Ann Ist Super Sanità 2025 | Vol. 61, No. 3: 163-172
www.iss.it/annali

Supplementary Materials for

Dietary supplements for human health. What do we really know? A systematic review of umbrella reviews

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Published on
Ann Ist Super Sanità 2025 Vol. 61, No. 3: 163-172
DOI: 10.4415/ ANN_25_03_02

This PDF file includes:

Table S1
Search string

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#1: "dietary supplements"[MeSH]

Table S2
Characteristics and main findings of the included studies

Study ID, reference	N. of reviews	Type of reviews	N. of primary studies (study design)	N. of patients	Population	Intervention	Main findings and conclusions	
Antonelli, 2019 [14]	5	SRs (4) + SR with MA (1)	- Median: 10, range: 4-24 (any design) - Median: 2, range: 2-4 (placebo-controlled trials)	Median: 590, range: 191-5,217	Patients with nonallergic diseases	Orally administered bee or flower pollen, or their extract (supplementation)	**Flower pollen** extracts may be useful for symptomatic benign prostatic hyperplasia and chronic prostatitis in men, as well as for vasomotor symptoms in women (good to poor quality of evidence). **Bee pollen** might be useful for the symptomatic management of adverse effects of cancer treatment or multiple sclerosis (good quality of evidence), but evidence is too limited	
Ao, 2022 [58]	11	SRs with MA	Range: 3-39 (obs. studies)	Not available	Not available	Spicy foods and chili pepper (dietary intervention)	The health effect of consuming **spicy food** and **chili peppers** is unclear. Direct correlations exist in consuming spicy food and risk of esophageal cancer, gastric cancer, and gallbladder cancer. Negative connections are reported between the intake of spicy food and chili pepper in metabolism, mortality, and CVD. No significant association exists in blood glucose, insulin, HOMA-IR, HbA1c or gastroesophageal reflux disease	
Apostolopoulou, 2020 [15]	17	SRs (1) + SRs with MA (16)	97 (RCTs)	9,013	Critically ill patients	Glutamine (administered *via* enteral/ parenteral nutrition, or intravenously)	**Glutamine** supplementation was not associated with overall mortality and intensive care unit length of stay (LOS). However, it may reduce the rate of infectious complications (low certainty of evidence). LOS was limited with the supplementation of glutamine (very low certainty of evidence), but this effect was diminished when only studies with low risk for bias were included	
Ashor, 2019 [59]	10	SRs with MA	Range: 3-44 (RCTs)	6,407	People aged ≥18 years	Vitamin C supplementation	Evidence on the effects of **vitamin C** supplementation on markers of CVD risk is weak. The effects on endothelial function were contrasting. One SR reported significant improvement in blood pressure, FBG, LDL-C, and TGs. No overall effects of vitamin C on arterial stiffness and blood concentration of insulin, TC, and HDL-C were found, but there was some evidence for significant improvements in subpopulations with higher BMI, FBG or TC, and low plasma concentration of vitamin C	
Bialy, 2020 [16]	9	SRs	- 78 (RCTs) - 126 (obs. studies)	Range: 16-12,861	Pregnant women	Vitamin D supplementation	**Vitamin D** showed no significant benefit in terms of preterm birth, stillbirth and caesarean section (high certainty of evidence)	
							Vitamin D showed no significant benefit in terms of pre-eclampsia (low certainty), gestational diabetes (very low certainty) and low birth weight (low certainty)	
							Vitamin D showed significant benefit in terms of gestational age (low certainty)	
Burrows, 2022 [17]	46	SRs	Not available (experimental studies, i.e., RCTs, pre-post studies)	Not available	Individuals with severe mental illness	Dietary interventions (omega-3 fatty acids, pre- and probiotics, folic acid, or tryptophan)	Most reviews supported the positive effects of considered dietary interventions (**omega-3 fatty acids, pre- and probiotics, folic acid, or tryptophan**), including positive effects on mental health outcomes (no information on the certainty of evidence)	
Chakhtoura, 2022 [55]	32	MA	Not available (RCTs)	6,407	People aged ≥18 years	Vitamin D supplementation, with or without calcium	**Vitamin D with calcium** reduces the risk of hip fractures and any fractures (no information on certainty of evidence)	
							Vitamin D alone did not reduce the risk of fractures (no information on the certainty of evidence)	
Chang, 2022 [38]	195	MA	970 (interventional studies)	Not available	Not available	Prebiotic and probiotics	**Prebiotic** and **probiotics** are generally safe and beneficial to a variety of human health outcomes. However, the quality of evidence is not high	
Choi, 2021 [56]	83	MA	Range: 5-26 (RCTs or obs. studies)	Range: 4,201-558,826	Not available	Omega-3 fatty acids supplementation	**Omega-3 fatty acids** supplementation reduced CV mortality. Statistical significance was maintained even in subgroup analysis of large-scale RCTs (more than 1,000 patients). However, many studies showed conflicting results	
Corrao, 2021 [60]	9	SRs with MA	Not available (clinical trials)	Not available	Not available	Vitamin D, vitamin C, melatonin, or zinc supplementation	Considered supplements have anti-inflammatory effects. An intake of 50,000 IU/month of **vitamin D** showed efficacy in reducing CRP. An amount of 1-2 g per day of **vitamin C** demonstrated efficacy both in CRP and endothelial function, and a dosage of **melatonin** ranging from 5 to 25 mg/day showed good evidence of efficacy in CRP, TNF, and IL-6. A dose of 50 mg/day of **zinc** showed positive results in CRP. Certainty of evidence ranged from moderate to high	
De Silvia Lopes, 2021 [79]	75	SRs	Range: 2-90 (clinical trials)	Range: 52-310,000	Anaemic or non-anaemic patients	Nutrition-specific interventions (e.g., zinc, zinc+iron) administered as supplements or fortified foods	**Iron** supplementation increased Hb levels in healthy children, adults, and elderly people. **Iron fortified foods** may increase Hb concentration and reduce the risk of anaemia. Daily **iron** supplementation may increase Hb levels and reduce the risk of anaemia in infants, preschoolers and school-age children, and pregnant and non-pregnant women. **Iron fortification of foods** in infants and use of iron pots in children may have prophylactic benefits for malaria endemicity low-risk populations. Certainty of evidence varied between high and very low	
De Spiegeleer, 2018 [61]	7	SRs with MA	Not available	Not available	Older people (≥65 years)	Vitamin D	**Vitamin D** significantly improved muscle strength and physical performance, especially in women with low baseline values (<25 nmol/l). Certainty of evidence was low	
Ellwood, 2020 [18]	10	SRs	- RCTs (93) - Obs. studies (1)	6,104	Infants	Probiotics	**Probiotics** were effective for the treatment of colic in breastfed infants (high-level evidence)	
Firouzabadi, 2022 [62]	28	SRs with MA	672 (RCTs)	273,523	Pregnant women, women during lactation and infants	Omega-3 fatty acids supplementation	**Omega-3 supplementation** during pregnancy reduced the risk of pre-eclampsia and low-birth weight, improved head circumference, and reduced severe retinopathy of prematurity and cholestasis in infants (moderate to high certainty of evidence)	
							Omega-3 supplementation showed favourable effects on preterm delivery, pre-natal/post-partum depression, glycaemic control, and markers of inflammation in pregnant women, and anthropometric measures, language development, visual acuity, and duration of ventilation in infants (low certainty of evidence)	
Fong, 2022 [39]	13	MA (12) + umbrella reviews (1)	Not available (RCTs)	Not available	Patients with T2D	Supplementation of chromium, vitamin C, vitamin D, probiotics, omega-3 fatty acids and polyphenols	**Chromium**, **vitamin C**, **vitamin D**, and **omega-3 fatty acids** reduced HbA1c (very low certainty evidence). **Probiotics** were superior to placebo for HbA1c. **Magnesium, zinc, vitamin C, probiotics,** and **polyphenols** were superior to placebo for FBG. **Vitamin D** was superior to placebo for insulin resistance	

Continues

Study ID, reference	N. of reviews	Type of reviews	N. of primary studies (study design)	N. of patients	Population	Intervention	Main findings and conclusions	
Ganmaa, 2022 [57]	62	MA (62)	RCTs (107)	Not available	Not available	Vitamin D supplementation	Current evidence regarding the effects of **vitamin D** supplementation on respiratory infections and chronic diseases is inconsistent (no information on the certainty of evidence)	
Gielen, 2021 [19]	13	SRs (7) + SRs with MA (6)	Not specified	Not available	People aged ≥65 years	Proteins, EAA, leucine, β-hydroxy-β-methylbutyrate, creatine, and multinutrient supplementation (with or without physical exercise)	Best evidence is available to recommend **leucine** because it has a significant effect on muscle mass in elderly people with sarcopenia. Protein supplementation on top of resistance training is recommended to increase muscle mass and strength, for obese persons and for ≥24 weeks. Certainty of evidence ranged from low to high	
Grgic, 2020 [37]	11	SRs	320 (crossover studies)	4,855	Apparently healthy individuals	Caffeine supplementation	**Caffeine** was ergogenic for aerobic endurance, muscle strength, muscle endurance, power, jumping performance and exercise speed. The certainty of evidence was generally moderate.	
Grgic, 2021 [75]	8	SRs with MA	110 (crossover studies)	1,101	Healthy people	Sodium bicarbonate supplementation	**Sodium bicarbonate** supplementation enhanced peak anaerobic power, anaerobic capacity, performance in endurance events lasting ~45 s to 8 min, muscle endurance, 2,000-m rowing performance, and high-intensity intermittent running. The certainty of evidence was moderate to high	
Hoang, 2021 [40]	50	MA	Not available (clinical trials)	Not available	Not available	*Zingiber officinale* Roscoe (ginger), *Hibiscus sabdariffa* L., *Aloe vera* spp., *Nigella sativa* L., or *Arthrospira platensis* (spirulina) supplementation	**Ginger** and ***Hibiscus sabdariffa* L.** reduced systolic blood pressure, while ***Aloe vera* spp., *Nigella sativa* L.,** and **spirulina** were associated with beneficial effects on both lipid profiles and glycaemic control. The results must be interpreted with caution due to potential heterogeneity. The certainty of evidence ranged from low to high	
Houzé, 2017 [63]	4	SRs with MA	Not available (clinical trials)	Not available	Patients with chronic pain	Antioxidants, *Cannabis sativa* spp., and *Rosa canina* L. supplementation	Inhaled ***Cannabis sativa* spp.** was efficient for chronic pain relief. Certainty of evidence was high	
Iqbal, 2019 [41]	16	MA	Not available (clinical trials)	Not available	Pregnant women	Iron, or iron+folic acid supplementation	**Iron** supplementation reduced the risk of iron deficiency and iron-deficiency anaemia and had some risk-reducing effects for low-birth-weight infants (no information on the certainty of evidence)	
Jafari, 2018 [20]	7	SRs	71 (RCTs)	4,688	Patients with CVDs	Coenzyme Q10 (CoQ10) supplementation	The **CoQ10** supplement may be a useful tool for managing patients with heart failure (good certainty of evidence)	
Kavyani, 2022 [42]	32	MA	Range: 2-68 (RCTs)	15,245	Adults with different health conditions	Omega-3 fatty acids supplementation	**Omega-3** supplementation significantly reduced CRP, TNF, and IL-6 levels. Omega-3 can be recommended as an adjuvant anti-inflammatory agent. Certainty of evidence ranged from moderate to high	
Keramati, 2022 [43]	7	MA	Range: 5-21 (RCTs)	6,203	Patients with T2D, PCOS or metabolic abnormalities	*Cinnamomum verum* Presl (cinnamon) supplementation	**Cinnamon** supplementation significantly reduced BW (moderate quality). Favourable results were obtained at a dose of ≥3 g/day and in patients with PCOS	
							Cinnamon supplementation significantly reduced BMI (low quality). Favourable results were obtained at a dose of ≥3 g/day and in patients with PCOS	
							Cinnamon had no effect on WC (low quality)	
Khan, 2019 [21]	9	SRs	277 (RCTs)	992,129	Adult patients	Nutritional supplements (antioxidants, β-carotene, vitamin B complex, multivitamins, selenium, vitamin A, vitamin B3, vitamin B6, vitamin C, vitamin E, vitamin D, calcium *plus* vitamin D, calcium, folic acid, iron, and omega-3 fatty acids	**Omega-3** fatty acids were associated with reduced risk for myocardial infarction and coronary heart disease (low certainty of evidence). **Folic acid** was associated with lower risk for stroke (low certainty of evidence)	
							Vitamin B6, vitamin A, multivitamins, antioxidants, and **iron** had no significant effect on mortality or CV disease outcomes (very low to moderate certainty of evidence)	
Kim, 2012 [22]	6	SRs	78 (RCTs)	Not available	Men with lower urinary tract symptoms secondary to benign prostatic hyperplasia	*Serenoa repens* extracts, β-sitosterol, *Pygeum africanum* Hook f. extracts and Cernilton® (rye grass pollen) supplementation	For ***Serenoa repens*** extracts, no specific effect on benign prostatic hyperplasia symptoms and urinary flow measures was observed (certainty of evidence ranged from low to high)	
							β-sitosterol, ***Pygeum africanum* Hook f.** extracts and **Cernilton®** were reviewed in one study each, and beneficial effects were observed for all three. Certainty of evidence ranged from moderate to high	
Kinshella, 2021 [44]	91	MA	Not available (RCTs)	Not available	Pregnant women	Vitamin D and/or calcium, omega-3, multiple micronutrients, and lipid-based nutrient supplementation	There is evidence that supports supplementation of **vitamin D and/or calcium, omega-3, multiple micronutrients**, and **lipid-based nutrients** in reducing the risks of adverse maternal and fetal health outcomes. However, these findings are limited by poor quality of evidence	
Liu, 2022 [45]	289	MA (245) + MR studies (44)	- 173 (obs. studies) - 72 (RCTs)	Not available	Not available	Vitamin D supplementation	**Vitamin D** supplementation is associated with a decreased risk for all-cause mortality (low quality of evidence)	
							Vitamin D supplementation did not reduce the risk for Alzheimer's disease, hypertension, schizophrenia, or T2D (low quality of evidence)	
Maretzke, 2020 [23]	74	SRs (73) + MR studies (1)	Not available (RCTs and obs. studies)	Not available	Not available	Vitamin D supplementation	SRs of RCTs support observational data on **vitamin D** supplementation only for the risk of acute respiratory tract infections and indicate beneficial therapeutic effects in vitamin D-deficient patients with asthma and COPD, while effects on major depression and T1D need to be further elucidated. MR studies do not consistently support the results of SRs	

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Study ID, reference	N. of reviews	Type of reviews	N. of primary studies (study design)	N. of patients	Population	Intervention	Main findings and conclusions	
Martin Ruiz, 2018 [24]	7	SRs	125 (RCTs)	345,829	Healthy adults or those at high risk of CVD	Vitamin D, omega-3 fatty acids, selenium, coenzyme Q10, vitamin K, vitamin A, vitamin C, vitamin E, calcium, folic acid, or β-carotene supplementation	Four reviews found a pooled statistically significant CV risk reduction with supplements of **vitamin D** and increased consumption of **omega-3 fatty acids** (no information on the certainty of evidence). Future studies are needed to establish if these interventions, alone or in combination, result in definitive long-term health benefits	
Mateussi, 2017 [25]	27	Cochrane SRs	Not available (clinical studies)	Not available	Healthy individuals or those diagnosed with any clinical condition	Vitamin D supplementation	Included reviews found moderate to high quality of evidence regarding the benefits of **vitamin** D for pregnant women (i.e., reduction of preterm birth risk and low-birth-weight risk), and for patients with asthma (reduction of severe exacerbations)	
							No benefit was found for **vitamin D** alone (without calcium) for preventing hip or any new fracture (moderate to high quality of evidence)	
McKenzie, 2016 [26]	9	SRs	35 (RCTs)	3,406	Patients with irritable bowel syndrome	Probiotics	Twelve out of 29 **probiotics** (41%) showed no symptom or quality of life benefits. No strain or dose specific probiotic was consistently effective to improve any symptoms of irritable bowel syndrome or quality of life. None of the RCTs were at low risk of bias	
Mehraban, 2021 [64]	141	SRs with MA	Range: 3-124 (controlled trials)	Not available	Not available	Vegetable oils, phytosterols, plant proteins, *Camellia sinensis* L. (green tea), *Curcuma longa* L. and curcumin	**Sunflower oil, green tea** and **plant proteins** reduced TC, LDL-C and TGs levels. Rice bran oil significantly increased HDL-C. **Phytosterols, curcumin, curcuminoid,** and ***Curcuma longa* L.** reduced TC, LDL-C and TGs, and increased HDL-C. Certainty of evidence was high in the majority of studies	
Michels, 2022 [27]	87	SRs	Not available (RCTs and obs. studies)	Not available	Not available	Prebiotics/probiotics/ synbiotics	522 associations were reported for **prebiotics/probiotics/synbiotics** with hyperglycemia, T2D, obesity, hyperlipidemia, hypertension, NAFLD, and MetS. Meta-evidence was highest for probiotics. Methodological quality was moderate in 62%, 12% low, and 26% critically low	
Moorthy, 2020 [28]	68	SRs	Not available (controlled trials)	Not available	Healthy population (aged 6 months to 49 years)	Iron, micronutrient powders and iron+folic acid supplementation	Daily and intermittent **iron** supplementation and **micronutrient powders** were associated with increased haemoglobin concentration in children aged <5y. Daily and intermittent **iron** supplementation among children older than 5y and **daily iron-folic acid supplementation** in pregnant women were associated with increased haemoglobin concentration. Similar results were obtained for reducing the risk of anemia. There is lack of evidence on the effects of the considered supplements	
Moslehi, 2023 [46]	25	MA	Range: 2-11 (RCTs)	Not available	Women with PCOS	Probiotics/synbiotics, curcumin, omega-3, vitamin D, or inositol supplementation	**Probiotics/synbiotics** reduced FBG, FI, and HOMA-IR (with moderate to high certainty of evidence) and total testosterone (with moderate certainty of evidence). **Curcumin** supplementation decreased FBG, FI, and HOMA-IR (with moderate certainty). There were also improvements in FI after taking **vitamin D** or **inositol** supplements (with moderate certainty of evidence). In subfertile women with PCOS, **inositol** increased the ovulation rates (with moderate certainty of evidence)	
Moslemi, 2022 [65]	23	SRs with MA	234 (clinical trials)	Not available	People aged ≥18 years	Vitamin D supplementation	**Vitamin D** supplementation significantly reduced serum CRP, TNF, and MDA concentrations. However, no significant changes were found for IL-6, total antioxidant capacity, and glutathione activity. Vitamin D could be considered an adjuvant therapy for relieving inflammation and oxidative stress. Almost all of the studies were of high methodological quality	
Motrico, 2023 [47]	1	MA	2 (RCTs)	305	Healthy women during the perinatal period	Preventive interventions for perinatal depression (selenium and omega-3 supplementation)	No significant effect was found for **selenium** and **omega-3** supplementation in reducing postpartum depressive symptoms compared with placebo. The strength of evidence was poorly reported and, in most cases, was low	
Musazadeh, 2022 [48]	29	MA	576 (clinical studies)	22,357	Obese people	Probiotics	**Probiotics** supplementation was significantly effective in decreasing BMI, BW, and WC. Greater effects on BW were observed when intervention duration was >8 weeks and on obese individuals. BMI was also greatly modified in participants with MetS and when intervention duration lasted for ≥12 weeks. The methodological quality was moderate in 83%, low in 10%, and critically low in 7% of included studies. These findings strongly recommend supplementation with probiotics in the management of obesity	
Musazadeh, 2023 [49]	10	MA	49 (RCTs)	24,510	Patients with depression	Vitamin D supplementation	There was a significant reduction in depression symptoms compared to placebo. These findings confirm the potential benefits of **vitamin D** supplementation in reducing the development and symptoms of depression. Certainty of evidence ranged from moderate to high	
Neil-Sztramko, 2022 [29]	9	SRs	170 (clinical trials)	8,847	Community-dwelling older adults	Physical activity or structured exercise, alone or combined with nutrition interventions (e.g., proteins, creatine, or vitamin D supplementation)	No evidence of benefit was found for **nutritional supplementation** with physical activity on combined aerobic/endurance activities, general physical activity, and mind-body exercise (low certainty of evidence)	
Neyestani, 2022 [66]	13	SRs with MA	317 (clinical trials)	24,482	Not available	*Camellia sinensis* L. (green tea) supplementation	Significant effects of **green tea** on BW, WC, systolic and diastolic blood pressure were found. There was a similar effect on FBG but not on other glycemic indicators. The findings also revealed a significant reduction in TC and LDL-C levels. Certainty of evidence ranged from low to high	

Continues

Study ID, reference	N. of reviews	Type of reviews	N. of primary studies (study design)	N. of patients	Population	Intervention	Main findings and conclusions	
Onakpoya, 2011 [67]	9	SRs with MA	135 (clinical trials)	7,756	Not available	Food supplements (i.e., guar gum, chromium picolinate, *Ephedra* spp. and ephedrine, *Citrus aurantium* L., conjugated linoleic acid, calcium, glucomannan, chitosan, *Camellia sinensis* L. (green tea)	**Guar gum**, ***Citrus aurantium* L.** and **conjugated linoleic acid** showed no effects on BW. Many studies were of low methodological quality	
							Chromium picolinate showed a significant effect on BW reduction in obese patients; ***Ephedra* spp**. and **ephedrine** supplementation revealed a significant short-term effect on BW; **glucomannan** reduced BW significantly, especially in obese patients; **chitosan** demonstrated short-term weight loss in obese and overweight people; **green tea** was efficacious for weight reduction and weight maintenance. Many studies were of low methodological quality	
Pagano, 2018 [30]	22	SRs	169 (RCTs)	12,465	People with CV, metabolic, neurodegenerative disorders, or inflammatory diseases	Curcumin supplementation	There is some evidence that **curcumin** can exert systemic antioxidant actions and may be effective i) in inflammatory conditions such as arthritis-related diseases and inflammatory bowel disease, ii) in reducing lipid levels and CV risk factors and iii) in skin diseases. Cautious positive results were reported for depressive disorders. Certainty of evidence ranged from low to high	
							Curcumin was not effective in Alzheimer's disease patients. Certainty of evidence ranged from low to high	
Philips, 2022 [35]	15	SRs	Not available	Not available	Older people or people with clinical conditions	β-hydroxy-β-methyl butyrate supplementation	Five studies found some evidence that β-hydroxy-β-methyl butyrate increased LSTM; the remaining 10 studies reported some evidence favouring no difference or insufficient evidence to determine an effect. Of the 12 studies that evaluated strength, 4 found some evidence, 5 found some evidence of no effect with one article finding some evidence in favour of patients in peri-hospitalized and no evidence for those that are community-dwelling, 4 had insufficient evidence to determine an effect, and one had insufficient evidence. No study reported a positive effect on physical function. Future studies are needed	
Posadzki, 2016 [31]	18	SRs	362 (clinical trials)	Not available	Patients with elevated blood lipid levels	*Allium sativum* L. (garlic), *Camellia sinensis* L. (green tea), Chinese herbal medicines, mushrooms, *Commiphora mukul* (guggul), Artichoke leaf extract, or red yeast rice	Most of the SRs (56%) furnished equivocal conclusions on the lipid lowering effects of **considered interventions**; 7 SRs (37%) arrived at positive conclusions, and 2 (7%) arrived at negative conclusions. Most of the SRs were of high methodological quality but evidence was conflicting	
Poscia, 2018 [68]	12	SRs with MA	614 (clinical trials)	Not available	Elderly people (≥65 years)	Vitamin D supplements, alone or combined with calcium, and protein-based formulas	Supplementation with **vitamin D** and other kinds of products was highly effective in preventing falls and fractures. Positive findings were also found for the elderly at risk of malnutrition and for older patients with dementia. Certainty of evidence ranged from moderate to high	
Rajwar, 2020 [32]	16	SRs	Not available (RCTs)	Not available	Women in reproductive age	Vitamin A, calcium, and vitamin D supplementation	Supplementation of **vitamin A** resulted in increased maternal serum retinol concentrations and breast milk retinol concentrations. It reduced the risk of anemia and maternal clinical infection. Certainty of evidence ranged from moderate to high	
							Calcium supplementation did not have any significant effect on BW, weight gain, and BMI. **Vitamin D** supplementation increased 25-hydroxy vitamin D levels but there was insufficient evidence for the effect on bone mineral density and serum calcium levels. Certainty of evidence ranged from moderate to high	
Rizzoli, 2018 [69]	Not available	SRs with MA	Not available (RCTs and obs. studies)	Not available	Not available	Dietary proteins	In older people with osteoporosis, **high protein intake** (≥0.8-g/kg body weight/day) is associated with higher BMD, slower rate of bone loss, and reduced risk of hip fracture. Intervention with dietary protein supplements attenuate age-related BMD decrease and reduce bone turnover marker levels, together with an increase in insulin-like growth factor and a decrease in parathyroid hormone (no information on the certainty of evidence)	
Schultz, 2016 [70]	Not available	SRs with MA	13 (not available)	Not available	Older adults (≥60 years) living in the community, with co-morbidities	Oral nutritional supplements (with and without resistance exercise training)	**Oral nutritional supplements** improved body composition, also in combination with resistance exercise training. The outcomes of lean mass and BW/BMI were responsive to nutritional interventions, but fat mass did not vary. Certainty of evidence ranged from moderate to high	
Schwingshackl, 2016 [50]	9	MA	266 (RCTs and obs. studies)	16,134	Healthy patients or patients with metabolic disorders or CVD	Garlic and garlic supplements	8 MA showed that **garlic** significantly reduced TC levels. The effect of garlic on systolic blood pressure showed consistent results across publications, demonstrating a substantial decrease in systolic and diastolic blood pressure levels following garlic interventions. Quality of evidence was moderate to good	
Shah, 2022 [71]	10	SRs with MA	744 (RCTs and obs. studies)	548,458	Hospitalized COVID-19 patients	Vitamin D supplementation	The MA of 7 SRs showed strong evidence that **vitamin D** supplementation reduces the risk of mortality, as well as the need for intensive care and mechanical ventilation in COVID-19 patients. However, the included studies were of different methodological quality (generally low)	
Theodoratou, 2014 [33]	87	SRs	Not available (RCTs)	Not available	Not available	Vitamin D supplementation	The direction of the effect and level of statistical significance was concordant only for birth weight (maternal **vitamin D** supplementation). Current evidence does not support the argument that vitamin D supplementation increases BMD or reduces the risk of fractures or falls in older people (no information on the quality of evidence)	
Unhapipatpong, 2023 [51]	11	MA	91 (RCTs)	5,615	Patients with PCOS or metabolic disorders (T2D, NAFLD, MetS)	Curcumin supplementation	**Curcumin** supplementation, especially in the bioavailability-enhanced form, significantly reduced BMI, BW, and WC. Significant effects were also seen in adults with obesity and diabetes. Curcumin supplementation should be an option for weight reduction. Certainty of evidence ranged from critically low to high	

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Study ID, reference	N. of reviews	Type of reviews	N. of primary studies (study design)	N. of patients	Population	Intervention	Main findings and conclusions	
Veronese, 2020 [72]	16	SRs with MA	- Median: 3; range: 2-34 (RCTs) - Median: 6; range: 3-32 (obs. studies)	RCTs -> median: 1225 range: 7-16,328 obs. studies -> median: 108,424 range: 606-2,589,742	Not available	Magnesium supplementation	Strong evidence from RCTs indicates that **magnesium** supplementation can decrease the risk of hospitalization in pregnant women and reduce the intensity/frequency of migraine. In observational studies, only one outcome presented highly suggestive evidence (lower incidence of T2D in people with higher magnesium intake at baseline) and one suggestive (lower incidence of stroke associated with higher magnesium intake at baseline)	
Vesco, 2015 [52]	Not available	MA	Not available	Not available	Adult, adolescents, and children with bipolar disorder	Omega-3 fatty acids supplementation	**Omega-3** supplementation may be a safe, adjunct intervention for treating bipolar disorder in children and adolescents, even in the presence of psychotic and anxious features (no information on the certainty of evidence)	
von Salmuth, 2021 [34]	28	SRs	Not available (RCTs and obs. studies)	Not available	Mothers, pregnant women, or women of reproductive age	Supplementation with macronutrients, multiple micronutrients, vitamin D, zinc, iron+folic acid and calcium, iodine, and vitamin B12	Prenatal supplementation with **macronutrients, multiple micronutrients, vitamin D, zinc, iron+folic acid and possibly calcium, iodine,** and **vitamin B12** in deficient women improved birth outcomes. Certainty of evidence ranged from low to high	
Xu, 2022 [73]	51	SRs with MA	Not available (RCTs and obs. studies)	Not available	Not available	Vitamin C supplementation	**Vitamin C** intake was associated with reduced risk of all-cause mortality, CVD, oesophageal cancer, gastric cancer, cervical cancer, and lung cancer with an increment of 50-100 mg per day. Beneficial associations were also identified for respiratory, neurological, ophthalmologic, musculoskeletal, renal, and dental outcomes. Certainty of evidence ranged from low to high	
Zarezadeh, 2022 [74]	48	SRs with MA	722 (RCTs)	37,035	Not available	Probiotics	**Probiotics** significantly decreased FBG, HbA1c, HOMA-IR, and insulin levels. Probiotics could be recommended as adjuvant anti-hyperglycaemic agents. Certainty of evidence ranged from low to high	
Zarezadeh, 2023 [53]	14	MA	234 (RCTs)	15,494	People aged ≥18 years	Probiotics	**Probiotics** decreased both systolic and diastolic blood pressure. Greater effects on systolic blood pressure were revealed in trials with a mean age of >50 years and the duration of intervention ≤10 weeks, as well as in patients with hypertension or diabetes. Diastolic blood pressure was also more reduced in studies with a dosage of $\geq 10^{10}$ colony forming units (CFU). Probiotics could be used for controlling high blood pressure. Certainty of evidence ranged from low to high	
Zeraattalab-Motlagh, 2021 [54]	30	MA	26 (RCTs)	2,474	Adult patients with T2D, MetS or NAFLD	Resveratrol supplementation	**Resveratrol** supplementation had beneficial effects on some outcomes such as blood pressure, lipid profile, glycemic control, and insulin resistance in T2D, WC in MetS, and BW and inflammation markers in NAFLD; however, for almost all outcomes, the certainty of evidence was very low to low, or the number of trials was too few. For HbA1c, there was evidence that resveratrol can exert clinically important effects in the short term (<12 weeks; moderate certainty of evidence) but the sample size was small	

Green flag: efficacy with high quality/certainty of evidence; light green flag: efficacy with low quality/certainty of evidence or without information on the quality/certainty of evidence; grey flag: inconclusive/conflicting results; red flag: inefficacy with high quality/certainty of evidence; orange flag: inefficacy with low quality/certainty of evidence or without information on the quality/certainty of evidence. BMI: body mass index; BW: body weight; BMD: bone mineral density; COPD: chronic obstructive pulmonary disease; CRP: C-reactive protein; CV: cardiovascular; CVD: cardiovascular disease; EEA: essential amino acids; FBG: fasting blood glucose; FI: fasting insulin; HbA1c: glycated haemoglobin; HOMA-IR: homeostasis model assessment of insulin resistance; IL: interleukin; LSTM: lean soft-tissue mass; LDL-C: low-density lipoprotein cholesterol; MA: meta-analysis; MDA: malondialdehyde; MetS: metabolic syndrome; MR: Mendelian randomisation studies; NAFLD: non-alcoholic fatty liver disease; obs: observational; PCOS: polycystic ovary syndrome; RCTs: randomized controlled trials; SRs: systematic reviews; T1D: type 1 diabetes; T2D: type 2 diabetes; TC: total cholesterol; TGs: triglycerides; TNF: tumour necrosis factor; WC: waist circumference.
Reference [79]: da Silva Lopes K, Yamaji N, Rahman MO, Suto M, Takemoto Y, Garcia-Casal MN, Ota E. Nutrition-specific interventions for preventing and controlling anaemia throughout the life cycle: an overview of systematic reviews. Cochrane Database Syst Rev. 2021;9(9):CD013092. doi: 10.1002/14651858.CD013092.