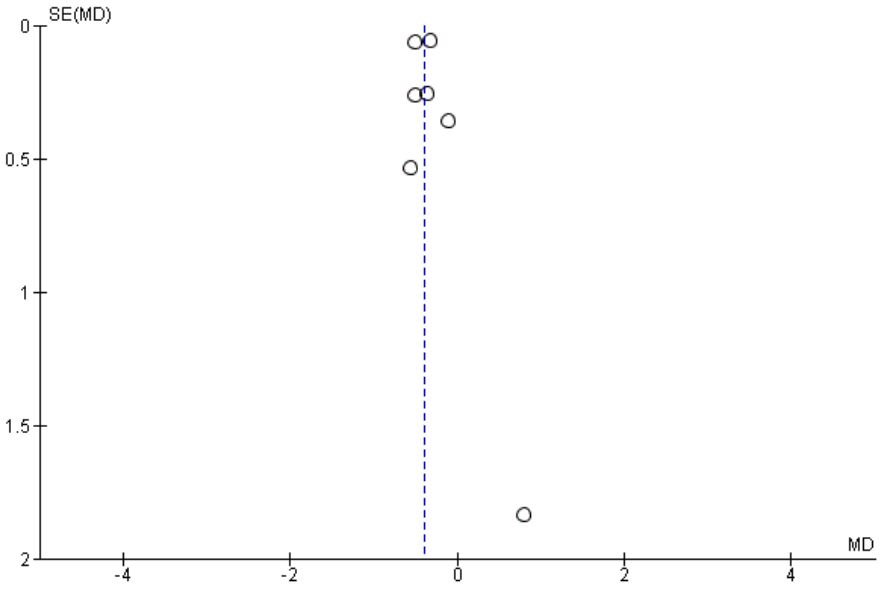

Figure 63: Funnel plot depicting the study precision for AA supplementation and glucose given as SE of MD against the MD effect estimated with 95 % CIs.
SE = standard error, MD = mean difference, CI = confidence interval

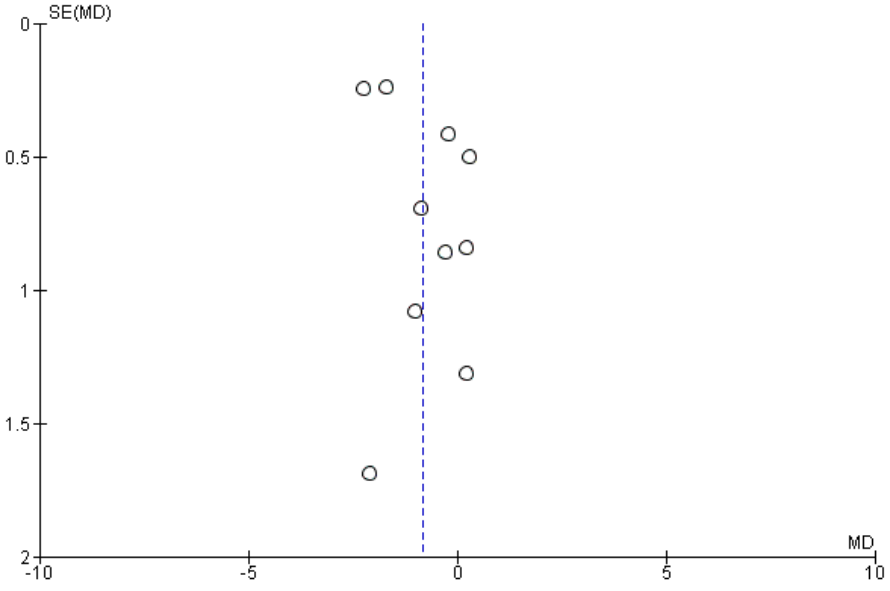

Figure 64: Funnel plot depicting the study precision for prebiotic supplementation and glucose given as SE of MD against the MD effect estimated with 95 % CIs.
SE = standard error, MD = mean difference, CI = confidence interval

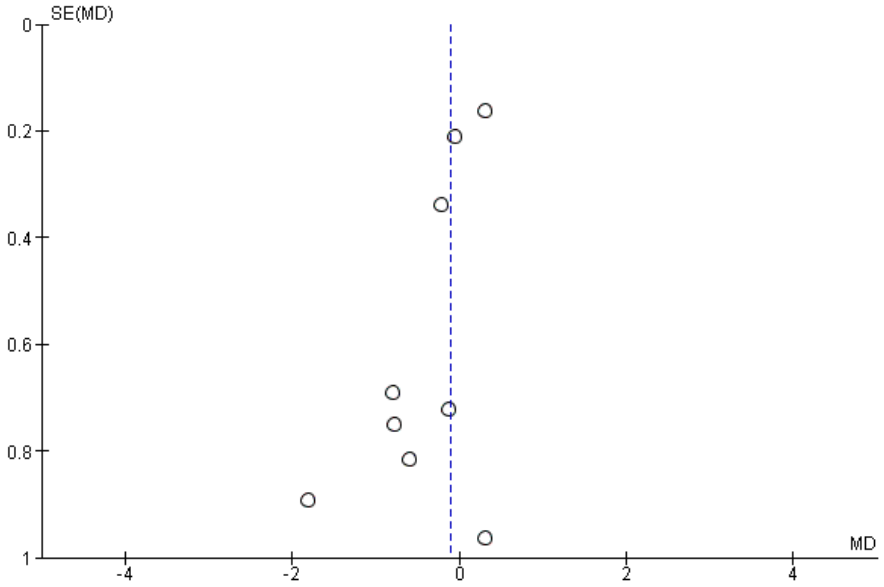

Figure 65: Funnel plot depicting the study precision for vitamin D supplementation and glucose given as SE of MD against the MD effect estimated with 95 % CIs.
SE = standard error, MD = mean difference, CI = confidence interval

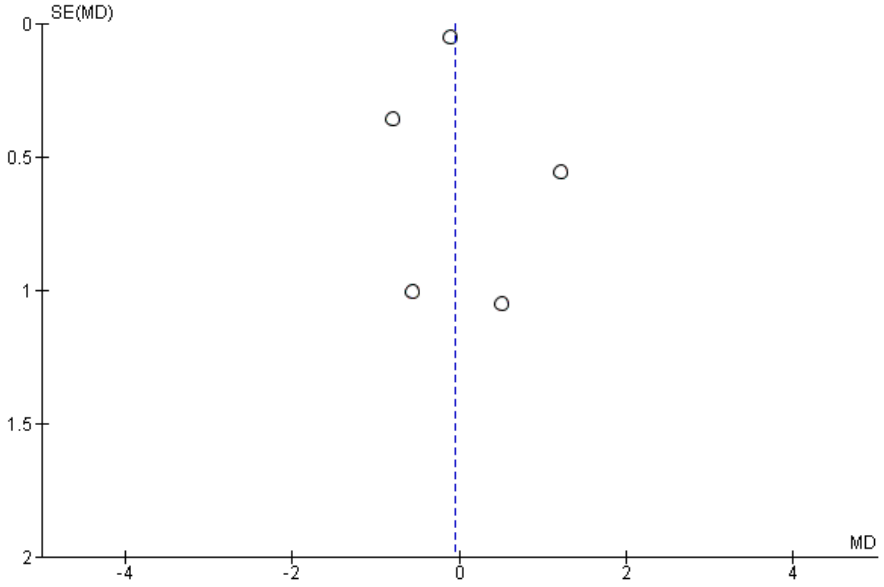

Figure 66: Funnel plot depicting the study precision for vitamin E supplementation and glucose given as SE of MD against the MD effect estimated with 95 % CIs.
SE = standard error, MD = mean difference, CI = confidence interval

8.11.3 Insulin

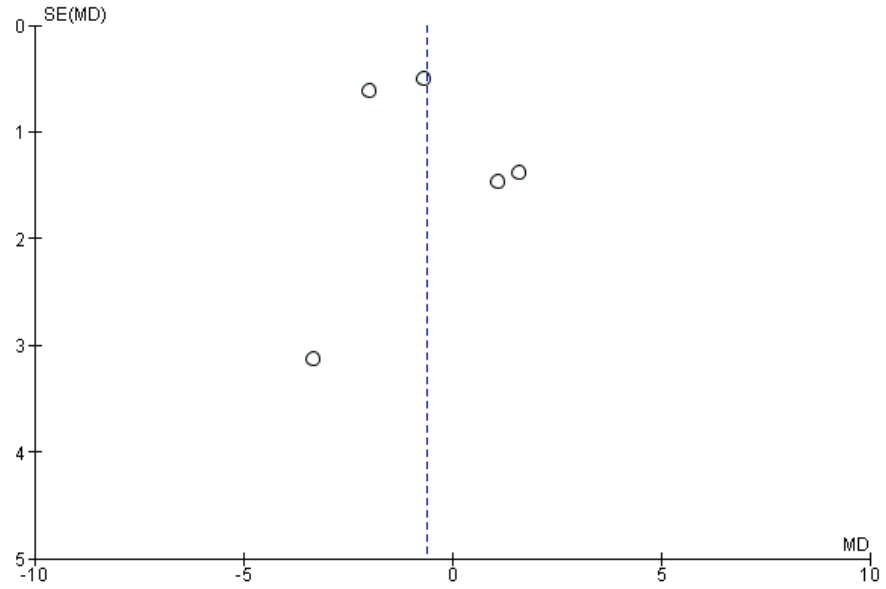

Figure 67: Funnel plot depicting the study precision for AA supplementation and insulin given as SE of MD against the MD effect estimated with 95 % CIs.
SE = standard error, MD = mean difference, CI = confidence interval

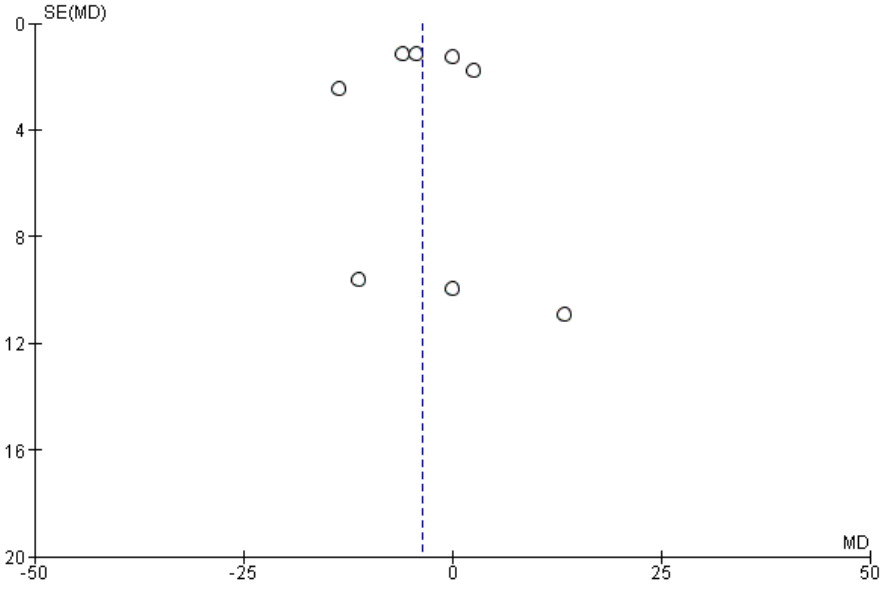

Figure 68: Funnel plot depicting the study precision for vitamin D supplementation and insulin given as SE of MD against the MD effect estimated with 95 % CIs.
SE = standard error, MD = mean difference, CI = confidence interval

8.11.4 HOMA-IR

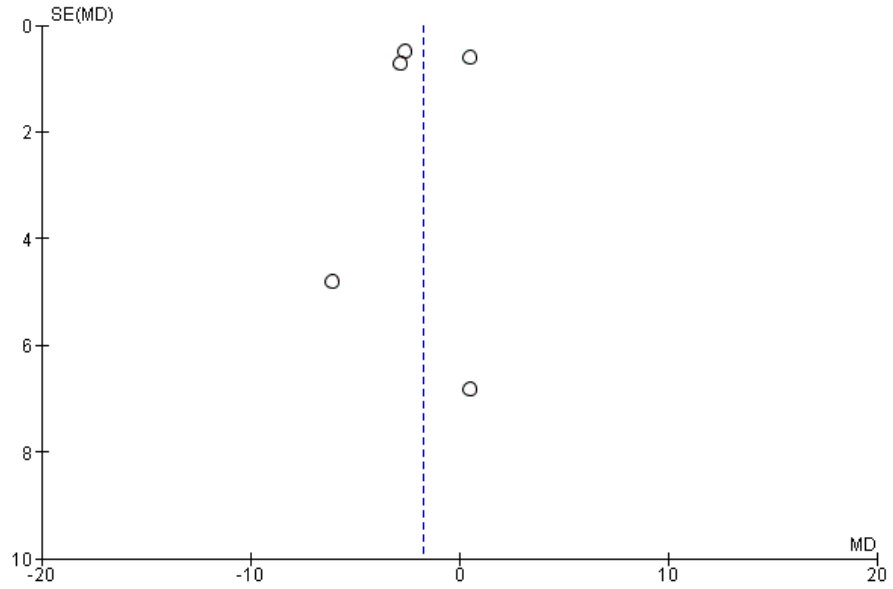

Figure 69: Funnel plot depicting the study precision for vitamin D supplementation and HOMA-IR given as SE of MD against the MD effect estimated with 95 % CIs.
SE = standard error, MD = mean difference, CI = confidence interval

8.11.5 QUICKI

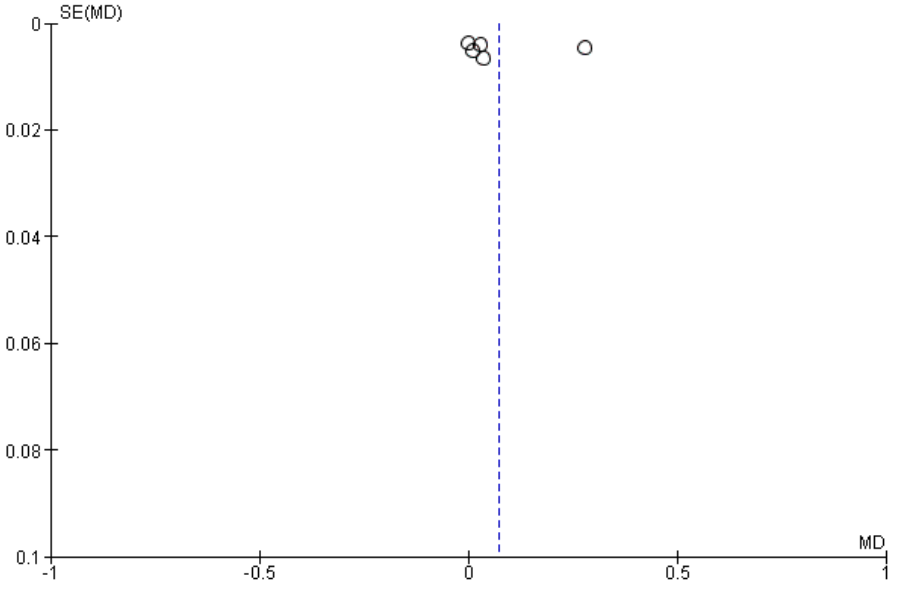

Figure 70: Funnel plot depicting the study precision for vitamin D supplementation and QUICKI given as SE of MD against the MD effect estimated with 95 % CIs.
SE = standard error, MD = mean difference, CI = confidence interval

9 Discussion

9.1 Summary of results and possible mechanisms of action

The goal of this systematic review and meta-analysis was to examine the effect of every supplement that has been used in RCTs with type 2 diabetics so far. A total of 26 different supplements and combinations of supplements out of the 56 different supplements and combinations used lead to significant decreases or increases in the outcome parameters. Table 5 summarizes how the supplements that produced significant forest plots impacted the different outcomes. The data is presented as mean differences. The numbers in the parantheses indicate how many different studies were involved in the formation of the result.

Table 5: Summary of statistically significant results

Supplement	HbA1c (%)	Glucose (mmol/L)	Insulin (µU/mL)	HOMA-IR	HOMA-beta	QUICKI	Adiponectin (µg/mL)	C-Peptide (ng/mL)	2-h 75g OGTT glucose (mmol/L)
AAs	-0.36 (7)	-0.40 (7)		-0.65 (4)			-1.00 (1)		
Prebiotics	-0.38 (7)	-0.83 (9)							
Vitamin E	-0.56 (4)			-0.55 (2)					
Flaxseed	-0.54 (3)	-0.98 (3)							
Berberine	-0.66 (2)	-0.76 (2)							-2.10 (1)
Silymarin	-1.92 (2)	-2.11 (2)							
Calcium + vitamin D	-1.40 (1)		-4.40 (1)	-2.50 (1)					
Pistachios	-0.40 (1)	-0.89 (1)							
Pycnogenol	-0.90 (1)	-1.98 (1)							
Zinc, vitamins, minerals	-0.68 (1)		+8.96 * (1)						
Melatonin + zinc	-2.09 (1)							+0.38 (1)	
Alpha-lipoic acid	-0.50 (1)								
Zinc	-0.60 (1)								
Diabetes-specific ONS	+1.85 (1)								
Vitamin C		-0.65 (4)	-2.66 (2)						
Probiotics		-0.85 (2)	-3.40 (1)	-2.00 (1)					
DAG		-0.74 (2)							
Caiapo		-0.73 (1)					-3.10 (1)		
***Agaricus blazei* Murill**			-5.70 ** (1)	-3.00 (1)					
Ginger			-2.01 (1)						
DJC			-1.10 (1)						
Magnesium				-1.20 (1)					
EPA				-1.00 (1)					
Nigella sativa				-22.50 (1)					
Synbiotics					-24.00 (1)				
Yeast						+0.02 (1)			

AAs = amino acids, DAG = diacylglycerol, DJC = Danzhijiangtang capsules, EPA = eicosapentaenoic acid, HbA1c = Glycated Haemoglobin, OGTT = oral glucose tolerance test
* unit: µmol/L, ** unit: UI/L

While the supplementation with melatonin and zinc has shown a very considerable positive effect on HbA1c (-2.09%) – especially for diabetics with HbA1c levels close to the diagnostic limit for diabetes –, this is merely the finding of a single study. Hence, this effect should further be investigated. The same applies for the effect of the Pycnogenol pill on glucose levels (-1.98 mmol/L), that of the mushroom ABM on insulin levels (-5.70UI/L) and the effect of the seeds of the Nigella sativa plant on HOMA-IR (-22.50). However, the positive impacts of flaxseed (-0.98 mmol/L), prebiotics (-0.83 mmol/L) and vitamin C (-0.65 mmol/L) on glucose levels and amino acids on HOMA-IR (-0.65) are farely big and are the results of the analyses of several studies (between three and nine trials). The positive effects from most supplements that have been used to change HbA1c levels in several trials are only small (between -0.36 and -0.56%) and might not have a big enough impact to improve a type 2 diabetic's condition. Further trials investigating the effect of zinc should be conducted since the combination of zinc, vitamins and minerals or melatonin and zinc had negative effects on insulin and C-Peptide levels in the studies included in this meta-analysis.

The effect of silymarin on HbA1c (-1.92%) and blood sugar (-2.11 mmol/L) found in this meta-analysis goes along with the findings of significant decreases in HbA1c (-1.07) and FBG (-26.86 mg/dL) reported in a meta-analysis by Voroneanu et al (144). This paper's findings on vitamin C and blood glucose (-0.65 mmol/L) also agree with those found in a meta-analysis by Tabatabaei-Malazy et al (standardized mean difference [SMD]: -20.59%) (145). While this meta-analysis coincides with several meta-analyses when it comes to the statistically significant influence of probiotics on FBG [-15.92 mg/dL (146), -0.52 mmol/L (147), MD: -0.98 mmol/L (148) and SMD: -0.61 mmol/L (149)], insulin [SMD: -0.38 (150)] and HOMA-IR [SMD: -2.10 (151) and SMD: -0.99 (150)], the results also differ with some meta-analyses when it comes to glucose (150), insulin (151) and HOMA-IR (147, 149) – these other meta-analyses were unable to report significant changes in these parameters.

Below, the main supplements that occurred in several of the 105 trials included in this meta-analysis and produced forest plots with significant or almost significant results and how they are thought to positively influence the prevalence and development of type 2 diabetes mellitus will be discussed briefly.

9.1.1 Vitamin D

Associations between the risk of diabetes mellitus type 2 and a low vitamin D status have been found in cohort studies (152-157). Further studies reported relationships between β-cell dysfunction, insulin resistance and serum vitamin D levels (12). Vitamin D is important because of its vitamin D receptors in pancreatic β-cells (12). This vitamin is able to improve the insulin sensitivity through the stimulation of insulin receptor expression and the activation of peroxisome proliferator activated receptor delta (PPAR-δ) (158-161). Additionally, the expression of calbindin-D28K (vitamin D dependent on the combination of proteins and calcium) has a positive influence on the β-cells from cytokine mediated cell death and therefore diminishes the risk of type 2 diabetes (162). Vitamin D also seems to modulate the effects of cytokines and nuclear transcription factors like NF-κB and therefore promotes pancreatic β-cell survival and improves insulin sensitivity (163).

9.1.2 Vitamin E

The risk of diabetes may be reduced through vitamin E most likely because of its antioxidant function (164, 165). It has been reported that the levels of vitamin C and vitamin E along with the concentration of other antioxidants are lower in diabetics when compared to healthy controls (166).

9.1.3 Vitamin C

Hyperclycaemia causes oxidative stress which results in a higher requirement of vitamin C in type 2 diabetics (167). Oxidative stress, HbA1c and fasting as well as postprandial blood sugar have been inversely correlated with plasma vitamin C levels (168, 169).

9.1.4 Zinc

As a cofactor for more than 300 enzymes including superoxide dismutase, the mineral zinc plays an important role in the antioxidant defense in type 2 diabetics (170). It also facilitates the neutralization and lowers the amount of free radicals in the body (171, 172). People suffering from type 2 diabetes undergo changes in zinc metabolism as well as superoxide dismutase activity, which may make zinc supplementation during the disease important to ensure a proper antioxidant defense (170).

9.1.5 Amino acids like L-carnitine or branched-chain amino acids

In contrast to the amino acids leucine and glycine that were examined in this meta-analysis as well, L-carnitine proved to be capable of significantly improving the glycaemic parameters HbA1c, blood glucose, HOMA-IR and adiponectin.

A positive effect of L-carnitine on blood sugar levels was also found in a meta-analysis by Vidal-Casariego et al (173). However, this study group was unable to find a significant change in HbA1c (173). The non-protein amino acid L-carnitine is found in food as well as it is synthesized endogenously and acts as a cofactor for the β-oxidation, facilitating the entrance of long chain fatty acid (FA) into the mitochondria as acylcarnitine esters (173). A reduction of this transport into the mitochondria results in an accumulation of triglycerides in the cytosol (173). This accumulation is connected to the pathogenesis of insulin resistance (173). Possible reasons as to why fatty acid dysregulation leads to insulin resistance could be the inhibition of glucose transporter type 4 (GLUT-4) translocation by long chain acyl-CoA, failures in insulin signalling caused by the aggregation of diacylglycerol (DAG) and acyl-CoA or mitochondrial stress and insulin resistance caused by accumulating non-metabolised fatty acids in the mitochondria (174).

Although this could not be demonstrated in this meta-analysis, branched-chain amino acids (BCAA) are also suggested to have a positive influence on the regulation of the glucose homeostasis (175, 176) and metabolic parameters like body composition, glycaemia levels and satiety (177). They have control over the release of hormones like leptin, ghrelin or glucagon-like peptide 1 (GLP-1) in fat deposits as well as in the gastrointestinal tract (177). These hormones are able

to influence the glycaemia levels and modulate the intake of food (178-183). Together with insulin, they change growth of energy-consuming tissues like the skeletal muscle or the adipose tissue by acting as anabolic signals (177). The BCAA leucine has an insulinotropic function (184, 185). It helps maintaining blood sugar homeostasis by improving sugar disposal, increases the availabitiy of amino acids for the synthesis of muscle protein and at the same time inhibits the breakdown of muscle protein (186).

9.1.6 Probiotics

Cani et al. were one of the first to demonstrate the direct role of gut microbiota in IR by showing that a high-fat diet increases certain gut bacteria that produce higher concentrations of lipopolysaccharide and trigger the progression of IR (187). Additional studies report about various bacterial metabolites that contribute to the blood sugar hemostasis (188). Compared to healthy individuals, type 2 diabetics show a significantly smaller amount of bacteria that produce butyrate (189, 190), a short chain fatty acid (SCFA) that constitutes a main energy source for the intestinal cells (191). Through mechanisms like the regulation of glucagon-like peptide 1 by binding to G protein-coupled receptors, SCFAs are able to enhance the secretion of insulin and hence, reduce the concentration of sugar in the blood (192). Short chain fatty acids also interact with histone deacetylases (151). These influence, among others, the expression of genes that are connected to the metabolism (193). Additionally, short chain fatty acids may also help keeping up the intestinal integrity and therefore directly inhibit the low-grade inflammatory response, a state closely related to T2DM (151). Clinical trials that infused feces from skinny subjects into insulin-resistant men with metoblic syndrome reported a greater amount of butyrate-producing bacteria and beneficial metoblic effects after the infusion (194).

9.1.7 Prebiotics

Prebiotic supplementation or prebiotic enriched diet may improve blood sugar homeostasis since there is a considerable interaction between dietary components like prebiotics and the gut bacteria (195). The microbiota is supposed to contribute to a low-grade inflammation that leads from a normal glucose tolerance to prediabetes and type 2 diabetes (187, 196-200).

9.1.8 Flaxseed

In flaxseed, the main n-3 fatty acid accounting for 55% of the total fatty acid content is alpha-linolenic acid (ALA), C18:3n-3, and the main lignan is secoisolariciresinol diglucoside (201). When investigating the influence of n-3 fatty acids on type 2 diabetic patients, fish oil containing eicosapentaenoic acid (EPA), C20:5n-3, and docosahexanoic acid (DHA), C22:6n-3 is usually used (202-205). Hence, it is important to evaluate the effects of ALA versus EPA and DHA (128). Secoisolariciresinol diglucoside is proposed to help prevent and delay the progression of diabetes due to its function as a precursor to antioxidant lignans *in vivo* (206-208).

9.1.9 Berberine

As a plant quaternary ammonium salt from the group of isoquinoline alkaloids, berberine can be extracted from many different plants (209). Berberine modulates PPAR protein expression and therefore regulates the lipid and sugar metabolism in the liver. A review by Pang et al has shown that berberine may be capable of enhancing the glucolipid metabolism (209). It also accumulates beneficial gut bacteria and inhibits harmful bacteria (210-213). Additionally, it could ameliorate insulin secretion and sensitivity and decrease the intestinal glucose absorption on top of its antioxidant activities that could tackle diabetic complications. (214-223)

9.1.10 Silymarin

Silymarin is the extract of milk thistle, *Silybum marianum,* an edible plant, and acts as an antioxidant (144). In a mice model, silymarin attenuates the continuous increase of plasma sugar induced by alloxan (224).

9.1.11 Diacylglycerol

Diacylglycerol naturally occurs in different edible oils like soybean, corn, safflower or olive oil (225). In previous studies with diabetics, diacylglycerol lowered HbA1c when combined with diet treatment (226) and diminished the fasting as well as the postprandial serum triacylglycerol levels (227, 228). Trials carried out with animals reported lower levels of serum leptin and insulin through the consumption of diacylglycerol (229).

9.1.12 Other rare supplements used for glycaemic control

Other supplements included in this meta-analysis, that sometimes even lead to statistically significant changes in glycaemic parameters but might not be well-known, are Pancreas Tonic, an Ayurvedic botanical mixture available in North America under the trades names AntiBetic or Pancreas Tonic (64); Pycnogenol, an extract from *Pinus maritima*, a French maritime pine, that exhibits considerable antioxidant functions and primarily consists of flavonoids and phenolic compounds such as taxifolin, catechin or epicatechin (230); Caiapo, an extract of the skin of a potato called *Ipomea batatas* grown in Japan's Kagawa region (85); DBCare, a traditional nutritional supplement sold in India that comprises 11 herbs and is obtainable electronically worldwide (114); *Momordica charantia (M. charantia)*, a plant also called Ampalaya with charantin, vicine and polypeptide *p* as its active ingredients – the later being structurally animal insulin alike (36); Nigella sativa seeds, an annual Ranunculaceae herbaceous plant with antioxidant properties (73); and the dry extract of *Gingko biloba* L. leaves, a natural antioxidant containing 20-27% flavonoids like quercetin, kaempferol, isorhamnetin or proanthocyanidins, 5-10% organic acids and 5-7% terpenoids (231, 232).

9.2 Limitations

This systematic review and meta-analysis is characterized by strenghts as well as limitations. First of all, it does not include unpublished data. The funnel plots show that the existance of a publication bias when it comes to the use of supplements to treat type 2 diabetes mellitus patients is very probable. The lack

of negative study results could be the result of journals being more likely to publish positive results as well as the conflict of interest that arises from the sources most supplement trials are funded with. The considerable heterogeneity found for some of the parameters may originate from the very heterogenic designs of the trials. Some studies worked solely with men, some only with women, some with both genders; the study duration ranked anywhere from 3 months all the way to 18 months; the treatment for the control groups also varied – some got a placebo, some got no treatment at all which didn't allow for an allocation concealment. Some trials did not really have a control group at all but instead compared two different supplement treatments like fish and flaxseed oil (94) or amino acids and magnesium (46). By doing so, these study groups basically implied the assumption that one treatment works for sure. Also the high number of 56 different supplements tested and the deficit of repetition of the same supplement by different study groups makes a comparison and a meta-analysis difficult. Many of the forest plots presented in this meta-analysis only include one or two publications and are thus of low informative value for a meta-analysis. The doses used and age groups studied also varied between the different trials. Additionally, the supplement/vitamin/mineral supplies at baseline were rarely established and therefore, it is not clear whether the supplementation substituted an already existing deficiency and thus lead to positive results or served as an addition on top of the adequate supply. All of these differing factors between the studies play important roles in the outcome of the trials.

However, this paper is also characterized by some major strenghts like the comprehensive search strategy that resulted in 105 publications from all over the world with a total number of 6763 participants included in the meta-analysis. This search was performed with previously defined in- and exclusion criteria. To the knowledge of the author of this paper, this is the first meta-analysis of this broad extent comparing all the supplements used in RCTs with type 2 diabetics that could be found. Furthermore, this review is registered in the PROSPERO database „International prospective register of systematic reviews".

10 Conclusion

This meta-analysis on trials with a study duration of at least 12 weeks shows that 24 ouf of the 56 supplements examined have a significant positive impact on glycaemic parameter in type 2 diabetics. Hence, supplement usage should be considered as a (complementary) therapy option for diabetes. However, caution should be exercised when it comes to vitamin/mineral combinations, zinc preperations, certain diabetes-specific ONS, and yeasts. So far, the numbers of trials examining the one and the same supplement are small. Thus to allow more precise recommendations on the use of supplements for the treatment of T2DM, further trials of the same study design should be performed with those supplements that showed first results indicating a considerable change of parameters into a positive direction such as probiotics, prebiotics, flaxseed, vitamin C and E, silymarin and berberine.

11 Abstract

Type 2 diabetes, formerly also called non-insulin-dependent diabetes mellitus or adult-onset diabetes, is characterized by an ineffectiveness of the body to use insulin (1). This type of diabetes accounts for approximately 90-95% of people with diabetes (2). There are several ways to achieve glycaemic control and improve insulin resistance such as diet, physical activity, weight reduction, oral glucose-lowering agents, subcutaneous insulin injections and possibly also the use of supplements (6). This systematic review and meta-analysis aimed to examine the influence of supplements on glycaemic parameters in adults suffering from diabetes mellitus type 2. The review included 122 randomized controlled trials examining type 2 diabetics after an intervention duration of at least 12 weeks. 105 of these studies were included in the meta-analysis. The statistical analysis was performed with the review manager 5.3 (Nordic Cochrane Center, Copenhagen).

Out of the 56 different supplements and combinations of supplements, 26 supplements and combinations lead to statistically significant changes in the outcome parameters. For example, HbA1c was significantly reduced through amino acids by 0.36% [95% confidence interval (CI) -0.67, -0.05], by 0.38% [95% CI -0.60, -0.16] through prebiotics, by 0.56% [95% CI -0.83, -0.29] through vitamin E, by 0.54% [95% CI -0.95, -0.12] through flaxseed, by 0.66% [95% CI -1.00, -0.33] through berberine and by 1.92% [95% CI -3.32, -0.51] through silymarin. Glucose levels were lowered by 0.40 mmol/L [95% CI -0.48, -0.32] through amino acids, by 0.83 mmol/L [95% CI -1.55, -0.10] through prebiotics, by 0.98 mmol/L [95% CI -1.18, -0.79] through flaxseed, by 0.76 mmol/L [95% CI -1.24, -0.29] through berberine, by 2.11 mmol/L [95% CI -3.69, -0.53] through silymarin, by 0.65 mmol/L [95% CI -1.07, -0.23] through vitamin C, by 0.85 mmol/L [95% CI -1.50, -0.21] through probiotics and by 0.74 mmol/L [95% CI -1.39, -0.09] through diacylglycerol. Vitamin C significantly decreased insulin by 2.66 µU/mL [95% CI -4.51, -0.82] and HOMA-IR was significantly reduced through amino acids by 0.65 95% CI -1.11, -0.20] and vitamin E by 0.55 [95% CI -0.65, -0.45].

At the same time, a significant increase in HbA1c was found through the supplementation of diabetes-specific oral nutritional supplements (+1.85% [95%

CI 1.02, 2.68]). A significant increase of 8.96 µmol/L [95% CI 0.99, 16.93] was also found for the influence of zinc, vitamins and minerals on insulin. Furthermore, yeast supplementation significantly increased QUICKI (+0.02 [95% CI 0.01, 0.03]) and melatonin and zinc supplementation significantly incrased C-Peptide levels (+0.38 ng/mL [95% CI 0.04, 0.72]).

Hence, it can be said that certain supplements such as probiotics, prebiotics, flaxseed, vitamin C and E, silymarin and berberine can have a positive influence on certain type 2 diabetics' glycaemic outcomes such as HbA1c, glucose, insulin and HOMA-IR. Thus, supplement usage should be considered as a (complementary) therapy option for diabetes. However, further trials of the same study design should be performed with those supplements that resulted in considerable decreases in parameters such as probiotics, prebiotics, flaxseed, vitamin C and E, silymarin and berberine in the first few trials.

12 Zusammenfassung

Typ 2 Diabetes, früher auch bekannt als nicht-insulinabhängiger Diabetes mellitus (NIDDM) oder Altersdiabetes, ist gekennzeichnet durch eine Unfähigkeit des Körpers, Insulin zu verarbeiten (1). Dieser Diabetestyp macht ca. 90-95% aller Diabetesfälle aus (2). Eine Ernährungsumstellung, Bewegung, Gewichtsreduktion, Blutzucker senkende Mittel, Insulinspritzen und vielleicht auch Nahrungsmittelsupplemente sind Möglichkeiten, den Blutzucker zu kontrollieren und die Insulinresistenz zu verbessern (6). Im Rahmen dieses systematischen Reviews/ dieser Meta-Analyse sollte der Einfluss von Nahrungsergänzungsmitteln auf die glykämischen Parameter erwachsener Typ 2 Diabetiker untersucht werden. 122 randomisierte kontrollierte Studien mit einer Mindestdauer von 12 Wochen wurden in den Review aufgenommen. 105 dieser Studien konnten in die Meta-Analyse eingeschlossen werden. Die statistische Analyse wurde mit dem Review Manager 5.3 (Nordic Cochrane Center, Kopenhagen) durchgeführt.

26 der 56 verschiedenen Supplementen und Kombinationen von Ergänzungsmitteln führten zu statistisch signifikanten Änderungen der Outcome-Parameter. Zum Beispiel wurde der Parameter HbA1c durch Aminosäuren um 0,36% [95% Konfidenzintervall (KI) -0,67; -0,05], durch Präbiotika um 0,38% [95% KI -0,60; -0,16], durch Vitamin E um 0,56% [95% KI -0,83; -0,29], durch Leinsamen um 0,54% [95% KI -0,95; -0,12], durch Berberin um 0,66% [95% KI -1,00; -0,33] und durch Silymarin um 1,92% [95% KI -3,32; -0,51] reduziert. Der Blutglukosespiegel wurde durch Aminosäuren um 0,40 mmol/L [95% KI -0,48; -0,32], durch Präbiotika um 0,83 mmol/L [95% KI -1,55; -0,10], durch Leinsamen um 0,98 mmol/L [95% KI -1,18; -0,79], durch Berberin um 0,76 mmol/L [95% KI -1,24; -0,29], durch Silymarin um 2,11 mmol/L [95% KI -3,69; -0,53], durch Vitamin C um 0,65 mmol/L [95% KI -1,07; -0,23], durch Probiotika um 0,85 mmol/L [95% KI -1,50; -0,21] und durch Diacylglycerol um 0,74 mmol/L [95% KI -1,39; -0,09] gesenkt. Vitamin C verringerte den Insulinlevel um 2,66 µU/mL [95% KI -4,51; -0,82] statistisch signifikant und HOMA-IR wurde durch Aminosäuren um 0,65 95% KI -1,11; -0,20] und durch Vitamin E um 0,55 [95% KI -0,65; -0,45] signifikant reduziert.

Gleichzeitig wurde jedoch der HbA1c-Wert durch Diabetes-spezifische orale Nahrungsmittelsupplemente signifikant erhöht (+1;85% [95% KI 1;02; 2;68]). Darüber hinaus führte die Supplementation von einer Kombination aus Zink, Vitaminen und Mineralstoffen zu einem Insulinanstieg um 8,96 µmol/L [95% KI 0;99; 16;93]. Außerdem steigerten Hefen den QUICKI um 0,02 [95% KI 0.01; 0.03] und C-Peptid nahm durch eine Kombination von Melatonin und Zink um 0,38 ng/mL [95% KI 0.04; 0.72] zu.

Diese Ergebnisse erlauben die Schlussfolgerung, dass gewisse Supplemente wie Pro- oder Präbiotika, Leinsamen, Vitamin C oder E, Silymarin und Berberin einen positiven Einfluss auf bestimmte glykämische Parameter diabetischer Patienten wie HbA1c, Blutzucker, Insulin und HOMA-IR haben können. Nahrungsergänzungsmittel sollten daher als (zusätzliche) Therapiemöglichkeit für Diabetes in Erwägung gezogen werden. Allerdings sollten noch weitere Studien desselben Studiendesigns mit denjenigen Supplementen, die bis jetzt zu bedeutenden Abnahmen geführt haben, wie Pro- und Präbiotika, Leinsamen, Vitamin C und E, Silymarin und Berberin, durchgeführt werden.

13 References

1. World Health Organization G. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: Diagnosis and classification of diabetes mellitus., 1999.
2. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2011;34 Suppl 1:S62-9. doi: 10.2337/dc11-S062.
3. Collaborators GBDCoD. Global, regional, and national age-sex specific mortality for 264 causes of death, 1980-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet (London, England) 2017;390(10100):1151-210. doi: 10.1016/S0140-6736(17)32152-9.
4. Disease GBD, Injury I, Prevalence C. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet (London, England) 2017;390(10100):1211-59. doi: 10.1016/S0140-6736(17)32154-2.
5. DALYs GBD, Collaborators H. Global, regional, and national disability-adjusted life-years (DALYs) for 333 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet (London, England) 2017;390(10100):1260-344. doi: 10.1016/S0140-6736(17)32130-X.
6. Asante E. Interventions to promote treatment adherence in type 2 diabetes mellitus. Br J Community Nurs 2013;18(6):267-74. doi: 10.12968/bjcn.2013.18.6.267.
7. World Health Organization G. Global report on diabetes. 2016.
8. International Diabetes Federation. IDF Diabetes Atlas Globally, IDF 2013;6th edition.
9. World Health Organization. The global burden of disease: 2004 update. 2004.
10. Information Evidence and Research (IER). Prevalence of raised fasting blood glucose, ages 18+, 2014. WHO, 2016.
11. Zatalia SR, Sanusi H. The role of antioxidants in the pathophysiology, complications, and management of diabetes mellitus. Acta medica Indonesiana 2013;45(2):141-7.
12. Valdes-Ramos R, Guadarrama-Lopez AL, Martinez-Carrillo BE, Benitez-Arciniega AD. Vitamins and type 2 diabetes mellitus. Endocrine, metabolic & immune disorders drug targets 2015;15(1):54-63.
13. American Diabetes Association. Economic costs of diabetes in the U.S. in 2012. Diabetes Care 2013;36(4):1033-46.
14. Agarwal AA, Jadhav PR, Deshmukh YA. Prescribing pattern and efficacy of anti-diabetic drugs in maintaining optimal glycemic levels in diabetic patients. Journal of basic and clinical pharmacy 2014;5(3):79-83. doi: 10.4103/0976-0105.139731.
15. Nagpal J, Bhartia A. Quality of diabetes care in the middle- and high-income group populace: the Delhi Diabetes Community (DEDICOM) survey. Diabetes Care 2006;29(11):2341-8. doi: 10.2337/dc06-0783.
16. Valeron PF, de Pablos-Velasco PL. [Limitations of insulin-dependent drugs in the treatment of type 2 diabetes mellitus]. Medicina clinica 2013;141 Suppl 2:20-5. doi: 10.1016/S0025-7753(13)70059-9.
17. Hanefeld M, Ganz X, Nolte C. [Hypoglycemia and cardiac arrhythmia in patients with diabetes mellitus type 2]. Herz 2014;39(3):312-9. doi: 10.1007/s00059-014-4086-1.
18. Nahin RL, Barnes PM, Stussman BJ. Expenditures on Complementary Health Approaches: United States, 2012. National health statistics reports 2016(95):1-11.
19. ORF. Gefährliches Geschäft mit Magnesium und Co. Internet: help.orf.at/stories/2820569. (19.01.2017). (accessed on 29 September 2017)
20. Verbraucherzentrale. Umfrage: Das halten Verbraucher von Nahrungsergänzungsmitteln. Internet: https://www.verbraucherzentrale.de/umfrage-das-halten-verbraucher-von-nahrungsergaenzungsmitteln. (02.01.2017). (accessed on 20 September 2017)
21. Akbari Fakhrabadi M, Zeinali Ghotrom A, Mozaffari-Khosravi H, Hadi Nodoushan H, Nadjarzadeh A. Effect of Coenzyme Q10 on Oxidative Stress, Glycemic Control and Inflammation in Diabetic Neuropathy: A Double Blind Randomized Clinical Trial. International journal for vitamin and nutrition research Internationale Zeitschrift fur Vitamin- und Ernahrungsforschung Journal international de vitaminologie et de nutrition 2014;84(5-6):252-60. doi: 10.1024/0300-9831/a000211.
22. Akilen R, Tsiami A, Devendra D, Robinson N. Glycated haemoglobin and blood pressure-lowering effect of cinnamon in multi-ethnic Type 2 diabetic patients in the UK: a randomized,

placebo-controlled, double-blind clinical trial. Diabetic medicine : a journal of the British Diabetic Association 2010;27(10):1159-67. doi: 10.1111/j.1464-5491.2010.03079.x.
23. Al-Maroof RA, Al-Sharbatti SS. Serum zinc levels in diabetic patients and effect of zinc supplementation on glycemic control of type 2 diabetics. Saudi Medical Journal 2006;27(3):344-50.
24. Anderson RA, Cheng N, Bryden NA, Polansky MM, Cheng N, Chi J, Feng J. Elevated intakes of supplemental chromium improve glucose and insulin variables in individuals with type 2 diabetes. Diabetes 1997;46(11):1786-91.
25. Anderson RA, Roussel AM, Zouari N, Mahjoub S, Matheau JM, Kerkeni A. Potential antioxidant effects of zinc and chromium supplementation in people with type 2 diabetes mellitus. Journal of the American College of Nutrition 2001;20(3):212-8.
26. Aro A, Uusitupa M, Voutilainen E, Hersio K, Korhonen T, Siitonen O. Improved diabetic control and hypocholesterolaemic effect induced by long-term dietary supplementation with guar gum in type 2 (insulin-independent) diabetes. Diabetologia 1981;21(1):29-33.
27. Ashraf R, Khan RA, Ashraf I. Garlic (Allium sativum) supplementation with standard antidiabetic agent provides better diabetic control in type 2 diabetes patients. Pak J Pharm Sci 2011;24(4):565-70.
28. Barchetta I, Del Ben M, Angelico F, Di Martino M, Fraioli A, La Torre G, Saulle R, Perri L, Morini S, Tiberti C, et al. No effects of oral vitamin D supplementation on non-alcoholic fatty liver disease in patients with type 2 diabetes: a randomized, double-blind, placebo-controlled trial. BMC medicine 2016;14:92. doi: 10.1186/s12916-016-0638-y.
29. Barre DE, Mizier-Barre KA, Griscti O, Hafez K. High dose flaxseed oil supplementation may affect fasting blood serum glucose management in human type 2 diabetics. Journal of oleo science 2008;57(5):269-73.
30. Bonsu NKA, Johnson S. Effects of inulin fibre Supplementation on Serum Glucose and Lipid Concentration in Patients with Type 2 Diabetes. Int J Diabetes & Metab 2012;21:80-6.
31. Boshtam M, Rafiei M, Golshadi ID, Ani M, Shirani Z, Rostamshirazi M. Long term effects of oral vitamin E supplement in type II diabetic patients. International journal for vitamin and nutrition research Internationale Zeitschrift fur Vitamin- und Ernahrungsforschung Journal international de vitaminologie et de nutrition 2005;75(5):341-6. doi: 10.1024/0300-9831.75.5.341.
32. Breslavsky A, Frand J, Matas Z, Boaz M, Barnea Z, Shargorodsky M. Effect of high doses of vitamin D on arterial properties, adiponectin, leptin and glucose homeostasis in type 2 diabetic patients. Clinical nutrition (Edinburgh, Scotland) 2013;32(6):970-5. doi: 10.1016/j.clnu.2013.01.020.
33. Cheng HH, Huang HY, Chen YY, Huang CL, Chang CJ, Chen HL, Lai MH. Ameliorative effects of stabilized rice bran on type 2 diabetes patients. Annals of nutrition & metabolism 2010;56(1):45-51. doi: 10.1159/000265850.
34. Cruz M, Maldonado-Bernal C, Mondragon-Gonzalez R, Sanchez-Barrera R, Wacher NH, Carvajal-Sandoval G, Kumate J. Glycine treatment decreases proinflammatory cytokines and increases interferon-gamma in patients with type 2 diabetes. J Endocrinol Invest 2008;31(8):694-9.
35. Dakhale GN, Chaudhari HV, Shrivastava M. Supplementation of vitamin C reduces blood glucose and improves glycosylated hemoglobin in type 2 diabetes mellitus: a randomized, double-blind study. Advances in pharmacological sciences 2011;2011:195271. doi: 10.1155/2011/195271.
36. Dans AM, Villarruz MV, Jimeno CA, Javelosa MA, Chua J, Bautista R, Velez GG. The effect of Momordica charantia capsule preparation on glycemic control in type 2 diabetes mellitus needs further studies. Journal of clinical epidemiology 2007;60(6):554-9. doi: 10.1016/j.jclinepi.2006.07.009.
37. de Oliveira AM, Rondo PH, Luzia LA, D'Abronzo FH, Illison VK. The effects of lipoic acid and alpha-tocopherol supplementation on the lipid profile and insulin sensitivity of patients with type 2 diabetes mellitus: a randomized, double-blind, placebo-controlled trial. Diabetes Res Clin Pract 2011;92(2):253-60. doi: 10.1016/j.diabres.2011.02.010.
38. Derosa G, Maffioli P, Ferrari I, D'Angelo A, Fogari E, Palumbo I, Randazzo S, Cicero AF. Comparison between orlistat plus l-carnitine and orlistat alone on inflammation parameters in obese diabetic patients. Fundamental & clinical pharmacology 2011;25(5):642-51. doi: 10.1111/j.1472-8206.2010.00888.x.

39. Derosa G, Maffioli P, Salvadeo SA, Ferrari I, Gravina A, Mereu R, D'Angelo A, Palumbo I, Randazzo S, Cicero AF. Sibutramine and L-carnitine compared to sibutramine alone on insulin resistance in diabetic patients. Internal medicine (Tokyo, Japan) 2010;49(16):1717-25.
40. Derosa G, Cicero AF, Gaddi A, Mugellini A, Ciccarelli L, Fogari R. The effect of L-carnitine on plasma lipoprotein(a) levels in hypercholesterolemic patients with type 2 diabetes mellitus. Clinical therapeutics 2003;25(5):1429-39.
41. Derosa G, D'Angelo A, Romano D, Maffioli P. A Clinical Trial about a Food Supplement Containing alpha-Lipoic Acid on Oxidative Stress Markers in Type 2 Diabetic Patients. Int J Mol Sci 2016;17(11). doi: 10.3390/ijms17111802.
42. de Valk HW, Verkaaik R, van Rijn HJ, Geerdink RA, Struyvenberg A. Oral magnesium supplementation in insulin-requiring Type 2 diabetic patients. Diabetic medicine : a journal of the British Diabetic Association 1998;15(6):503-7. doi: 10.1002/(sici)1096-9136(199806)15:6<503::aid-dia596>3.0.co;2-m.
43. Eftekhari MH, Akbarzadeh M, Dabbaghmanesh MH, Hasanzadeh J. Impact of treatment with oral calcitriol on glucose indices in type 2 diabetes mellitus patients. Asia Pacific journal of clinical nutrition 2011;20(4):521-6.
44. Eibl NL, Kopp HP, Nowak HR, Schnack CJ, Hopmeier PG, Schernthaner G. Hypomagnesemia in type II diabetes: effect of a 3-month replacement therapy. Diabetes Care 1995;18(2):188-92.
45. Elwakeel NM, Hazaa HH. Effect of omega 3 fatty acids plus low-dose aspirin on both clinical and biochemical profiles of patients with chronic periodontitis and type 2 diabetes: a randomized double blind placebo-controlled study. Journal of periodontal research 2015;50(6):721-9. doi: 10.1111/jre.12257.
46. Eriksson J, Kohvakka A. Magnesium and ascorbic acid supplementation in diabetes mellitus. Annals of nutrition & metabolism 1995;39(4):217-23.
47. Faghihi T, Radfar M, Barmal M, Amini P, Qorbani M, Abdollahi M, Larijani B. A randomized, placebo-controlled trial of selenium supplementation in patients with type 2 diabetes: effects on glucose homeostasis, oxidative stress, and lipid profile. American journal of therapeutics 2014;21(6):491-5. doi: 10.1097/MJT.0b013e318269175f.
48. Fang ZH, Liu Y, Bao TT, Ni YQ, Liu J, Shi GB, Wu JP, Yang JP, Zhang H. Effect of Danzhijiangtang capsule on monocyte chemoattractant protein-1 mRNA expression in newly diagnosed diabetes subclinical vascular lesions. World J Gastroenterol 2013;19(19):2963-8. doi: 10.3748/wjg.v19.i19.2963.
49. Farvid MS, Jalali M, Siassi F, Hosseini M. Comparison of the effects of vitamins and/or mineral supplementation on glomerular and tubular dysfunction in type 2 diabetes. Diabetes Care 2005;28(10):2458-64.
50. Feinglos MN, Gibb RD, Ramsey DL, Surwit RS, McRorie JW. Psyllium improves glycemic control in patients with type-2 diabetes mellitus. Bioactive Carbohydrates and Dietary Fibre 2013;I:156-61.
51. Fenercioglu AK, Saler T, Genc E, Sabuncu H, Altuntas Y. The effects of polyphenol-containing antioxidants on oxidative stress and lipid peroxidation in Type 2 diabetes mellitus without complications. J Endocrinol Invest 2010;33(2):118-24. doi: 10.3275/6564.
52. Firouzi S, Majid HA, Ismail A, Kamaruddin NA, Barakatun-Nisak MY. 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(4):1535-50. doi: 10.1007/s00394-016-1199-8.
53. Foster M, Chu A, Petocz P, Samman S. Zinc transporter gene expression and glycemic control in post-menopausal women with Type 2 diabetes mellitus. Journal of trace elements in medicine and biology : organ of the Society for Minerals and Trace Elements (GMS) 2014;28(4):448-52. doi: 10.1016/j.jtemb.2014.07.012.
54. Ginter E, Zdichynec B, Holzerova O, Ticha E, Kobza R, Koziakova M, Cerna O, Ozdin L, Hruba F, Novakova V, et al. Hypocholesterolemic effect of ascorbic acid in maturity-onset diabetes mellitus. International journal for vitamin and nutrition research Internationale Zeitschrift fur Vitamin- und Ernahrungsforschung Journal international de vitaminologie et de nutrition 1978;48(4):368-73.
55. Goh KP, Lee HY, Lau DP, Supaat W, Chan YH, Koh AF. Effects of resveratrol in patients with type 2 diabetes mellitus on skeletal muscle SIRT1 expression and energy expenditure. International journal of sport nutrition and exercise metabolism 2014;24(1):2-13. doi: 10.1123/ijsnem.2013-0045.

56. Grotz VL, Henry RR, McGill JB, Prince MJ, Shamoon H, Trout JR, Pi-Sunyer X. Lack of effect of sucralose on glucose homeostasis in subjects with type 2 diabetes. Journal of the American Dietetic Association 2003;103(12):1607-12. doi: 10.1016/s0002-8223(03)01364-6.
57. Gualano B, V DESP, Roschel H, Artioli GG, Neves M, Jr., De Sa Pinto AL, Da Silva ME, Cunha MR, Otaduy MC, Leite Cda C, et al. Creatine in type 2 diabetes: a randomized, double-blind, placebo-controlled trial. Medicine and science in sports and exercise 2011;43(5):770-8. doi: 10.1249/MSS.0b013e3181fcee7d.
58. Guimaraes MM, Martins Silva Carvalho AC, Silva MS. Chromium nicotinate has no effect on insulin sensitivity, glycemic control, and lipid profile in subjects with type 2 diabetes. J Am Coll Nutr 2013;32(4):243-50. doi: 10.1080/07315724.2013.816598.
59. Gullestad L, Jacobsen T, Dolva LO. Effect of magnesium treatment on glycemic control and metabolic parameters in NIDDM patients. Diabetes Care 1994;17(5):460-1.
60. Gunasekara P, Hettiarachchi M, Liyanage C, Lekamwasam S. Effects of zinc and multimineral vitamin supplementation on glycemic and lipid control in adult diabetes. Diabetes, metabolic syndrome and obesity : targets and therapy 2011;4:53-60. doi: 10.2147/DMSO.S16691.
61. Hosseinzadeh P, Javanbakht MH, Mostafavi SA, Djalali M, Derakhshanian H, Hajianfar H, Bahonar A, Djazayery A. Brewer's Yeast Improves Glycemic Indices in Type 2 Diabetes Mellitus. Int J Prev Med 2013;4(10):1131-8.
62. Hosseinzadeh-Attar M, Kolahdouz Mohammadi R, Eshraghian M, Nakhjavani M, Khorrami E, Ebadi M, Esteghamati A. Reduction in asymmetric dimethylarginine plasma levels by coenzyme Q10 supplementation in patients with type 2 diabetes mellitus. Minerva endocrinologica 2015;40(4):259-66.
63. Hove KD, Brons C, Faerch K, Lund SS, Rossing P, Vaag A. Effects of 12 weeks of treatment with fermented milk on blood pressure, glucose metabolism and markers of cardiovascular risk in patients with type 2 diabetes: a randomised double-blind placebo-controlled study. European Journal of Endocrinology 2015;172(1). doi: 10.1530/eje-14-0554.
64. Hsia SH, Bazargan M, Davidson MB. Effect of Pancreas Tonic (an ayurvedic herbal supplement) in type 2 diabetes mellitus. Metabolism: clinical and experimental 2004;53(9):1166-73.
65. Hsu CH, Liao YL, Lin SC, Hwang KC, Chou P. The mushroom Agaricus blazei Murill in combination with metformin and gliclazide improves insulin resistance in type 2 diabetes: A randomized, double-blinded, and placebo-controlled clinical trial. Journal of Alternative and Complementary Medicine 2007;13(1):97-102. doi: 10.1089/acm.2006.6054.
66. Hsu CH, Liao YL, Lin SC, Tsai TH, Huang CJ, Chou P. Does supplementation with green tea extract improve insulin resistance in obese type 2 diabetics? A randomized, double-blind, and placebo-controlled clinical trial. Alternative medicine review : a journal of clinical therapeutic 2011;16(2):157-63.
67. Huseini HF, Larijani B, Heshmat R, Fakhrzadeh H, Radjabipour B, Toliat T, Raza M. The efficacy of Silybum marianum (L.) Gaertn. (silymarin) in the treatment of type II diabetes: a randomized, double-blind, placebo-controlled, clinical trial. Phytotherapy research : PTR 2006;20(12):1036-9. doi: 10.1002/ptr.1988.
68. Hussain SA. Silymarin as an adjunct to glibenclamide therapy improves long-term and postprandial glycemic control and body mass index in type 2 diabetes. J Med Food 2007;10(3):543-7. doi: 10.1089/jmf.2006.089.
69. Hussain SA, Khadim HM, Khalaf BH, Ismail SH, Hussein KI, Sahib AS. Effects of melatonin and zinc on glycemic control in type 2 diabetic patients poorly controlled with metformin. Saudi Med J 2006;27(10):1483-8.
70. Jafari T, Faghihimani E, Feizi A, Iraj B, Javanmard SH, Esmaillzadeh A, Fallah AA, Askari G. Effects of vitamin D-fortified low fat yogurt on glycemic status, anthropometric indexes, inflammation, and bone turnover in diabetic postmenopausal women: A randomised controlled clinical trial. Clinical nutrition (Edinburgh, Scotland) 2016;35(1):67-76. doi: 10.1016/j.clnu.2015.02.014.
71. Jayagopal V, Albertazzi P, Kilpatrick ES, Howarth EM, Jennings PE, Hepburn DA, Atkin SL. Beneficial effects of soy phytoestrogen intake in postmenopausal women with type 2 diabetes. Diabetes Care 2002;25(10):1709-14. doi: 10.2337/diacare.25.10.1709.
72. Jorde R, Figenschau Y. Supplementation with cholecalciferol does not improve glycaemic control in diabetic subjects with normal serum 25-hydroxyvitamin D levels. Eur J Nutr 2009;48(6):349-54. doi: 10.1007/s00394-009-0020-3.

73. Kaatabi H, Bamosa AO, Badar A, Al-Elq A, Abou-Hozaifa B, Lebda F, Al-Khadra A, Al-Almaie S. Nigella sativa improves glycemic control and ameliorates oxidative stress in patients with type 2 diabetes mellitus: placebo controlled participant blinded clinical trial. PLoS One 2015;10(2):e0113486. doi: 10.1371/journal.pone.0113486.
74. Kajanachumpol S, Srisurapanon S, Supanit I, Roongpisuthipong C, Apibal S. Effect of zinc supplementation on zinc status, copper status and cellular immunity in elderly patients with diabetes mellitus. Journal of the Medical Association of Thailand = Chotmaihet thangphaet 1995;78(7):344-9.
75. Kampmann U, Mosekilde L, Juhl C, Moller N, Christensen B, Rejnmark L, Wamberg L, Orskov L. Effects of 12 weeks high dose vitamin D3 treatment on insulin sensitivity, beta cell function, and metabolic markers in patients with type 2 diabetes and vitamin D insufficiency - a double-blind, randomized, placebo-controlled trial. Metabolism: clinical and experimental 2014;63(9):1115-24. doi: 10.1016/j.metabol.2014.06.008.
76. Kleefstra N, Houweling ST, Jansman FG, Groenier KH, Gans RO, Meyboom-de Jong B, Bakker SJ, Bilo HJ. Chromium treatment has no effect in patients with poorly controlled, insulin-treated type 2 diabetes in an obese Western population: a randomized, double-blind, placebo-controlled trial. Diabetes Care 2006;29(3):521-5.
77. Krul-Poel YH, Westra S, ten Boekel E, ter Wee MM, van Schoor NM, van Wijland H, Stam F, Lips PT, Simsek S. Effect of Vitamin D Supplementation on Glycemic Control in Patients With Type 2 Diabetes (SUNNY Trial): A Randomized Placebo-Controlled Trial. Diabetes Care 2015;38(8):1420-6. doi: 10.2337/dc15-0323.
78. Lasaite L, Spadiene A, Savickiene N, Skesters A, Silova A. The effect of Ginkgo biloba and Camellia sinensis extracts on psychological state and glycemic control in patients with type 2 diabetes mellitus. Natural product communications 2014;9(9):1345-50.
79. Lee IT, Chan YC, Lin CW, Lee WJ, Sheu WH. Effect of cranberry extracts on lipid profiles in subjects with Type 2 diabetes. Diabetic medicine : a journal of the British Diabetic Association 2008;25(12):1473-7. doi: 10.1111/j.1464-5491.2008.02588.x.
80. Leenders M, Verdijk LB, van der Hoeven L, van Kranenburg J, Hartgens F, Wodzig WK, Saris WH, van Loon LJ. Prolonged leucine supplementation does not augment muscle mass or affect glycemic control in elderly type 2 diabetic men. The Journal of nutrition 2011;141(6):1070-6. doi: 10.3945/jn.111.138495.
81. Levin ER, Hanscom TA, Fisher M, Lauvstad WA, Lui A, Ryan A, Glockner D, Levin SR. The influence of pyridoxine in diabetic peripheral neuropathy. Diabetes Care 1981;4(6):606-9.
82. Li D, Zhang Y, Liu Y, Sun R, Xia M. Purified anthocyanin supplementation reduces dyslipidemia, enhances antioxidant capacity, and prevents insulin resistance in diabetic patients. The Journal of nutrition 2015;145(4):742-8. doi: 10.3945/jn.114.205674.
83. Li D, Xu T, Takase H, Tokimitsu I, Zhang P, Wang Q, Yu X, Zhang A. Diacylglycerol-induced improvement of whole-body insulin sensitivity in type 2 diabetes mellitus: a long-term randomized, double-blind controlled study. Clinical nutrition (Edinburgh, Scotland) 2008;27(2):203-11. doi: 10.1016/j.clnu.2008.01.009.
84. Liu CY, Huang CJ, Huang LH, Chen IJ, Chiu JP, Hsu CH. Effects of Green Tea Extract on Insulin Resistance and Glucagon-Like Peptide 1 in Patients with Type 2 Diabetes and Lipid Abnormalities: A Randomized, Double-Blinded, and Placebo-Controlled Trial. Plos One 2014;9(3). doi: 10.1371/journal.pone.0091163.
85. Ludvik B, Hanefeld M, Pacini G. Improved metabolic control by Ipomoea batatas (Caiapo) is associated with increased adiponectin and decreased fibrinogen levels in type 2 diabetic subjects. Diabetes, obesity & metabolism 2008;10(7):586-92. doi: 10.1111/j.1463-1326.2007.00752.x.
86. Mackenzie T, Leary L, Brooks WB. The effect of an extract of green and black tea on glucose control in adults with type 2 diabetes mellitus: double-blind randomized study. Metabolism: clinical and experimental 2007;56(10):1340-4. doi: 10.1016/j.metabol.2007.05.018.
87. Magnoni D, Rouws CH, Lansink M, van Laere KM, Campos AC. Long-term use of a diabetes-specific oral nutritional supplement results in a low-postprandial glucose response in diabetes patients. Diabetes Res Clin Pract 2008;80(1):75-82. doi: 10.1016/j.diabres.2007.10.027.
88. Malaguarnera M, Vacante M, Avitabile T, Malaguarnera M, Cammalleri L, Motta M. L-Carnitine supplementation reduces oxidized LDL cholesterol in patients with diabetes. The American journal of clinical nutrition 2009;89(1):71-6. doi: 10.3945/ajcn.2008.26251.

89. Manzella D, Barbieri M, Ragno E, Paolisso G. Chronic administration of pharmacologic doses of vitamin E improves the cardiac autonomic nervous system in patients with type 2 diabetes. The American journal of clinical nutrition 2001;73(6):1052-7.
90. Martin J, Wang ZQ, Zhang XH, Wachtel D, Volaufova J, Matthews DE, Cefalu WT. Chromium picolinate supplementation attenuates body weight gain and increases insulin sensitivity in subjects with type 2 diabetes. Diabetes Care 2006;29(8):1826-32. doi: 10.2337/dc06-0254.
91. Mashavi M, Hanah R, Boaz M, Gavish D, Matas Z, Fux A, Shargorodsky M. Effect of homocysteine-lowering therapy on arterial elasticity and metabolic parameters in metformin-treated diabetic patients. Atherosclerosis 2008;199(2):362-7. doi: 10.1016/j.atherosclerosis.2007.11.037.
92. Mason SA, Della Gatta PA, Snow RJ, Russell AP, Wadley GD. Ascorbic acid supplementation improves skeletal muscle oxidative stress and insulin sensitivity in people with type 2 diabetes: Findings of a randomized controlled study. Free radical biology & medicine 2016;93:227-38. doi: 10.1016/j.freeradbiomed.2016.01.006.
93. Mayr P, Kuhn KS, Klein P, Stover JF, Pestana EA. A Diabetes-specific Oral Nutritional Supplement Improves Glycaemic Control in Type 2 Diabetes Patients. Experimental and clinical endocrinology & diabetes : official journal, German Society of Endocrinology [and] German Diabetes Association 2016;124(7):401-9. doi: 10.1055/s-0042-100909.
94. McManus RM, Jumpson J, Finegood DT, Clandinin MT, Ryan EA. A comparison of the effects of n-3 fatty acids from linseed oil and fish oil in well-controlled type II diabetes. Diabetes Care 1996;19(5):463-7.
95. Mehrdadi P, Kolahdouz Mohammadi R, Alipoor E, Eshraghian MR, Esteghamati A, Hosseinzadeh-Attar MJ. The Effect of Coenzyme Q10 Supplementation on Circulating Levels of Novel Adipokine Adipolin/CTRP12 in Overweight and Obese Patients with Type 2 Diabetes. Experimental and clinical endocrinology & diabetes : official journal, German Society of Endocrinology [and] German Diabetes Association 2017;125(3):156-62. doi: 10.1055/s-0042-110570.
96. Mirfeizi M, Mehdizadeh Tourzani Z, Mirfeizi SZ, Asghari Jafarabadi M, Rezvani HR, Afzali M. Controlling type 2 diabetes mellitus with herbal medicines: A triple-blind randomized clinical trial of efficacy and safety. J Diabetes 2016;8(5):647-56. doi: 10.1111/1753-0407.12342.
97. Mitra A, Bhattacharya D. Effects of longlerm study of combination of neutraceuticals in non-insulindependent diabetes mellitus patients. Journal of Food Science and Technology-Mysore 2006;43(5):477-83.
98. Mobini R, Tremaroli V, Stahlman M, Karlsson F, Levin M, Ljungberg M, Sohlin M, Perkins R, Perkins R, Baackhed F, et al. Metabolic effects of Lactobacillus reuteri DSM 17938 in people with type 2 diabetes: A randomized controlled trial. Diabetes Obesity & Metabolism 2017;19(4):579-89. doi: 10.1111/dom.12861.
99. Morgan WA, Raskin P, Rosenstock J. A comparison of fish oil or corn oil supplements in hyperlipidemic subjects with NIDDM. Diabetes Care 1995;18(1):83-6.
100. Navarrete-Cortes A, Ble-Castillo JL, Guerrero-Romero F, Cordova-Uscanga R, Juarez-Rojop IE, Aguilar-Mariscal H, Tovilla-Zarate CA, Lopez-Guevara Mdel R. No effect of magnesium supplementation on metabolic control and insulin sensitivity in type 2 diabetic patients with normomagnesemia. Magnes Res 2014;27(2):48-56. doi: 10.1684/mrh.2014.0361.
101. Niemi MK, Keinanen-Kiukaanniemi SM, Salmela PI. Long-term effects of guar gum and microcrystalline cellulose on glycaemic control and serum lipids in type 2 diabetes. European journal of clinical pharmacology 1988;34(4):427-9.
102. Nikooyeh B, Neyestani TR, Tayebinejad N, Alavi-Majd H, Shariatzadeh N, Kalayi A, Zahedirad M, Heravifard S, Salekzamani S. Daily intake of vitamin D- or calcium-vitamin D-fortified Persian yogurt drink (doogh) attenuates diabetes-induced oxidative stress: evidence for antioxidative properties of vitamin D. Journal of human nutrition and dietetics : the official journal of the British Dietetic Association 2014;27 Suppl 2:276-83. doi: 10.1111/jhn.12142.
103. Nikooyeh B, Neyestani TR, Farvid M, Alavi-Majd H, Houshiarrad A, Kalayi A, Shariatzadeh N, Gharavi A, Heravifard S, Tayebinejad N, et al. Daily consumption of vitamin D- or vitamin D + calcium-fortified yogurt drink improved glycemic control in patients with type 2 diabetes: a randomized clinical trial. The American journal of clinical nutrition 2011;93(4):764-71. doi: 10.3945/ajcn.110.007336.
104. Norris LE, Collene AL, Asp ML, Hsu JC, Liu LF, Richardson JR, Li D, Bell D, Osei K, Jackson RD, et al. Comparison of dietary conjugated linoleic acid with safflower oil on body

composition in obese postmenopausal women with type 2 diabetes mellitus. The American journal of clinical nutrition 2009;90(3):468-76. doi: 10.3945/ajcn.2008.27371.
105. Ogawa S, Abe T, Nako K, Okamura M, Senda M, Sakamoto T, Ito S. Eicosapentaenoic acid improves glycemic control in elderly bedridden patients with type 2 diabetes. The Tohoku journal of experimental medicine 2013;231(1):63-74.
106. Pan A, Sun J, Chen Y, Ye X, Li H, Yu Z, Wang Y, Gu W, Zhang X, Chen X, et al. Effects of a flaxseed-derived lignan supplement in type 2 diabetic patients: a randomized, double-blind, cross-over trial. PLoS One 2007;2(11):e1148. doi: 10.1371/journal.pone.0001148.
107. Paolisso G, Balbi V, Volpe C, Varricchio G, Gambardella A, Saccomanno F, Ammendola S, Varricchio M, D'Onofrio F. Metabolic benefits deriving from chronic vitamin C supplementation in aged non-insulin dependent diabetics. J Am Coll Nutr 1995;14(4):387-92.
108. Paolisso G, D'Amore A, Galzerano D, Balbi V, Giugliano D, Varricchio M, D'Onofrio F. Daily vitamin E supplements improve metabolic control but not insulin secretion in elderly type II diabetic patients. Diabetes Care 1993;16(11):1433-7.
109. Parham M, Heidari S, Khorramirad A, Hozoori M, Hosseinzadeh F, Bakhtyari L, Vafaeimanesh J. Effects of pistachio nut supplementation on blood glucose in patients with type 2 diabetes: a randomized crossover trial. The review of diabetic studies : RDS 2014;11(2):190-6. doi: 10.1900/rds.2014.11.190.
110. Pedersen C, Gallagher E, Horton F, Ellis RJ, Ijaz UZ, Wu HH, Jaiyeola E, Diribe O, Duparc T, Cani PD, et al. Host-microbiome interactions in human type 2 diabetes following prebiotic fibre (galacto-oligosaccharide) intake. British Journal of Nutrition 2016;116(11):1869-77. doi: 10.1017/s0007114516004086.
111. Pick ME, Hawrysh ZJ, Gee MI, Toth E, Garg ML, Hardin RT. Oat bran concentrate bread products improve long-term control of diabetes: a pilot study. J Am Diet Assoc 1996;96(12):1254-61. doi: 10.1016/s0002-8223(96)00329-x.
112. Racek J, Trefil L, Rajdl D, Mudrova V, Hunter D, Senft V. Influence of chromium-enriched yeast on blood glucose and insulin variables, blood lipids, and markers of oxidative stress in subjects with type 2 diabetes mellitus. Biol Trace Elem Res 2006;109(3):215-30. doi: 10.1385/bter:109:3:215.
113. Rodriguez-Moran M, Guerrero-Romero F. Elevated concentrations of C-reactive protein in subjects with type 2 diabetes mellitus are moderately influenced by glycemic control. J Endocrinol Invest 2003;26(3):216-21. doi: 10.1007/bf03345160.
114. Rotman-Pikielny P, Ness-Abramof R, Charach G, Roitman A, Zissin R, Levy Y. Efficacy and safety of the dietary supplement DBCare(R) in patients with type 2 diabetes mellitus and inadequate glycemic control. J Am Coll Nutr 2014;33(1):55-62. doi: 10.1080/07315724.2014.870008.
115. Roussel AM, Kerkeni A, Zouari N, Mahjoub S, Matheau JM, Anderson RA. Antioxidant effects of zinc supplementation in Tunisians with type 2 diabetes mellitus. Journal of the American College of Nutrition 2003;22(4):316-21.
116. Rytter E, Vessby B, Asgard R, Ersson C, Moussavian S, Sjodin A, Abramsson-Zetterberg L, Moller L, Basu S. Supplementation with a combination of antioxidants does not affect glycaemic control, oxidative stress or inflammation in type 2 diabetes subjects. Free radical research 2010;44(12):1445-53. doi: 10.3109/10715762.2010.515219.
117. Ryu OH, Lee S, Yu J, Choi MG, Yoo HJ, Mantero F. A prospective randomized controlled trial of the effects of vitamin D supplementation on long-term glycemic control in type 2 diabetes mellitus of Korea. Endocr J 2014;61(2):167-76.
118. Sarbolouki S, Javanbakht MH, Derakhshanian H, Hosseinzadeh P, Zareei M, Hashemi SB, Dorosty AR, Eshraghian MR, Djalali M. Eicosapentaenoic acid improves insulin sensitivity and blood sugar in overweight type 2 diabetes mellitus patients: a double-blind randomised clinical trial. Singapore medical journal 2013;54(7):387-90.
119. Scroggie DA, Albright A, Harris MD. The effect of glucosamine-chondroitin supplementation on glycosylated hemoglobin levels in patients with type 2 diabetes mellitus: a placebo-controlled, double-blinded, randomized clinical trial. Arch Intern Med 2003;163(13):1587-90. doi: 10.1001/archinte.163.13.1587.
120. Shab-Bidar S, Neyestani TR, Djazayery A. Vitamin D receptor Cdx-2-dependent response of central obesity to vitamin D intake in the subjects with type 2 diabetes: a randomised clinical trial. The British journal of nutrition 2015;114(9):1375-84. doi: 10.1017/s0007114515003049.

121. Shab-Bidar S, Neyestani TR, Djazayery A, Eshraghian MR, Houshiarrad A, Gharavi A, Kalayi A, Shariatzadeh N, Zahedirad M, Khalaji N, et al. Regular consumption of vitamin D-fortified yogurt drink (Doogh) improved endothelial biomarkers in subjects with type 2 diabetes: a randomized double-blind clinical trial. BMC medicine 2011;9:125. doi: 10.1186/1741-7015-9-125.
122. Shidfar F, Rajab A, Rahideh T, Khandouzi N, Hosseini S, Shidfar S. The effect of ginger (Zingiber officinale) on glycemic markers in patients with type 2 diabetes. Journal of complementary & integrative medicine 2015;12(2):165-70. doi: 10.1515/jcim-2014-0021.
123. Shimizu H, Ohtani K, Tanaka Y, Sato N, Mori M, Shimomura Y. Long-term effect of eicosapentaenoic acid ethyl (EPA-E) on albuminuria of non-insulin dependent diabetic patients. Diabetes Res Clin Pract 1995;28(1):35-40.
124. Solerte SB, Gazzaruso C, Schifino N, Locatelli E, Destro T, Ceresini G, Ferrari E, Fioravanti M. Metabolic effects of orally administered amino acid mixture in elderly subjects with poorly controlled type 2 diabetes mellitus. The American journal of cardiology 2004;93(8a):23a-9a. doi: 10.1016/j.amjcard.2003.11.006.
125. Solerte SB, Fioravanti M, Locatelli E, Bonacasa R, Zamboni M, Basso C, Mazzoleni A, Mansi V, Geroutis N, Gazzaruso C. Improvement of blood glucose control and insulin sensitivity during a long-term (60 weeks) randomized study with amino acid dietary supplements in elderly subjects with type 2 diabetes mellitus. The American journal of cardiology 2008;101(11a):82e-8e. doi: 10.1016/j.amjcard.2008.03.006.
126. Strobel F, Reusch J, Penna-Martinez M, Ramos-Lopez E, Klahold E, Klepzig C, Wehrle J, Kahles H, Badenhoop K. Effect of a randomised controlled vitamin D trial on insulin resistance and glucose metabolism in patients with type 2 diabetes mellitus. Hormone and metabolic research = Hormon- und Stoffwechselforschung = Hormones et metabolisme 2014;46(1):54-8. doi: 10.1055/s-0033-1358453.
127. Tajabadi-Ebrahimi M, Sharifi N, Farrokhian A, Raygan F, Karamali F, Razzaghi R, Taheri S, Asemi Z. A Randomized Controlled Clinical Trial Investigating the Effect of Synbiotic Administration on Markers of Insulin Metabolism and Lipid Profiles in Overweight Type 2 Diabetic Patients with - Coronary Heart Disease. Experimental and Clinical Endocrinology & Diabetes 2017;125(1):21-7. doi: 10.1055/s-0042-105441.
128. Taylor CG, Noto AD, Stringer DM, Froese S, Malcolmson L. Dietary milled flaxseed and flaxseed oil improve N-3 fatty acid status and do not affect glycemic control in individuals with well-controlled type 2 diabetes. J Am Coll Nutr 2010;29(1):72-80.
129. Turpeinen AK, Kuikka JT, Vanninen E, Yang J, Uusitupa MI. Long-term effect of acetyl-L-carnitine on myocardial 123I-MIBG uptake in patients with diabetes. Clinical autonomic research : official journal of the Clinical Autonomic Research Society 2000;10(1):13-6.
130. Tutuncu NB, Bayraktar M, Varli K. Reversal of defective nerve conduction with vitamin E supplementation in type 2 diabetes: a preliminary study. Diabetes Care 1998;21(11):1915-8.
131. Uusitupa M, Tuomilehto J, Karttunen P, Wolf E. Long term effects of guar gum on metabolic control, serum cholesterol and blood pressure levels in type 2 (non-insulin-dependent) diabetic patients with high blood pressure. Annals of clinical research 1984;16 Suppl 43:126-31.
132. Vaisman N, Niv E, Izkhakov Y. Catalytic amounts of fructose may improve glucose tolerance in subjects with uncontrolled non-insulin-dependent diabetes. Clinical nutrition (Edinburgh, Scotland) 2006;25(4):617-21. doi: 10.1016/j.clnu.2005.11.013.
133. von Hurst PR, Stonehouse W, Coad J. Vitamin D supplementation reducdes insulin resistance in South Asian women living in New Zealand who are insulin resistand and vitamin D deficient - a randomised, placebo-controlled trial. British Journal of Nutrition 2010;103:549-55.
134. Vuksan V, Sung MK, Sievenpiper JL, Stavro PM, Jenkins AL, Di Buono M, Lee KS, Leiter LA, Nam KY, Arnason JT, et al. Korean red ginseng (Panax ginseng) improves glucose and insulin regulation in well-controlled, type 2 diabetes: results of a randomized, double-blind, placebo-controlled study of efficacy and safety. Nutrition, metabolism, and cardiovascular diseases : NMCD 2008;18(1):46-56. doi: 10.1016/j.numecd.2006.04.003.
135. Wainstein J, Stern N, Heller S, Boaz M. Dietary cinnamon supplementation and changes in systolic blood pressure in subjects with type 2 diabetes. J Med Food 2011;14(12):1505-10. doi: 10.1089/jmf.2010.0300.
136. Watts GF, Playford DA, Croft KD, Ward NC, Mori TA, Burke V. Coenzyme Q(10) improves endothelial dysfunction of the brachial artery in Type II diabetes mellitus. Diabetologia 2002;45(3):420-6. doi: 10.1007/s00125-001-0760-y.

137. Wolffenbuttel BH, Sels JP, Heesen BJ, Menheere PP, Nieuwenhuijzen Kruseman AC. [Effects of dietary fiber and insulin treatment on serum levels of lipids and lipoprotein (a) in patients with type II diabetes mellitus]. Nederlands tijdschrift voor geneeskunde 1992;136(15):739-42.
138. Yin J, Xing H, Ye J. Efficacy of berberine in patients with type 2 diabetes mellitus. Metabolism: clinical and experimental 2008;57(5):712-7. doi: 10.1016/j.metabol.2008.01.013.
139. Yiu YF, Yiu KH, Siu CW, Chan YH, Li SW, Wong LY, Lee SW, Tam S, Wong EW, Lau CP, et al. Randomized controlled trial of vitamin D supplement on endothelial function in patients with type 2 diabetes. Atherosclerosis 2013;227(1):140-6. doi: 10.1016/j.atherosclerosis.2012.12.013.
140. Zhang Y, Li X, Zou D, Liu W, Yang J, Zhu N, Huo L, Wang M, Hong J, Wu P, et al. Treatment of type 2 diabetes and dyslipidemia with the natural plant alkaloid berberine. The Journal of clinical endocrinology and metabolism 2008;93(7):2559-65. doi: 10.1210/jc.2007-2404.
141. Zheng JS, Wang L, Lin M, Yang H, Li D. BMI status influences the response of insulin sensitivity to diacylglycerol oil in Chinese type 2 diabetic patients. Asia Pacific journal of clinical nutrition 2015;24(1):65-72. doi: 10.6133/apjcn.2015.24.1.01.
142. Zibadi S, Rohdewald PJ, Park D, Watson RR. Reduction of cardiovascular risk factors in subjects with type 2 diabetes by Pycnogenol supplementation. Nutrition research (New York, NY) 2008;28(5):315-20. doi: 10.1016/j.nutres.2008.03.003.
143. Uusitupa M, Kumpulainen J, Voutilainen E, Sarlund H, Hersio K, Pyorala K, Koivistoinen P, Lehto J. [The effect of chromium supplementation on glucose tolerance, insulin response and serum lipids in maturity-onset diabetes]. Duodecim; laaketieteellinen aikakauskirja 1984;100(1):29-34.
144. Voroneanu L, Nistor I, Dumea R, Apetrii M, Covic A. Silymarin in Type 2 Diabetes Mellitus: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. J Diabetes Res 2016;2016:5147468. doi: 10.1155/2016/5147468.
145. Tabatabaei-Malazy O, Nikfar S, Larijani B, Abdollahi M. Influence of ascorbic acid supplementation on type 2 diabetes mellitus in observational and randomized controlled trials; a systematic review with meta-analysis. Journal of pharmacy & pharmaceutical sciences : a publication of the Canadian Society for Pharmaceutical Sciences, Societe canadienne des sciences pharmaceutiques 2014;17(4):554-82.
146. Zhang QQ, Wu YC, Fei XQ. Effect of probiotics on glucose metabolism in patients with type 2 diabetes mellitus: A meta-analysis of randomized controlled trials. Medicina-Lithuania 2016;52(1):28-34. doi: 10.1016/j.medici.2015.11.008.
147. Sun J, Buys NJ. Glucose- and glycaemic factor-lowering effects of probiotics on diabetes: a meta-analysis of randomised placebo-controlled trials. British Journal of Nutrition 2016;115(7):1167-77. doi: 10.1017/s0007114516000076.
148. Samah S, Ramasamy K, Lim SM, Neoh CF. Probiotics for the management of type 2 diabetes mellitus: A systematic review and meta-analysis. Diabetes Research and Clinical Practice 2016;118:172-82. doi: 10.1016/j.diabres.2016.06.014.
149. Li CF, Li X, Han HQ, Cui HL, Peng M, Wang GL, Wang ZQ. Effect of probiotics on metabolic profiles in type 2 diabetes mellitus: A meta-analysis of randomized, controlled trials. Medicine 2016;95(26). doi: 10.1097/md.0000000000004088.
150. Yao K, Zeng L, He Q, Wang W, Lei J, Zou X. Effect of Probiotics on Glucose and Lipid Metabolism in Type 2 Diabetes Mellitus: A Meta-Analysis of 12 Randomized Controlled Trials. Medical science monitor : international medical journal of experimental and clinical research 2017;23:3044-53.
151. Kasinska MA, Drzewoski J. Effectiveness of probiotics in type 2 diabetes: a meta-analysis. Polskie Archiwum Medycyny Wewnetrznej-Polish Archives of Internal Medicine 2015;125(11):803-13.
152. Afzal S, Brondum-Jacobsen P, Bojesen SE, Nordestgaard BG. Genetically low vitamin D concentrations and increased mortality: Mendelian randomisation analysis in three large cohorts. Bmj 2014;349:g6330. doi: 10.1136/bmj.g6330.
153. Gagnon C, Lu ZX, Magliano DJ, Dunstan DW, Shaw JE, Zimmet PZ, Sikaris K, Grantham N, Ebeling PR, Daly RM. Serum 25-hydroxyvitamin D, calcium intake, and risk of type 2 diabetes after 5 years: results from a national, population-based prospective study (the Australian Diabetes, Obesity and Lifestyle study). Diabetes Care 2011;34(5):1133-8. doi: 10.2337/dc10-2167.

154. Knekt P, Laaksonen M, Mattila C, Harkanen T, Marniemi J, Heliovaara M, Rissanen H, Montonen J, Reunanen A. Serum vitamin D and subsequent occurrence of type 2 diabetes. Epidemiology 2008;19(5):666-71. doi: 10.1097/EDE.0b013e318176b8ad.
155. Liu S, Song Y, Ford ES, Manson JE, Buring JE, Ridker PM. Dietary calcium, vitamin D, and the prevalence of metabolic syndrome in middle-aged and older U.S. women. Diabetes Care 2005;28(12):2926-32.
156. Pittas AG, Dawson-Hughes B, Li T, Van Dam RM, Willett WC, Manson JE, Hu FB. Vitamin D and calcium intake in relation to type 2 diabetes in women. Diabetes Care 2006;29(3):650-6.
157. Song Y, Wang L, Pittas AG, Del Gobbo LC, Zhang C, Manson JE, Hu FB. Blood 25-hydroxy vitamin D levels and incident type 2 diabetes: a meta-analysis of prospective studies. Diabetes Care 2013;36(5):1422-8. doi: 10.2337/dc12-0962.
158. Guo J, Xiao Z, Xue X, Liu X, Lu Y, Yin X, Ma K. 25-Hydroxyvitamin D is closely related with the function of the pancreatic islet beta cells. Pak J Med Sci 2013;29(3):809-13.
159. Mitri J, Muraru MD, Pittas AG. Vitamin D and type 2 diabetes: a systematic review. Eur J Clin Nutr 2011;65(9):1005-15. doi: 10.1038/ejcn.2011.118.
160. van Etten E, Mathieu C. Immunoregulation by 1,25-dihydroxyvitamin D3: basic concepts. The Journal of steroid biochemistry and molecular biology 2005;97(1-2):93-101. doi: 10.1016/j.jsbmb.2005.06.002.
161. Wolden-Kirk H, Rondas D, Bugliani M, Korf H, Van Lommel L, Brusgaard K, Christesen HT, Schuit F, Proost P, Masini M, et al. Discovery of molecular pathways mediating 1,25-dihydroxyvitamin D3 protection against cytokine-induced inflammation and damage of human and male mouse islets of Langerhans. Endocrinology 2014;155(3):736-47. doi: 10.1210/en.2013-1409.
162. Mitri J, Pittas AG. Vitamin D and diabetes. Endocrinology and metabolism clinics of North America 2014;43(1):205-32. doi: 10.1016/j.ecl.2013.09.010.
163. Seshadri KGT, Rajendran BA. Role of Vitamin D on Diabetes. Endocrinol Mebol 2011;1(2):47-56.
164. Ebesunun MO, Obajobi EO. Elevated plasma homocysteine in type 2 diabetes mellitus: a risk factor for cardiovascular diseases. The Pan African medical journal 2012;12:48.
165. Polidori MC, Mecocci P, Stahl W, Parente B, Cecchetti R, Cherubini A, Cao P, Sies H, Senin U. Plasma levels of lipophilic antioxidants in very old patients with type 2 diabetes. Diabetes/metabolism research and reviews 2000;16(1):15-9.
166. Odum EP, Ejilemele AA, Wakwe VC. Antioxidant status of type 2 diabetic patients in Port Harcourt, Nigeria. Niger J Clin Pract 2012;15(1):55-8. doi: 10.4103/1119-3077.94099.
167. Mandl J, Szarka A, Banhegyi G. Vitamin C: update on physiology and pharmacology. British journal of pharmacology 2009;157(7):1097-110. doi: 10.1111/j.1476-5381.2009.00282.x.
168. Carter P, Gray LJ, Talbot D, Morris DH, Khunti K, Davies MJ. Fruit and vegetable intake and the association with glucose parameters: a cross-sectional analysis of the Let's Prevent Diabetes Study. Eur J Clin Nutr 2013;67(1):12-7. doi: 10.1038/ejcn.2012.174.
169. Mazloom Z, Hejazi N, Dabbaghmanesh MH, Tabatabaei HR, Ahmadi A, Ansar H. Effect of vitamin C supplementation on postprandial oxidative stress and lipid profile in type 2 diabetic patients. Pakistan journal of biological sciences : PJBS 2011;14(19):900-4.
170. Cruz KJC, de Oliveira ARS, Marreiro DD. Antioxidant role of zinc in diabetes mellitus. World Journal of Diabetes 2015;6(2):333-7. doi: 10.4239/wjd.v6.i2.333.
171. Carocho M, Ferreira IC. A review on antioxidants, prooxidants and related controversy: natural and synthetic compounds, screening and analysis methodologies and future perspectives. Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association 2013;51:15-25. doi: 10.1016/j.fct.2012.09.021.
172. Prasad AS. Zinc in human health: effect of zinc on immune cells. Molecular medicine 2008;14(5-6):353-7. doi: 10.2119/2008-00033.Prasad.
173. Vidal-Casariego A, Burgos-Pelaez R, Martinez-Faedo C, Calvo-Gracia F, Valero-Zanuy MA, Luengo-Perez LM, Cuerda-Compes C. Metabolic effects of L-carnitine on type 2 diabetes mellitus: systematic review and meta-analysis. Experimental and clinical endocrinology & diabetes : official journal, German Society of Endocrinology [and] German Diabetes Association 2013;121(4):234-8. doi: 10.1055/s-0033-1333688.
174. Mynatt RL. Carnitine and type 2 diabetes. Diabetes/metabolism research and reviews 2009;25 Suppl 1:S45-9. doi: 10.1002/dmrr.987.

175. Lynch CJ, Adams SH. Branched-chain amino acids in metabolic signalling and insulin resistance. Nature reviews Endocrinology 2014;10(12):723-36. doi: 10.1038/nrendo.2014.171.
176. Wang TJ, Larson MG, Vasan RS, Cheng S, Rhee EP, McCabe E, Lewis GD, Fox CS, Jacques PF, Fernandez C, et al. Metabolite profiles and the risk of developing diabetes. Nature medicine 2011;17(4):448-53. doi: 10.1038/nm.2307.
177. Yoon MS. The Emerging Role of Branched-Chain Amino Acids in Insulin Resistance and Metabolism. Nutrients 2016;8(7). doi: 10.3390/nu8070405.
178. Chen Q, Reimer RA. Dairy protein and leucine alter GLP-1 release and mRNA of genes involved in intestinal lipid metabolism in vitro. Nutrition 2009;25(3):340-9. doi: 10.1016/j.nut.2008.08.012.
179. Lynch CJ, Gern B, Lloyd C, Hutson SM, Eicher R, Vary TC. Leucine in food mediates some of the postprandial rise in plasma leptin concentrations. American journal of physiology Endocrinology and metabolism 2006;291(3):E621-30. doi: 10.1152/ajpendo.00462.2005.
180. Potier M, Darcel N, Tome D. Protein, amino acids and the control of food intake. Curr Opin Clin Nutr Metab Care 2009;12(1):54-8. doi: 10.1097/MCO.0b013e32831b9e01.
181. Salehi A, Gunnerud U, Muhammed SJ, Ostman E, Holst JJ, Bjorck I, Rorsman P. The insulinogenic effect of whey protein is partially mediated by a direct effect of amino acids and GIP on beta-cells. Nutr Metab (Lond) 2012;9(1):48. doi: 10.1186/1743-7075-9-48.
182. Torres-Leal FL, Fonseca-Alaniz MH, Teodoro GF, de Capitani MD, Vianna D, Pantaleao LC, Matos-Neto EM, Rogero MM, Donato J, Jr., Tirapegui J. Leucine supplementation improves adiponectin and total cholesterol concentrations despite the lack of changes in adiposity or glucose homeostasis in rats previously exposed to a high-fat diet. Nutr Metab (Lond) 2011;8(1):62. doi: 10.1186/1743-7075-8-62.
183. Xu G, Li Y, An W, Li S, Guan Y, Wang N, Tang C, Wang X, Zhu Y, Li X, et al. Gastric mammalian target of rapamycin signaling regulates ghrelin production and food intake. Endocrinology 2009;150(8):3637-44. doi: 10.1210/en.2009-0372.
184. Floyd JC, Jr., Fajans SS, Pek S, Thiffault CA, Knopf RF, Conn JW. Synergistic effect of essential amino acids and glucose upon insulin secretion in man. Diabetes 1970;19(2):109-15.
185. Manders RJ, Koopman R, Sluijsmans WE, van den Berg R, Verbeek K, Saris WH, Wagenmakers AJ, van Loon LJ. Co-ingestion of a protein hydrolysate with or without additional leucine effectively reduces postprandial blood glucose excursions in Type 2 diabetic men. The Journal of nutrition 2006;136(5):1294-9.
186. Manders RJ, Little JP, Forbes SC, Candow DG. Insulinotropic and muscle protein synthetic effects of branched-chain amino acids: potential therapy for type 2 diabetes and sarcopenia. Nutrients 2012;4(11):1664-78. doi: 10.3390/nu4111664.
187. Cani PD, Amar J, Iglesias MA, Poggi M, Knauf C, Bastelica D, Neyrinck AM, Fava F, Tuohy KM, Chabo C, et al. Metabolic endotoxemia initiates obesity and insulin resistance. Diabetes 2007;56(7):1761-72. doi: 10.2337/db06-1491.
188. Delzenne NM, Cani PD, Everard A, Neyrinck AM, Bindels LB. Gut microorganisms as promising targets for the management of type 2 diabetes. Diabetologia 2015;58(10):2206-17. doi: 10.1007/s00125-015-3712-7.
189. Karlsson FH, Tremaroli V, Nookaew I, Bergstrom G, Behre CJ, Fagerberg B, Nielsen J, Backhed F. Gut metagenome in European women with normal, impaired and diabetic glucose control. Nature 2013;498(7452):99-103. doi: 10.1038/nature12198.
190. Qin J, Li Y, Cai Z, Li S, Zhu J, Zhang F, Liang S, Zhang W, Guan Y, Shen D, et al. A metagenome-wide association study of gut microbiota in type 2 diabetes. Nature 2012;490(7418):55-60. doi: 10.1038/nature11450.
191. Hamer HM, Jonkers D, Venema K, Vanhoutvin S, Troost FJ, Brummer RJ. Review article: the role of butyrate on colonic function. Alimentary pharmacology & therapeutics 2008;27(2):104-19. doi: 10.1111/j.1365-2036.2007.03562.x.
192. Tremaroli V, Backhed F. Functional interactions between the gut microbiota and host metabolism. Nature 2012;489(7415):242-9. doi: 10.1038/nature11552.
193. Davie JR. Inhibition of histone deacetylase activity by butyrate. The Journal of nutrition 2003;133(7 Suppl):2485S-93S.
194. Vrieze A, Van Nood E, Holleman F, Salojarvi J, Kootte RS, Bartelsman JF, Dallinga-Thie GM, Ackermans MT, Serlie MJ, Oozeer R, et al. Transfer of intestinal microbiota from lean donors increases insulin sensitivity in individuals with metabolic syndrome. Gastroenterology 2012;143(4):913-6 e7. doi: 10.1053/j.gastro.2012.06.031.

195. Barengolts E. VITAMIN D AND PREBIOTICS MAY BENEFIT THE INTESTINAL MICROBACTERIA AND IMPROVE GLUCOSE HOMEOSTASIS IN PREDIABETES AND TYPE 2 DIABETES. Endocrine Practice 2013;19(3):497-510. doi: 10.4158/ep12263.ra.
196. Defronzo RA. Banting Lecture. From the triumvirate to the ominous octet: a new paradigm for the treatment of type 2 diabetes mellitus. Diabetes 2009;58(4):773-95. doi: 10.2337/db09-9028.
197. Guarner F, Malagelada JR. Gut flora in health and disease. Lancet 2003;361(9356):512-9. doi: 10.1016/S0140-6736(03)12489-0.
198. Ley RE, Turnbaugh PJ, Klein S, Gordon JI. Microbial ecology: human gut microbes associated with obesity. Nature 2006;444(7122):1022-3. doi: 10.1038/4441022a.
199. Turnbaugh PJ, Ridaura VK, Faith JJ, Rey FE, Knight R, Gordon JI. The effect of diet on the human gut microbiome: a metagenomic analysis in humanized gnotobiotic mice. Science translational medicine 2009;1(6):6ra14. doi: 10.1126/scitranslmed.3000322.
200. Vijay-Kumar M, Aitken JD, Carvalho FA, Cullender TC, Mwangi S, Srinivasan S, Sitaraman SV, Knight R, Ley RE, Gewirtz AT. Metabolic syndrome and altered gut microbiota in mice lacking Toll-like receptor 5. Science 2010;328(5975):228-31. doi: 10.1126/science.1179721.
201. Bozan B, Temelli F. Chemical composition and oxidative stability of flax, safflower and poppy seed and seed oils. Bioresource technology 2008;99(14):6354-9. doi: 10.1016/j.biortech.2007.12.009.
202. Kabir M, Catalano KJ, Ananthnarayan S, Kim SP, Van Citters GW, Dea MK, Bergman RN. Molecular evidence supporting the portal theory: a causative link between visceral adiposity and hepatic insulin resistance. American journal of physiology Endocrinology and metabolism 2005;288(2):E454-61. doi: 10.1152/ajpendo.00203.2004.
203. Mostad IL, Bjerve KS, Bjorgaas MR, Lydersen S, Grill V. Effects of n-3 fatty acids in subjects with type 2 diabetes: reduction of insulin sensitivity and time-dependent alteration from carbohydrate to fat oxidation. The American journal of clinical nutrition 2006;84(3):540-50.
204. Rasic-Milutinovic Z, Perunicic G, Pljesa S, Gluvic Z, Sobajic S, Djuric I, Ristic D. Effects of N-3 PUFAs supplementation on insulin resistance and inflammatory biomarkers in hemodialysis patients. Renal failure 2007;29(3):321-9. doi: 10.1080/08860220601184092.
205. Vessby B, Uusitupa M, Hermansen K, Riccardi G, Rivellese AA, Tapsell LC, Nalsen C, Berglund L, Louheranta A, Rasmussen BM, et al. Substituting dietary saturated for monounsaturated fat impairs insulin sensitivity in healthy men and women: The KANWU Study. Diabetologia 2001;44(3):312-9.
206. Hu C, Yuan YV, Kitts DD. Antioxidant activities of the flaxseed lignan secoisolariciresinol diglucoside, its aglycone secoisolariciresinol and the mammalian lignans enterodiol and enterolactone in vitro. Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association 2007;45(11):2219-27. doi: 10.1016/j.fct.2007.05.017.
207. Paolisso G, Giugliano D. Oxidative stress and type 2 diabetes mellitus. Int Diabetes Monitor 1998;10:1-6.
208. Rajesha J, Murthy KN, Kumar MK, Madhusudhan B, Ravishankar GA. Antioxidant potentials of flaxseed by in vivo model. J Agric Food Chem 2006;54(11):3794-9. doi: 10.1021/jf053048a.
209. Pang B, Zhao LH, Zhou Q, Zhao TY, Wang H, Gu CJ, Tong XL. Application of berberine on treating type 2 diabetes mellitus. International journal of endocrinology 2015;2015:905749. doi: 10.1155/2015/905749.
210. Ahuja S, Shankar P. Association between westernized diets, gut microbiome, and obesity and related disorders. Agro Food Industry Hi-Tech 2015;26(2):28-32.
211. Han J, Lin H, Huang W. Modulating gut microbiota as an anti-diabetic mechanism of berberine. Medical science monitor : international medical journal of experimental and clinical research 2011;17(7):RA164-7.
212. Xie W, Gu D, Li J, Cui K, Zhang Y. Effects and action mechanisms of berberine and Rhizoma coptidis on gut microbes and obesity in high-fat diet-fed C57BL/6J mice. PLoS One 2011;6(9):e24520. doi: 10.1371/journal.pone.0024520.
213. Zhang X, Zhao Y, Zhang M, Pang X, Xu J, Kang C, Li M, Zhang C, Zhang Z, Zhang Y, et al. Structural changes of gut microbiota during berberine-mediated prevention of obesity and insulin resistance in high-fat diet-fed rats. PLoS One 2012;7(8):e42529. doi: 10.1371/journal.pone.0042529.
214. Chen QM, Xie MZ. [Studies on the hypoglycemic effect of Coptis chinensis and berberine]. Yao xue xue bao = Acta pharmaceutica Sinica 1986;21(6):401-6.

215. Chueh WH, Lin JY. Berberine, an isoquinoline alkaloid in herbal plants, protects pancreatic islets and serum lipids in nonobese diabetic mice. J Agric Food Chem 2011;59(14):8021-7. doi: 10.1021/jf201627w.
216. Chueh WH, Lin JY. Protective effect of berberine on serum glucose levels in non-obese diabetic mice. International immunopharmacology 2012;12(3):534-8. doi: 10.1016/j.intimp.2012.01.003.
217. Derosa G, Maffioli P, Cicero AF. Berberine on metabolic and cardiovascular risk factors: an analysis from preclinical evidences to clinical trials. Expert opinion on biological therapy 2012;12(8):1113-24. doi: 10.1517/14712598.2012.704014.
218. Kim SH, Shin EJ, Kim ED, Bayaraa T, Frost SC, Hyun CK. Berberine activates GLUT1-mediated glucose uptake in 3T3-L1 adipocytes. Biol Pharm Bull 2007;30(11):2120-5.
219. Kong WJ, Zhang H, Song DQ, Xue R, Zhao W, Wei J, Wang YM, Shan N, Zhou ZX, Yang P, et al. Berberine reduces insulin resistance through protein kinase C-dependent up-regulation of insulin receptor expression. Metabolism: clinical and experimental 2009;58(1):109-19. doi: 10.1016/j.metabol.2008.08.013.
220. Singh IP, Mahajan S. Berberine and its derivatives: a patent review (2009 - 2012). Expert Opin Ther Pat 2013;23(2):215-31. doi: 10.1517/13543776.2013.746314.
221. Vuddanda PR, Chakraborty S, Singh S. Berberine: a potential phytochemical with multispectrum therapeutic activities. Expert opinion on investigational drugs 2010;19(10):1297-307. doi: 10.1517/13543784.2010.517745.
222. Yang J, Yin J, Gao H, Xu L, Wang Y, Xu L, Li M. Berberine improves insulin sensitivity by inhibiting fat store and adjusting adipokines profile in human preadipocytes and metabolic syndrome patients. Evidence-based complementary and alternative medicine : eCAM 2012;2012:363845. doi: 10.1155/2012/363845.
223. Zhang Q, Xiao X, Feng K, Wang T, Li W, Yuan T, Sun X, Sun Q, Xiang H, Wang H. Berberine Moderates Glucose and Lipid Metabolism through Multipathway Mechanism. Evidence-based complementary and alternative medicine : eCAM 2011;2011. doi: 10.1155/2011/924851.
224. Khazim K, Gorin Y, Cavaglieri RC, Abboud HE, Fanti P. The antioxidant silybin prevents high glucose-induced oxidative stress and podocyte injury in vitro and in vivo. American journal of physiology Renal physiology 2013;305(5):F691-700. doi: 10.1152/ajprenal.00028.2013.
225. D'alonzo R, Kozarek W, Wade R. Glyceride composition of processed fats and oils as determined by glass capillary gas chromatography. J am Oil Chem Soc 1982;59:292-5.
226. Yamamoto K, Asakawa H, Tokunaga K, Watanabe H, Matsuo N, Tokimitsu I, Yagi N. Long-term ingestion of dietary diacylglycerol lowers serum triacylglycerol in type II diabetic patients with hypertriglyceridemia. The Journal of nutrition 2001;131(12):3204-7.
227. Tada N, Shoji K, Takeshita M, Watanabe H, Yoshida H, Hase T, Matsuo N, Tokimitsu I. Effects of diacylglycerol ingestion on postprandial hyperlipidemia in diabetes. Clinica chimica acta; international journal of clinical chemistry 2005;353(1-2):87-94. doi: 10.1016/j.cccn.2004.10.006.
228. Yamamoto K, Takeshita M, Tokimitsu I, Watanabe H, Mizuno T, Asakawa H, Tokunaga K, Tatsumi T, Okazaki M, Yagi N. Diacylglycerol oil ingestion in type 2 diabetic patients with hypertriglyceridemia. Nutrition 2006;22(1):23-9. doi: 10.1016/j.nut.2005.04.009.
229. Murase T, Mizuno T, Omachi T, Onizawa K, Komine Y, Kondo H, Hase T, Tokimitsu I. Dietary diacylglycerol suppresses high fat and high sucrose diet-induced body fat accumulation in C57BL/6J mice. Journal of lipid research 2001;42(3):372-8.
230. Coates P, Blackman MR, Cragg G, Levine M, Moss J, White J. Encyclopedia of dietary supplements. 2005:545-53.
231. European Scientific Cooperative on Phytotherapy (ESCOP). Gingko folium. ESCOP, ed ESCOP Monographs: The scientific foundation for Herbal Medicinal Products 2003(2nd Edition):178-210.
232. Wichtl M. Herbal Drugs and Phytopharmaceuticals: A Handbook for Practice on a Scientific Basis. Medpharm Scientific Publishers, Stuttgart, Germany 2004:251-4.

14 Appendix

The following pages summarize the non-significant forest plots of all the supplements for the 9 different parameters examined.

14.1 HbA1c

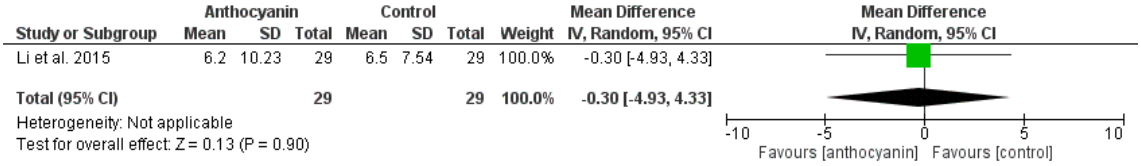

Figure 71: Forest plot for HbA1c after anthocyanin supplementation vs. control.

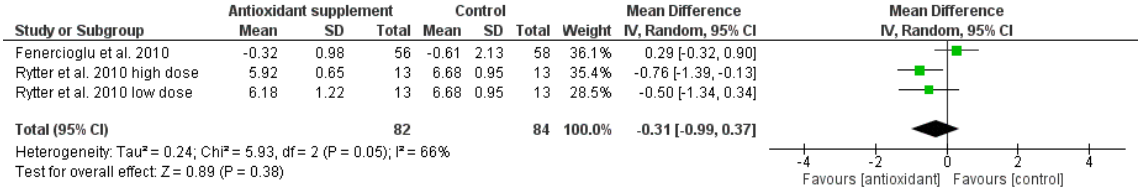

Figure 72: Forest plot for HbA1c after antioxidant supplementation vs. control.

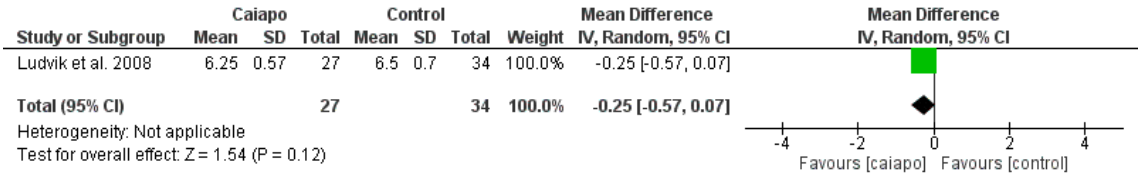

Figure 73: Forest plot for HbA1c after Caiapo supplementation vs. control.

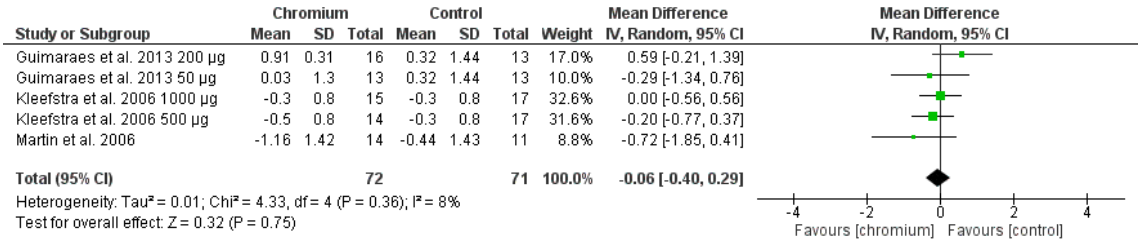

Figure 74: Forest plot for HbA1c after chromium supplementation vs. control.

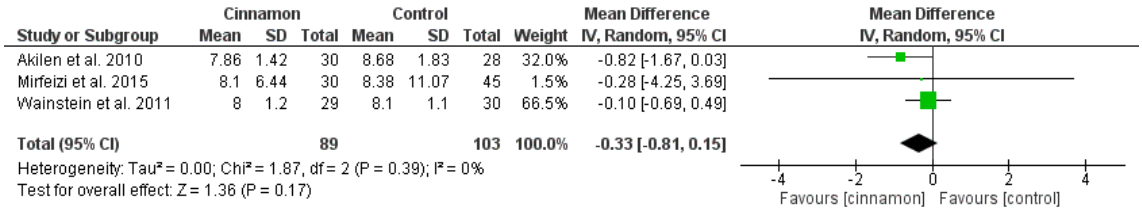

Figure 75: Forest plot for HbA1c after cinnamon supplementation vs. control.

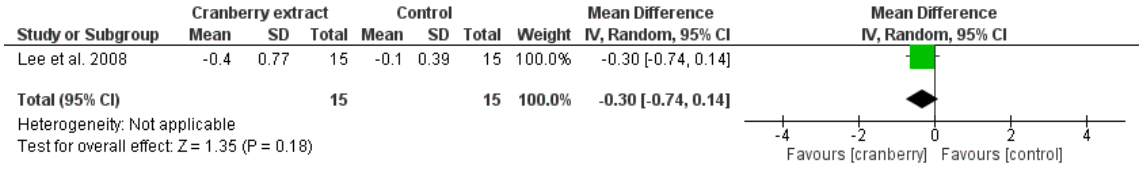

Figure 76: Forest plot for HbA1c after cranberry extract supplementation vs. control.

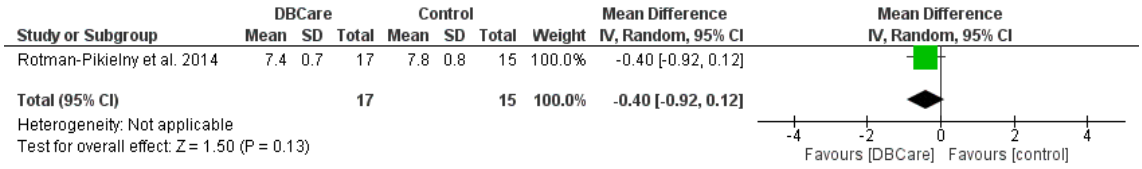

Figure 77: Forest plot for HbA1c after DBCare supplementation vs. control.

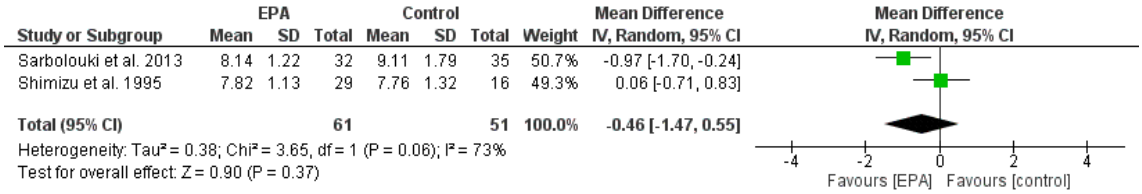

Figure 78: Forest plot for HbA1c after EPA supplementation vs. control.

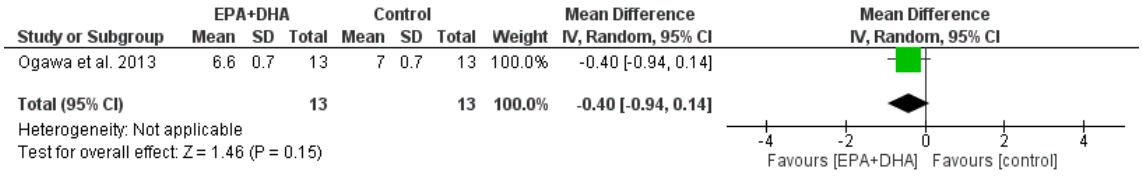

Figure 79: Forest plot for HbA1c after EPA and DHA supplementation vs. control.

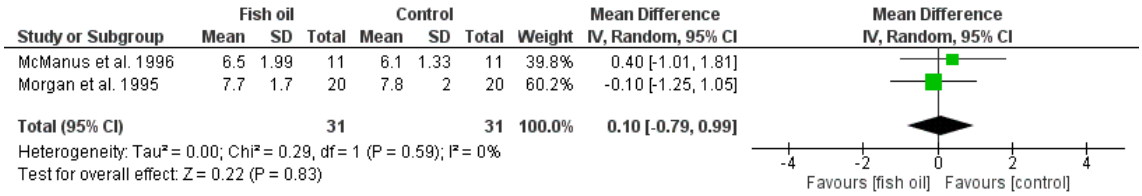

Figure 80: Forest plot for HbA1c after fish oil supplementation vs. control.

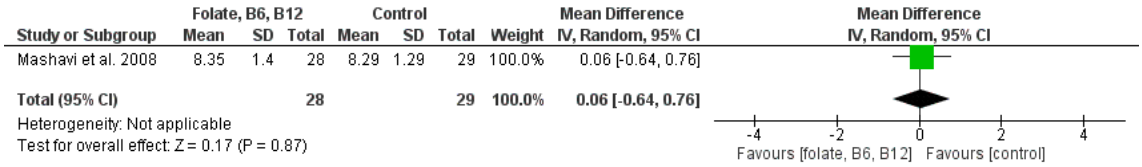

Figure 81: Forest plot for HbA1c after folate, B6 and B12 supplementation vs. control.

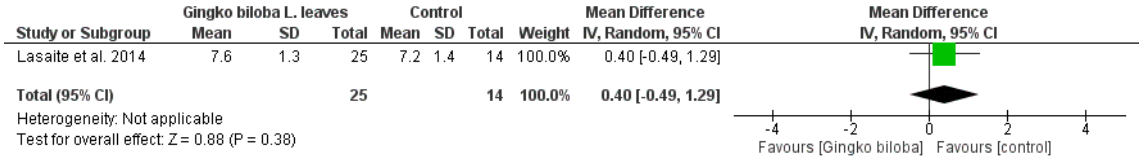

Figure 82: Forest plot for HbA1c after *G. biloba* L. leaf supplementation vs. control.

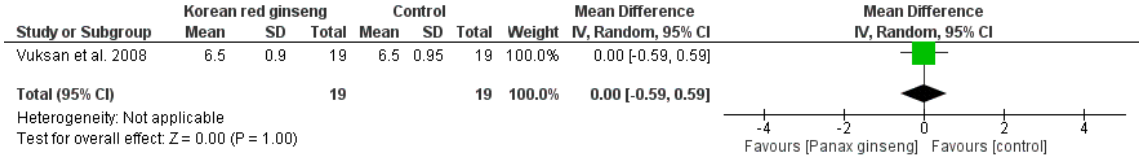

Figure 83: Forest plot for HbA1c after Korean red ginseng supplementation vs. control.

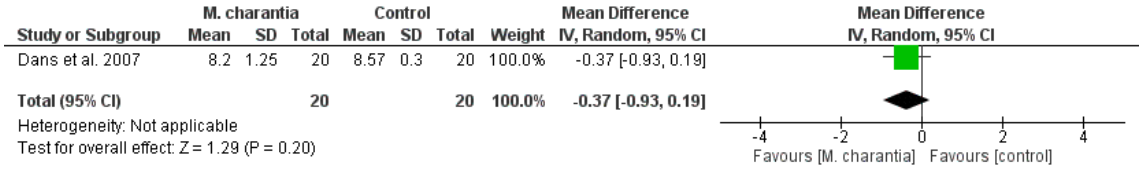

Figure 84: Forest plot for HbA1c after *M. charantia* supplementation vs. control.

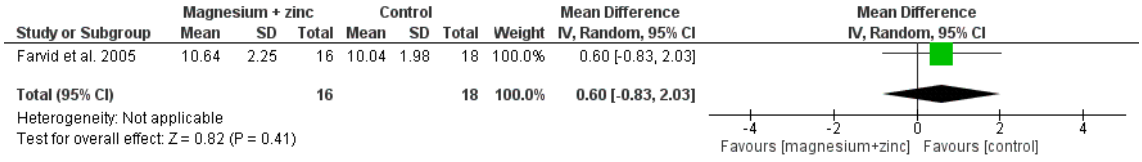

Figure 85: Forest plot for HbA1c after magnesium and zinc supplementation vs. control.

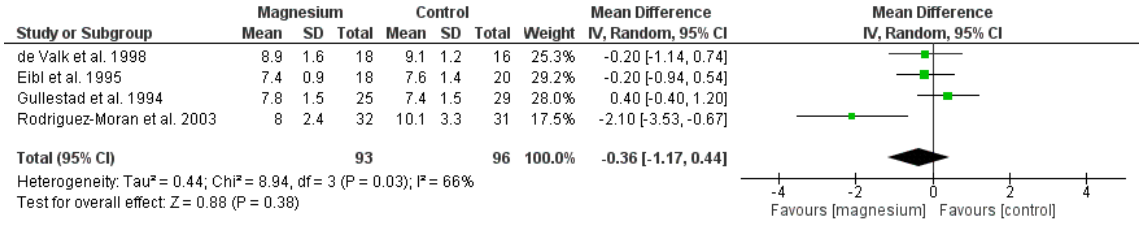

Figure 86: Forest plot for HbA1c after magnesium supplementation vs. control.

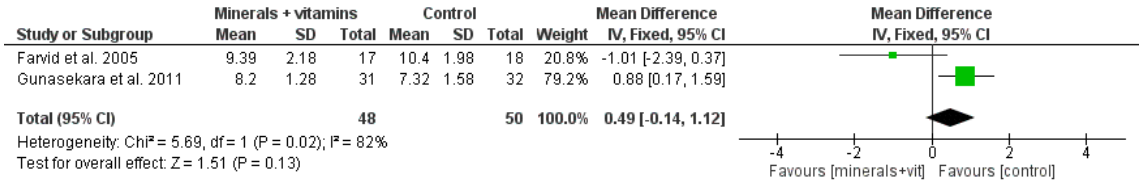

Figure 87: Forest plot for HbA1c after mineral and vitamin supplementation vs. control.

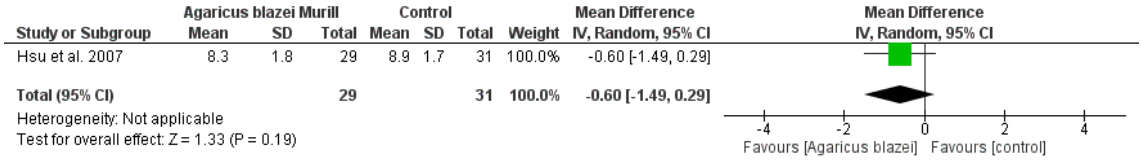

Figure 88: Forest plot for HbA1c after ABM supplementation vs. control.

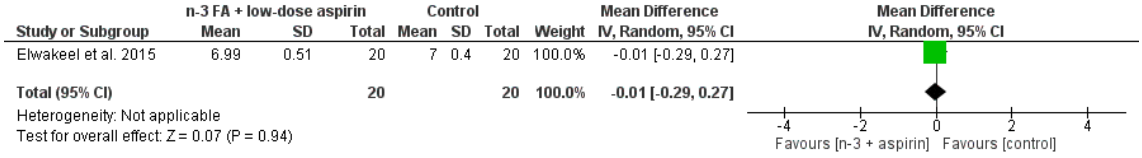

Figure 89: Forest plot for HbA1c after n-3 fatty acid and low-dose aspirin supplementation vs. control.

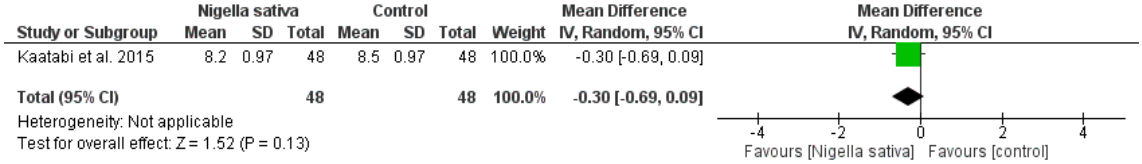

Figure 90: Forest plot for HbA1c after N. sativa supplementation vs. control.

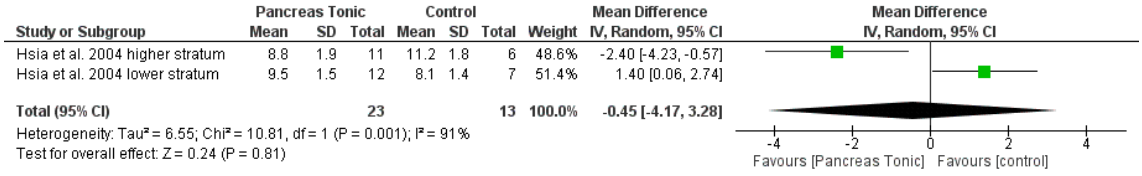

Figure 91: Forest plot for HbA1c after Pancreas Tonic supplementation vs. control.

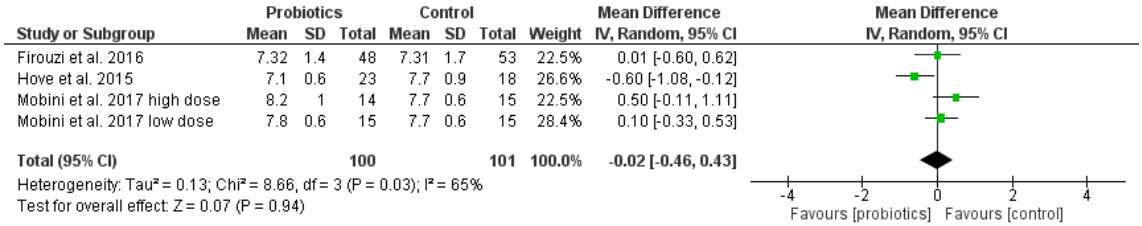

Figure 92: Forest plot for HbA1c after probiotic supplementation vs. control.

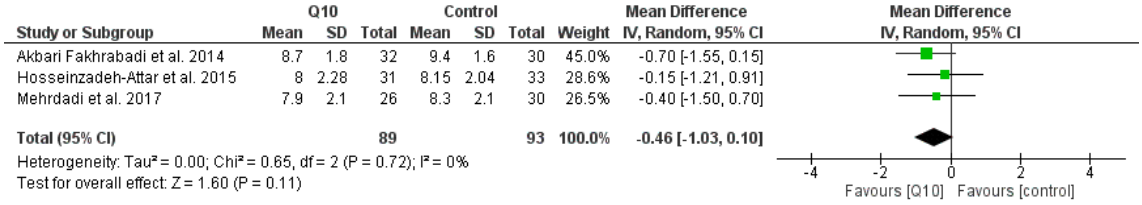

Figure 93: Forest plot for HbA1c after Q10 supplementation vs. control.

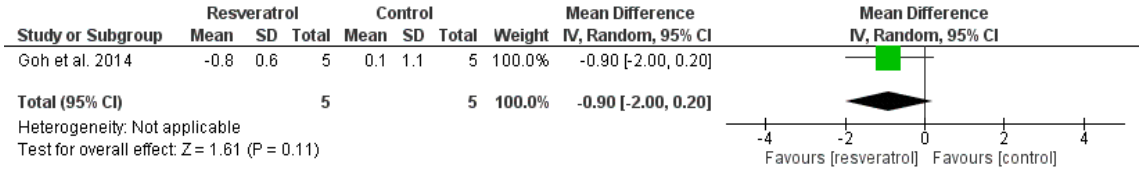

Figure 94: Forest plot for HbA1c after resveratrol supplementation vs. control.

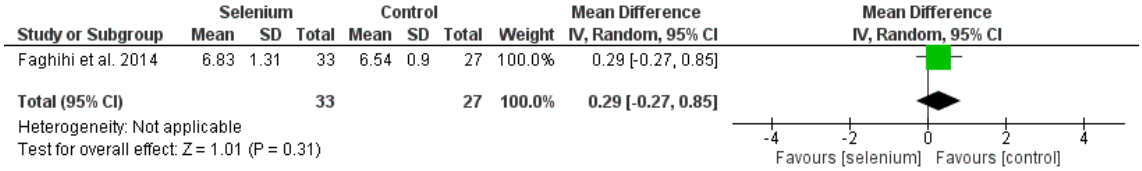

Figure 95: Forest plot for HbA1c after selenium supplementation vs. control.

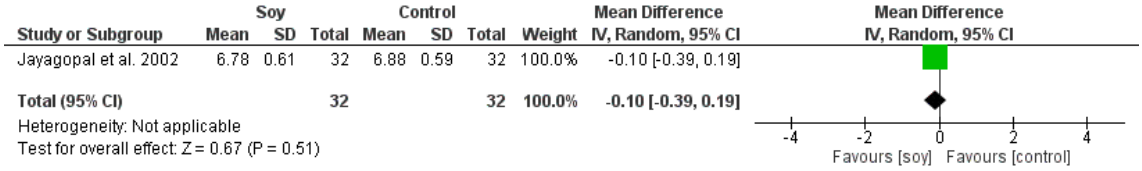

Figure 96: Forest plot for HbA1c after soy supplementation vs. control.

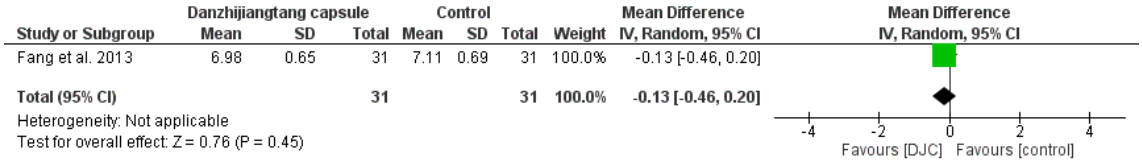

Figure 97: Forest plot for HbA1c after DJC supplementation vs. control.

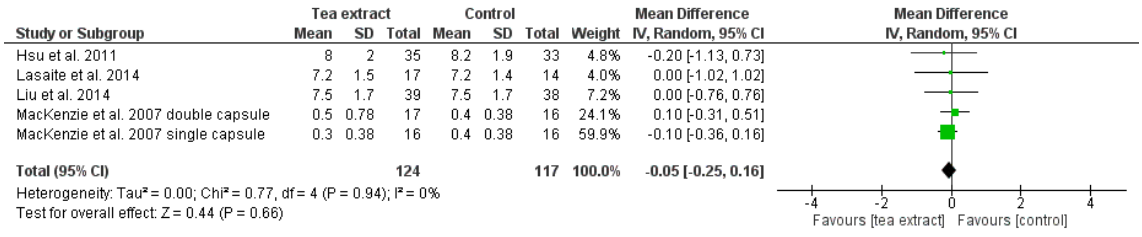

Figure 98: Forest plot for HbA1c after tea extract supplementation vs. control.

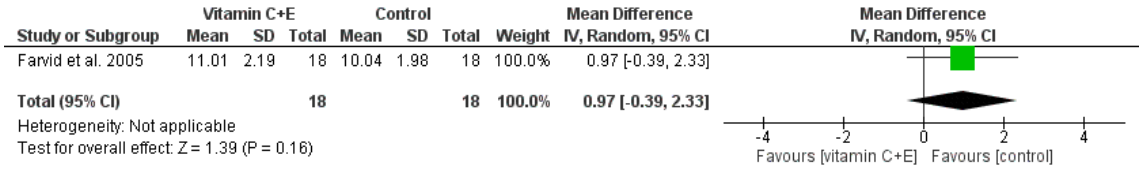

Figure 99: Forest plot for HbA1c after vitamin C and E supplementation vs. control.

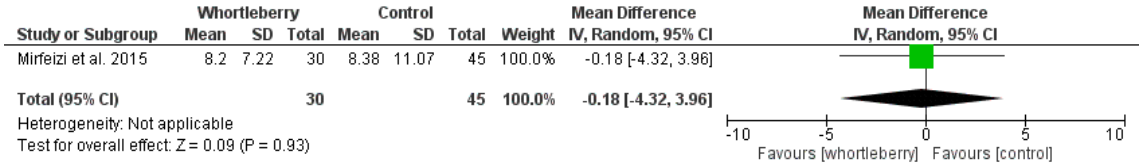

Figure 100: Forest plot for HbA1c after whortleberry supplementation vs. control.

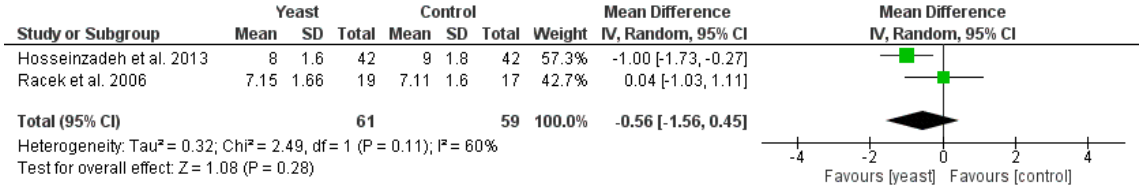

Figure 101: Forest plot for HbA1c after yeast supplementation vs. control.

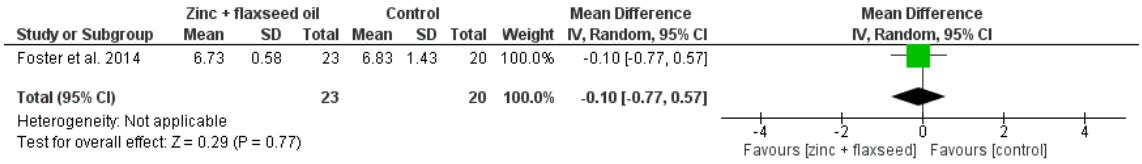

Figure 102: Forest plot for HbA1c after zinc and flaxseed oil supplementation vs. control.

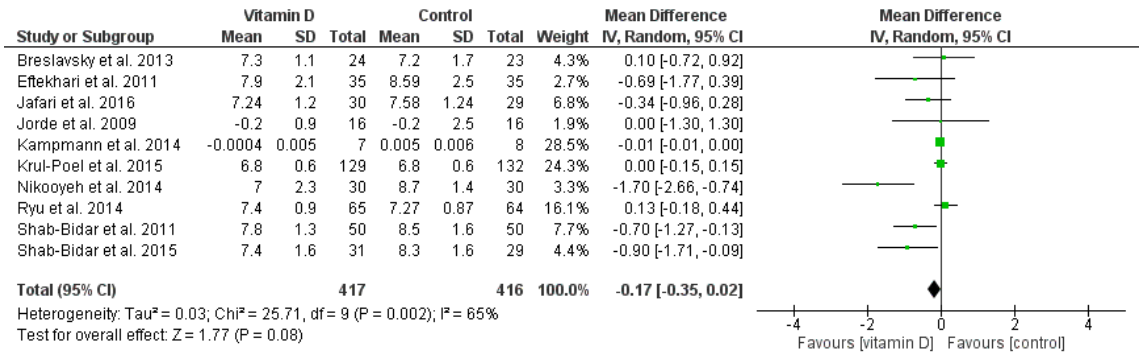

Figure 103: Forest plot for HbA1c after vitamin D supplementation vs. control.

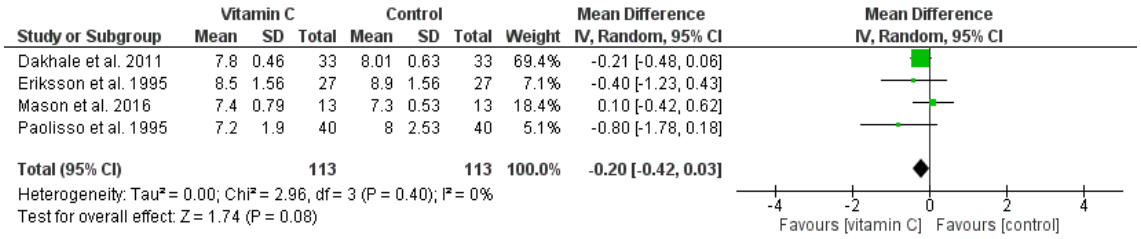

Figure 104: Forest plot for HbA1c after vitamin C supplementation vs. control.

14.2 Glucose

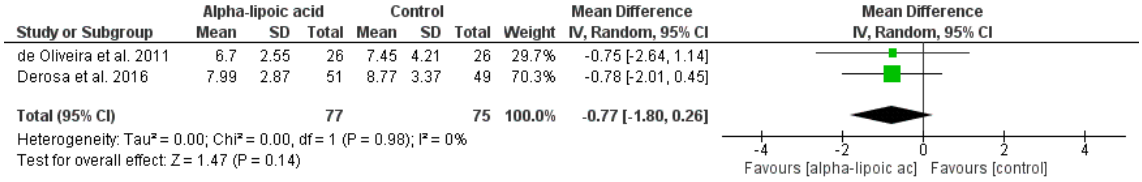

Figure 105: Forest plot for glucose after alpha-lipoic acid supplementation vs. control.

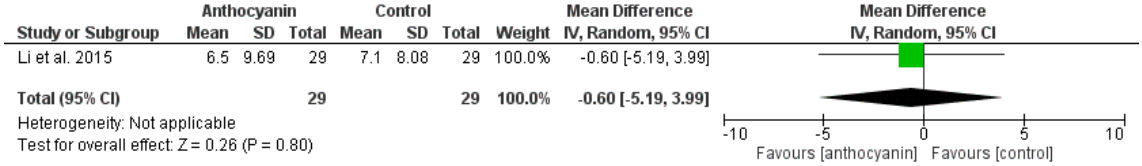

Figure 106: Forest plot for glucose after anthocyanin supplementation vs. control.

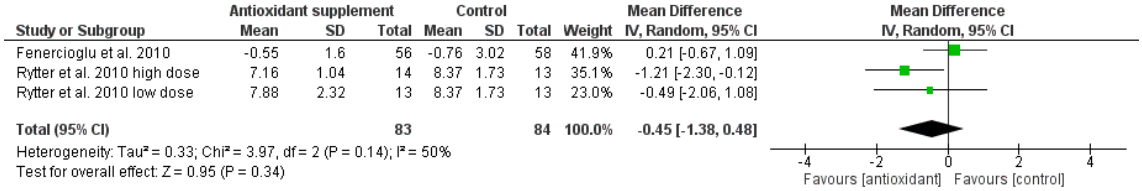

Figure 107: Forest plot for glucose after antioxidant supplementation vs. control.

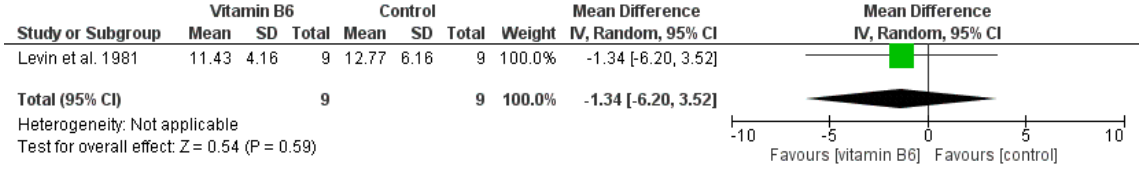

Figure 108: Forest plot for glucose after vitamin B6 supplementation vs. control.

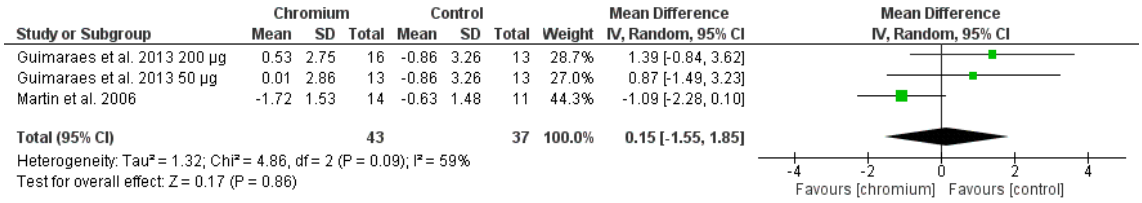

Figure 109: Forest plot for glucose after chromium supplementation vs. control.

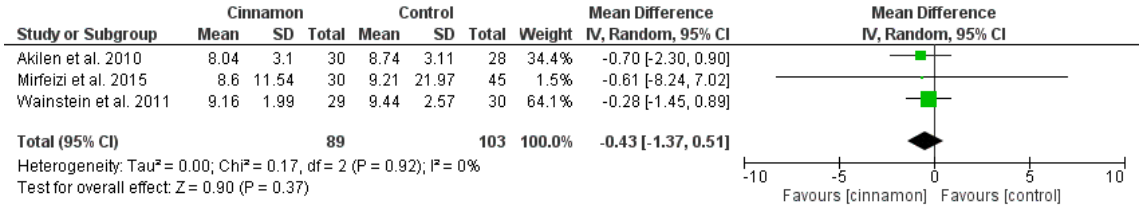

Figure 110: Forest plot for glucose after cinnamon supplementation vs. control.

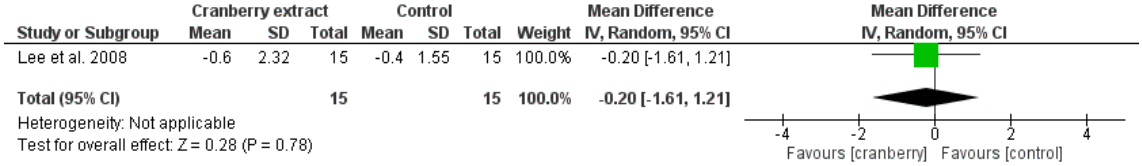

Figure 111: Forest plot for glucose after cranberry extract supplementation vs. control.

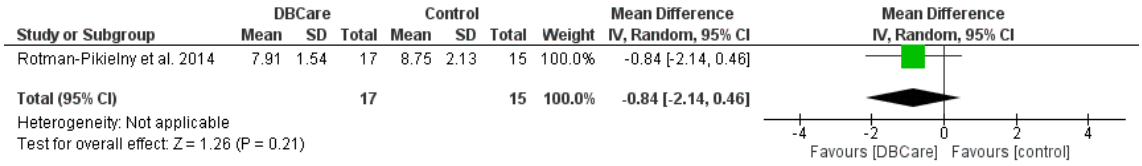

Figure 112: Forest plot for glucose after DBCare supplementation vs. control.

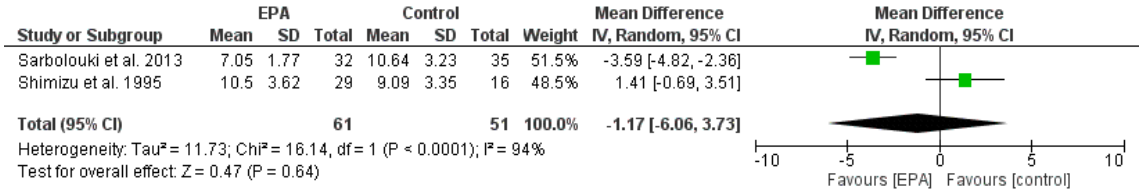

Figure 113: Forest plot for glucose after EPA supplementation vs. control.

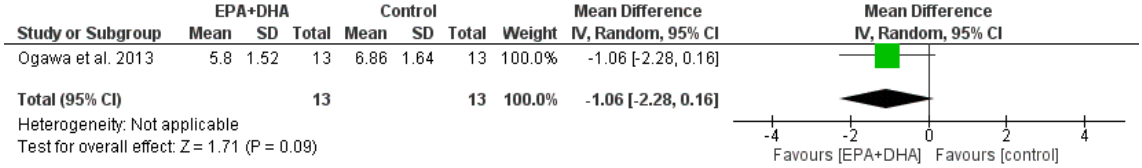

Figure 114: Forest plot for glucose after EPA and DHA supplementation vs. control.

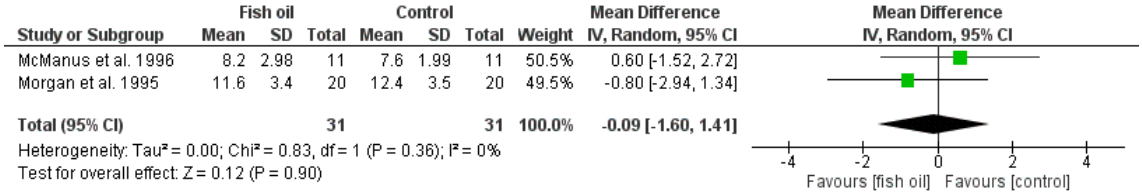

Figure 115: Forest plot for glucose after fish oil supplementation vs. control.

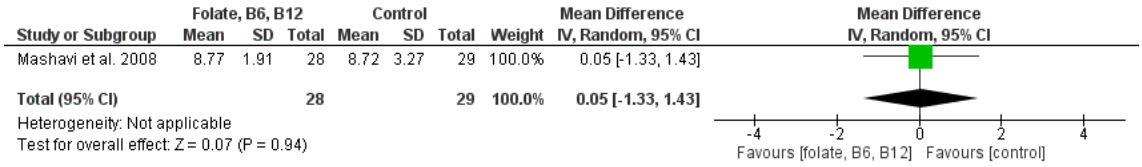

Figure 116: Forest plot for glucose after folate, B6 and B12 supplementation vs. control.

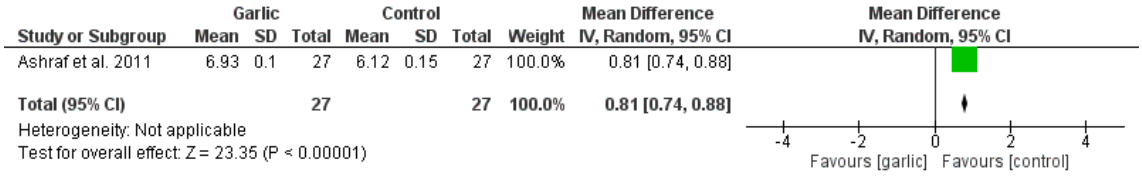

Figure 117: Forest plot for glucose after garlic supplementation vs. control.

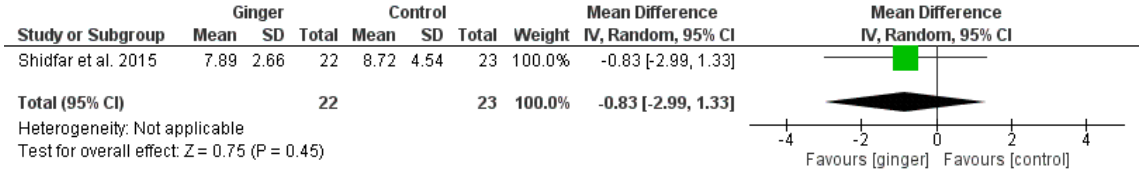

Figure 118: Forest plot for glucose after ginger supplementation vs. control.

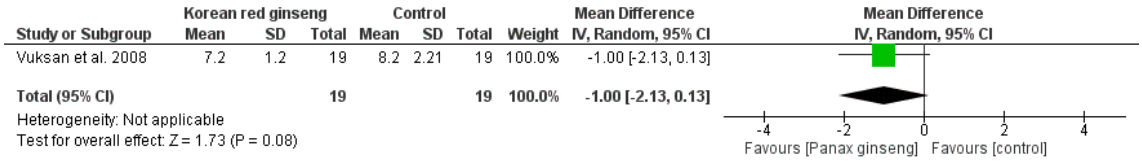

Figure 119: Forest plot for glucose after Korean red ginseng supplementation vs. control.

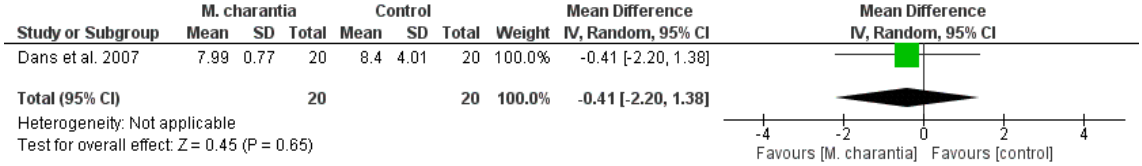

Figure 120: Forest plot for glucose after *M. charantia* supplementation vs. control.

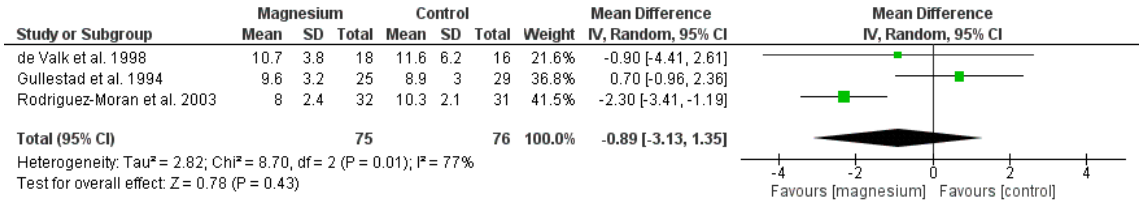

Figure 121: Forest plot for glucose after magnesium supplementation vs. control.

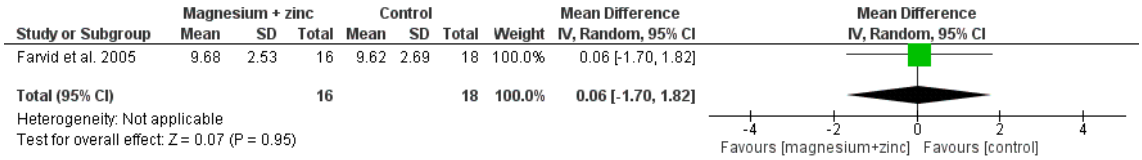

Figure 122: Forest plot for glucose after magnesium and zinc supplementation vs. control.

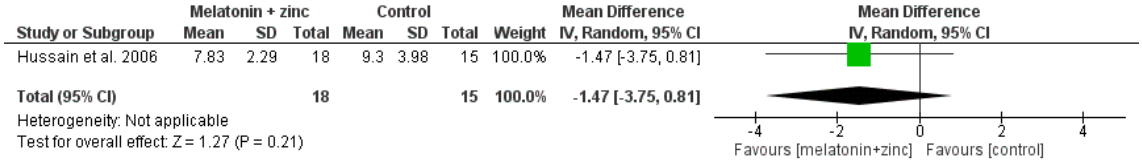

Figure 123: Forest plot for glucose after melatonin and zinc supplementation vs. control.

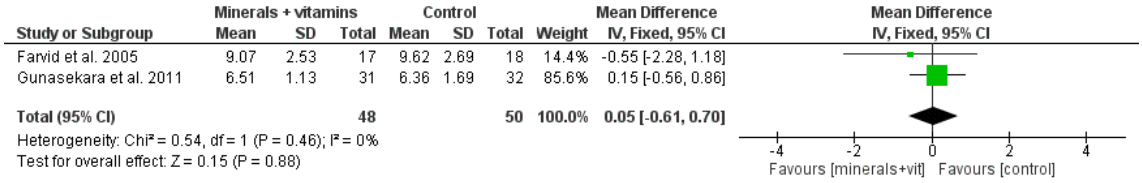

Figure 124: Forest plot for glucose after mineral and vitamin supplementation vs. control.

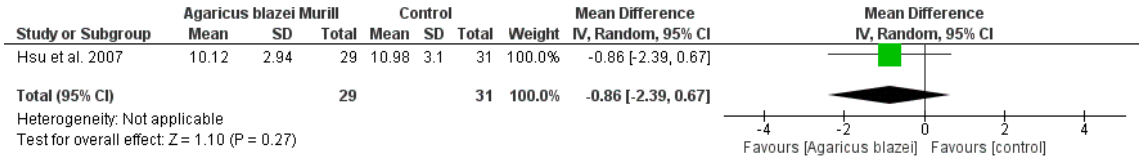

Figure 125: Forest plot for glucose after ABM supplementation vs. control.

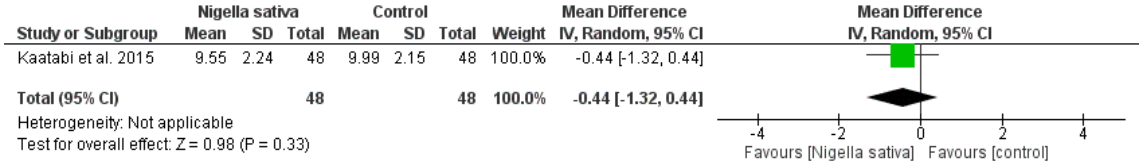

Figure 126: Forest plot for glucose after N. sativa supplementation vs. control.

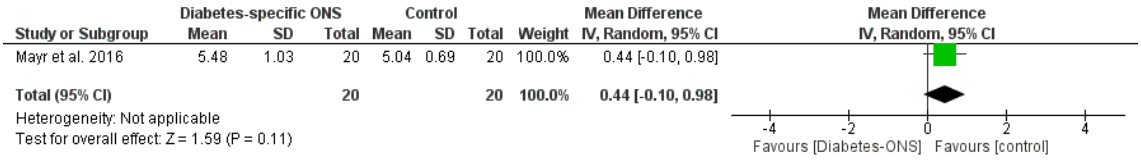

Figure 127: Forest plot for glucose after diabetes-specific ONS vs. control.

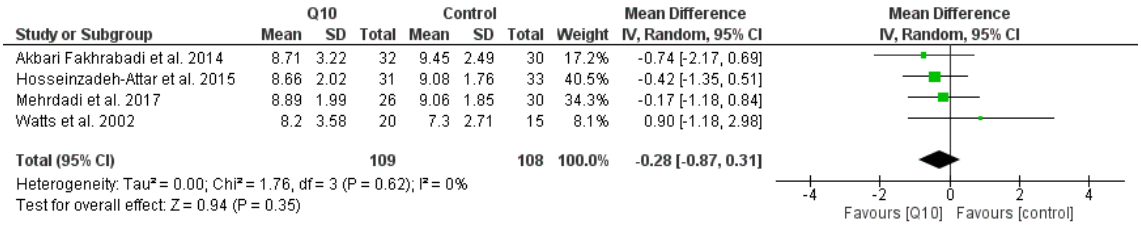

Figure 128: Forest plot for glucose after Q10 supplementation vs. control.

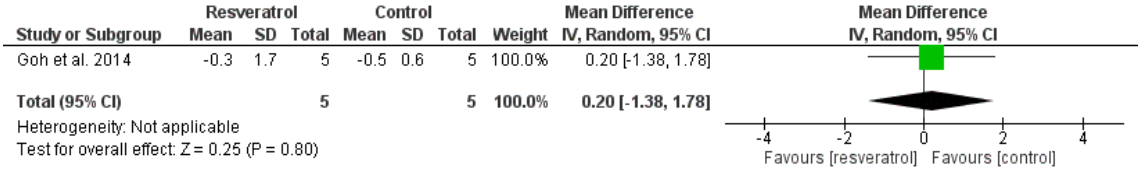

Figure 129: Forest plot for glucose after resveratrol supplementation vs. control.

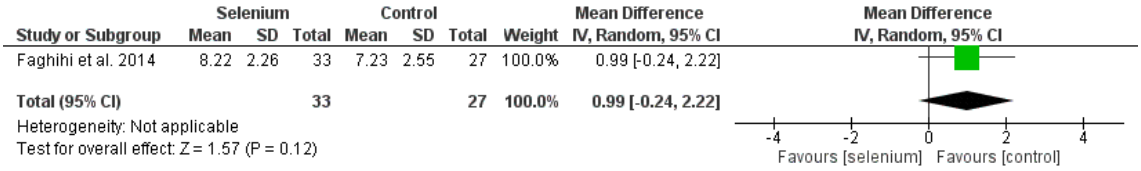

Figure 130: Forest plot for glucose after selenium supplementation vs. control.

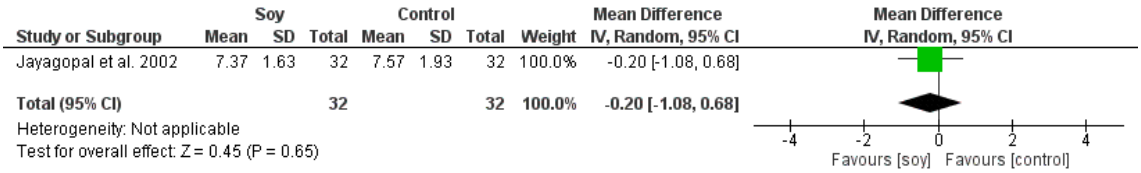

Figure 131: Forest plot for glucose after soy supplementation vs. control.

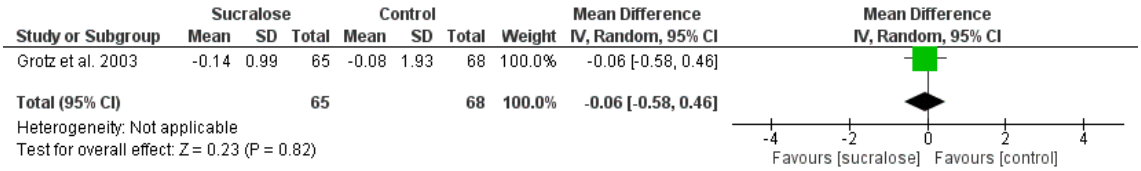

Figure 132: Forest plot for glucose after sucralose supplementation vs. control.

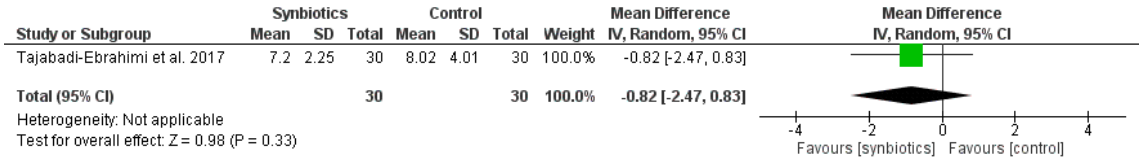

Figure 133: Forest plot for glucose after synbiotic supplementation vs. control.

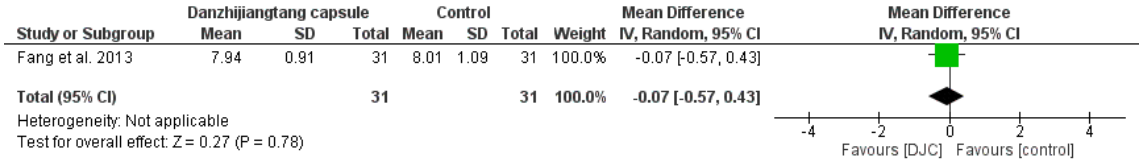

Figure 134: Forest plot for glucose after DJC supplementation vs. control.

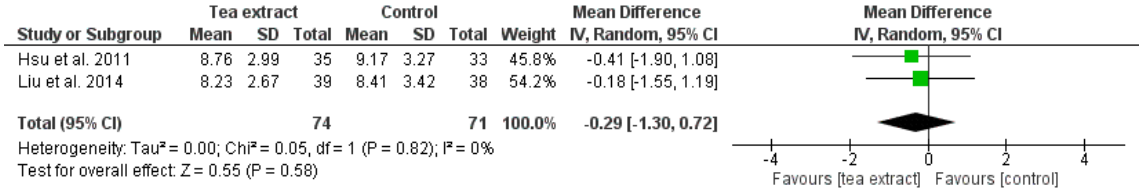

Figure 135: Forest plot for glucose after tea extract supplementation vs. control.

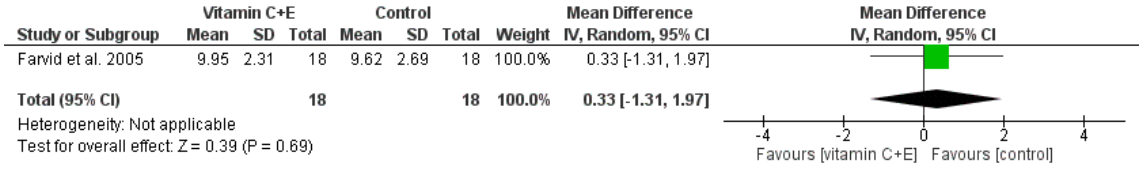

Figure 136: Forest plot for glucose after vitamin C and E supplementation vs. control.

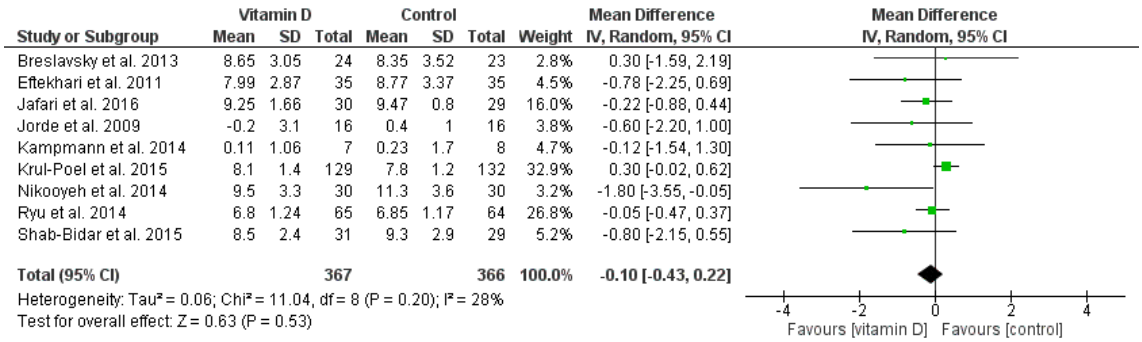

Figure 137: Forest plot for glucose after vitamin D supplementation vs. control.

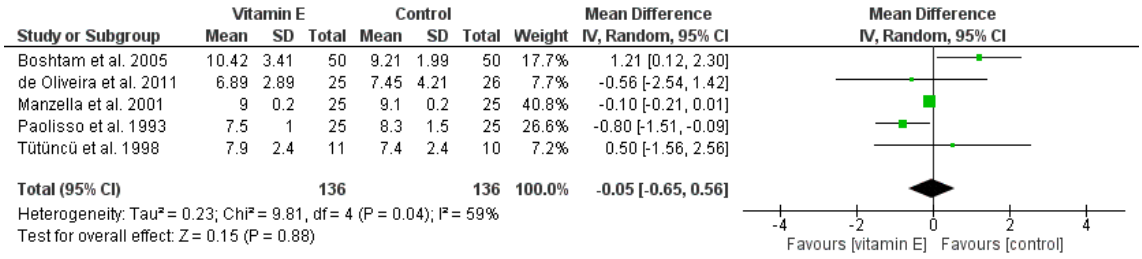

Figure 138: Forest plot for glucose after vitamin E supplementation vs. control.

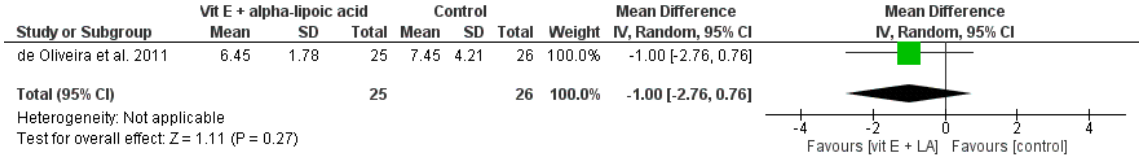

Figure 139: Forest plot for glucose after vitamin E and alpha-lipoic acid supplementation vs. control.

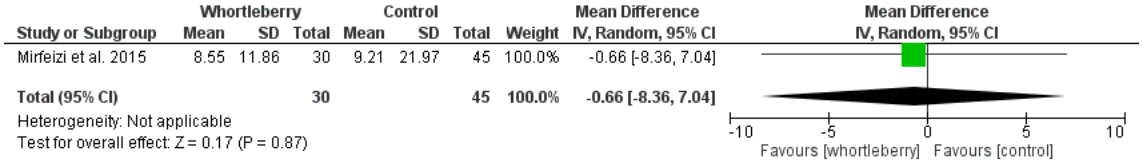

Figure 140: Forest plot for glucose after whortleberry supplementation vs. control.

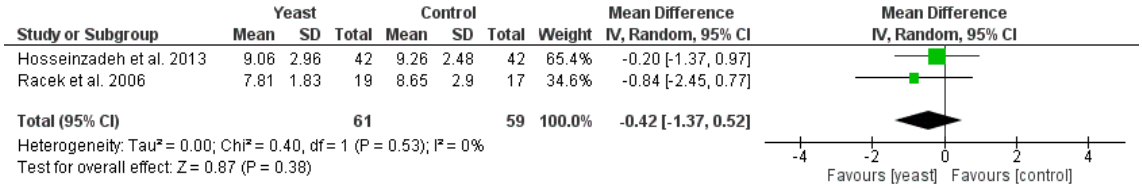

Figure 141: Forest plot for glucose after yeast supplementation vs. control.

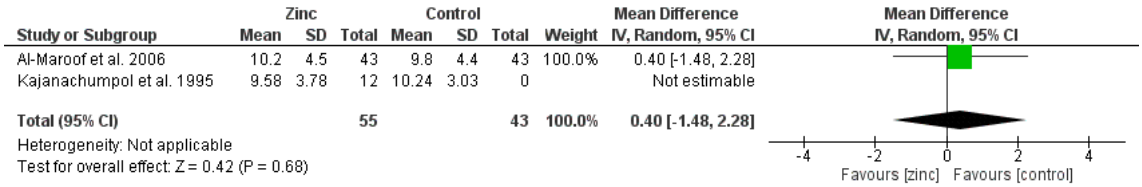

Figure 142: Forest plot for glucose after zinc supplementation vs. control.

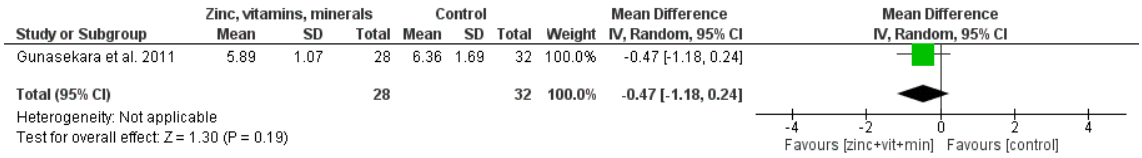

Figure 143: Forest plot for glucose after zinc, vitamin and mineral supplementation vs. control.

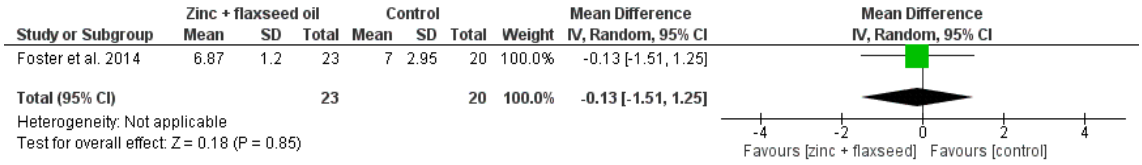

Figure 144: Forest plot for glucose after zinc and flaxseed oil supplementation vs. control.

14.3 Insulin

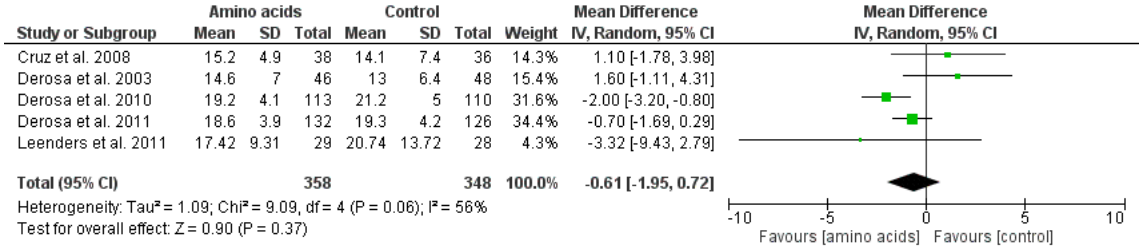

Figure 145: Forest plot for insulin after amino acid supplementation vs. control.

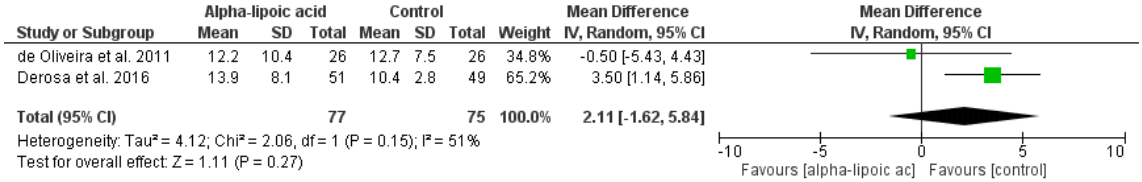

Figure 146: Forest plot for insulin after alpha-lipoic acid supplementation vs. control.

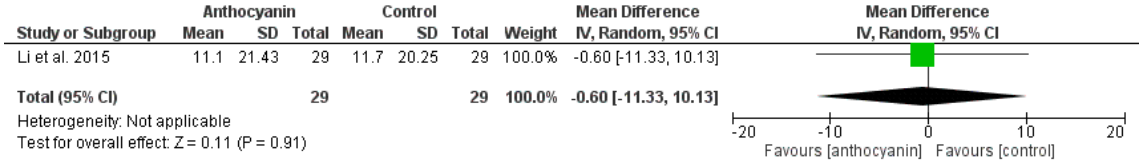

Figure 147: Forest plot for insulin after anthocyanin supplementation vs. control.

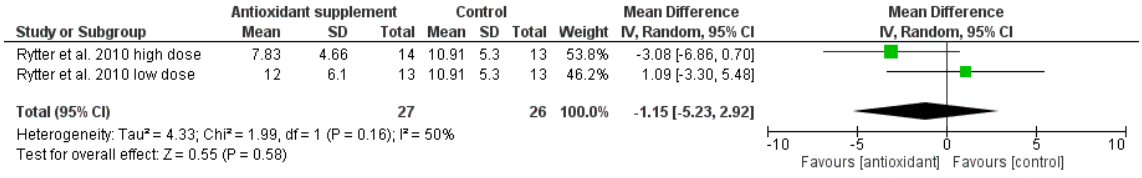

Figure 148: Forest plot for insulin after antioxidant supplementation vs. control.

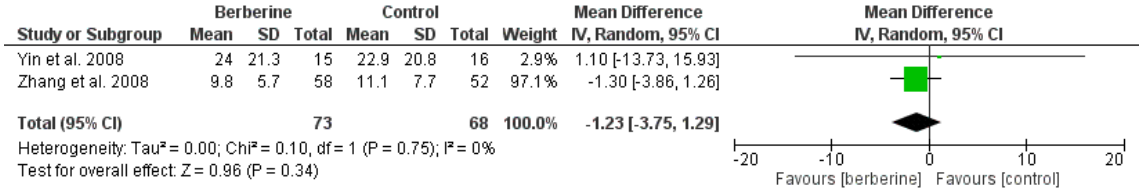

Figure 149: Forest plot for insulin after berberine supplementation vs. control.

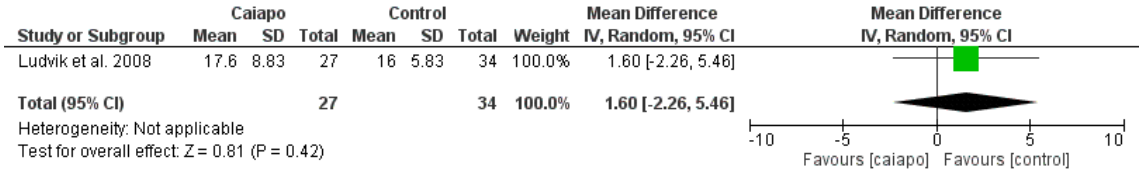

Figure 150: Forest plot for insulin after Caiapo supplementation vs. control.

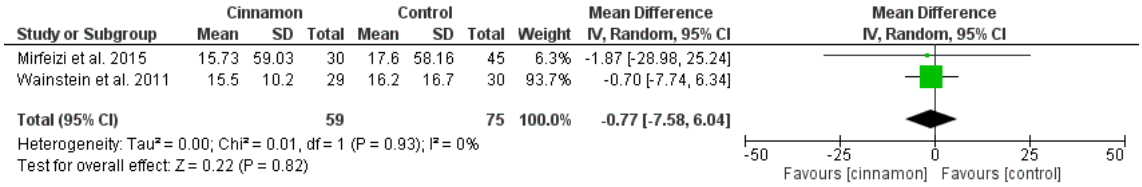

Figure 151: Forest plot for insulin after cinnamon supplementation vs. control.

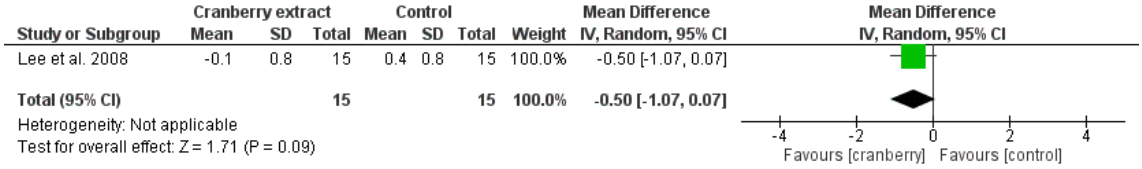

Figure 152: Forest plot for insulin after cranberry extract supplementation vs. control.

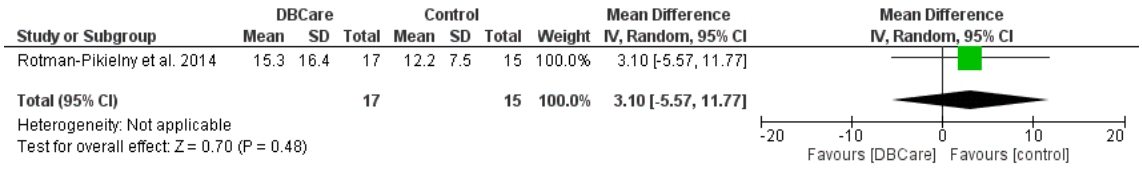

Figure 153: Forest plot for insulin after DBCare supplementation vs. control.

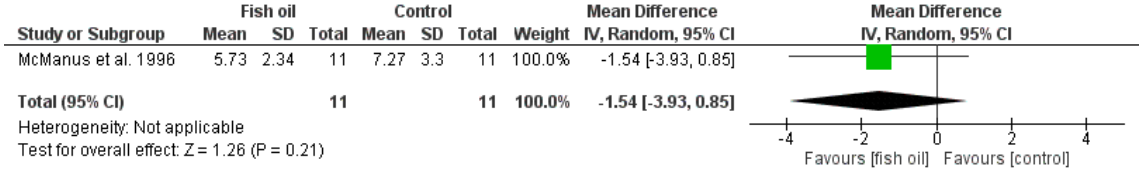

Figure 154: Forest plot for insulin after fish oil supplementation vs. control.

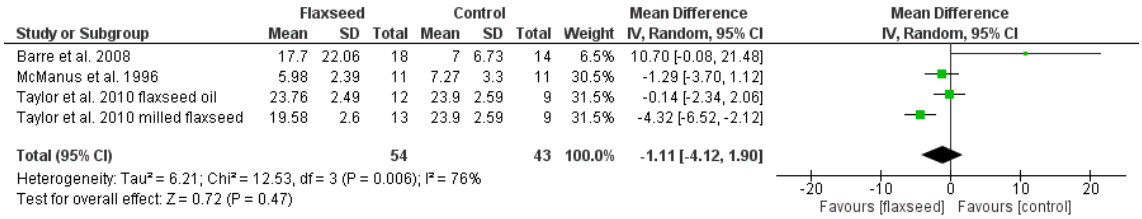

Figure 155: Forest plot for insulin after flaxseed supplementation vs. control.

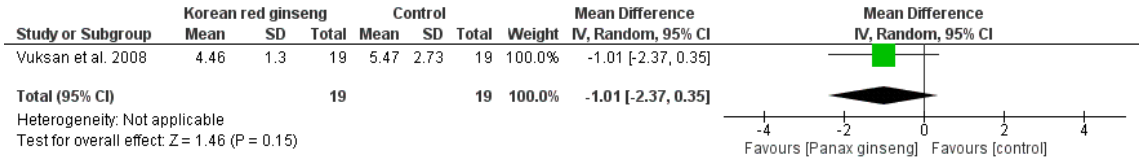

Figure 156: Forest plot for insulin after Korean red ginseng supplementation vs. control.

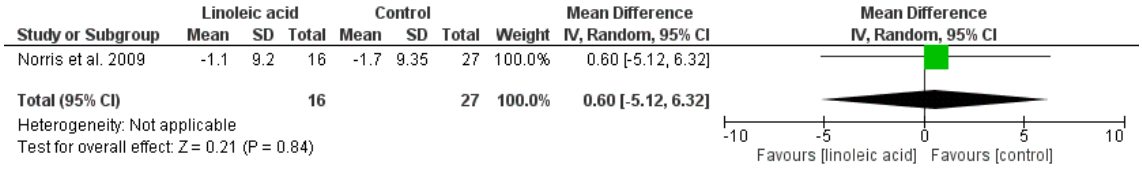

Figure 157: Forest plot for insulin after linoleic acid supplementation vs. control.

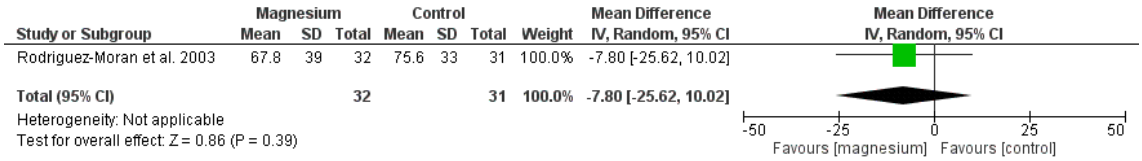

Figure 158: Forest plot for insulin after magnesium supplementation vs. control.

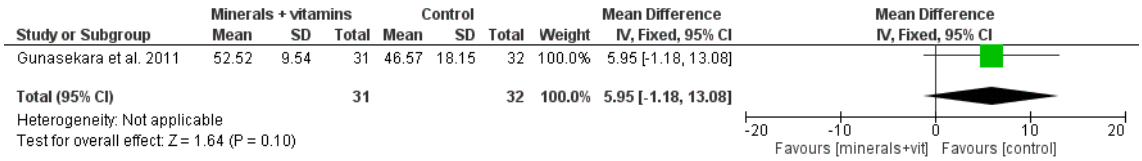

Figure 159: Forest plot for insulin after mineral and vitamin supplementation vs. control.

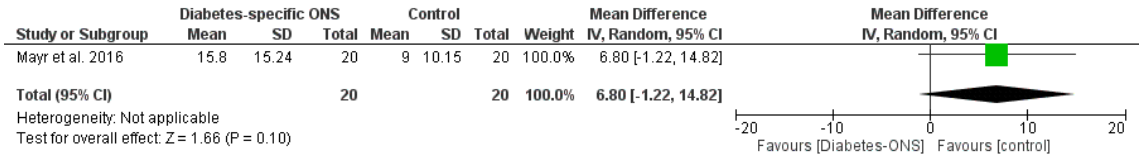

Figure 160: Forest plot for insulin after diabetes-specific ONS vs. control.

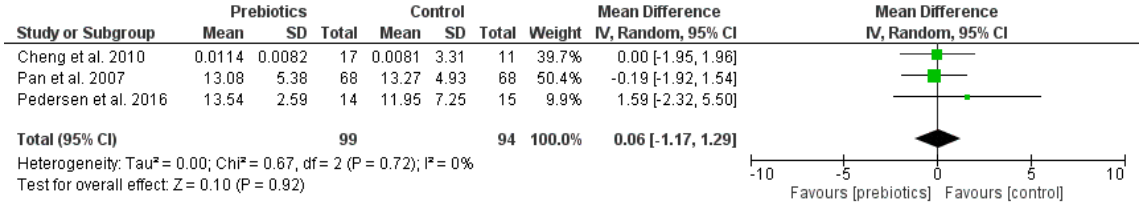

Figure 161: Forest plot for insulin after prebiotic supplementation vs. control.

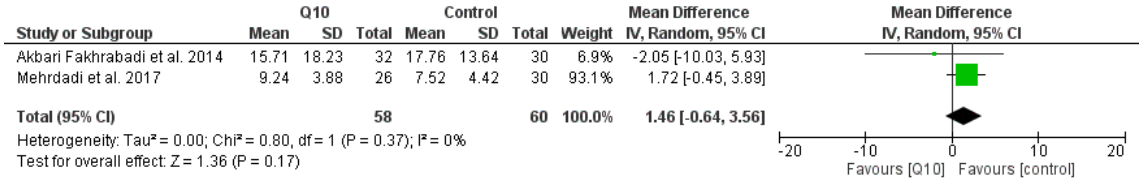

Figure 162: Forest plot for insulin after Q10 supplementation vs. control.

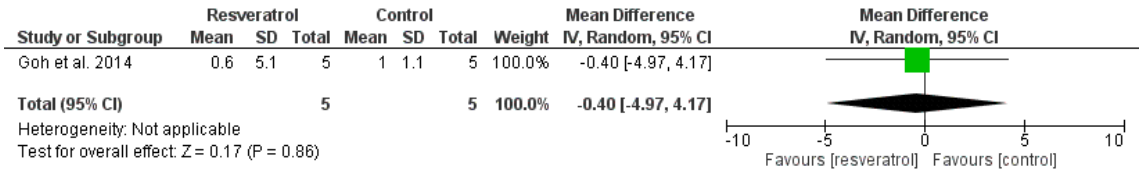

Figure 163: Forest plot for insulin after resveratrol supplementation vs. control.

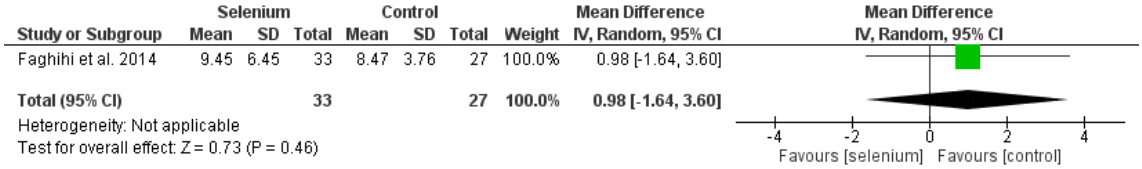

Figure 164: Forest plot for insulin after selenium supplementation vs. control.

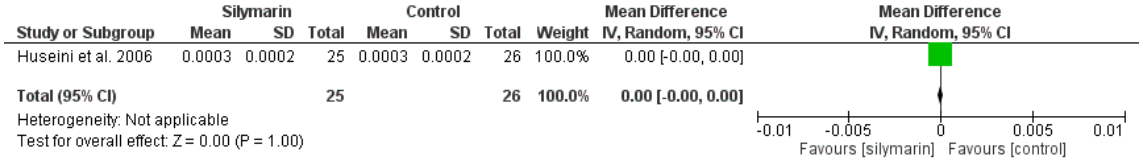

Figure 165: Forest plot for insulin after silymarin supplementation vs. control.

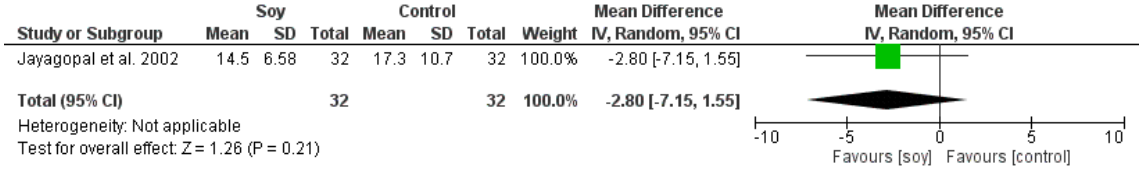

Figure 166: Forest plot for insulin after soy supplementation vs. control.

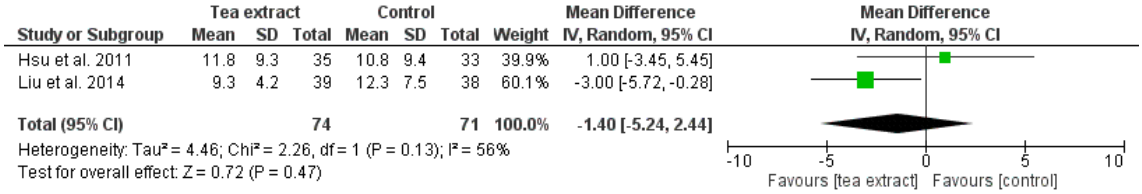

Figure 167: Forest plot for insulin after tea extract supplementation vs. control.

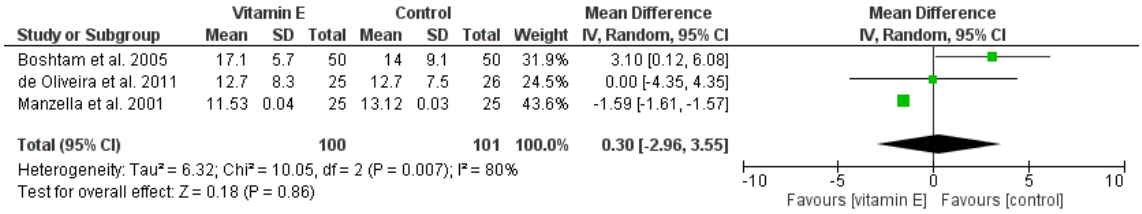

Figure 168: Forest plot for insulin after vitamin E supplementation vs. control.

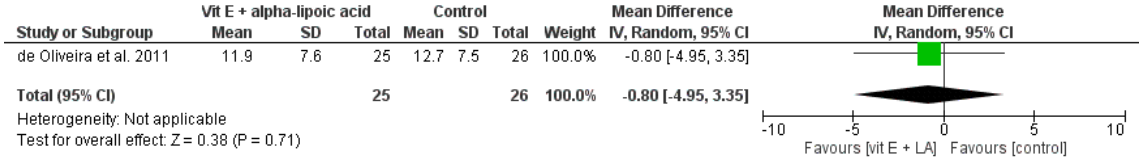

Figure 169: Forest plot for insulin after vitamin E and alpha-lipoic acid supplementation vs. control.

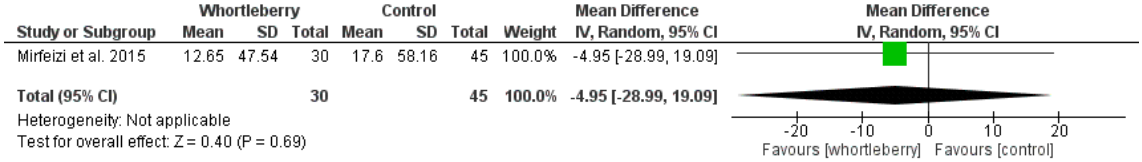

Figure 170: Forest plot for insulin after whortleberry supplementation vs. control.

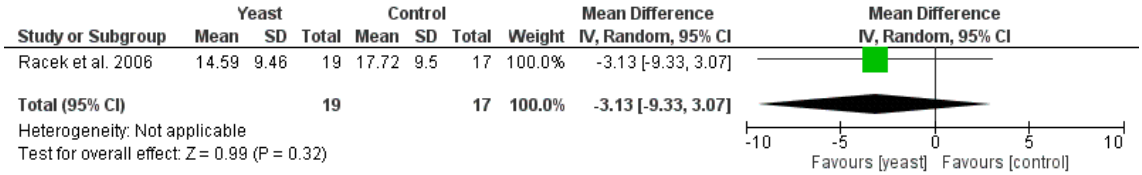

Figure 171: Forest plot for insulin after yeast supplementation vs. control.

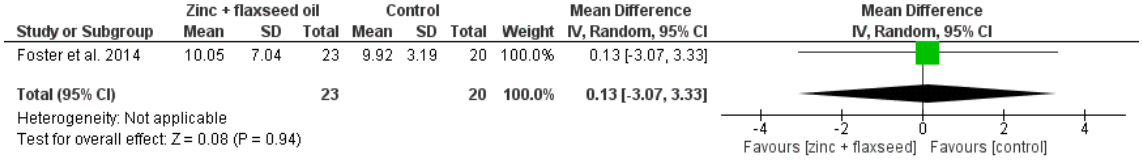

Figure 172: Forest plot for insulin after zinc and flaxseed oil supplementation vs. control.

14.4 HOMA-IR

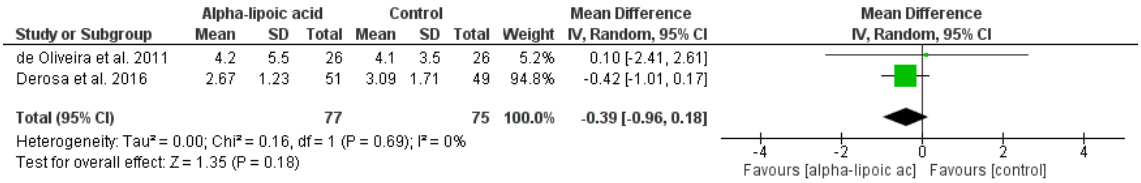

Figure 173: Forest plot for HOMA-IR after alpha-lipoic acid supplementation vs. control.

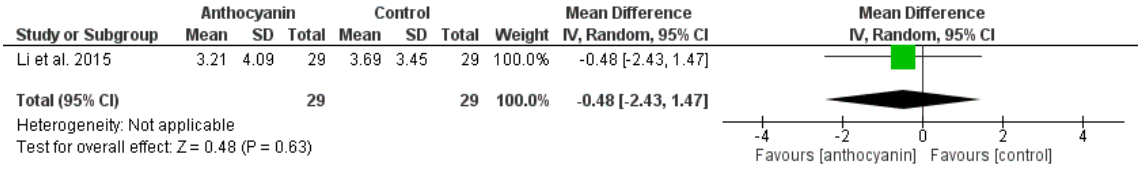

Figure 174: Forest plot for HOMA-IR after anthocyanin supplementation vs. control.

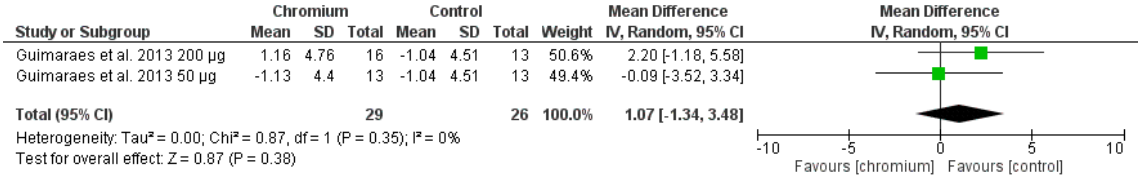

Figure 175: Forest plot for HOMA-IR after chromium supplementation vs. control.

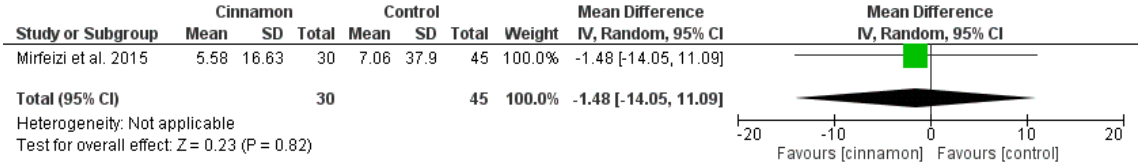

Figure 176: Forest plot for HOMA-IR after cinnamon supplementation vs. control.

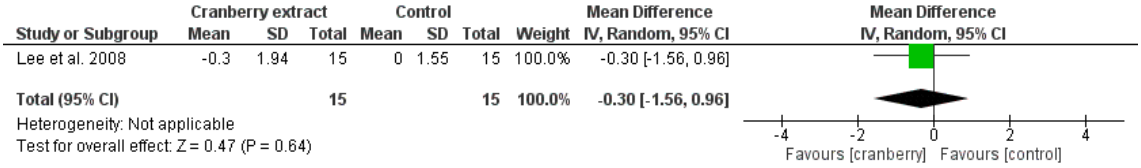

Figure 177: Forest plot for HOMA-IR after cranberry extract supplementation vs. control.

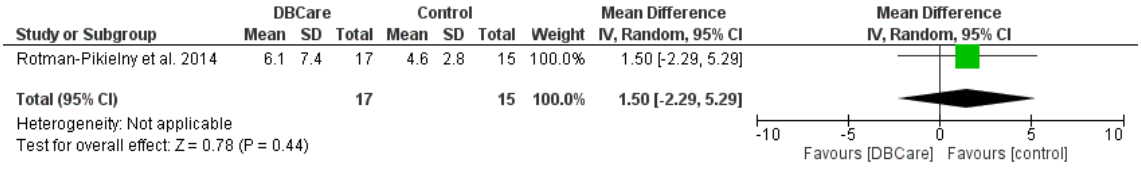

Figure 178: Forest plot for HOMA-IR after DBCare supplementation vs. control.

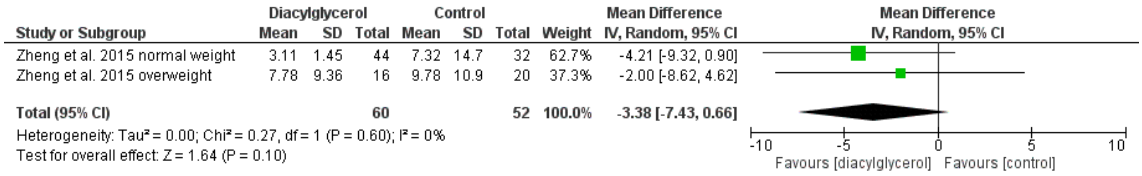

Figure 179: Forest plot for HOMA-IR after DAG supplementation vs. control.

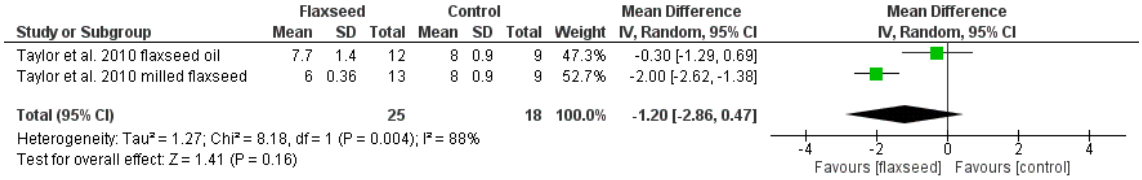

Figure 180: Forest plot for HOMA-IR after flaxseed supplementation vs. control.

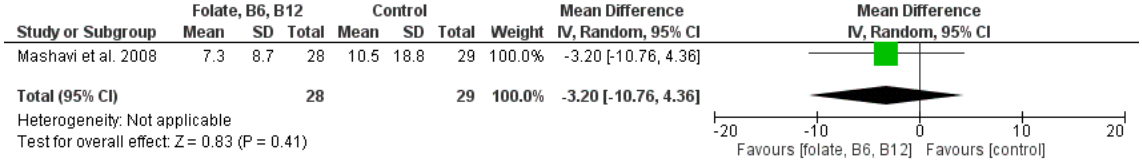

Figure 181: Forest plot for HOMA-IR after folate, B6 and B12 supplementation vs. control.

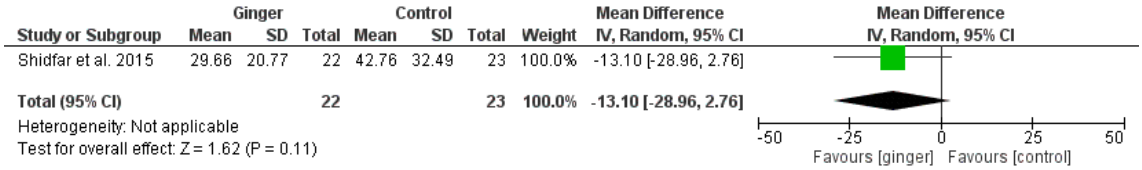

Figure 182: Forest plot for HOMA-IR after ginger supplementation vs. control.

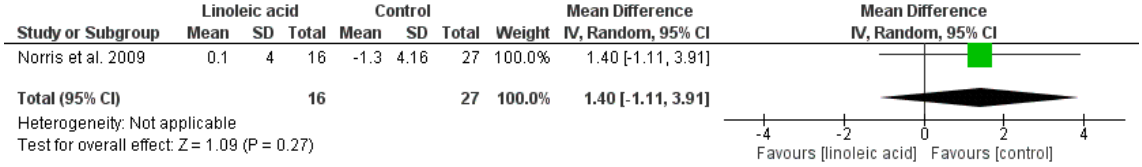

Figure 183: Forest plot for HOMA-IR after linoleic acid supplementation vs. control.

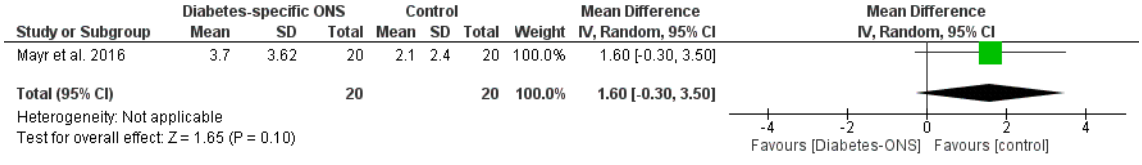

Figure 184: Forest plot for HOMA-IR after diabetes-specific ONS vs. control.

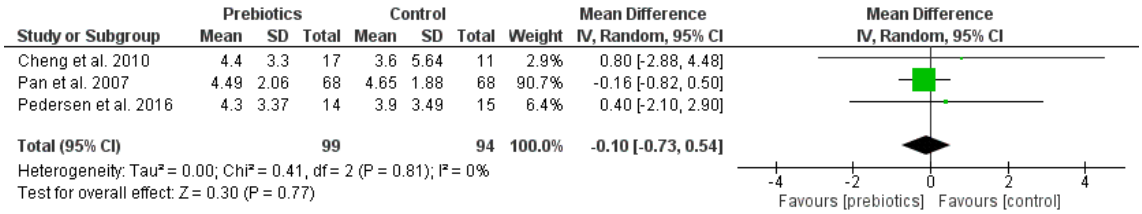

Figure 185: Forest plot for HOMA-IR after prebiotic supplementation vs. control.

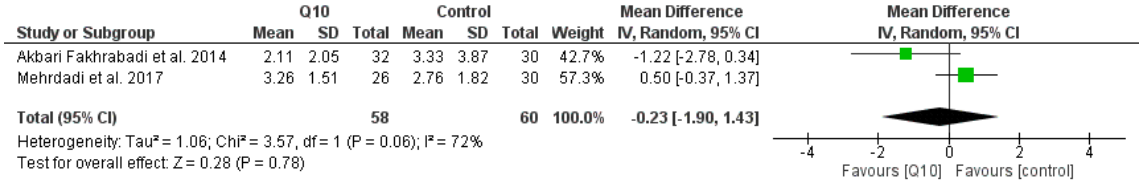

Figure 186: Forest plot for HOMA-IR after Q10 supplementation vs. control.

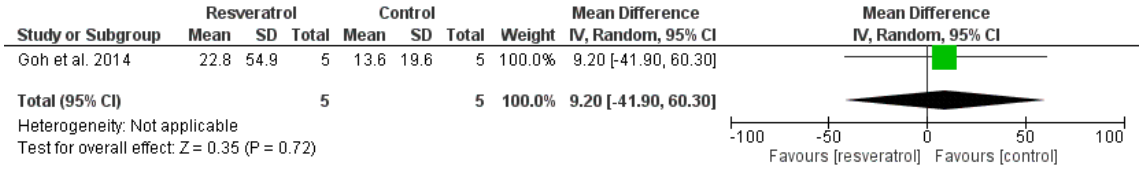

Figure 187: Forest plot for HOMA-IR after resveratrol supplementation vs. control.

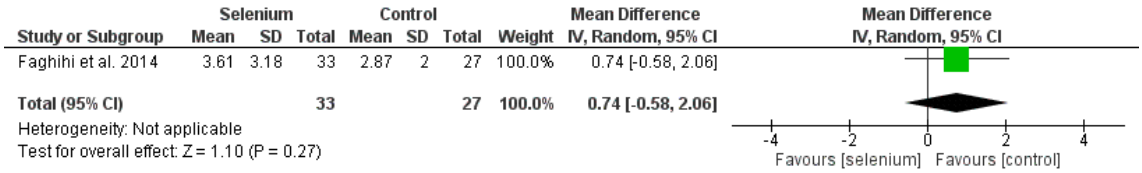

Figure 188: Forest plot for HOMA-IR after selenium supplementation vs. control.

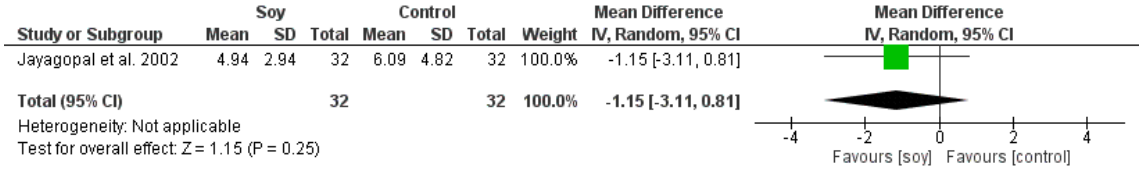

Figure 189: Forest plot for HOMA-IR after soy supplementation vs. control.

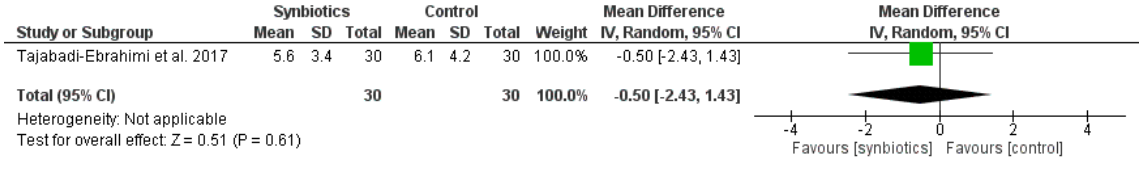

Figure 190: Forest plot for HOMA-IR after synbiotic supplementation vs. control.

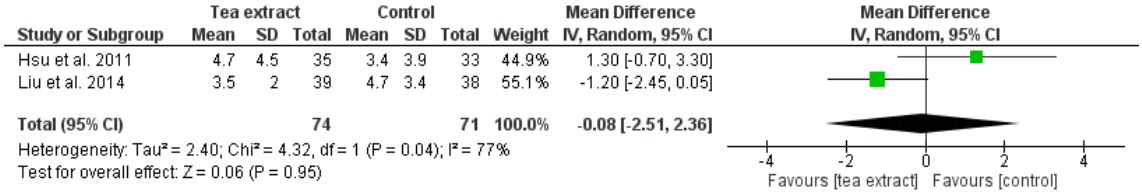

Figure 191: Forest plot for HOMA-IR after tea extract supplementation vs. control.

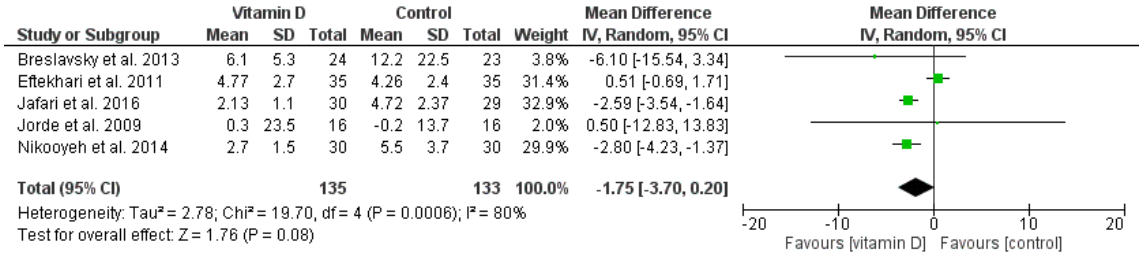

Figure 192: Forest plot for HOMA-IR after vitamin D supplementation vs. control.

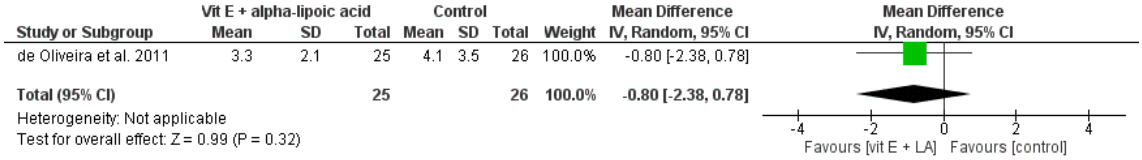

Figure 193: Forest plot for HOMA-IR after vitamin E and alpha-lipoic acid supplementation vs. control.

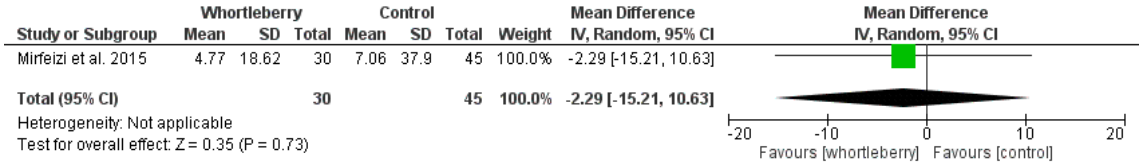

Figure 194: Forest plot for HOMA-IR after whortleberry supplementation vs. control.

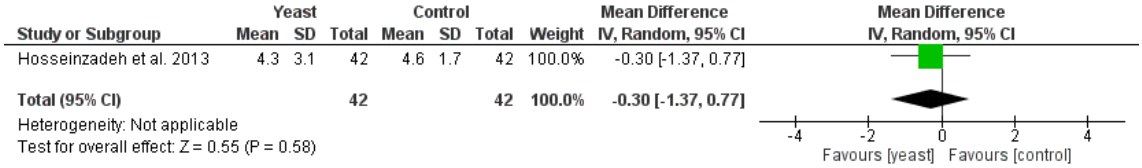

Figure 195: Forest plot for HOMA-IR after yeast supplementation vs. control.

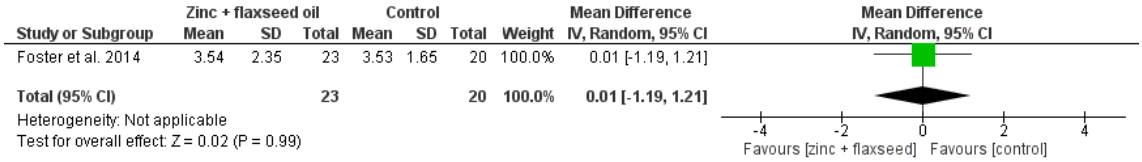

Figure 196: Forest plot for HOMA-IR after zinc and flaxseed oil supplementation vs. control.

14.5 HOMA-beta

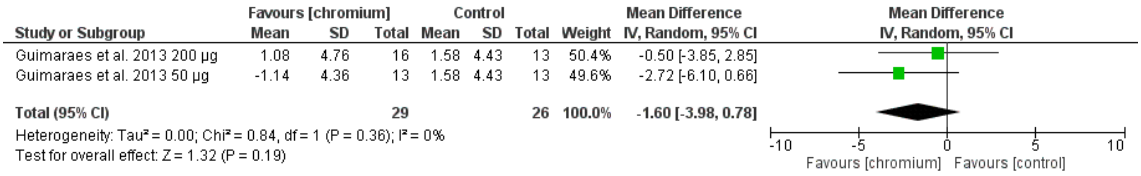

Figure 197: Forest plot for HOMA-beta after chromium supplementation vs. control.

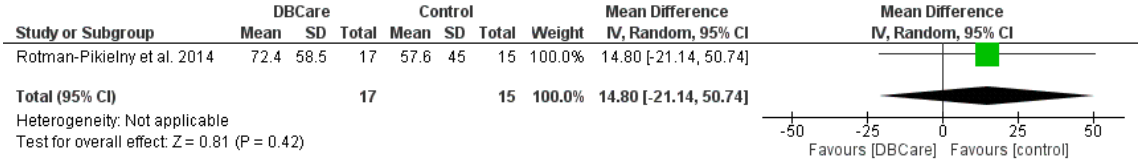

Figure 198: Forest plot for HOMA-beta after DBCare supplementation vs. control.

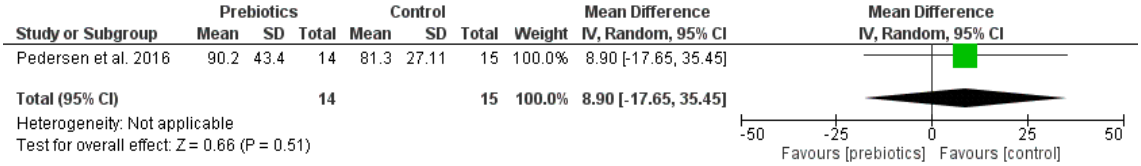

Figure 199: Forest plot for HOMA-beta after prebiotic supplementation vs. control.

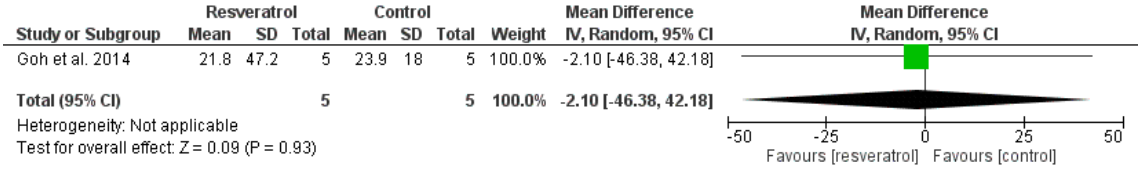

Figure 200: Forest plot for HOMA-beta after resveratrol supplementation vs. control.

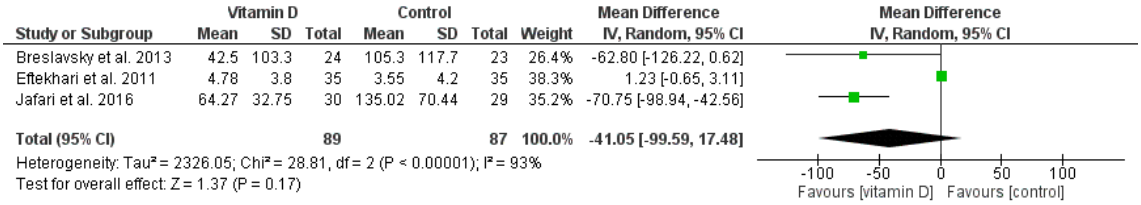

Figure 201: Forest plot for HOMA-beta after vitamin D supplementation vs. control.

14.6 QUICKI

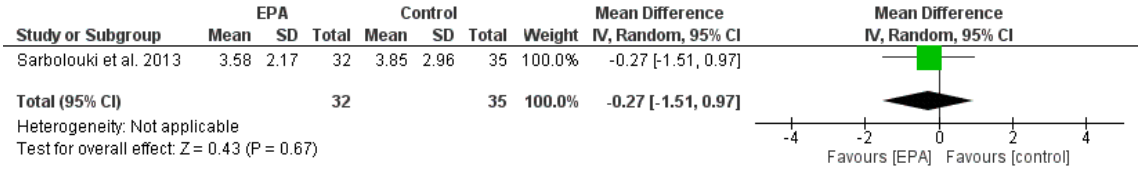

Figure 202: Forest plot for QUICKI after EPA supplementation vs. control.

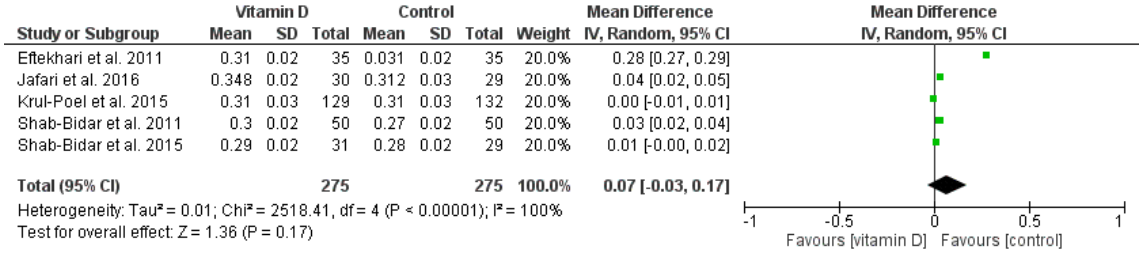

Figure 203: Forest plot for QUICKI after vitamin D supplementation vs. control.

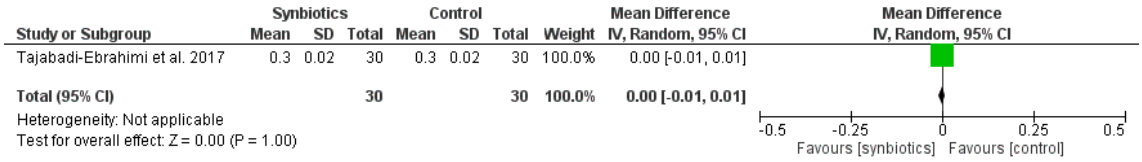

Figure 204: Forest plot for QUICKI after synbiotic supplementation vs. control.

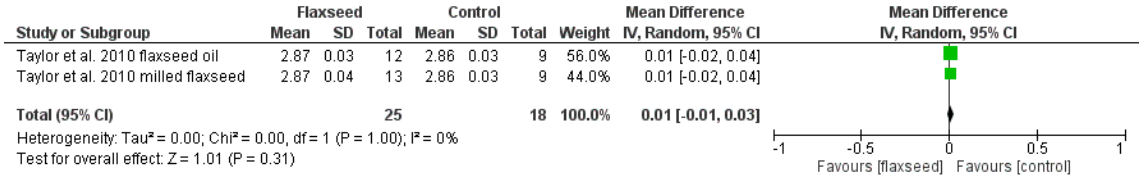

Figure 205: Forest plot for QUICKI after flaxseed supplementation vs. control.

14.7 Adiponectin

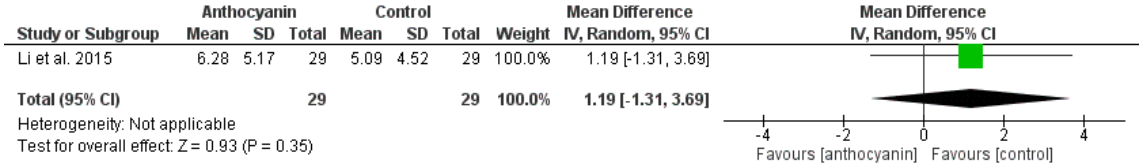

Figure 206: Forest plot for adiponectin after anthocyanin supplementation vs. control.

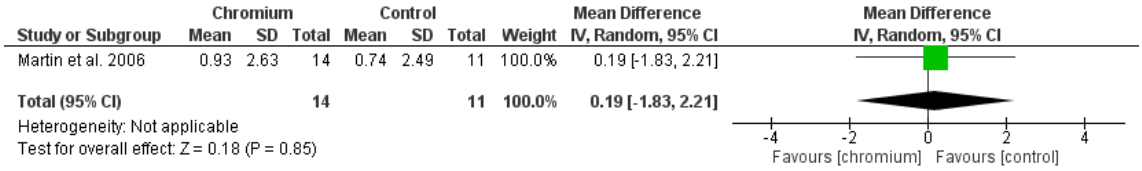

Figure 207: Forest plot for adiponectin after chromium supplementation vs. control.

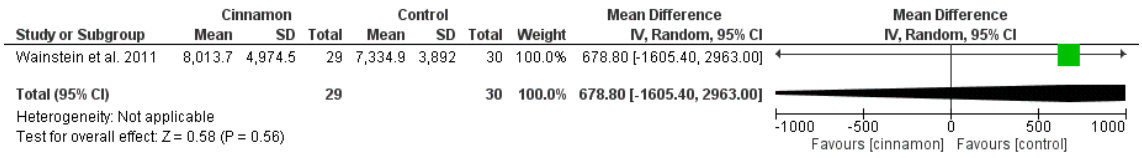

Figure 208: Forest plot for adiponectin after cinnamon supplementation vs. control.

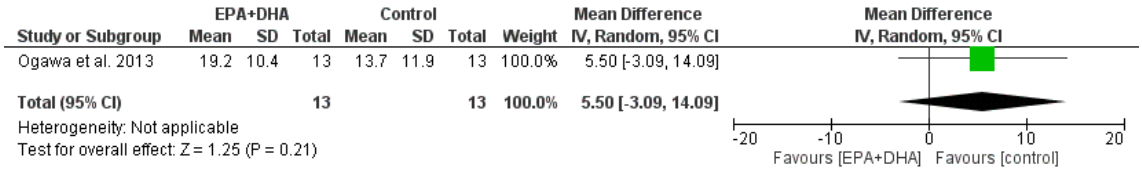

Figure 209: Forest plot for adiponectin after EPA and DHA supplementation vs. control.

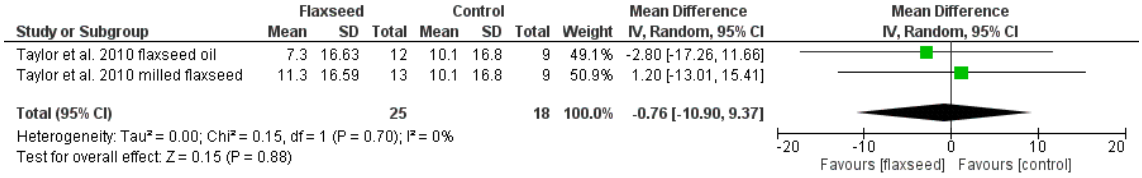

Figure 210: Forest plot for adiponectin after flaxseed supplementation vs. control.

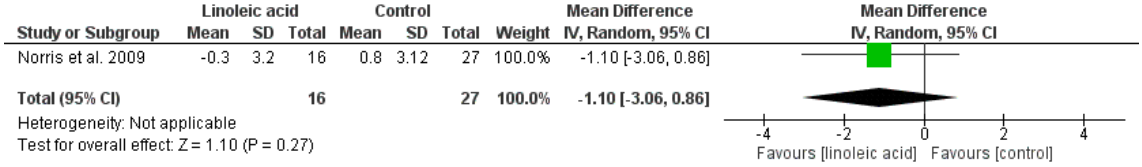

Figure 211: Forest plot for adiponectin after linoleic acid supplementation vs. control.

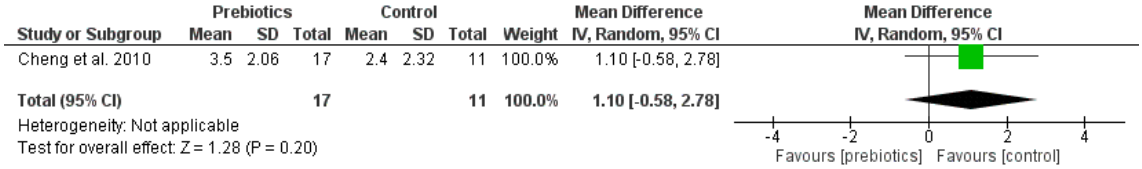

Figure 212: Forest plot for adiponectin after prebiotic supplementation vs. control.

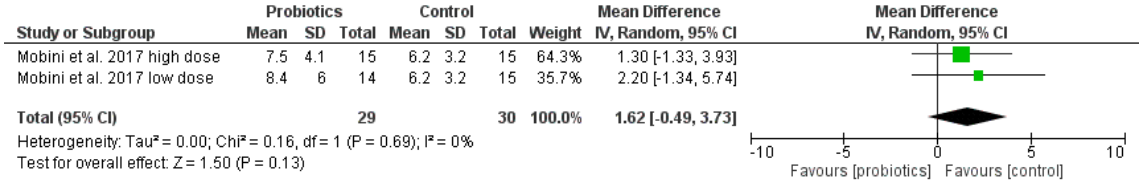

Figure 213: Forest plot for adiponectin after probiotic supplementation vs. control.

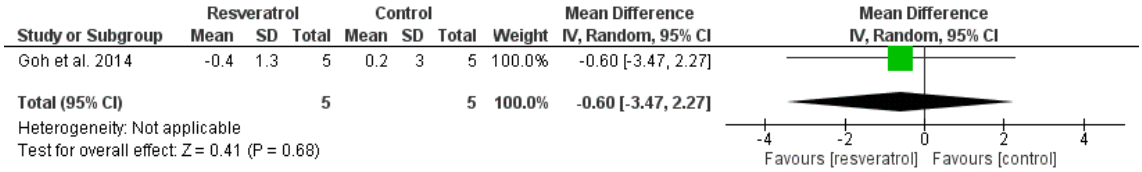

Figure 214: Forest plot for adiponectin after resveratrol supplementation vs. control.

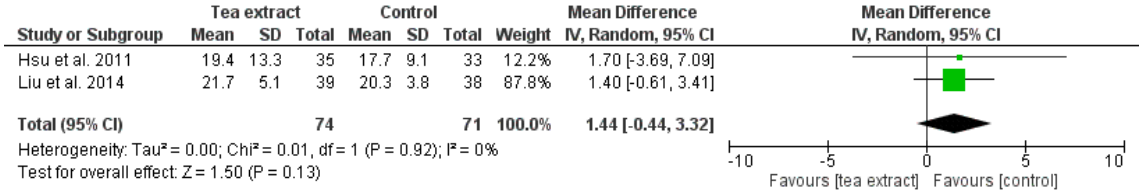

Figure 215: Forest plot for adiponectin after tea extract supplementation vs. control.

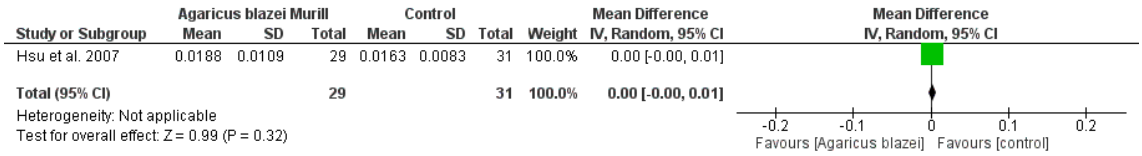

Figure 216: Forest plot for adiponectin after ABM supplementation vs. control.

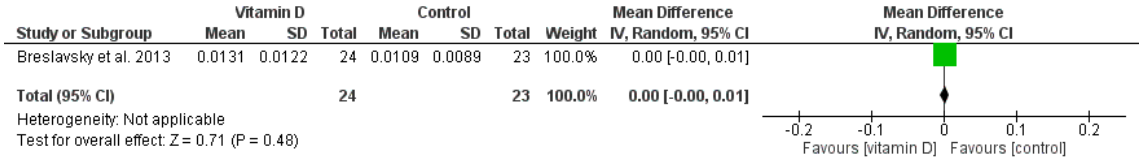

Figure 217: Forest plot for adiponectin after vitamin D supplementation vs. control.

14.8 C-Peptide

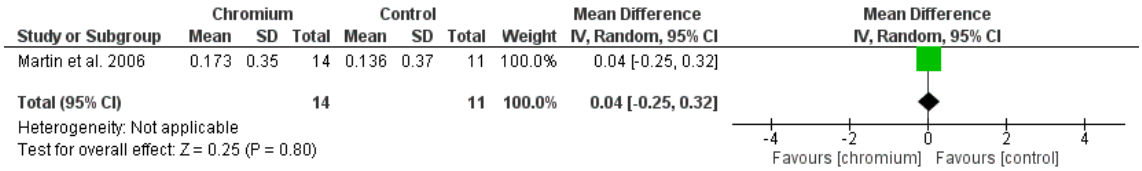

Figure 218: Forest plot for C-Peptide after chromium supplementation vs. control.

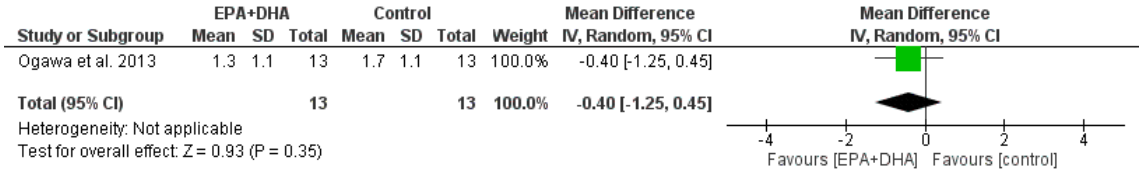

Figure 219: Forest plot for C-Peptide after EPA and DHA supplementation vs. control.

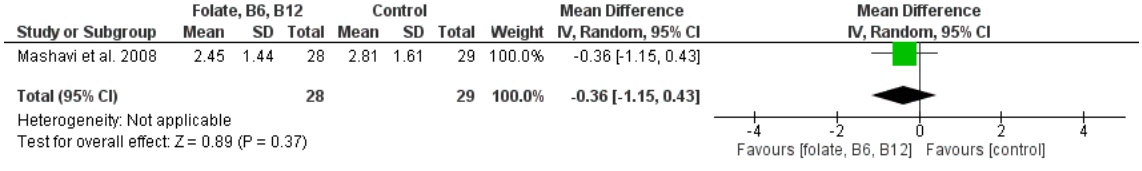

Figure 220: Forest plot for C-Peptide after folate, B6 and B12 supplementation vs. control.

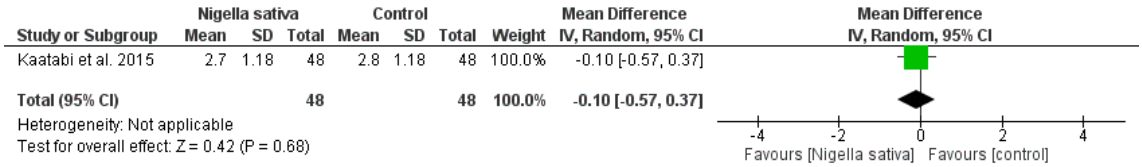

Figure 221: Forest plot for C-Peptide after N. sativa supplementation vs. control.

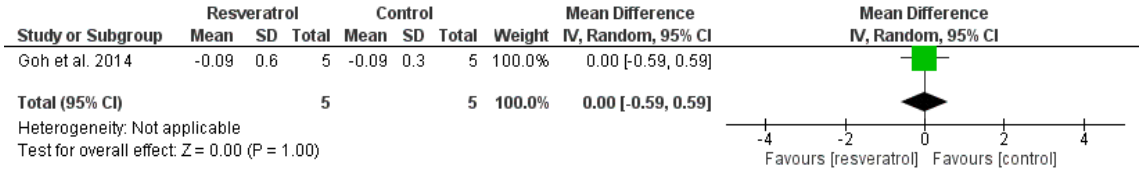

Figure 222: Forest plot for C-Peptide after resveratrol supplementation vs. control.

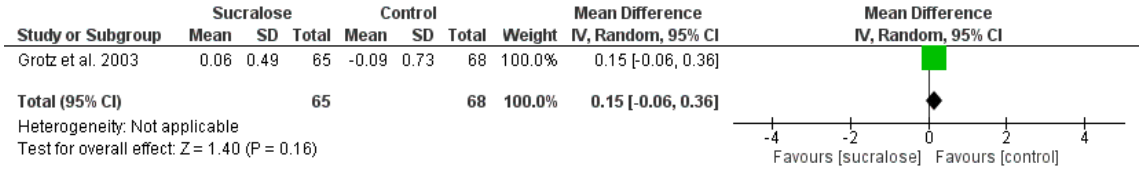

Figure 223: Forest plot for C-Peptide after sucralose supplementation vs. control.

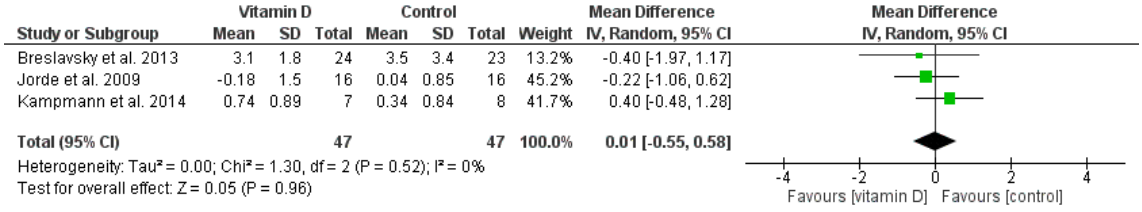

Figure 224: Forest plot for C-Peptide after vitamin D supplementation vs. control.

14.9 2-h 75 g OGTT glucose

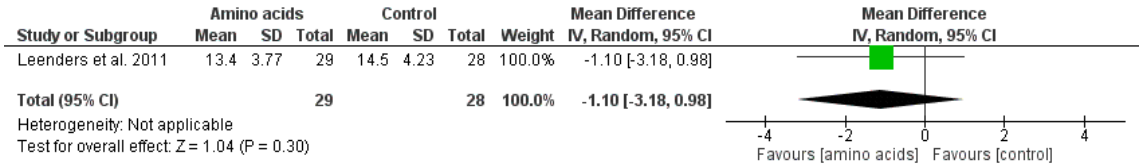

Figure 225: Forest plot for 2-h 75 g OGTT glucose after amino acid supplementation vs. control.