

Examine®

STUDY SUMMARIES



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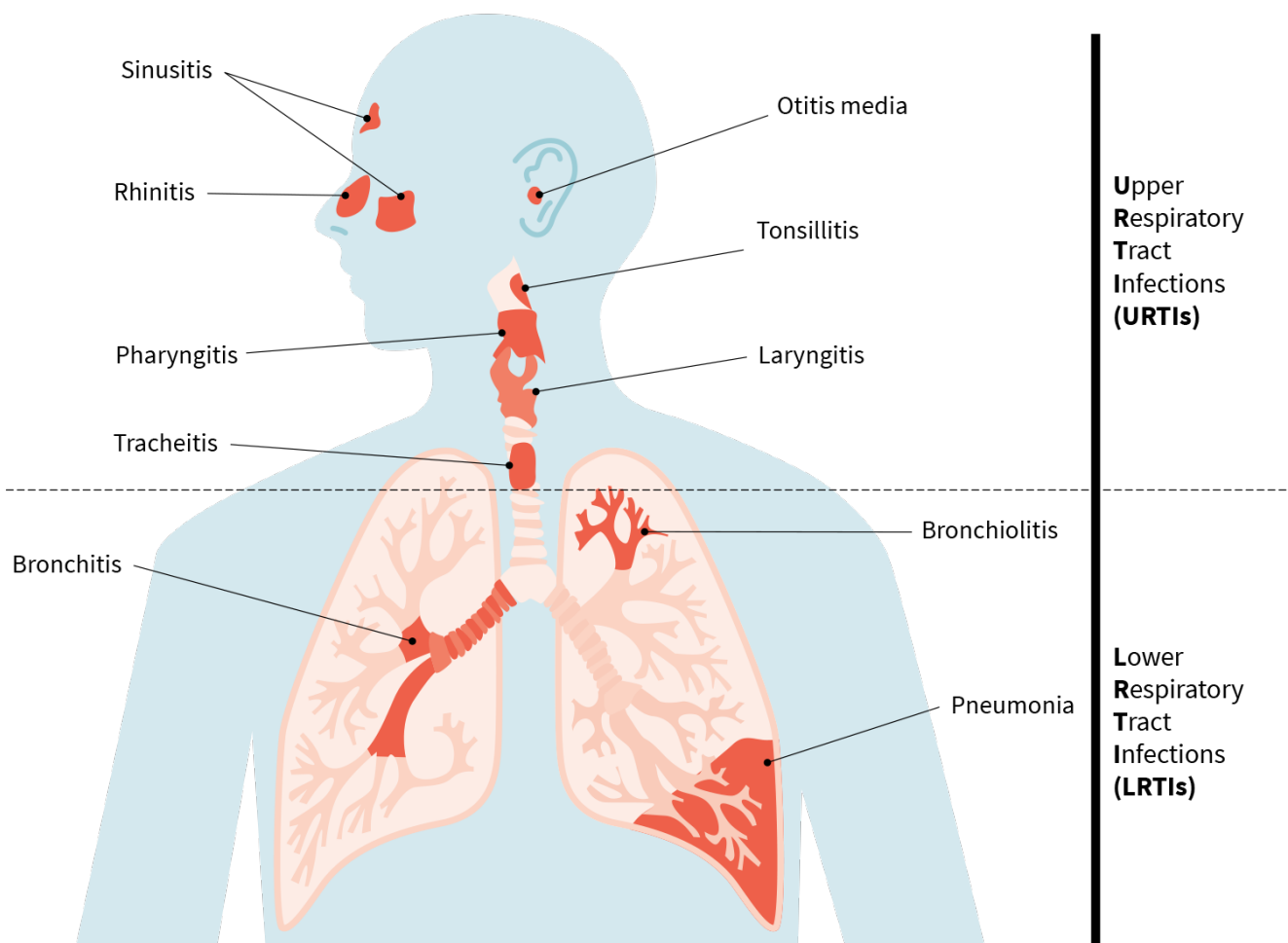
Infant formulas with prebiotics, probiotics, or synbiotics for the prevention of respiratory tract infections

Infant formulas with added pre-/pro-/synbiotics had a protective effect against respiratory tract infections in infants and young children.

Background

Respiratory tract infections (RTIs) affect parts of the body involved in breathing, such as the nose, throat, or lungs. They're especially common in the first few years of life.

Various types of upper and lower respiratory tract infections



Compared to formula-feeding, breastfeeding has been associated with a lower incidence of RTIs^[11] and a healthier gut microflora (less pathogenic bacteria, more *Bifidobacteria* and *Lactobacilli*).^[12] If the two observations are causally related, then some prebiotics, probiotics, or synbiotics (which combine prebiotics and probiotics) may protect infants against RTIs.

The study

This meta-analysis of 15 *randomized controlled trials* (RCTs) compared “biotic formulas” (infant formulas containing prebiotics, probiotics, or synbiotics) to control formulas for their effects on the incidence of RTIs. The total 3,805 infants and children were healthy and up to four years old at the start of the interventions, which lasted between three months and five years.

Subgroup analyses were performed based on the type of supplement (prebiotics [7 trials], probiotics [7 trials], and synbiotics [3 trials]) and the type of outcome (*upper respiratory tract infections* [URTIs; 8 trials], *lower respiratory tract infections* [LRTIs; 3 trials], and RTIs [8 trials]).

The URTIs were laryngitis, pharyngitis, rhinitis, sinusitis, tonsillitis, tracheitis, and otitis media. The LRTIs were bronchiolitis, bronchitis, and pneumonia. The RTIs involved both URTIs and LRTIs.

The results

In the overall analysis, biotic formulas reduced RTI risk by 11% (compared to control).

In the subgroup analyses, the risk reduction was statistically significant only for RTIs — so not for URTIs, LRTIs, or any of the three types of supplement. (This may be due to the small number of trials in each subgroup rendering the analysis insufficiently powered to detect an effect.)

The methodological quality of all trials was good, and no evidence of publication bias was found.

Note

There was considerable heterogeneity in the main analysis and in most of the subgroup analyses. The trials differed with regard to the type and dose of pre-/pro-/synbiotic, making it difficult to establish an optimal regimen.

The big picture

This was the first meta-analysis to examine the effects of biotic formulas on the incidence of RTIs in infants and young children, but its findings are consistent with those of previous meta-analyses of RCTs examining the effects of probiotics on RTIs.

- A 2014 meta-analysis looked at children and adults who developed common acute respiratory infectious conditions. It found that probiotics (particularly *Bifidobacteria* and *Lactobacilli*) resulted in moderate reductions in sickness duration and total sick days.^[13]
- A 2015 meta-analysis looked at children and adults. It found that probiotics reduced URTI duration, cold-related school absence, antibiotic use, and the number of participants experiencing episodes of acute URTI.^[14]
- A 2016 meta-analysis looked at children. It found that probiotics reduced the number of children with at least one RTI.^[15]
- A 2020 meta-analysis looked at adults. It found that probiotics reduced the incidence, episode rate, and episode duration of URTIs.^[16]

You may also be interested in [our analysis](#) of a 2016 RCT involving 33 athletes. Of the 16 participants who self-reported a URTI episode, 11 were in the placebo group and 5 in the probiotic group.

Digging Deeper: How does it work?

Pre-/pro-/synbiotics may prevent RTIs through various mechanisms:

- They may regulate systemic immune responses by producing exopolysaccharides^[17] and by increasing the number and activity of leukocytes, neutrophils, and natural killer cells.^[18]
- They may decrease inflammation by decreasing the expression of proinflammatory cytokines and increasing the expression of anti-inflammatory cytokines.^[19]
- They may compete with pathogenic bacteria for adhesion sites in the intestinal epithelium.^[20]

The effects of cold exposure on brown fat and energy expenditure

Winter swimmers and control participants exhibited a similar degree of brown-fat activity when exposed to the cold; in warm temperatures, however, only the control participants exhibited brown-fat activity. Both groups experienced a modest increase in energy expenditure when exposed to the cold, with a greater increase observed in the winter swimmers

Background

There are two types of body fat: *white adipose tissue* (WAT), by far the more common, and *brown adipose tissue* (BAT), which produces heat when the body is exposed to the cold.^{[30][31]} BAT is present in the neck, along the spine, and in the supraclavicular area (where it is most active).^[32] Early research in mice suggested that the calories burned by BAT activation could help protect against obesity,^[33] but studies in humans are needed for confirmation.

The study

Because repeated exposure to the cold is associated with increased BAT activity,^{[34][35]} this crossover *randomized controlled trial* (RCT) assessed whether BAT activity differed between 8 winter swimmers and 8 controls exposed to both cold and warm temperatures. The secondary outcomes were energy expenditure, gene expression in WAT, and skin and core body temperature.

The 8 winter swimmers were Danish men aged 18–35. They swam at least twice a week and were in at least their second swimming season. They were matched to 8 controls for age, [BMI](#), and [VO₂max](#). All but one of the winter swimmers (and none of the controls) regularly used a sauna.

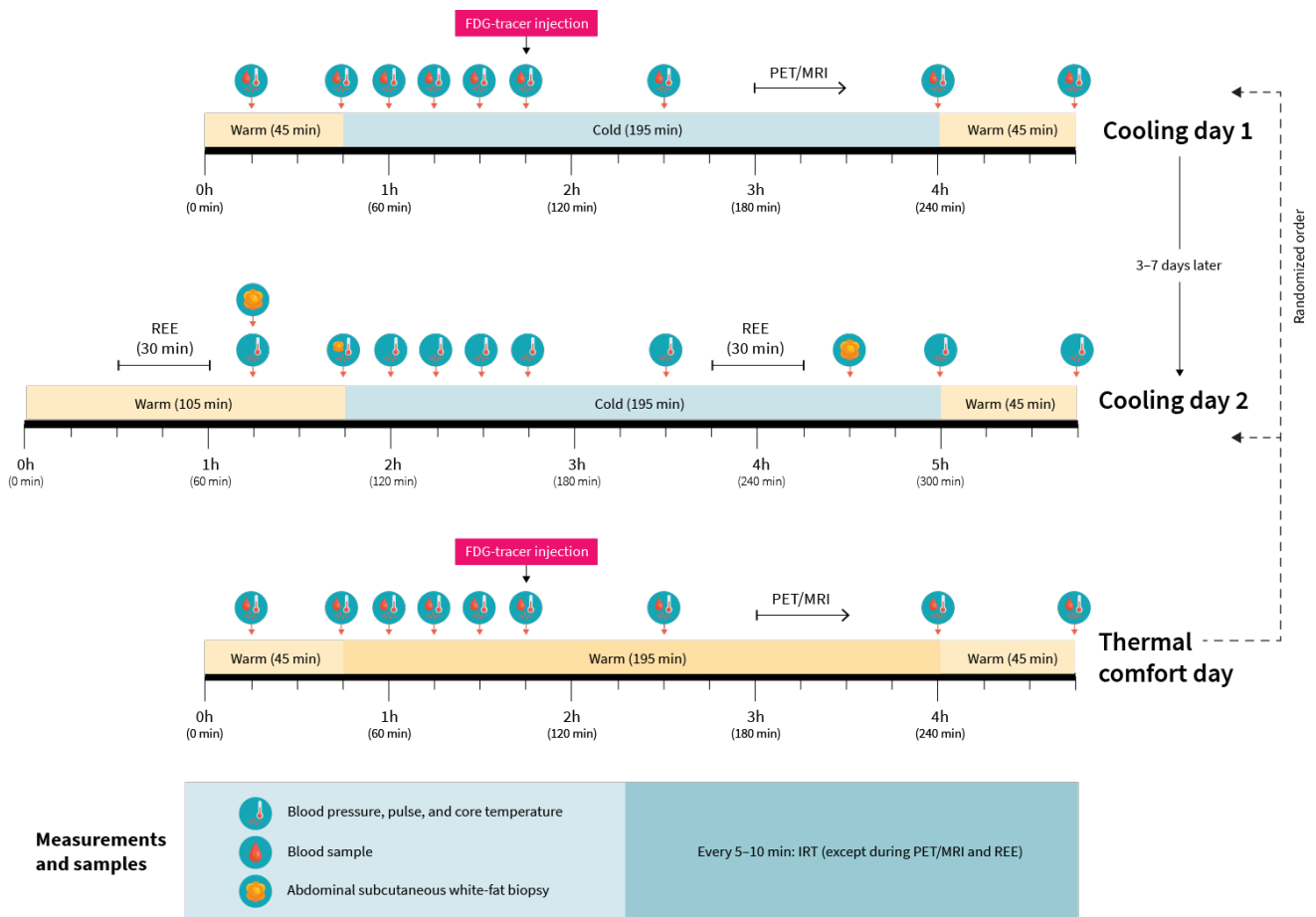
All 16 participants completed all three study visits, but they were randomly assigned to start with “cooling day 1” (followed by “cooling day 2” and “thermal-comfort day”) or “thermal-comfort day” (followed by “cooling day 1” and “cooling day 2”).

- For *cooling day 1*, the participants spent 285 minutes in two water-perfused cooling/heating blankets. For the first and last 45 minutes, the blankets were set to warm (27–33°C / 81–91°F). In between, for 195 minutes, the temperature was set at a level that had the participants feeling cold but not shivering. At various time points, BAT activity was assessed, blood samples were collected, and pulse and core temperature were measured.
- For *cooling day 2* (3–7 days later), the blanket protocol was the same, except that the initial warm period lasted 60 minutes longer (105 instead of 45) to allow the participants to relax for 30 minutes before their *resting energy expenditure* (REE) was first assessed. Their REE was assessed twice: during the initial warm period and during the cold period. Each assessment used indirect calorimetry, lasted 30 minutes, and was followed by a subcutaneous WAT biopsy (so the researchers could look for genetic factors related to lipid metabolism).
- For *thermal-comfort day*, the blanket was kept warm (≈32°C / ≈90°F) for the whole 285 minutes. Like on cooling day 1, BAT activity was assessed, blood samples were collected, and pulse and core temperature were measured.

BAT activity is often assessed via FDG-PET/CT scan: a person is injected with a *fluoro-D-glucose* (FDG) tracer and later scanned via *positron emission tomography/computed tomography* (PET/CT).^[30] In the present RCT, the participants were injected with the FDG tracer (2-deoxy-2-[¹⁸F]FDG) 105 minutes into each visit; one hour later, still wrapped in their blankets, they were scanned using PET and *magnetic resonance imaging* (MRI) to assess the uptake of the FDG tracer into their BAT.

At all three study visits, supraclavicular BAT activity was indirectly assessed by measuring skin temperature via *infrared thermography* (IRT) every 5–10 minutes, except during PET/MRI scans and REE measurements.

RCT protocol



Several months later, the investigators ran a follow-up study: over 24 hours, they measured the variations in both core temperature and supraclavicular skin temperature in 11 of the original participants (5 winter swimmers and 6 controls) and collected blood samples at various time points.

The results

Both groups had similar levels of BAT activity (as assessed via FDG uptake) during the cold period, but only the control group exhibited BAT activity during the warm period. Compared to the controls, the winter swimmers had a higher supraclavicular skin temperature during the cold period.

During the cold period, REE was higher in the winter swimmers than in the controls. During the warm period, there was no difference between the two groups. During the cold period, REE increased by ≈ 950 kcal/day in the winter swimmers and ≈ 450 kcal/day in the controls; in other words, during the cold-period 30-minute REE testing, the winter swimmers burned ≈ 20 kcal more than during the warm-period 30-minute REE testing, while the controls burned only ≈ 9 kcal more.

Based on the WAT biopsies, there were modest between-group differences in gene expression regulating lipid metabolism: the winter swimmers had higher expression of ELOVL6, a marker for *de novo lipogenesis*, and lower expression of PLIN1, a gene that encodes a protein protecting lipid droplets from breakdown.

The follow-up study found that, over 24 hours, compared to the controls, the winter swimmers had a lower core temperature but a higher supraclavicular skin temperature.

Note

The results suggest that, compared to other people, people regularly exposed to both very cold (winter swimming) and very warm (sauna) temperatures exhibit higher REE when exposed to cold temperatures and lower BAT activity when exposed to warm temperatures. The authors hypothesized that the winter swimmers were better able to adapt to cold temperatures by using more energy to generate more heat, and to warm temperatures by increasing heat loss and decreasing heat production (and thus BAT activity).

While the cold-induced increase in REE was *statistically* significant, it is unlikely to be *clinically* significant

for people looking to lose fat. Cooling increased REE by ≈ 950 kcal/day in the winter swimmers and ≈ 450 kcal/day in the controls; that's just ≈ 40 kcal/hour for the winter swimmers and ≈ 19 kcal/hour for the controls. The energy cost of exercise is much higher.

The big picture

In other studies, the effect of brown fat on energy expenditure in cold temperatures ranged from 25 to 400 kcal/day,^{[36][37]} and individuals with obesity have been observed to have lower levels of BAT activity.^[38]

Fermented *Rhus verniciflua* Stokes extract for improving markers of liver function and blood lipids [↗](#)

Supplementation with fermented Rhus verniciflua Stokes extract did not improve markers of liver function or blood lipids in healthy Korean adults.

Background

Toxicodendron vernicifluum is also known as Chinese lacquer tree and was previously known as *Rhus verniciflua* Stokes. It is an Asian tree species, the sap of which has been used in traditional Chinese medicine. *Fermented Rhus verniciflua Stokes extract* (FRVE) contains the flavonoids fustin and fisetin and has been reported to improve markers of liver function and blood lipids in mice. However, the effect of FRVE on the aforementioned outcomes has not been examined in humans.

The study

In this 12-week randomized controlled trial, 52 healthy Korean adults (average age of 33 years) took either 800 milligrams of FRVE (containing 129 milligrams of fustin and 59 milligrams of fisetin) or a placebo while maintaining their usual lifestyle and dietary habits.

The primary outcome was *aspartate aminotransferase* (AST, a marker of liver function). The secondary outcomes were the markers of liver function *alanine aminotransferase* (ALT) and *gamma-glutamyl transferase* (GGT), as well as blood lipid parameters.

The results

There were no changes over time or differences between groups in the primary or secondary outcomes.

Note

It's worth keeping in mind that the trial was performed in young healthy adults, which means that the results cannot be generalized to other populations.



Adherence to the Mediterranean diet may decrease the risk of depression [✉](#)

A greater adherence to a Mediterranean dietary pattern was associated with a lower risk of depression in middle-aged Swedish women.

Background

Some evidence has suggested diet as a modifiable risk factor for depression.^[4] The Mediterranean diet has been associated with various health benefits, but studies on its association with depression have yielded mixed results.

The study

This cohort study included data from a random sample of 42,515 Swedish women (average age of 39.5 years) over an average follow-up period of 20.4 years.

Dietary data were collected using an 80-item food frequency questionnaire and were compared to the Swedish National Food Administration database. Clinical depression diagnoses were extracted from the National Patient Register.

Adherence to the *Mediterranean diet pattern* (MDP) was calculated according to a previously used [scale](#) that indexes components of the MDP (vegetables, fruits and nuts, cereals, legumes, dairy products, fish and seafood, meat, alcohol, and monounsaturated-to-saturated fat ratio) and scores individuals based on their consumption level above or below the cohort median (i.e., "0" for intake below/above the cohort median for more/less healthy components and "1" for intake below/above the cohort median for less/more healthy components). A score of 9 was considered as indicative of maximal adherence to a MDP.

The confounding variables in the analysis included demographic and lifestyle factors, anthropometric profile, and medical history.

The results

A greater adherence to MDP (score >3) was associated with a lower risk of depression compared to low MDP adherence (score ≤3). The association became stronger with increasing age and in analysis restricted to more severe forms of depression.

The risk of depression decreased by 5% for every increase in adherence score.

Note

The self-reported dietary data may temper our confidence in the results, but it's worth mentioning that the cutoffs for MDP adherence scoring are rather strong.

Antioxidant vitamin and carotenoid intake is associated with sperm quality parameters

In male partners of subfertile couples, higher intakes of alpha-carotene, beta-carotene, and vitamin D were linked to a reduced risk of low sperm concentration, low total sperm count, and low semen volume, while a higher intake of lycopene was linked to an increased risk of low sperm concentration and low total sperm count.

Background

Oxidative stress may negatively affect sperm quality, thus contributing to male infertility. Therefore, the intake of dietary antioxidants may be linked to sperm quality parameters.

The study

The researchers conducting this cross-sectional analysis used data from a prospective cohort study to examine the associations between dietary antioxidant intake and sperm quality parameters in 323 men who were referred to a fertility clinic in Milan, Italy.

The researchers used a food frequency questionnaire to collect information on the participants' diets. To account for potential confounders, the researchers made statistical adjustments for age, alcohol intake, smoking, and days of abstinence.

The results

Of the 323 men, 19.1% had low semen volume (less than 1.5 mL), 31.4% had low sperm concentration (less than 15.0 million/mL), 26.8% had low sperm motility (less than 32%), and 33.0% had low total sperm count (less than 39.0 million/ejaculate).

Higher alpha-carotene intake was associated with a reduced risk of low sperm concentration, and both higher alpha- and beta-carotene intakes were associated with a lower risk of low total sperm count. On the other hand, higher lycopene intake was associated with an increased risk of low sperm concentration and low total sperm count. Higher vitamin D intake was associated with a reduced risk of low semen volume.

Note

Although the researchers adjusted the analyses for some potential confounders, it's possible that there is residual or unmeasured confounding that affected the results.

Hot tea is again linked to esophageal cancer

Although tea and its polyphenols may have anticancer properties, drinking hot tea is linked to a twofold higher risk of esophageal cancer.

Background

While animal and *in vitro* studies suggest that tea and its polyphenols may inhibit tumor formation and growth,^[21] observational human studies looking at the potential link between tea intake and cancer have produced mixed results, with some of the studies even linking tea intake to a higher risk of esophageal cancer.

These inconsistent results may be due to various confounding factors, notably drinking temperature. A 2019 prospective study we summarized [here](#) found that, compared to drinking tea colder than 60°C (140°F), drinking tea hotter than 60°C was associated with a 40% higher risk of esophageal cancer.^[22] This time, the study we're summarizing is a meta-analysis.

The study

This meta-analysis of 12 case-control studies totaling 5,253 cases and 8,273 controls looked for an association between esophageal cancer risk and hot-tea drinking. Subgroup analyses were based on tea intake (hot tea vs. no tea), tea temperature (hot vs. warm), tea type (green vs. others), cancer type (esophageal carcinoma vs. esophageal squamous-cell carcinoma), study region (China vs. others), and year of study publication (2000–2010 vs. 2011–2020).

The studies were conducted in China (9), Iran (1), Kenya (1), and Eastern Turkey (1). The types of tea consumed, in the studies that provided this information, were green tea (5 studies), black tea (1 study), and oolong tea (1 study).

The results

Compared to drinking no tea or warm tea (including lukewarm), drinking hot tea (including very hot) was associated with a twofold increase in esophageal cancer risk.

There was no heterogeneity in this analysis, and the association remained statistically significant in all subgroups. The results did not materially change in the sensitivity analysis, either. Finally, there was no evidence of publication bias, and the methodological quality was high in 10 of the 12 studies.

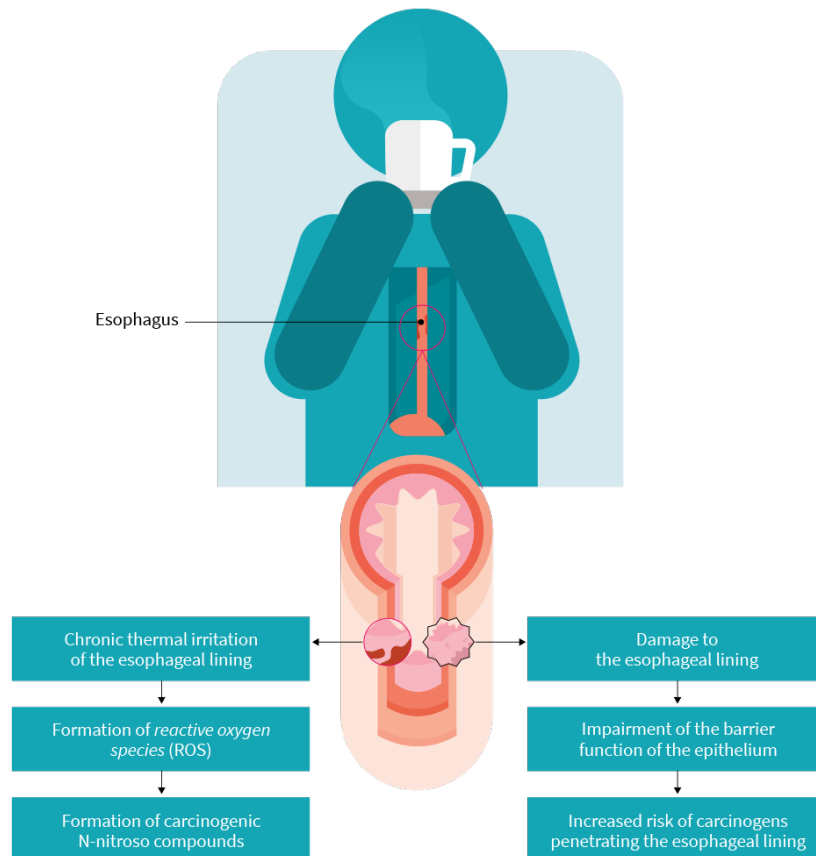
Note

All 12 studies included in the meta-analysis were case-control studies, which are vulnerable to selection bias (where individuals selected as controls are unrepresentative of the population that produced the cases) and recall bias (where individuals in the case group are more likely to recall a certain risk factor — in this case, hot-tea drinking — relative to individuals in the control group).

The big picture

The present meta-analysis linked hot tea to a twofold higher risk of esophageal cancer. Similarly, two 2015 meta-analyses linked hot food/beverages to an almost twofold higher risk of esophageal cancer.^{[23][24]}

How might hot tea be carcinogenic?



One potential explanation is that chronic thermal irritation of the membrane that lines the esophagus might stimulate the formation of *reactive nitrogen species* (ROS), such as [nitric oxide](#), and subsequently of carcinogenic N-nitroso compounds.^[25] Consistent with this idea, higher rates of mutations of the TP53 gene have been reported in samples of esophageal tumors collected in geographical areas where drinking hot beverages is considered an important risk factor for esophageal cancer.^{[26][27]} The TP53 gene provides instructions for making a tumor-suppressor protein, and mutations in this gene have been associated with *nitric oxide synthase* (NOS) activity.^[28]

Another potential explanation is that hot food and beverages may damage the membrane that lines the esophagus. This damage could impair the barrier function of the esophageal epithelium, thereby increasing the risk of harm from exposure to carcinogenic substances, such as alcohol and tobacco.^[29]

Lactobacillus rhamnosus GG supplementation in children with cow's milk allergy

Supplementation with the probiotic strain Lactobacillus rhamnosus GG in children aged ≤ 3 years who had cow's milk allergy was associated with improvements in milk tolerability rates and fecal occult blood rates.

Background

Certain probiotics have been investigated for their potential beneficial effects on *cow's milk allergy* (CMA), one of the most common food allergies in infants and children. Although a [2007 Cochrane meta-analysis](#) reported that there was insufficient evidence to recommend the use of probiotics in the prevention of allergic disease and food hypersensitivity in infants, it also found that all trials that reported benefits used probiotic supplements containing the *Lactobacillus rhamnosus* GG (LGG) strain. This study was an updated meta-analysis that examined the effects of LGG on CMA in children.

The study

This meta-analysis of 8 studies (7 randomized controlled trials and 1 prospective cohort study) examined the effects of LGG in the treatment of allergic symptoms in 696 children aged ≤ 3 years with CMA. The outcomes examined were milk tolerance rate (5 studies involving 565 children), severity of atopic dermatitis (2 studies involving 103 children), and fecal occult blood rate (hidden blood in stool; 2 studies involving 136 children).

Most studies compared i) an extensively hydrolyzed whey or casein formula containing LGG (treatment) to ii) an extensively hydrolyzed whey or casein formula alone or containing microcrystalline cellulose (control). The duration of the randomized controlled trials was between 1 month to 12 months, and the duration of the prospective cohort study was 3 years.

The results

Compared to the control, LGG supplementation was associated with two times greater milk tolerability rates (moderate certainty of evidence) and almost three times lower rates of fecal occult blood (low certainty of evidence).

Vitamin E slows bone resorption

This 12-week randomized controlled trial demonstrated that supplemental vitamin E can slow bone resorption in postmenopausal women with osteopenia.

Background

Oxidative stress is a pathophysiological driver of aging that provokes bone resorption and contributes to the development of osteoporosis (i.e., low bone mass). Decreases in estrogen after menopause are associated with increased oxidative stress.^[1] Vitamin E is a lipid-soluble vitamin with antioxidant and anti-inflammatory properties that may slow bone resorption and loss. Could supplemental vitamin E have benefits for postmenopausal women?

The study

This 12-week randomized controlled trial involved 52 postmenopausal women with osteopenia (average age of 63) who took either a vitamin E supplement (400 IU, mixed tocopherols) or a placebo daily.

The participants were not vitamin D deficient and did not have a history of bone disease, cancer, eating disorders, or malabsorption. The participants in both groups also received 600 milligrams of calcium carbonate twice per day and 20,000 IU of vitamin D once per week.

The primary outcomes were changes in a bone resorption marker (serum C-terminal telopeptide of type I collagen) and a bone formation marker (N-terminal propeptide of type I procollagen), as measured by an electrochemiluminescence immunoassay.

The results

Vitamin E supplementation prevented the bone resorption marker from increasing, but it increased by 35% in the placebo group compared to baseline.

Note

Despite promising findings, further research involving assessment of vitamin E levels, dietary intake, lifestyle habits, and antioxidant and inflammatory markers, alongside monitoring of biomarkers for bone turnover, would strengthen these results and the understanding of vitamin E's role in bone turnover and slowing of osteopenia.

Vitamin D for migraine prevention

In migraine sufferers, vitamin D supplementation improved the number of headache attacks per month, the number of headache days per month, and headache-related disability.

Background

Low vitamin D status has been linked to different pain-related disorders, including migraine. Although a number of trials have examined the effects of vitamin D supplementation on migraine symptoms, the findings have been mixed. What does the totality of the available evidence say?

The study

This meta-analysis of 6 randomized controlled trials examined the effects of vitamin D supplementation, compared to placebo (5 trials) or the usual care (1 trial), in 301 migraine sufferers.

The primary outcome was the number of headache attacks per month (3 trials). The secondary outcomes were the number of headache days per month (3 trials), the *migraine disability assessment questionnaire* (MIDAS) score (3 trials), migraine attack duration (2 trials), and headache severity (3 trials).

The average age of the participants was between 10 and 45 years. In 5 trials, the daily vitamin D dose averaged 2,000–7,150 IU, while 1 trial used a dose of 500,000 IU per week (average of approximately 71,500 IU per day). The treatment duration was between 8 and 24 weeks.

The results

Compared to the control, vitamin D supplementation improved the number of headache attacks per month (–2.7), the number of headache days per month (–1.6), and the MIDAS score (–5.7).

All trials were of high methodological quality.

Note

The word “migraine” comes from the Greek “ἡμικρανία” (hemi-krania) which translates to “half-skull.” This makes sense because migraines typically affect half of the head.

Are proinflammatory diets linked to lower bone mineral density in Mediterranean populations?

In a Mediterranean population of older adults with overweight/obesity and metabolic syndrome, a proinflammatory diet was associated with lower bone mineral density.

Background

The *modified dietary inflammatory score* (M-DIS) is a tool used to estimate the inflammatory potential of the diet. According to the findings of observational research, a higher M-DIS is associated with lower *bone mineral density* (BMD) in populations who follow a Western dietary pattern. However, research examining the association between the M-DIS and BMD in Mediterranean populations is lacking.

The study

This cross-sectional analysis was conducted in a subset of 1,134 older adults with overweight/obesity and metabolic syndrome from the [PREDIMED-Plus](#) trial. The analysis examined the associations between the M-DIS and BMD in a Mediterranean population.

The M-DIS was assessed using food frequency questionnaires, and BMD was measured at the femur, lumbar spine, and hip using dual-energy X-ray absorptiometry (DXA).

The researchers made adjustments for a number of potential confounders, including age, sex, BMI, calorie intake, prevalence of type 2 diabetes, education level, smoking status, physical activity, use of antidiabetic drugs, and use of calcium or vitamin D supplements.

The results

Participants with the highest M-DIS, compared to the lowest, had a 0.02 lower BMD at the femur, and a 0.03 lower BMD at the hip. Moreover, participants with the highest M-DIS, compared to the lowest, were more likely to have low BMD at the femur and at the hip.

Note

Despite the adjustments made for the potential effects of confounding variables, residual or unmeasured confounding is still possible.

Are plant-based diets associated with lower bone mineral density?

Compared to omnivorous diets, vegan and vegetarian diets may be associated with lower bone mineral density, particularly in women.

Background

Previous studies have found that vegetarians and vegans have lower *bone mineral density* (BMD) than omnivores, possibly due to lower BMI and lower intakes of calcium and protein.^{[5][6]} This meta-analysis explored the effects of plant-based diets on BMD at different sites of the body and assessed how variables such as gender may influence BMD.

The study

This meta-analysis of 17 cross-sectional studies (13,888 participants) compared BMD at the lumbar spine, femoral neck, and whole body in people eating plant-based or omnivorous diets.

The results

The pooled results showed that compared to omnivores, both vegetarians and vegans had lower BMD at the lumbar spine and the femoral neck, but only vegans had lower whole-body BMD. A subgroup analysis found that these differences in BMD were more pronounced in women.

Note

The researchers note several limitations of this analysis including (but not limited to) the following: the majority of the studies enrolled only women, the populations enrolled in the studies varied greatly, and none of the included studies measured whether the participants had low BMD before starting a vegetarian or vegan diet.



Does animal protein increase the risk of gestational diabetes?

A higher intake of total animal protein (particularly red meat) was associated with an increased risk of gestational diabetes.

Background

In Malaysia, meat consumption has continued to rise, with the greatest increase in red meat. Obesity rates in childbearing women have also risen, increasing the risk of *gestational diabetes* (GDM). Is the amount and type of protein consumed during pregnancy associated with GDM?

The study

This prospective cohort study in 452 participants (30 years of age on average) explored the association between the amount and types of protein consumed during each trimester of pregnancy and the risk of developing gestational diabetes. The participants' diets were assessed using a 126-item semiquantitative food frequency questionnaire validated for Malaysia (the country in which the study was conducted). Oral glucose tolerance tests were performed between 28 and 32 weeks of pregnancy.

The results

Of the 452 participants, 48 (10.62%) developed GDM. Most of the participants consumed 10–20% of their total daily calories from protein before pregnancy until the second trimester. Participants in the highest tertile of total animal protein intake (≥ 42.15 grams per day or g/day), and specifically red meat (≥ 2.94 g/day or equivalent to roughly 12 grams of cooked red meat per day), had a greater risk of developing GDM, particularly in the second trimester, compared to those in the middle tertile. However, participants in the highest tertile for egg protein intake had a lower risk of GDM than those in the middle tertile for egg protein.

Note

Overall, this cohort consumed a relatively low amount of red meat (24.4 g/day on average). It's possible that the association between red meat and an increased risk of GDM may be due to the common cooking methods of the region, which include fried meat with high-sugar or high-fat sauces that contribute to higher overall fat and calorie intake.

Dietary factors related to hormonal profiles in pubertal girls



Greater intakes of total protein, animal protein, and total calories were associated with higher bioavailable estrogen in pubertal girls. Greater total and soluble fiber intake were associated with lower estrogen and higher sex hormone-binding globulin.

Background

Increasing fiber and decreasing saturated fat and animal protein have been associated with a decreased risk of breast cancer. Early puberty in girls has also been associated with an increased risk of hormonal cancers, including breast cancer. Does diet composition at puberty influence estrogen and *sex hormone-binding globulin* (SHBG) levels in girls?

The study

This study in 260 girls from the Cincinnati puberty cohort of the Breast Cancer and the Environment Research Program analyzed the relationship between diet and estrogen and SHBG levels cross-sectionally (at the time of puberty) and longitudinally (over a period of time). The participants were enrolled in the cohort between 6 and 7 years of age and were followed every 6 months to measure estrogen and SHBG levels 18 months before the onset of puberty (measured by the stage of breast development) and 6 months after. The participants completed 24-hour dietary recall logs every 3 months.

The results

The food logs showed that the cohort's average daily macronutrient intake consisted of 1,764 calories, 64.2 grams of fat, 241.2 grams of carbohydrates, 61.7 grams of total protein, 40.8 grams of animal protein, 12.6 grams of fiber, 4.1 grams of soluble fiber, and 8.4 grams of insoluble fiber.

The cross-sectional analysis found that higher estrone concentrations at puberty were associated with higher total protein and animal protein. Lower SHBG was associated with a greater intake of total calories, total fat, and animal protein. The ratio of estrone to SHBG (a measure of bioavailable estrogen) was associated with total caloric intake, total protein intake, and animal protein intake.

The longitudinal analysis found that lower estradiol levels were associated with greater insoluble fiber intake. Higher estrone levels were associated with a greater intake of animal protein, and higher SHBG was associated with a greater intake of soluble fiber and a lower intake of total protein. The ratio of estrone to SHBG was positively associated with animal protein.

Low-glycemic-index diets for women with polycystic ovary syndrome [↗](#)

Low-glycemic-index diets improved clinical outcomes (emotional health, body hair, and fertility) and a range of metabolic, hormonal, and anthropometric outcomes more than control diets in women with polycystic ovary syndrome and overweight/obesity.

Background

Polycystic ovary syndrome (PCOS), the most common endocrine disorder in women of reproductive age, is associated with a number of endocrine and metabolic abnormalities. *Low glycemic index* (LGI) diets, which are characterized by the consumption of foods known to minimize large fluctuations in blood glucose levels, have been investigated for their potential beneficial effects on a range of parameters in women with PCOS. This meta-analysis summarized the findings of the available clinical research on the effects of LGI diets in women with PCOS.

The study

This meta-analysis of 8 randomized controlled trials examined the effects of LGI diets, compared to control diets, on a range of outcomes in 412 women with PCOS and overweight/obesity.

The outcomes examined included:

- Clinical outcomes (emotional health, body hair, fertility, and menstrual problems). These were measured in 3 trials with the Polycystic Ovary Syndrome Questionnaire (PCOSQ) using a 7-point scale.
- Markers of glycemic control (including fasting glucose, 2-hour glucose, fasting insulin, 2-hour insulin, and insulin resistance).
- Blood lipids (total cholesterol, LDL cholesterol, HDL cholesterol, total cholesterol to HDL cholesterol ratio, and triglycerides).
- Hormones (including sex hormone-binding globulin, lutenizing hormone, follicle-stimulating hormone, and testosterone).
- Anthropometrics (including BMI, bodyweight, waist circumference, and fat mass).

The control diets were the high-glycemic-index diet, low-calorie diet, normal glycemic diet, low-fat diet, therapeutic lifestyle changes, and conventional hypocaloric diet.

The results

Compared to the control diets, LGI diets improved emotional health (mean difference of -1.97), body hair (mean difference of -0.4), and fertility (difference of 1.45). They also improved several other outcomes, including 2-hour insulin, insulin resistance, all blood lipids, sex hormone-binding globulin, lutenizing hormone, follicle-stimulating hormone, testosterone, waist circumference, and fat mass.

Do dietary interventions improve fertility outcomes in women with polycystic ovary syndrome?

In women with polycystic ovary syndrome, fertility appeared to be improved by low-carbohydrate diets, and hormonal profiles were improved by calorie-restricted diets.

Background

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders among women of reproductive age. Women with PCOS often have insulin resistance and high levels of androgens (so-called “male hormones”), and this hormonal profile negatively affects fertility. Previous analyses have focused on pharmaceutical or single-nutrient interventions, and therefore, this meta-analysis explored the role of diet in improving fertility outcomes in women with PCOS.

The study

This meta-analysis of 20 randomized controlled trials (1,113 participants) assessed the effects of diet on pregnancy, miscarriage, and ovulation rates among women with PCOS. Additional analyses included menstrual cycle regularity, *anti-Müllerian hormone* (AMH; women with PCOS have high AMH) levels, free androgen index (FAI), *sex hormone-binding globulin* (SHBG) levels, total *testosterone* (T) levels, and the Ferriman-Gallway score (a scale for hirsutism or excessive body hair).

The dietary patterns used in the studies were a low-carbohydrate diet (9 studies), a low glycemic diet (6 studies), the DASH diet (4 studies), and the Mediterranean diet (1 study). The duration of the diets ranged from 1 month to 1 year.

The results

Overall, clinical pregnancy rates, ovulation rates, and menstrual function were improved and miscarriage rates were reduced by dietary modifications. Further analysis showed that the Mediterranean and low-carbohydrate diets were more beneficial for pregnancy rates and menstrual regularity.

Dietary interventions also reduced AMH, FAI (low-carbohydrate and calorie-restricted diets were more beneficial), T (longer-duration calorie-restricted interventions showed larger reductions), and hirsutism (as measured by the Ferriman-Gallway score) and increased SHBG (only longer-duration calorie-restricted diets had this effect).



Olive leaf extract improves body composition and metabolic indices in women with obesity alongside a weight loss diet [↗](#)

In young and middle-aged women with obesity, supplementation with olive leaf extract alongside a weight loss diet, compared to a weight loss diet alone, reduced body weight and fat mass and improved a number of metabolic parameters.

Background

In both animal and human studies, supplementation with *olive leaf extract* (OLE), which is rich in the polyphenol oleuropein, has exhibited antiobesity, antilipidemic, and insulin-sensitizing properties. However, no studies have examined the effects of OLE in humans following a weight loss diet.

The study

In this 8-week randomized controlled trial, 70 women with obesity (ages 18–50) took either 250 mg of OLE (standardized to contain 50 mg of oleuropein) or a placebo while also following a hypocaloric diet designed to cause weight loss. In both study groups, the diets were made up of 55% carbohydrates, 30% fat, and 15% protein.

The primary outcomes were anthropometric indices (body weight and body composition), blood lipids (total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides), markers of glycemic control (fasting blood glucose, fasting insulin, and insulin resistance), and the hormones leptin and adiponectin. In their analyses, the researchers adjusted for a number of potential confounding variables, including age, physical activity, and calorie intake and macronutrient intakes.

The results

Compared to placebo, OLE improved body weight (–4.1 vs. –2.8 kg), BMI (–1.6 vs. –1.1), fat mass (–2.6 vs. –1.3 kg), total cholesterol (–10.5 vs. –2.5 mg/dL), LDL cholesterol (–11.8 vs. –3.2 mg/dL), and fasting blood glucose (–4.3 vs. –0.5 mg/dL). Supplementation also reduced leptin and increased adiponectin concentrations.

***Caralluma fimbriata* extract supplementation may provide minor benefits for body measurements, but not appetite suppression**

Adults with overweight and obesity supplementing with Caralluma fimbriata extract showed reduced waist circumference and waist:hip ratio, but no effects on appetite or metabolic markers.

Background

Caralluma fimbriata is an edible cactus traditionally used in India to suppress hunger. While a limited number of clinical trials have examined the potential appetite-suppressing and antiobesity effects of *Caralluma fimbriata* extract, a meta-analysis pooling the available data was needed to evaluate the overall effects of the supplement.

The study

This meta-analysis of 4 randomized controlled trials examined the effects of *Caralluma fimbriata* extract, compared to placebo, on the following measurements in a total of 269 adult participants with overweight and obesity:

Anthropometric indices

- Body weight, 4 trials
- BMI, 4 trials
- Waist circumference, 3 trials
- Hip circumference, 3 trials
- Waist:hip ratio, 2 trials

Markers of appetite

- Feeling of fullness, 3 trials
- Hunger, 3 trials
- Desire to eat, 3 trials
- Thoughts of food, 2 trials

Blood lipids and blood glucose

- Total cholesterol, 2 trials
- HDL cholesterol, 2 trials
- LDL cholesterol, 2 trials
- Triglycerides, 2 trials
- Blood glucose, 2 trials

The participants were 18 to 70 years old. In all 4 trials, participants took 1 gram of *Caralluma fimbriata* extract per day. The intervention duration ranged from 8 to 12 weeks.

The results

Supplementing *Caralluma fimbriata* extract reduced waist circumference by 1.6 cm (0.63 inches) and waist:hip ratio by 0.06, but did not affect any of the other outcomes, compared to placebo.

All trials were of good methodological quality.

Note

Most of the analyses included only 2 or 3 trials. This reduces confidence in the results.

Can body composition be beat with betaine?

This meta-analysis found that betaine supplementation did not change any measures of body composition, although its effects on water retention may influence the accuracy of body composition measurements

Background

Betaine (technically a class of related molecules, though it most commonly refers to trimethylglycine) is an amino acid derivative that can be found in wheat products, spinach, beets, and other select foods. It plays a vital role in methylation in the body and also acts as an osmoregulator (maintains water balance, like creatine). Although some studies report associations between betaine concentrations and/or supplementation and measures of body composition, others show no significant changes.

The study

This meta-analysis included 12 randomized controlled trials that examined the effect of betaine supplementation on body composition and dietary intakes in 369 participants.

The daily dosage of betaine ranged from 1.5 to 20 grams/day, and trial durations ranged from 2 to 52 weeks. The mean age of participants in the included studies ranged from 21 to 59 years.

Measures of body composition included body mass, body mass index, fat mass, body fat percentage, and fat free mass. Dietary intakes were evaluated, including carbohydrate, protein, fat, and total energy measures.

Subgroup analyses based on age (<40 or ≥ 40 years), BMI (18.5–24.9, 25–29.9, or ≥30) , study duration (<8 or ≥8 weeks), intervention dosage (>4 or ≤4 grams/day), and health status (presence/absence of chronic disease) were also conducted.

The results

Betaine supplementation did not change any measures of body composition. The subgroup analyses demonstrated similar results.

A negligible increase in protein intake (3.56 grams) was the only change in dietary intake following betaine supplementation, when compared to a control.

Note

Betaine's role as an osmoregulator may alter the accuracy of body composition measurements, as hydration status can influence body composition measurements.^[8]



Cumin seeds may improve body composition and blood lipid measurements in the context of metabolic syndrome [↗](#)

Adults with at least one component of metabolic syndrome who supplemented cumin seeds experienced improvements in some anthropometric parameters and blood lipids. However, the certainty of the evidence was ranked as low or very low.

Background

Cuminum cyminum, commonly known as cumin, is an aromatic plant native to the Mediterranean region, northern Egypt, Iran, and India. The seeds of the plant, which are rich in a wide spectrum of phenols and flavonoids, have been investigated for their potential beneficial effects on body composition and blood lipids. However, previous trials have produced mixed results.

The study

This meta-analysis of 8 randomized controlled trials examined the effects of cumin seed supplementation on anthropometric parameters and blood lipids in a total of 486 adults with at least one component of the metabolic syndrome.

The anthropometric parameters were BMI (8 trials) and waist circumference (4), and the blood lipids of interest were total cholesterol (8), LDL cholesterol (7), HDL cholesterol (7), and triglycerides (8). The average age of the participants was between 36 and 59 years. Cumin seeds were taken as oil, powder, or extract in doses ranging from 25 to 2,000 mg per day for 8–24 weeks. All of the trials were conducted in Iran.

The results

Supplementation with cumin seeds improved BMI by 0.88 kg/m² and total cholesterol by 3.96 mg/dL, compared to placebo. When the researchers adjusted for publication bias, supplementation with cumin seeds also improved waist circumference, HDL cholesterol, and triglycerides. However, the certainty of the evidence was low or very low for all outcomes, which reduces confidence in the results.

The acute, chronic, and cessation effects of smoking on arterial stiffness

Short-term (acute) smoking increases arterial stiffness, and smoking cessation may decrease it, but the effect of chronic smoking is less clear.

Background

Smoking contributes to endothelial dysfunction (blood vessel narrowing) and can worsen arterial stiffness, an indicator of vascular aging that is independently associated with the risk of cardiovascular events and mortality. However, the beneficial effects of smoking cessation on measures of arterial stiffness are not completely clear.

The study

This meta-analysis included 13 studies (7 nonrandomized controlled trials, 5 randomized crossover trials, and 1 randomized controlled trial) that evaluated the acute (7 studies), chronic (7), cessation (6) and maintenance effects (5) of smoking on arterial stiffness in both healthy and unhealthy adults (aged 23–54 years).

The included studies involved sample sizes ranging from 6 to 160 participants, four different methods for measurement of *pulse wave velocity* (PWv; an indicator of arterial stiffness, measured in m/s^[21]), and assessment time points ranging from 0 to 50 min (acute), 1 to 15 months (chronic), and 3 to 15 months (cessation).

The results

Smoking cessation had a moderate effect (3.5% difference) on reducing PWv compared to the maintenance of smoking (i.e., the difference would be noticeable to someone with training and background knowledge, like a doctor). However, the analysis showed a high level of heterogeneity.

Smoking (both conventional cigarettes and electronic cigarettes) had moderate (10% difference) and small (4.7%) effects, respectively, on acute increases in PWv. The chronic effect of smoking did not show significant results on PWv, but it also demonstrated publication bias.

Subgroup analyses demonstrated effective reductions in PWv after smoking cessation for healthy individuals only.

Additionally, the researchers noted that the assessment time points for smoking cessation may confound estimates of its effect on arterial stiffness.

Note

The effect of smoking cessation vs. maintenance appeared to be biased by one particular study, and the high level of heterogeneity suggests cautious interpretation.

Are carbohydrates and fats associated with cardiovascular disease risk in women?

Moderate carbohydrate intake was associated with the lowest risk of cardiovascular disease, and increasing saturated fat intake was not associated with cardiovascular disease or mortality.

Background

Historically, a low-fat/high-carbohydrate diet was the mainstay recommendation for reducing *cardiovascular disease* (CVD) risk, but results from some recent studies contradict this recommendation. For instance, one study found that postmenopausal women who reduced their fat intake to no more than 20% of daily energy did not have a lower risk of CVD over an 8-year follow-up period.^[9] Furthermore, an observational study reported an association between high carbohydrate intake and an increased risk of all-cause mortality, whereas total fat intake and types of fat were associated with lower mortality.^[10] What is the association between carbohydrate and saturated fat intake and CVD risk and all-cause mortality in women?

The study

This was an analysis of the Longitudinal Study on Women's Health in which 9,899 women (52 years of age on average) were followed for 15 years. The participants were divided into quintiles according to their self-reported carbohydrate and saturated fat intakes. The primary outcome was newly diagnosed cardiovascular disease and stroke. The secondary outcomes were all-cause mortality, hypertension, obesity, and type 2 diabetes.

The results

After 15 years of follow-up, there were 1,199 incidents of cardiovascular disease, 470 deaths, 4,198 cases of hypertension, 3,588 cases of obesity, and 1,218 cases of type 2 diabetes.

A carbohydrate intake between 41% and 43% of total calories was associated with a 44% lower odds of developing cardiovascular disease compared to the lowest intake (<37.1%). Carbohydrate intake was not associated with total mortality, but an increasing percentage of total calories from carbohydrates was associated with reduced odds of obesity, type 2 diabetes, and hypertension.

Saturated fat intake was not associated with total mortality or cardiovascular disease risk. Furthermore, increasing saturated fat intake was inversely associated with hypertension, type 2 diabetes, and obesity.

Note

One of the authors has declared competing interests.

Ashwagandha root extract for improving cognitive function, stress, happiness, and sleep quality in individuals with stress

□

Supplementation with a sustained-release ashwagandha root extract product improved some aspects of cognitive function — as well as perceived stress, happiness, and sleep quality — in healthy men and women with moderate levels of perceived stress.

Background

Chronic stress and stress hormones may negatively affect cognitive abilities, sleep, and psychological well-being. Some research suggests that the root extract of ashwagandha, an herb commonly used in Ayurveda practices, may reduce stress and stress hormones, and it may also improve cognitive function, sleep, and quality of life. This trial examined these potential effects.

The study

In this 90-day randomized controlled trial, 125 healthy men and women, aged 20–55 years with moderate levels of perceived stress, took capsules containing either 300 milligrams of sustained-release ashwagandha root extract (Prolanza™) or a placebo.

The primary outcome was cognitive function measured using the Cambridge Neuropsychological Test Automated Battery (CANTAB). The secondary outcomes were perceived stress, serum cortisol levels, happiness (measured with the Oxford Happiness Questionnaire), sleep quality (measured with the Pittsburgh Sleep Quality Index), and levels of serum brain-derived neurotrophic factor (a neurotrophin that plays important roles in cognitive performance and brain morphology developments).

The results

Recall memory (an aspect of cognitive function) improved with ashwagandha by 19% but did not change with placebo, and the differences between groups at the end of the intervention were statistically significant.

The total error rate in recalling patterns (another aspect of cognitive function) nonsignificantly improved by 25% with ashwagandha and nonsignificantly worsened with placebo by 29%, and the differences between groups at the end of the intervention was statistically significant.

The secondary outcomes of perceived stress, serum cortisol levels, happiness, and sleep quality improved more with ashwagandha, compared to placebo.

Note

It's worth noting that the trial was funded by Inventia Healthcare Ltd. and Laila Nutraceuticals (the manufacturers of Prolanza™) and that some of the researchers were employees of these companies at the time of the study.

The authors did not report total CANTAB scores and focused on discussing the positive findings. Also, CANTAB is a scale designed to measure cognitive dysfunction in patients with various neurological conditions,^[2] and some research suggests that CANTAB may not be able to accurately measure cognitive function in healthy adults.^[3] Therefore, it is possible that CANTAB is not a good measure of cognitive function in healthy adults.

Dietary metabolites and cognitive decline

This cohort study found positive and negative associations between certain food/microbial metabolites and age-related cognitive decline but emphasized the complexity of these relationships, the interindividual variation, and the need for greater validation and understanding of global biological/metabolic pathways (i.e., systems biology).

Background

Diet is a modifiable lifestyle factor for healthy aging and *age-related cognitive decline* (ARCD). Despite suggested mechanisms and specific dietary components such as antioxidant and anti-inflammatory bioactive components, inconsistent findings make it difficult to determine the role of diet in the pathogenesis of ARCD. Moreover, few studies have evaluated microbial influence or used metabolomic analysis.

The study

This study used targeted metabolomics techniques to analyze blood samples from two study centers (Bordeaux: 418 participants, Dijon: 424 participants) of the Three-City Cohort, which recruited older subjects who were free from dementia at the time of blood sample collection.

ARCD was evaluated using five neuropsychological tests, including the Mini-Mental State Examination and Trail-Making tests (parts A and B), and association with subsequent ARCD was evaluated over a 12-year follow-up period.

The results

Metabolites of cocoa (e.g., 3-methylxanthine), coffee (e.g., 2-furoylglycine), mushrooms (e.g., ergothioneine), and red wine (e.g., cis-resveratrol 3-sulfate), as well as microbial metabolites of polyphenol-rich foods (e.g., phenolic acids), demonstrated an inverse association with ARCD.

Metabolites related to unhealthy dietary components, including artificial sweeteners (e.g., saccharin) and alcohol (e.g., ethyl sulfate), were associated with ARCD.

Note

Initially, the Bordeaux sample set was used to test and “discover” potential metabolites that were associated with subsequent ARCD. The Dijon sample set was meant to be used to validate the metabolites identified in the Bordeaux sample. However, when the predictive potential of the metabolite panel identified in the Bordeaux sample (24 metabolites) was tested, it demonstrated poor sensitivity and specificity for metabolite signatures in the Dijon sample set.

When the “discovery” analysis was performed on the Dijon sample set, 20 metabolites were associated with ARCD, 7 of which were common with the Bordeaux sample set. Moreover, differences were found between the two datasets (e.g., caffeine metabolites were found to increase and decrease ARCD risk in either dataset). This suggests that although there is some overlap and validation, the field of metabolomics and systems biology requires more data and a greater understanding to produce practical takeaways.

The authors suggested that changes in metabolites involved in the gut-brain axis, such as the neurotransmitters dopamine and serotonin and B-group vitamins, may also play a role in ARCD. These observations are interesting, but again, it's difficult to assess the certainty of these relationships.

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