Examine®

Cardiovascular Health Supplement Guide

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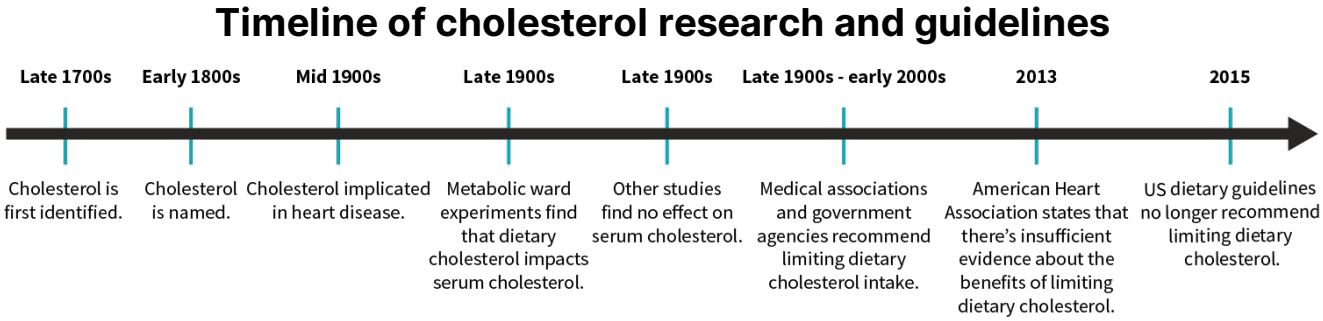
Introduction

For three decades, the cholesterol issue was clear: too much cholesterol in your blood is bad, and both dietary cholesterol and saturated fat should be kept to a minimum. But in recent years, media headlines have shown mixed messages.

A typical nutrition enthusiast will take sides, either shying away from butter or adding it to everything, even their coffee. Some low-carbers tend to downplay cholesterol concerns — even celebrate their high numbers[1] — while some vegans brandish their rock-bottom numbers[2][3] as proof that eggs and meat are better avoided.

If it's your first time at Cholesterol Club, you have to fight. Fight dogma that is, with scientific evidence as your only weapon. You have to dare consider cardiovascular health as a whole, rather than either magnify or ignore the role of dietary fat and serum cholesterol.



References: Olson. *J Nutr*. 1998.[4] ● Duff. *Am J Med*. 1951.[5] ● Clarke et al. *BMJ*. 1997.[6] ● Brownawell and Falk. *Nutr Rev*. 2010.[7] ● Stone et al. *J Am Coll Cardiol*. 2014.[8]

Saturated fat versus specific foods

First published in 1970, the *Seven Country Study* led by Ancel Keys suggested that dietary saturated fat raised serum cholesterol levels and therefore increased the risk of cardiovascular disease.[9] Within the academic and medical communities, this conclusion was widely accepted as fact, and it influences official dietary guidelines even today.

Recent evidence, however, is more mixed. Whether serum cholesterol and heart health are affected by saturated-fat intake appears to depend on what saturated fat is replacing (or is being replaced by).[10]

Even the source of the saturated fat matters. Randomized controlled trials have shown that a diet high in saturated fat *from butter* led to an increase in LDL-C (the "bad cholesterol"), but that a diet equally high in saturated fat *from cheese* might not.[11] And to add to the confusion, the most recent evidence suggests that butter has, at worst, a minor effect on cardiovascular health,[12] despite its increasing LDL-C more than do olive oil and coconut oil, and HDL-C (the "good cholesterol") less than does coconut oil.[13]

The evidence on coconut products is equally conflicted. Though purified oil tends to perform worse than coconut meat, the magnitude of its effect on cardiovascular health is uncertain — probably because wider dietary patterns have a much greater impact on cardiovascular health.[14]

🔍 ***Digging Deeper:*** **Are you cuckoo for coconuts?**

You may love coconuts, or might even guzzle coconut oil for its health benefits, but have you ever eaten an entire coconut in one seating? Probably not. A single coconut of average size contains 400 grams of meat (1,400 kcal). Aside from water, this meat is composed of fat (133 grams, including 18 grams of MCTs — *medium-chain triglycerides*), carbs (35 grams of fiber. and 25 grams of sugar), and more protein than you'd expect (13 grams). Combined, coconut's fiber, sorbitol (a sugar alcohol that naturally occurs in some plants), and MCTs can result in a prolonged toilet stay.

Consuming the equivalent amount of fat through a few tablespoons of coconut oil might not cause any digestive issues, since fiber and sorbitol are both subtracted, but the evidence linking coconut oil with a reduction in cardiovascular risk factors is mixed.[15] While there is evidence of good health in island cultures with high coconut intakes,[16] we cannot conclude that these cultures owe their good health to coconuts. And even if coconuts are a healthy *component* of these cultures' simple diets, it doesn't follow that isolated coconut oil is healthy too — especially when *added* to most modern diets.

Still, when it comes to its effect on your cholesterol, coconut oil compares favorably to both butter and olive oil.[17] Compared to butter, it causes a higher increase in HDL-C (the "good cholesterol") and a lower increase in LDL-C (the "bad cholesterol"). Compared to olive oil, it causes a higher increase in HDL-C and a smaller increase in LDL-C.

Test results matter, but they can be misleading

The standard lipid panel is a relatively poor reflection of your cardiovascular health. It estimates how much cholesterol, triglycerides, LDL-C, and HDL-C are in your blood, but it ignores better indicators of cardiovascular health.

LDL particle count is far more important than LDL-C levels. LDL infiltration is a major cause of inflammation, which is a prerequisite to atherosclerosis (a hardening and narrowing of the arteries),[18] and the more particles you have, the more can infiltrate your artery walls. LDL particle size is another potentially important factor, for the smaller and denser LDL particles might find infiltration easier, but its predictive ability is greatly reduced once particle number is accounted for.[19]

So, simply keeping your LDL-C levels in check won't protect you from heart attacks. In fact, one study found that nearly half of hospital patients admitted for cardiovascular disease had ideal levels of LDL-C.[20] Furthermore, some studies have associated low LDL-C levels with cancer, depression, and infectious diseases — although whether low LDL-C is a cause or a consequence of these conditions is uncertain.[21]

🔍 ***Digging Deeper:*** **Is LDL-C really "bad cholesterol"?**

Low-density lipoprotein (LDL) delivers cholesterol to the cells that need it. *High-density lipoprotein* (HDL) removes excess cholesterol from the bloodstream.

A quick Internet search will probably convince you that *LDL cholesterol* (LDL-C) is nefarious. It's beyond question at this point that, in certain populations, lowering LDL-C helps reduce the risk of coronary events.[22]

But cholesterol is also key to, notably, hormone production and the structure of cell membranes, so it certainly isn't inherently bad. LDL particles ferry cholesterol over to cells where it can be used.

If your LDL-C is extremely low, that could even be a sign that something is wonky within your body. One reason relates to infection: both HDL and LDL are needed to fight infection, and severe infection is linked to a reduction in both. Very low LDL-C levels (≤70 mg/dL) have been associated with higher risks of both cancer malignancy and sepsis (a life-threatening complication of infection),[23] not to mention an overall higher risk of death;[24] it is however possible that the diseases *cause* low LDL-C, rather than the reverse.

Not everyone agrees that very low LDL-C levels are risky,[25] but it should be noted that some of the reviews concluding that risks are low were funded by companies producing LDL-C–lowering drugs.[21] The overall takeaway is that the health effects of low LDL-C levels are far from certain, with well-documented cardiovascular benefits on one side and less-well-quantified risks on the other. If your LDL levels are very low, you should probably do a little bit of digging into these topics.

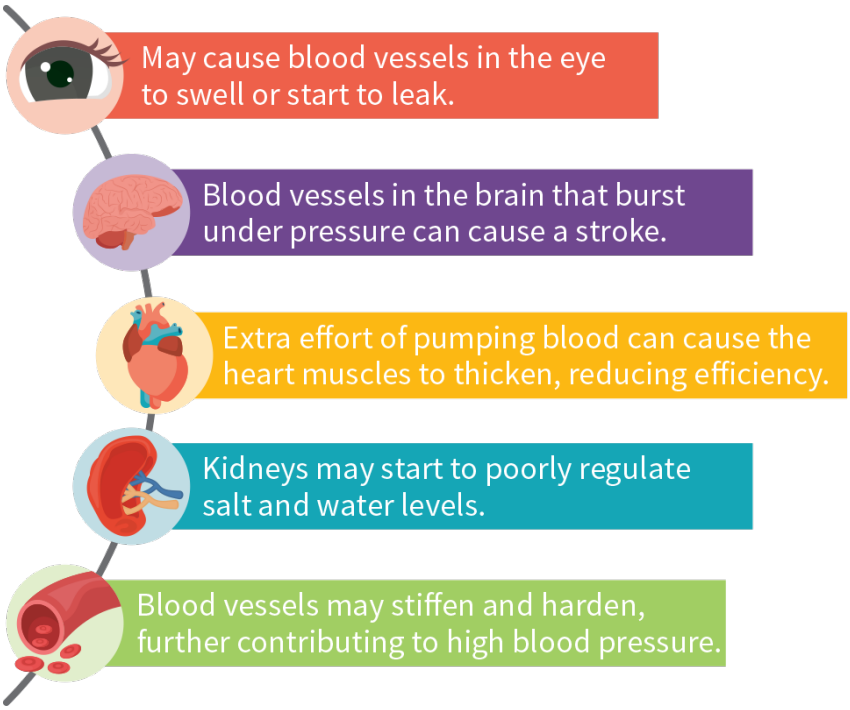
Still, even the standard lipid panel can provide useful information — if we look at ratios. On their own, cholesterol, triglycerides, LDL-C, and HDL-C are relatively poor indicators of cardiovascular health, but the ratio of total cholesterol to HDL-C is a strong indicator of heart disease risk,[26] and the ratio of triglycerides to HDL-C is a strong predictor of heart disease severity,[27][28] insulin resistance,[29] and LDL particle size.[30]

Beyond blood lipids

Even a savvy member of Cholesterol Club — a veteran who looks at ratios and LDL particle size — needs to realize that there's more to cardiovascular health than blood lipids.

For instance, LDL particles aren't the only factor involved in the inflammation necessary for arterial plaque formation. And of course, *blood pressure* (BP) also plays a central role in heart health: cardiovascular disease risk is strongly associated with an increase in BP, even when BP is still within normal range.[31]

Complications of high blood pressure

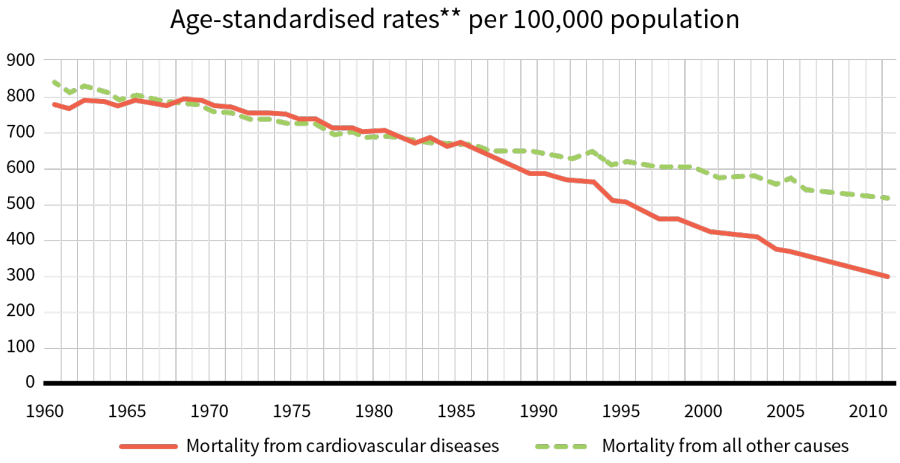


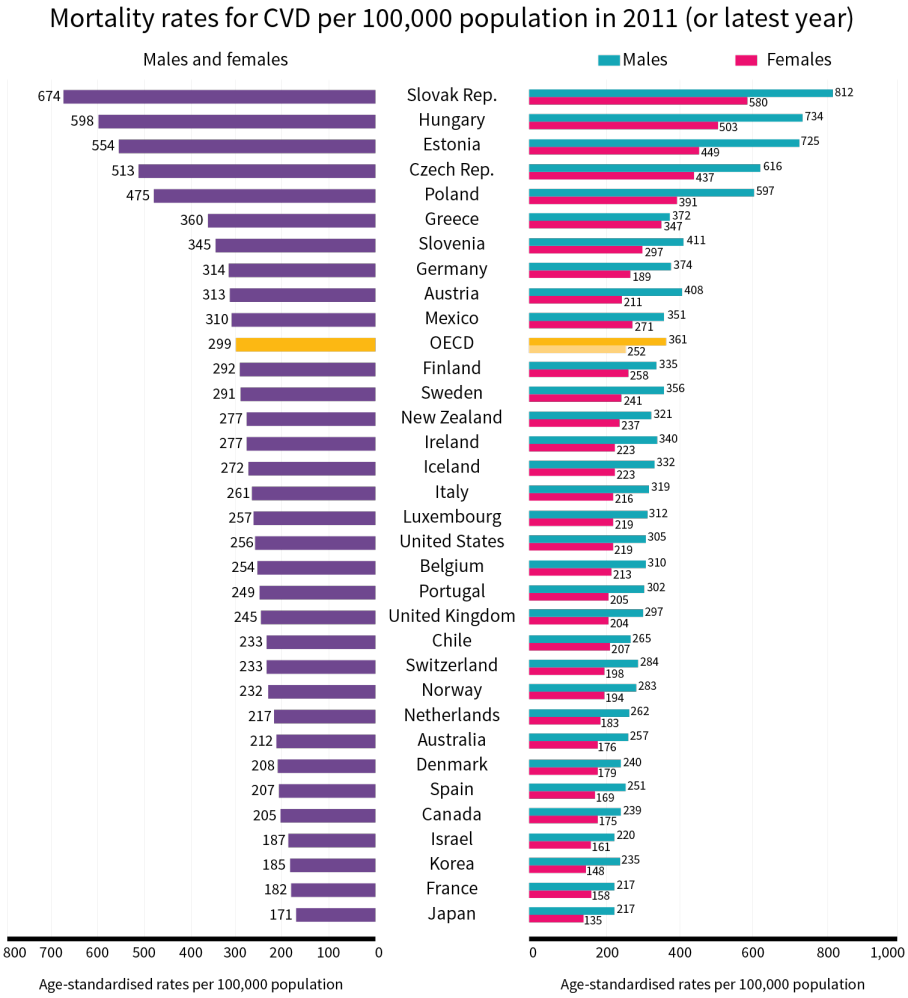
In sum, blood lipids are but one piece of the cardiovascular health puzzle: they shouldn't be ignored, but neither should they turn into an obsession. Some supplements show evidence for potentially aiding cardiovascular health through a variety of mechanisms — some involving blood lipids, some not. None of these supplements, however, will be able to counteract an unhealthy diet; rather, they should be seen as helpful adjuncts to a healthy diet and lifestyle.

Healthy foods, well-chosen supplements — those may complicate your life a little, but they can prolong it too. Published in 2019, a research letter on the "trends in cardiometabolic mortality in the United States, 1999–2017"[32] reports that, "while *cardiovascular disease* (CVD) death rates declined by approximately 36% from 2000 to 2014,[33] CVD remains the leading cause of mortality among US adults."

Kamal Patel, Co-founder and Director
MBA, MPH, PhD(c) in Nutrition

Mortality rates for cardiovascular diseases and all other causes of death in OECD countries*





* In 2013, the Organization for Economic Cooperation and Development comprises 36 member countries.

** Age-adjusted rates are a statistical tool that allows us to compare different age groups while reducing the potential confounding effect age may have on a health outcome.

Reference: OECD Health Statistics. 2013. DOI:10.1787/health-data-en

Combos

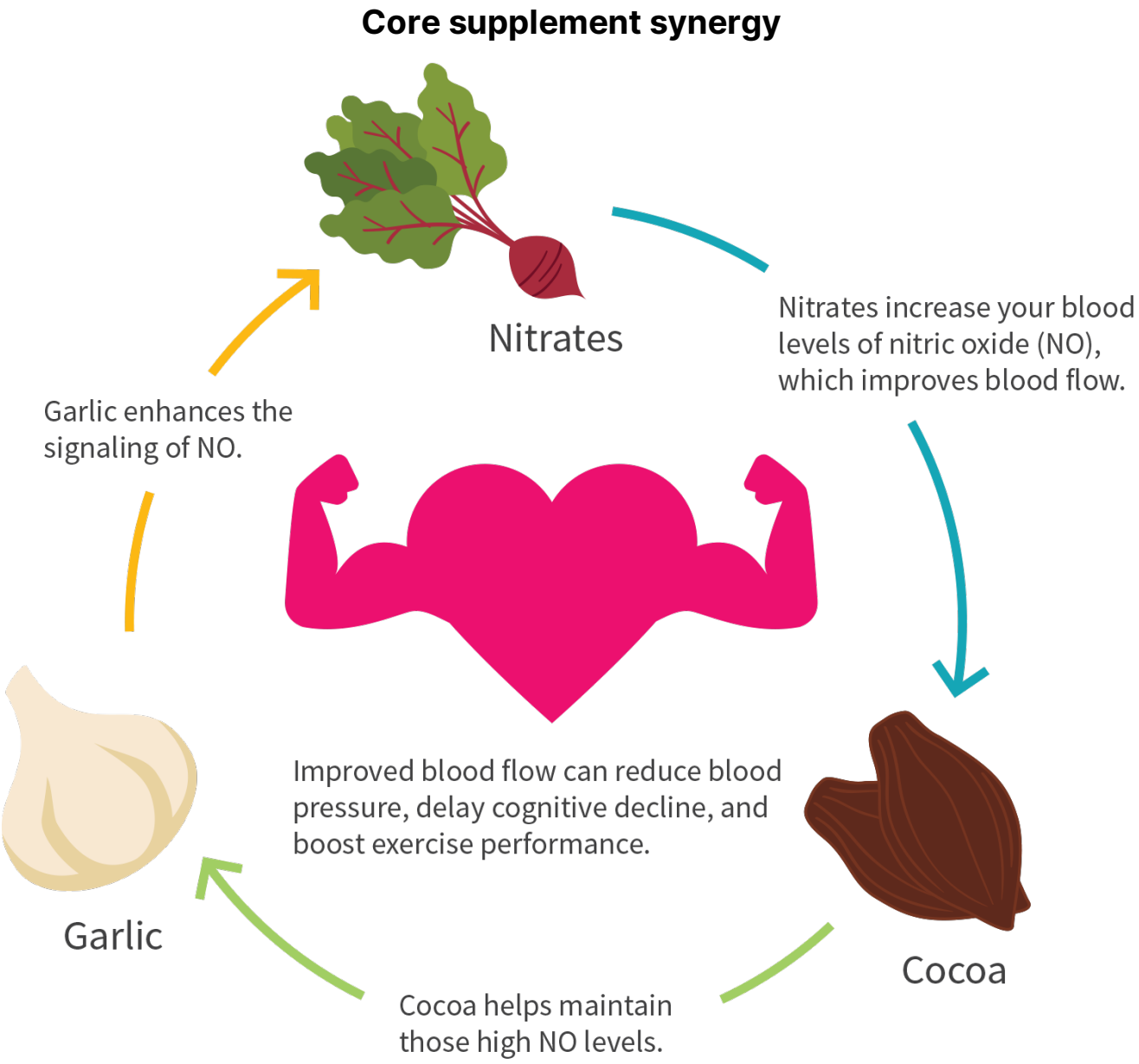
Core Combo

Take 1 g of cocoa polyphenols, for instance by eating about 30 g of cocoa powder or 40g of dark chocolate with a 75% cocoa content.

Take 3 to 6 cloves of garlic (or 600–1,200 mg of an aged garlic extract) over several meals.

Take nitrate-rich vegetables. Aim for 6.4–12.8 mg of nitrates per kilogram of body weight per day (2.9–5.8 mg/lb/day), either over several meals or in one sitting a couple of hours before exercise.

Those three supplements are hypotensive agents, so start at the low end of the dosage range and monitor your blood pressure.



💡 ***Tip:*** **Try one combo alone for a few weeks**

Taking too many supplements at once may prevent you from determining which ones are truly working. Start with just one of the combos suggested here for a couple of weeks before you consider making any modification, such as adding another supplement, altering a supplements dosage, or incorporating the supplements from an additional combo.

When adding another supplement to your regimen, be methodical. For example, you may wish to take all the supplements from two combos. Select the combo that you wish to try first and take this for a couple of weeks. Then, add one supplement from the second combo and wait another week to see how it affects you. Continue this process until you've added all the supplements you wish to.

If a supplement appears in two combos you wish to combine, don't stack the doses; instead, combine the ranges. For instance, if the range is 2–4 mg in one combo and 3–6 mg in the other, your new range becomes 2–6 mg. Always start with the lower end of the range — especially in this case, since the reason why one of the ranges has a lower ceiling in one combo may be due to a synergy with another supplement in the same combo. Reading through the full supplement entry may help you decide which dose to aim for, but if you're not sure, lower is usually safer.

Specialized Combos

For people with no heart complications practicing preventive care

In addition to the core supplements, take 200 mcg of vitamin K_2 MK-7 with a food containing fat. (Adding 500–1,000 mcg of vitamin K_1 may provide additional benefits.)

Adding to this food 500 mg of an olive leaf extract standardized to at least 16% oleuropein can reduce LDL-C oxidation — an effect thought to be cardioprotective. For a better chance to also reduce blood pressure, you could try increasing the dose to 1,000 mg (i.e., 1 g).

For people who have suffered a heart attack

After consultation with your physician, take the core supplements with 5–9 g of carnitine, 1.5–3 g of taurine, and 15 g of D-ribose, in three divided doses spread through the day. Take 90–150 mg of CoQ_{10} with a food containing fat.

For people with varicose veins or with leg swelling caused by sitting

If the core supplements do not solve the problem within a month, add a venotropic — either 100–200 mg of Pycnogenol at breakfast or one of the following options twice a day, 12 hours apart.

- 375–750 mg of *butcher's broom* (i.e., 750–1,500 mg/day)
- 50–75 mg of *horse chestnut* (i.e., 100–150 mg/day)
- 400 mg of *diosmin* with 100 mg of *hesperidin* (i.e., 1,000 mg/day in total)

Like the core supplements (cocoa, garlic, and nitrates), Pycnogenol is a hypotensive agent.

Other Options

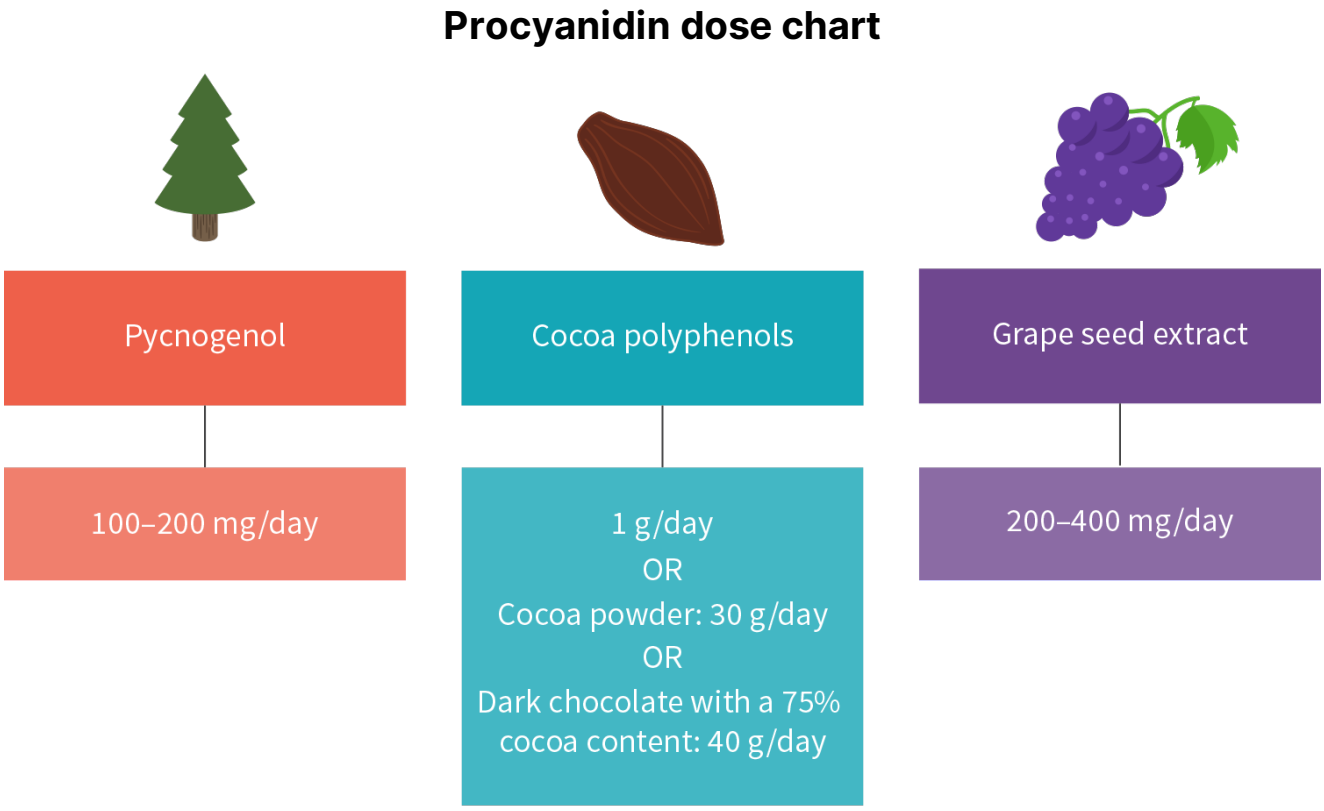
People with elevated triglycerides can add fish oil to any combo. Get 4 g of combined EPA and DHA per day by eating fatty fish (e.g., 280 g of salmon) or by taking fish oil softgels (with food, to reduce the chance of fishy burps). Vegans and vegetarians have the option of taking algal oil softgels.

People with elevated LDL-C levels have the option of taking a supplement with only EPA (4 g still). EPA and DHA are weak antiplatelet agents; combined with other blood thinners (such as garlic, a core supplement), they may prolong bleeding time.

People with hypertension (i.e., high blood pressure) or prehypertension can add *trans*-resveratrol to any combo: 150–3,000 mg/day, with or without food.

Because glutathione may slow down the rate of *nitric oxide* (NO) breakdown in the bloodstream, adding 200 mg of glutathione to your nitrates might prove synergistic.

Should the core cocoa polyphenols (1 g) fail to help you after a month, you could try replacing them with a grape seed extract (200–400 mg). Should the grape seed extract fail to help you after a month, you could try replacing it with Pycnogenol (100–200 mg). Take your grape seed extract or Pycnogenol once a day with a meal.



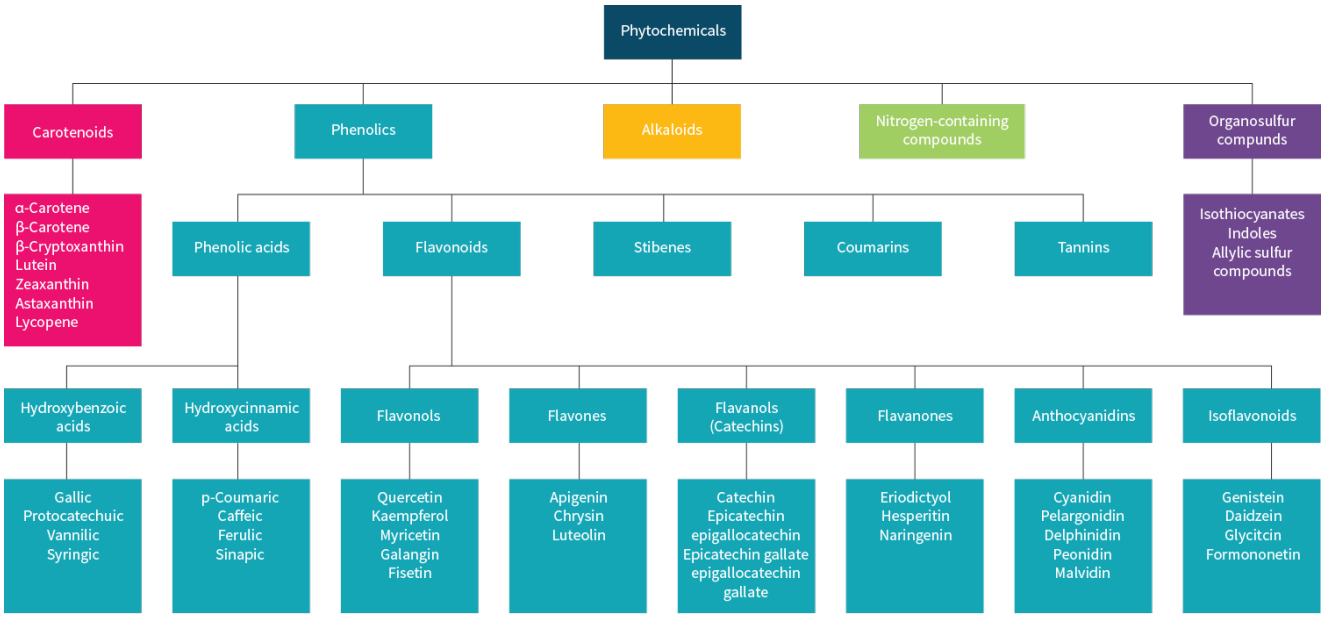
Primary Supplements

Cocoa

What makes *cocoa* a core supplement

Low *nitric oxide* (NO) levels can cause blood vessels to narrow, leading to reduced blood flow. Like the flavonoids in grape seed and Pycnogenol, (-)-epicatechin and other flavonoids in cocoa can help support NO levels, and research shows that cocoa does improve blood flow. Cocoa might also cause a minor decrease in blood pressure in people with hypertension (i.e., high blood pressure), but it has no effect on heart rate.

Classification hierarchy of polyphenols



Judging from a study on a grape seed extract, the improvement in blood flow from cocoa might be negated by the flavonoid quercetin, whose concurrent supplementation should therefore be avoided.

Taking cocoa with other hypotensive agents could cause low blood pressure. Hypotensive agents can be pharmaceuticals but also supplements — garlic, notably, but also nitrates, grape seed extracts, or pine bark extracts, to mention only the supplements presented in this guide.

How to take *cocoa*

The standard daily dose for *cocoa polyphenols* is 1 g, which you can get by eating about 30 g of cocoa powder or 40 g of dark chocolate with a 75% cocoa content. Neither milk chocolate nor white chocolate is a good source of polyphenols.

💡 ***Tip:*** **Why don't you recommend brands or specific products?**

For two reasons:

- We don't test physical products. What our researchers do — all day, every day — is analyze peer-reviewed studies on supplements and nutrition.
- We go to great lengths to protect our integrity. As you've probably noticed, we don't sell supplements, or even show ads from supplement companies, even though either option would generate a lot more money than our Supplement Guides ever will — and for a lot less work, too.

If we recommended any brands or specific products, our integrity would be called into question, so … we can't do it. That being said, in the interest of keeping you safe, we drew a short list of steps you should take if a product has caught your interest.

Garlic

What makes *garlic* a core supplement

Garlic enhances *nitric oxide* (NO) signaling, but its lowering action on blood pressure is mostly due to its enhancing hydrogen sulfide (H_2S) signaling.

Garlic may also fight atherosclerosis (a hardening and narrowing of the arteries). *First*, garlic can cause a decrease in *low-density lipoprotein* LDL-C) and an increase in *high-density lipoprotein* (HDL-C) and thus help prevent cholesterol from clogging the arteries. *Second*, garlic can help prevent excess calcium from stiffening the arteries.

Garlic has antiplatelet properties. While this is yet another attribute of garlic that can improve blood flow, it may be a problem for people taking blood thinners, be they antiplatelet agents (such as aspirin) or anticoagulants (such as warfarin/Coumadin and acenocoumarol/Sintrom).

Taking too much garlic, or taking garlic with other hypotensive agents, could cause low blood pressure. Hypotensive agents can be pharmaceuticals but also supplements, such as nitrates, cocoa, grape seed extracts, or pine bark extracts, to mention only the supplements presented in this guide.

Garlic can interact with several pharmaceuticals other than blood thinners and hypotensive agents, notably contraceptives and drugs used to treat tuberculosis and HIV. If you take any medication, talk to your physician before supplementing garlic.

How to take *garlic*

To maximize the benefits of garlic, eat 3–6 cloves daily over several meals. You should first cut or crush them, to activate their bioactive compounds, then cook them or eat them raw.

Supplementation can provide the same benefits. If you dislike the smell or taste of garlic, or if you wish to avoid the bad breath that comes from eating the cloves, take 600–1,200 mg of an aged garlic extract daily.

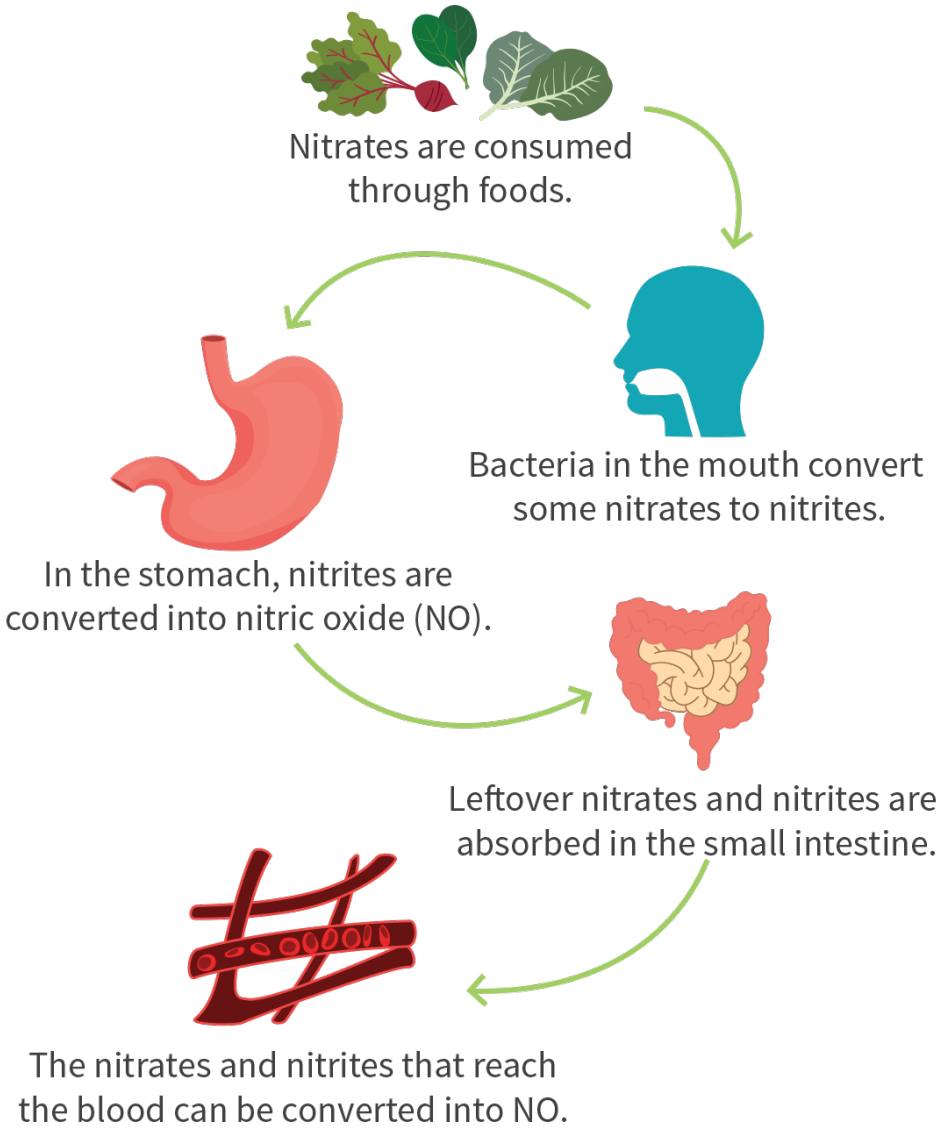
Too much garlic daily (12 cloves) or at once (6 cloves, or 1,200 mg of an aged garlic extract) could cause low blood pressure, especially if taken with other hypotensive agents, and prolong bleeding time. Eating 8 cloves in a day is enough to strongly reduce the efficacy of the anti-HIV drug saquinavir (Fortovase, Invirase).

Nitrates

What makes *nitrates* a core supplement

Nitrates break down into nitrites, which circulate in the body and are turned into *nitric oxide* (NO) as needed. Elevated NO levels are associated with better blood flow and lower blood pressure.

How nitrates are converted into nitric oxide



Nitrates do not exist as dietary supplements, unfortunately, because of regulations against high quantities of sodium nitrate (a food additive frequently added to meat products). Nitrates can be found in different

foods, however, notably beetroot and leafy green vegetables. Beetroot extract capsules will not provide enough nitrates to affect blood flow, but beetroot powder (⅛ the weight of raw beetroot) and beetroot juice are valid options.

Taking nitrates with other hypotensive agents could cause low blood pressure. Hypotensive agents can be pharmaceuticals but also supplements — garlic, notably, but also cocoa, grape seed extracts, or pine bark extracts, to mention only the supplements presented in this guide.

Leafy greens are often rich in vitamin K_1, a fat-soluble vitamin that helps with blood clotting and so might decrease the effectiveness of blood thinners, especially anticoagulants (such as warfarin/Coumadin and acenocoumarol/Sintrom). If you take a blood thinner, you should consult with your physician before consuming a lot of leafy greens.

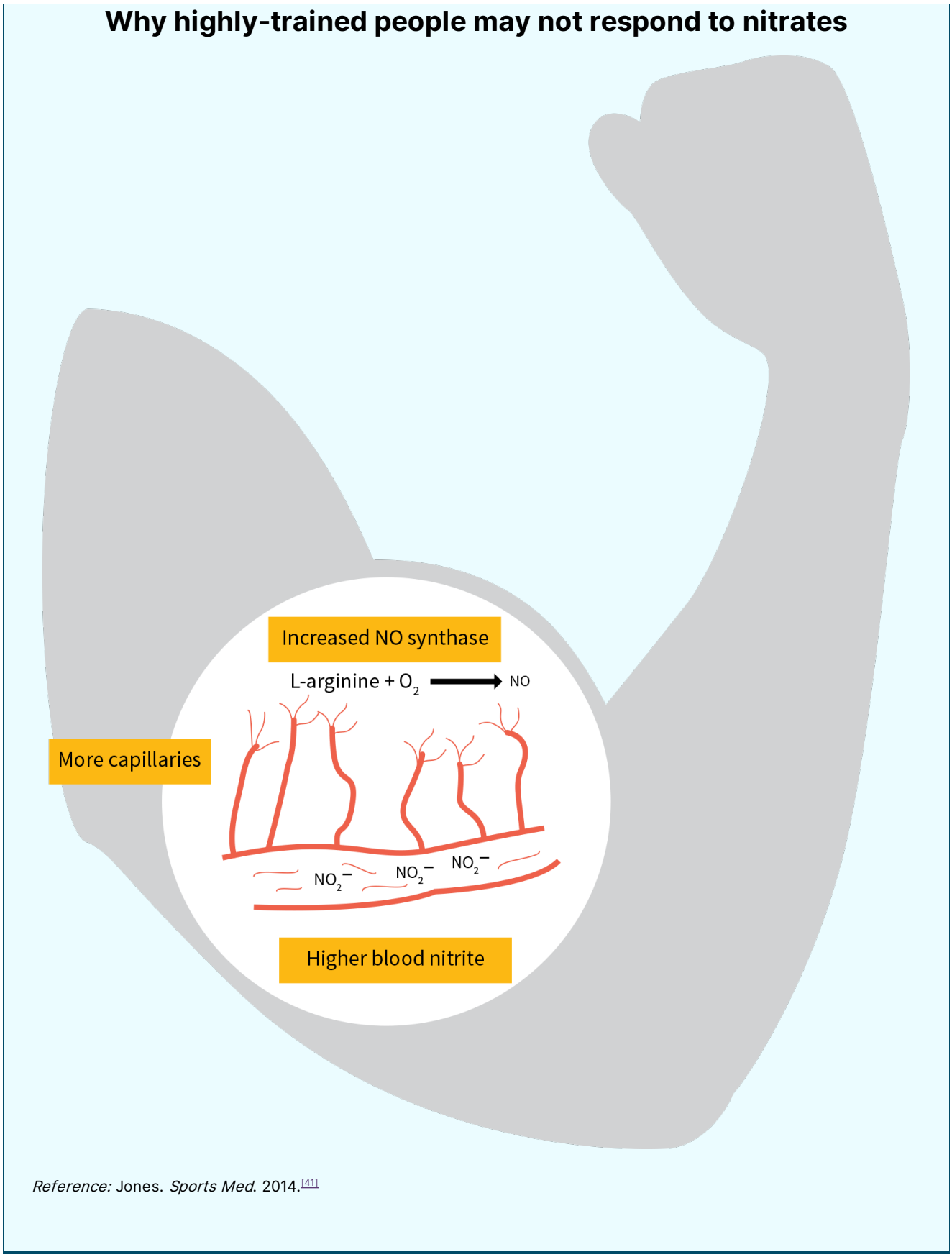
Due to their goitrogen content, cruciferous vegetables can reduce thyroid hormone production if regularly consumed in high amounts, such as those needed for nitrate supplementation. If you tend to eat a lot of cruciferous vegetables (such as cabbage, collard greens, or kale), make sure to also get enough iodine — through iodine-rich foods (such as cod, shrimp, milk, yogurt, or cottage cheese), iodine-fortified foods (such as iodized salt), or supplements (75–150 mcg/day).

🔍 ***Digging Deeper:*** **How training status interacts with nitrate's effects**

From what's known,[34] well-trained people get less benefit from nitrate supplementation, with highly-trained athletes getting little to no performance benefits.[35][36][37] But it's too early to say this with great certainty.

There are several reasons why this could be the case, though, with some shown in the figure below. One reason is that exercise improves the body's ability to make its own nitric oxide through higher plasma nitrite,[38] which is converted to nitric oxide in acidic and low-oxygen conditions, and increased nitric oxide synthase.[39] These two factors could make supplementing it less important.

Athletic muscles also have more capillaries running through them so that they get relatively more blood;[40] thus, there may not be much room for blood flow improvement through nitrate supplementation in well-trained individuals.



Reference: Jones. *Sports Med*. 2014.[41]

How to take *nitrates*

Aim for 6.4–12.8 mg of nitrates per kilogram of body weight (2.9–5.8 mg/lb).

Because the nitrate content of beet-based sports supplements (juice, powder, concentrate) vary so greatly,[42] it's important to check the amount of nitrate the product delivers per serving. Remember to

follow these guidelines to find a quality supplement.

Nitrate intake by bodyweight

BODYWEIGHT lb / kg	2.9 (6.4)	3.4 (7.5)	3.9 (8.5)	4.3 (9.5)	4.8 (10.5)	5.2 (11.5)	5.8 (12.8)	mg/lb (mg/kg)
*100	45*	288	338	383	428	473	518	576	mg
*125	57*	365	428	485	542	599	656	730	mg
*150	68*	435	510	578	646	714	782	870	mg
*175	79*	506	593	672	751	830	909	1,011	mg
*200	91*	582	683	774	865	956	1,047	1,165	mg
*225	102*	653	765	867	969	1,071	1,173	1,306	mg
*250	113*	723	848	961	1,074	1,187	1,300	1,446	mg
*275	125*	800	938	1,063	1,188	1,313	1,438	1,600	mg

Nitrate-rich vegetables (mg per 100 g)

NITRATE-RICH VEGETABLES	Nitrates (mg)	Total Oxalate (mg)	Soluble Oxalate (mg)	Vitamin K~1~ (mcg)
Arugula/rocket	362.4	7.1	<0.5	108.6
Turnip greens	346.7	50	—	251
Dill	259	159	60	0
Collard greens	254.5	450	—	437.1
Spinach	248.5	656	542.6	482.9
Swiss chard	236.3	964	207.7	830
Turnips	217.4	210	—	0.1
Rhubarb	199.9	805	223	29.3
Beetroot	199.2	121	74.9	0.2
Celery	196.4	17.5	<0.5	29.3
Mustard greens	187.5	128.7	—	257.5
Radish	177.3	9.2	<0.5	1.3
Lettuce	168.9	13.6	<0.5	126.3
Watercress	164	10	<0.5	250
Bok choy	162	2	—	45.5
Kale	137.5	20	—	704.8
Parsley	130.47	136	76	1,640

This table is composed of averages from multiple samples. Farming techniques, transport, storage conditions, and cooking methods can all greatly affect the actual nitrate and oxalate content of your food.

References: Jackson et al. *Nutr Res Rev*. 2017[43] ● Lidder and Webb. *Br J Clin Pharmacol*. 2013[44] ● Griesenbeck et al. *Nutr J*. 2009[45] ● Tamme et al. *Food Addit Contam*. 2006[46] ● Siener et al. *Food Chem*. 2006[47] ● Hönow and Hesse. *Food Chem*. 2002[48] ● Santamaria et al. *J. Sci. Food Agric*. 1999[49] ● Dr. Duke's Phytochemical and Ethnobotanical databases ● FoodData Central

Those vegetables can be consumed whole or in liquid form (juice, shake, or purée) over several meals. They can also be drunk in one sitting a couple of hours before exercise.

Since the bacteria in saliva play a role in activating dietary nitrates, do not use an antibacterial mouthwash too often, and especially not shortly before consuming nitrate-rich foods. Moreover, the cooking time, if any, should be brief: although cooking reduces the oxalate content more than the nitrate content, the loss of nitrates after fifteen minutes of cooking can still exceed 50%.

Vegetables sorted by nitrate content (mg per 100 g)

NITRATE CONTENT	VEGETABLES
Very high (250+)	Arugula/rocket, collard greens, dill, turnip greens
High (100 to <250)	Beetroot, bok choy, celeriac, celery, kale, kohlrabi, lettuce, mustard greens, parsley, radish, rhubarb, spinach, swiss chard, turnip, watercress
Moderate (50 to <100)	Broccoli, cabbage, cauliflower, endive, savoy cabbage
Low (20 to <50)	Chicory, eggplant, fennel, green beans, green onion, leek, pumpkin/squash
Very low (<20)	Artichoke, asparagus, broad bean, brussels sprouts, carrot, cucumber, dry beans, garlic, lima beans, maize, mushroom, onion, peas, pepper, sweet potato, tomato, white potato

References: Jackson et al. *Nutr Res Rev.* 2017.[43] ● Hord et al. *Am J Clin Nutr.* 2009.[50] ● Jones. *Sports Med.* 2014.[41]

Most vegetables rich in nitrates are also rich in oxalate, which can increase the risk of kidney stones. People already at an increased risk of forming kidney stones, as well as people with oxalosis or hyperoxaluria, should keep their oxalate intake to a minimum.

Other people need not ban all oxalate from their diet, but if you consume high amounts of nitrates (and the dosage range in this guide certainly qualifies) more than twice a week, favor oxalate-poor vegetables. And if you do eat oxalate-rich foods on occasion, consider cooking them and/or pairing them with calcium-rich foods, in order to reduce oxalate absorption.

Vegetables sorted by total oxalate content (mg per 100 g)

OXALATE CONTENT	VEGETABLES
Very high (100+)	Beetroot, collard greens, dill, mustard greens, parsley, rhubarb, spinach, swiss chard, turnips
High (10 to <100)	Cauliflower, celery, kale, lettuce, turnip greens
Moderate (2 to <10)	Arugula/rocket, asparagus, carrot, radish, sweet potato, watercress
Low (<2)	Bok choy, cabbage, radicchio

Because glutathione may slow down the rate of NO breakdown in the bloodstream, adding 200 mg of N-acetylcysteine (NAC) to your nitrates might prove synergistic.

Secondary Supplements

Carnitine

What makes *carnitine* a core supplement

Carnitine plays a role in cognition,[51] energy metabolism,[52] and cardiovascular health.[53][54][55] Though your body can synthesize it out of lysine and methionine, two amino acids, nearly three-fourths of the carnitine in omnivorous people comes from the meat, fish, eggs, and dairy products they consume.

Selected food sources of carnitine

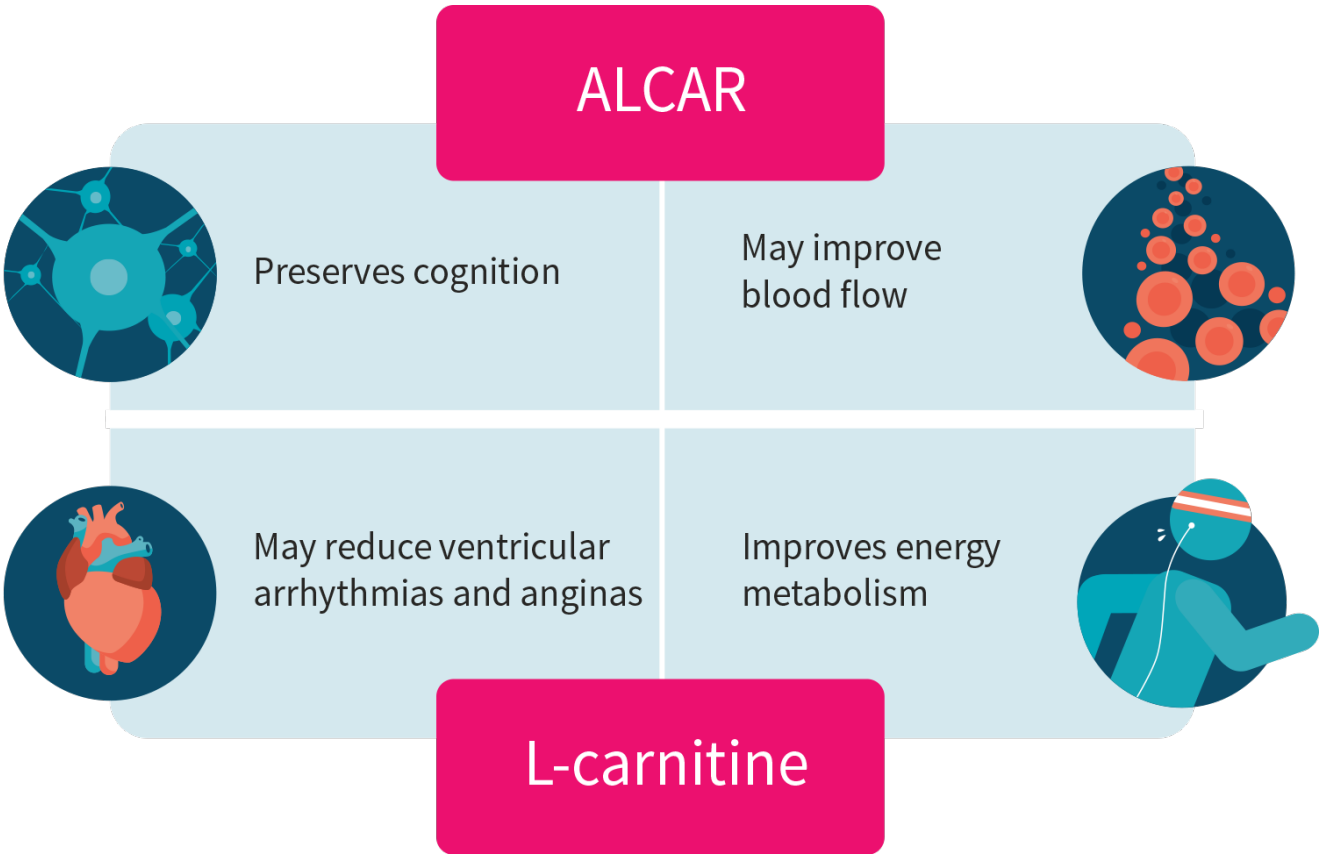
FOOD	PORTION	MILLIGRAMS (mg)
Beefsteak, cooked	4 oz	56–162
Ground beef, cooked	4 oz	87–99
Whole milk	1 cup	8
Codfish, cooked	4 oz	4–7
Chicken breast, cooked	4 oz	3–5
Ice cream	½ cup	3
Cheddar cheese	2 oz	2
Whole-wheat bread	2 slices	0.2
Asparagus, cooked	½ cup	0.1

Adapted from Carnitine: Fact Sheet for Health Professionals. NIH ODS. Last updated October 10, 2017; accessed October 27, 2019

Your body's ability to synthesize carnitine decreases as you age. In seniors, carnitine supplementation may reduce muscular fatigue, and preliminary evidence suggests that it may improve muscular control.

Also, people who have suffered a heart attack can supplement carnitine as an add-on treatment to possibly lower the risk of both abnormal heartbeats in the lower chambers (i.e., ventricular arrhythmia) and pain in the chest or limbs caused by poor blood circulation (i.e., angina).[56]

Summary of carnitine's benefits



Adverse effects are generally rare, but some cases of upset stomachs have been reported. Higher doses of L-carnitine (2 g/day or more) can be converted into the compound trimethylamine, which in *some* people can give a fishy odor to urine, sweat, or breath.

Carnitine and its derivatives might interact negatively with some pharmaceuticals, including anticoagulants (such as warfarin/Coumadin and acenocoumarol/Sintrom). People on thyroid medication or with hypothyroidism may also wish to forgo carnitine, as it might depress thyroid hormone levels.

How to take *carnitine*

In people at risk but who have not yet suffered cardiovascular complications, 500–2,000 mg of *L-carnitine* per day might offer some protection when taken in conjunction with prescribed medical therapies. People who have already suffered a heart attack, however, would need *at least* 2,000 mg (i.e., 2 g) and preferably 5,000–9,000 mg (i.e., 5–9 g) to see a reduction in arrhythmia, angina, and all-cause mortality.

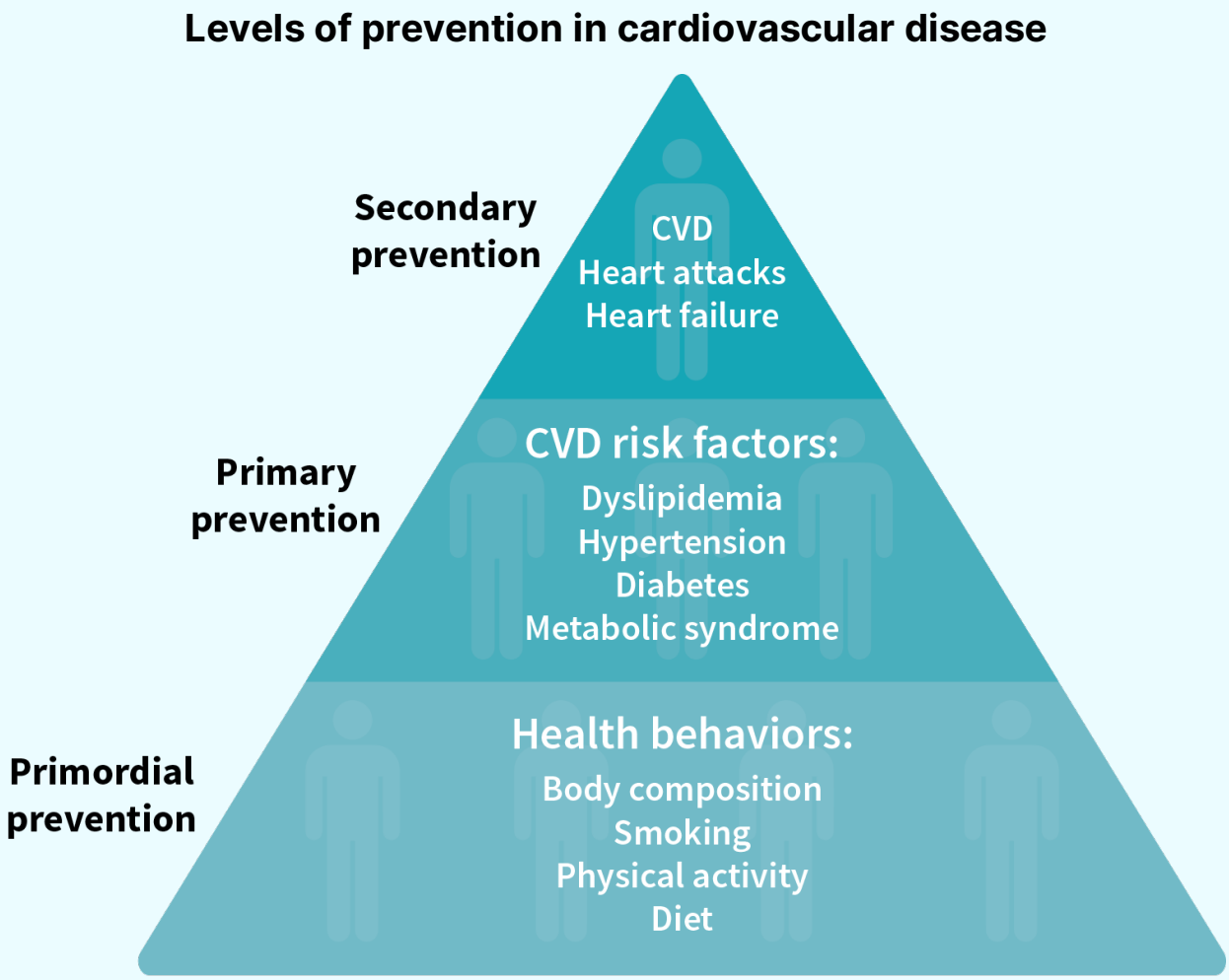
L-carnitine can also be consumed as *L-carnitine L-tartrate* (LCLT) or *glycine propionyl-L-carnitine* (GPLC).

- You can supplement 500–2,000 mg of L-carnitine through 750–3,000 mg of LCLT or GPLC.
- You can supplement 5,000–9,000 mg of L-carnitine through 7,500–13,500 mg of LCLT or GPLC.

However, neither LCLT nor GPLC has proven advantages over regular L-carnitine, both are more expensive, and GPLC also clumps easily in moist environments.

🔍 ***Digging Deeper:*** **Levels of prevention for CVD**

Public health and medical interventions are often focused on preventing negative health outcomes. There are multiple types of prevention: primordial, primary, and secondary. These types of prevention are summarized below.



Reference: Hong et al. *J Am Coll Cardiol.* 2017.[57]

Primordial prevention is aimed at stopping the risk factors for CVD from ever developing. An example would be aiming to maintain blood pressure in someone who already has normal blood pressure.

Primary prevention means preventing an initial event from happening, like getting heart disease or a first heart attack, by modifying its risk factors. An example would be lowering high cholesterol to prevent a first heart attack.

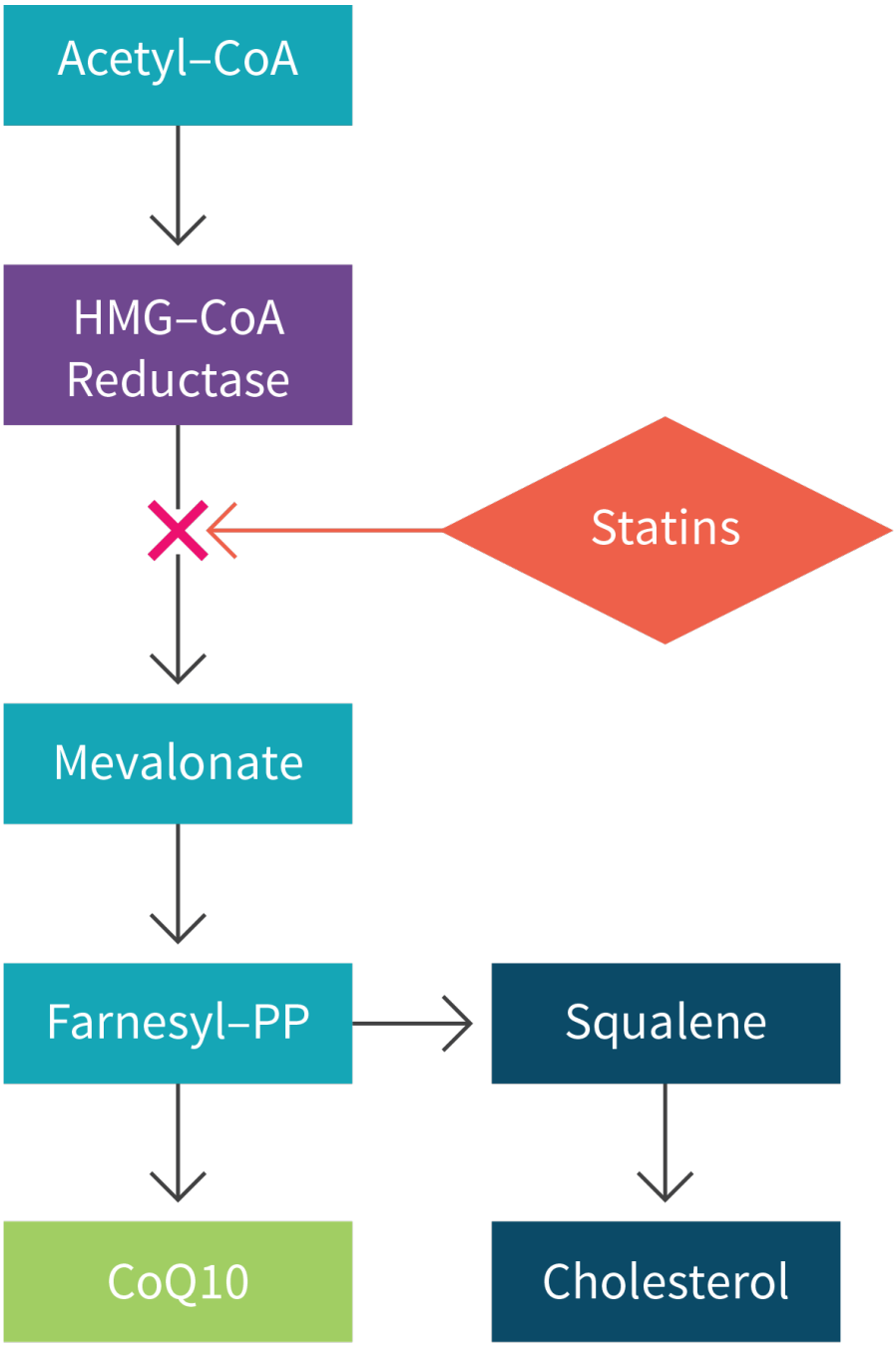
Secondary prevention aims to prevent the progression or another occurrence of an existing disease, like preventing a second stroke in someone who's already had one.

What makes *CoQ$_{10}$* a primary option

Coenzyme Q_{10} (CoQ_{10}) is found mostly in mitochondria, the "power plants" in our cells. Our bodies produce it, yet supplementation can provide additional benefits, such as reducing the risk of further heart complications in people who have suffered a heart attack. More research is needed to determine if CoQ_{10} can also benefit people with less severe cardiac damage.

Statin medications (i.e., cholesterol lowering drugs) can lower CoQ_{10} levels in the body. If you are taking statins, talk to your physician about supplementing CoQ_{10}.

How statins lower CoQ~10~



Statins, such as atorvastatin (Lipitor), inhibit the enzyme HMG–CoA reductase in the mevalonate pathway. In such a way, they can decrease your cholesterol levels, but also your production of CoQ_{10}. Supplementing CoQ_{10} can help offset this decrease.

How to take *CoQ_{10}*

Take 90–150 mg of CoQ_{10} once a day with a meal containing fat.

Higher doses (200–300 mg) result in higher levels of CoQ_{10} in the body, but more research is needed to determine if those higher levels translate into greater cardiovascular protection.

Fish Oil

What makes *fish oil* a primary option

Essential fatty acids (EFAs) are *polyunsaturated fatty acids* (PUFAs) your body needs and cannot produce. There are only two kinds of EFAs: linoleic acid (LA) and alpha-linolenic acid (ALA). Neither is very active, so your body transforms the former into notably arachidonic acid (AA) and the latter into eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). LA and AA are omega-6 fatty acids, while ALA, EPA, and DHA are omega-3 fatty acids. EPA and DHA make for most of the PUFAs in fish oil.

Fish oil can reliably reduce triglyceride levels. Even in people with normal triglyceride levels, it can reduce inflammation and high blood pressure, and consequently plaque formation and the risk of atherosclerosis (a hardening and narrowing of the arteries). In this fashion, fish oil can benefit cardiovascular health, though most recent studies have found no evidence that it actually lowers the risk of heart attack.

Supplements with only EPA or DHA are also available. Whereas DHA is marginally better than EPA at reducing triglycerides levels, it can cause a modest increase in low-density lipoprotein ((LDL-C), the “bad cholesterol”).

Though to a lesser extent than garlic, omega-3 fatty acids have antiplatelet properties. While this is yet another attribute of EPA or DHA that could improve blood flow, it might be a problem for people taking blood thinners, be they antiplatelet agents (such as aspirin) or anticoagulants (such as warfarin/Coumadin and acenocoumarol/Sintrom). Omega-3 fatty acids may also lower blood pressure and increase fasting blood sugar levels.

🔍 ***Digging Deeper:*** **Oxidized fish oil**

Fish oil can go rancid and oxidize when exposed to oxygen, heat, or light. These oils are particularly susceptible to oxidation because of their very-long-chain polyunsaturated fatty acids. The oxidation level is measured using three values.

1. Peroxide value (PV)
2. Anisidine value (AV)
3. Total oxidation value (TOTOX)

The PV is a measure of primary oxidation products (peroxides) and AV a measure of secondary oxidation (aldehydes and ketones). The TOTOX value is calculated using the formula AV + 2PV. The lower the TOTOX value, the better the oil quality will be. The Global Organization for EPA and DHA Omega-3 recommends a TOTOX value of no more than 26.

Oxidation of fish oils can be highly variable. One 2015 study found that nearly 50% of commercial fish oils exceeded the maximum recommended TOTOX value.[58] while others have found very good compliance with TOTOX limits.[59][60] Taken together, the divergent results demonstrate just how widely the quality of commercially available fish oil supplement can be.

Evidence for the health effects of consuming oxidized fish oils is a bit mixed. For healthy individuals, it would appear that there is a lack of obvious short-term health damage from consuming oxidized fish oil. One study showed no difference in circulating levels of oxidized LDL-C or inflammatory markers after seven weeks of oxidized fish oil supplementation.[61]

However, in people with high levels of cholesterol and triglycerides, consumption of highly oxidized fish oils can minimize its efficiency at improving metabolic markers like fasting glucose, total cholesterol, and triglycerides.[62]

How to take *fish oil*

To reduce triglyceride levels, get 4 g of combined EPA and DHA per day by eating fatty fish (e.g., 280 g of salmon) or by taking fish oil softgels (with food, to reduce the chance of fishy burps). Vegans and vegetarians have the option of taking algal oil softgels.

For general health and cardiovascular support, take 300–600 mg of combined EPA and DHA a day. This dose can be achieved simply by eating fatty fish several times a week.

If your LDL levels are too high, you could replace the EPA+DHA combination with an equal dose of just EPA.

Taking fish oil with a food reduces the chance of fishy burps.

Grape Seed

What makes *grape seed* a primary option

Low *nitric oxide* (NO) levels can cause blood vessels to narrow, leading to reduced blood flow. Like the flavonoids in cocoa and pine bark, procyanidins and other flavonoids in grape seeds can help support NO levels.

Studies on grape seed extracts have reported minor reductions in heart rate and, possibly as a consequence, in blood pressure. There was no improvement in blood flow, or only to a small extent in people with vascular risk factors, such as high blood pressure. This possible improvement in blood flow may be negated by the flavonoid quercetin, whose concurrent supplementation should therefore be avoided.

Taking a grape seed extract with other hypotensive agents could cause low blood pressure. Hypotensive agents can be pharmaceuticals but also supplements — garlic, notably, but also nitrates, cocoa, or pine bark extracts, to mention only the supplements presented in this guide.

How to take *grape seed*

Take 200–400 mg of a grape seed extract once a day with a meal.

Resveratrol

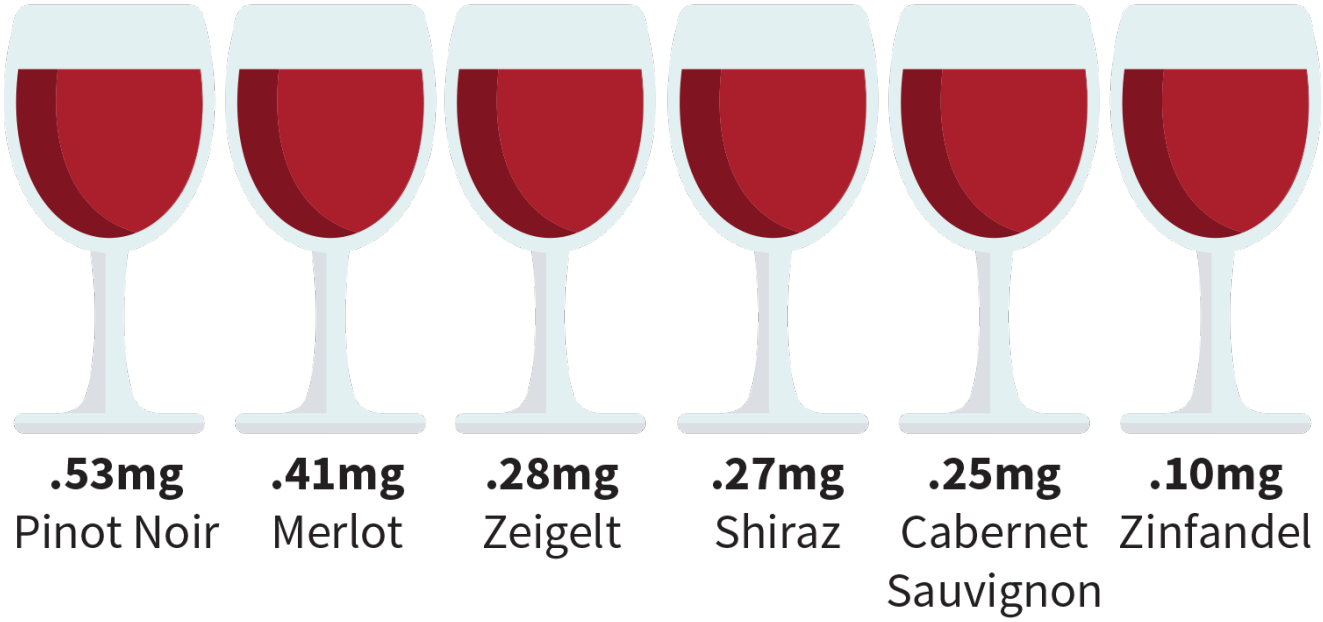
What makes *resveratrol* a primary option

Much of the initial excitement surrounding resveratrol (a fat-soluble polyphenol found notably in peanuts, berries, grapes, and red wine) stemmed from cell culture studies and animal trials. As the research progressed into humans, evidence began to emerge that resveratrol could raise insulin sensitivity and decrease fat stores, blood lipids, blood pressure, and inflammatory markers; however, media articles much overhyped the relatively small effects seen in these studies.

In people with hypertension (i.e., high blood pressure) or prehypertension, resveratrol can produce a minor reduction in blood pressure: about 5 mmHg systolic and 3 mmHg diastolic. These numbers may fail to impress you, but keep in mind they are averages over hundreds of people — individual results do vary.

Resveratrol is an umbrella term for different isomers, the most active being *trans*-resveratrol.

Average trans-resveratrol content of various red wines per 5-ounce glass



Reference: Stervbo et al. *Food Chemistry*. 2007. DOI:10.1016/j.foodchem.2006.01.047

How to take *resveratrol*

Take 150–3,000 mg of *trans-resveratrol* a day, with or without food.

Maximum benefit is usually experienced after three months of continuous supplementation.

Taurine

What makes *taurine* a primary option

Taurine (L-taurine) is one of the most abundant amino acids in the body, with particularly high concentrations in the heart tissue, where it is thought to help maintain cell membranes and regulate heartbeats. It is not an essential amino acid], since our bodies can make it from vitamin B_6, methionine, and cysteine; however, supplementation can modestly but reliably reduce blood pressure in people with congestive heart failure, hypertension (i.e., high blood pressure), or prehypertension. Likewise, in people with congestive heart failure, taurine can modestly but reliably improve cardiac function.

How to take *taurine*

Daily dosage ranges from 1.5 to 6 g, though 3 g is currently considered the upper limit for safe lifetime supplementation. Whichever dosage you go with, split it into 2 or 3 doses a day, with or without food.

Venotropics

What makes *venotropics* a primary option

Venotropics can improve the rate at which the blood returns to the heart. They are used to treat *chronic venous insufficiency* (CVI), which is characterized by blood pooling in extremities. They can also be used to treat leg swelling caused by prolonged sitting or to reduce varicose veins.

Daflon (90% diosmin, 10% hesperidin) was the first venotropic, but it is slightly less effective than Pycnogenol. Butcher's broom (*Ruscus aculeatus*) and horse chestnut (*Aesculus hippocastanum*) also have venotropic properties.

Pycnogenol is a patented pine bark extract standardized to 65–75% procyanidin. Grape seed extracts, being also rich in procyanidins, might offer similar benefits, but there is currently no study on the subject.

How to take *venotropics*

Take 100–200 mg of *Pycnogenol* with breakfast. Alternatively, take one of the following options twice a day, 12 hours apart.

- 375–750 mg of *butcher's broom* (i.e., 750–1,500 mg/day)
- 50–75 mg of *horse chestnut* (i.e., 100–150 mg/day)
- 400 mg of *diosmin* with 100 mg of *hesperidin* (i.e., 1,000 mg/day in total).

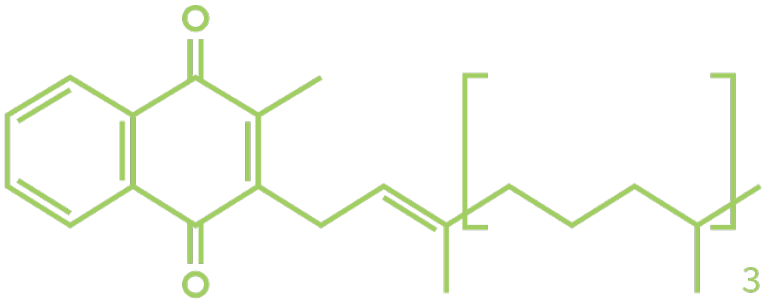
Vitamin K

What makes *vitamin K* a primary option

Vitamin K is an umbrella term for a variety of molecules with similar but distinct structures.

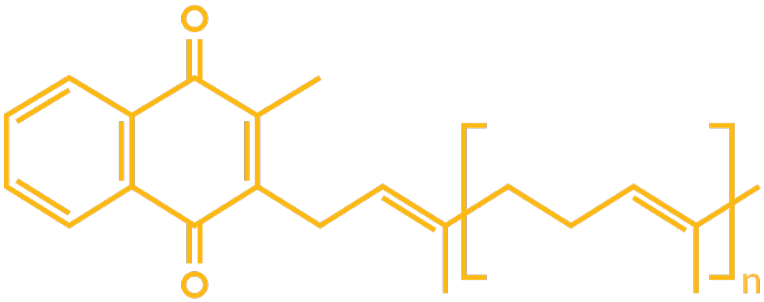
- K_1 (phylloquinone) is a molecule found in plants.
- K_2 (menaquinone) is a group of molecules.
    - K_2 MK-4 is mostly found in animal products.
    - K_2 MK-7 is mostly found in fermented foods.

The K vitamins

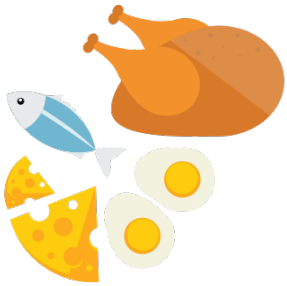


Phylloquinone (Vitamin K_1)

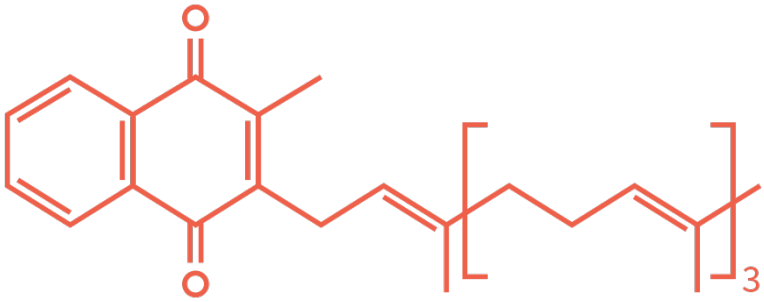
Found in plants



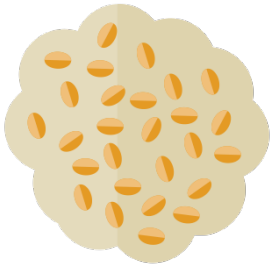
Menaquinone-4 (Vitamin K_2 MK-4)



Found in animal products



Menaquinone-7 (Vitamin K_2 MK-7)



Found in fermented foods

In all its forms, vitamin K is fat-soluble and supports blood clotting and calcium regulation; it helps ensure that more calcium gets deposited in bone and less in soft tissues.

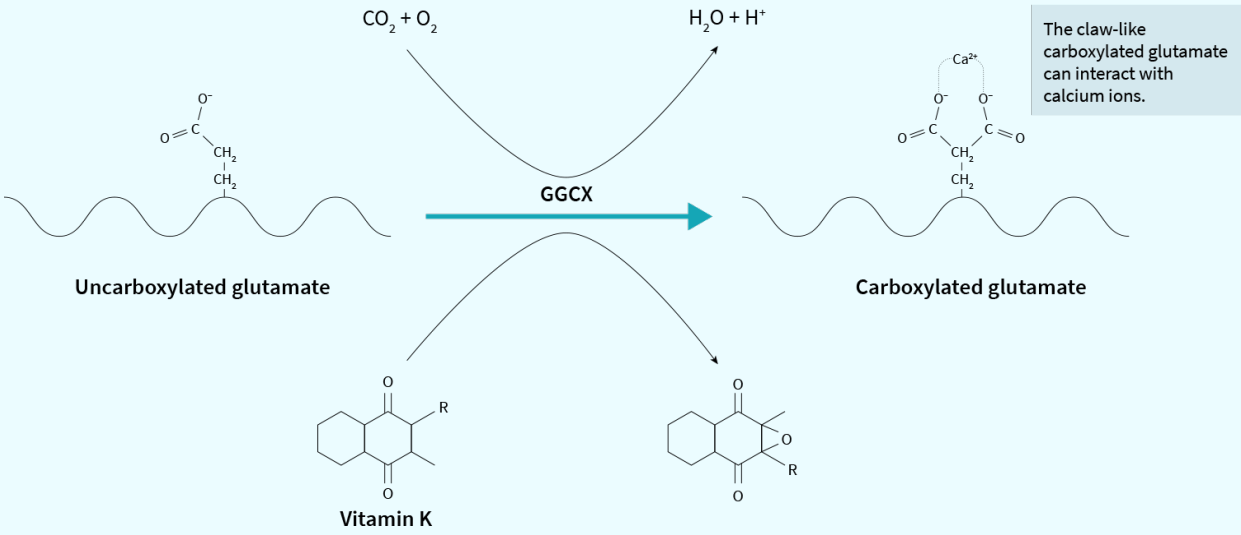
🔍 ***Digging Deeper:*** **How does vitamin K affect calcification?**

Vitamin K is a necessary cofactor for enzymes that catalyze some carboxylation reactions, a process in which a molecule of carbon dioxide is transferred onto one of over a dozen different proteins in the body.

In the case of the enzyme *gamma-glutamyl carboxylase* (GGCX), for example, vitamin K likely gets oxidized to facilitate the removal of a proton from a glutamate residue in a protein — a removal needed for GGCX to carboxylate the protein in a following step.[63][64]

On the protein, this process creates a chemical group resembling a two-pronged claw and carrying two negative charges. This group can grab free calcium ions, which each carry two positive charges. The protein can then transport these ions and utilize them as needed, resulting in effects on blood coagulation, bone metabolism, and possibly the removal of calcium from arteries.

The carboxylation mechanism of vitamin K



Put simply, vitamin K makes a bunch of proteins good at grabbing calcium and moving it around in the body as needed.

Hence, vitamin K can both strengthen bones and reduce cardiovascular risk. However, there are notable differences between the different forms.

After being absorbed by your intestines, K_1 is taken up by your liver (where vitamin K is used to make clotting proteins, which are then released into your blood) at a higher rate than MK-4, whereas MK-4 is taken up by soft tissues at a higher rate than K_1. This should make K_1 better at supporting coagulation (i.e., blood clotting), and MK-4 better at preventing calcium from being deposited in the arteries.

Some K_1 converts indirectly to MK-4, but how much is unknown. Diets naturally rich in K_1 do not seem to reduce cardiovascular risk, but trials supplementing high K_1 doses have noted some reduction in coronary artery calcification. The reason may be that, in many plants, K_1 is tightly bound to chloroplasts (organelles that contain chlorophyll and conduct photosynthesis), so you could be absorbing very little of what you eat.

Unlike MK-4, MK-7 has been used in trials looking at arterial stiffness and atherosclerosis (a hardening and narrowing of the arteries), and we can say it is likely good at both supporting coagulation and preventing coronary calcification. It is important to note that cardiovascular research has not compared K_1 to K_2, or MK-4 to MK-7.

Vitamin K is usually safe. Supplementation might cause some nausea or stomach upset, but those effects are uncommon.

K_1 is present mostly in leafy green vegetables, many of which are cruciferous. If you plan to increase your K_1 intake through plant foods, be aware that cruciferous vegetables contain goitrogens and thus can reduce thyroid hormone production. If you tend to eat a lot of cruciferous vegetables, such as kale, make sure to also get enough iodine — through iodine-rich foods (such as cod, shrimp, milk, yogurt, or cottage cheese), iodine-fortified foods (such as iodized salt), or supplements (75–150 mcg/day).

Micrograms of vitamin K per 100 grams of food

FOODS	K~1~	K~2~ MK-4	K~2~ MK-7
Collards	440	0	0
Spinach	360–380	0	0
Broccoli	113–180	0	0
Cabbage	98–145	0	0
Natto	Not measured	0	939–998
Chicken	0–4.5	8.5–60	0
Pork	0–3.4	2.1–6	0.5–0.12
Beef	0.7–2.4	1.1–15	0–0.12
Beef liver	2.7	0.82	18.2
Egg	0.3–12	7–9	Not measured
Egg yolk	Not measured	15.5–64	0
Butter	7	15–21	0
Blue cheese	Not measured	Not measured	2.5–22
Cheddar	2.1	10.2	0–2.3

References: Fu et al. *J Agric Food Chem*. 2016.[65] ● Manoury et al. *J Dairy Sci*. 2013.[66] ● Booth. *Food Nutr Res*. 2012.[67] ● Kamao et al. *J Nutr Sci Vitaminol (Tokyo)*. 2007.[68] ● Elder et al. *J Agric Food Chem*. 2006.[69] ● Schurgers and Vermeer. *Haemostasis*. 2000.[70] ● Booth et al. *J Am Diet Assoc*. 1996.[71] ● Shimogawara and Muto. *Arch Biochem Biophys*. 1992.[72] ● Hirauchi et al. *J Chromatogr*. 1989.[73]

How to take *vitamin K*

The doses below reflect the doses used in studies; they are much higher than the minimum amount of vitamin K you need to avoid deficiency-related issues:

Adequate Intake (AI) for vitamin K (mcg)

AGE	MALE	FEMALE	PREGNANT	LACTATING

AGE	MALE	FEMALE	PREGNANT	LACTATING
0–6 months	2.0	2.0	—	—
7–12 months	2.5	2.5	—	—
1–3 years	30	30	—	—
4–8 years	55	55	—	—
9–13 years	60	60	—	—
14–18 years	75	75	75	75
>18 years	120	90	90	90

Reference: Institute of Medicine. Vitamin K (chapter 5 in *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*. The National Academies Press. 2001.)[74]

As we saw, different forms of vitamin K have different metabolisms and distributions within the body, so taking more than one form may be beneficial.

Take 200 mcg (0.2 mg) of *MK-7* and, optionally, 500–1,000 mcg (0.5–1 mg) of *K_1*. MK-4 is theoretically better than K_1 (for cardiovascular health), but there are not enough data to support a dosage.

Vitamin K being fat soluble, it is better absorbed when taken with a fat-containing food or supplement (e.g., fish oil)

Do not supplement with vitamin K if you have been prescribed blood thinners (i.e., anticoagulants) that work by hindering vitamin K's blood-clotting properties (such as warfarin/Coumadin and acenocoumarol/Sintrom). If you have been prescribed a diet low in vitamin K, you may need to strictly track your vitamin K intake to ensure it stays consistent.

Promising Supplements

D-Ribose

What makes *D-Ribose* a secondary option

Adenosine triphosphate (ATP) has been called “life’s energy currency”; it powers our cells. Its levels remain depressed following events that damage the heart tissue, such as heart attacks. Without enough ATP, the heart can suffer from dysfunctions, such as the inability to pump properly (and thus fill up with adequate amounts of blood).

D-Ribose is a monosaccharide that helps replenish ATP stores. Its supplementation when ATP levels are depressed looks beneficial, but research is still limited. To date, only four studies have investigated D-ribose supplementation in seniors with congestive heart failure, all of whom were on various medications to treat their condition. The majority were senior males, with only ten females being included across all four studies.

Preliminary evidence suggests that D-ribose may help the heart pump blood, with results ranging from very minor effects to moderate improvements.

How to take *D-Ribose*

Take 5 g of D-ribose three times a day (i.e., 15 g/day) with or without food.

Olive Leaf

What makes *olive leaf* a secondary option

The oxidation of low-density lipoprotein (LDL-C, the “bad cholesterol”) is one of the main contributors to plaque formation. Oleuropein and other phenolic compounds in the leaf of the olive tree (*Olea europaea*) can reduce LDL oxidation. Therefore, olive leaf extracts should reduce plaque buildup in arteries, but this has yet to be confirmed by dedicated studies.

How to take *olive leaf*

Choose an olive leaf extract standardized to at least 16% oleuropein. To reduce LDL oxidation, take 500 mg/day. To more reliably reduce blood pressure, take 1,000 mg/day. Since LDL oxidation increases after a meal, taking your extract with a meal might be optimal.

Some studies have found benefits from doses as low as 10 mg/day. Consuming olive oil as part of your diet

may provide you with the same cardiovascular benefits as supplementing such a low dose of olive leaf extract.

Pycnogenol

What makes *Pycnogenol* a secondary option

Low *nitric oxide* (NO) levels can cause blood vessels to narrow, leading to reduced blood flow. Like the flavonoids in cocoa and grape seeds, procyanidins and other flavonoids in pine bark can help support NO levels.

Pycnogenol is a patented pine bark extract standardized to 65–75% procyanidin. It is the best-studied source of procyanidins, but also the most expensive. It can improve blood flow, might cause a minor decrease in blood pressure in people with hypertension (i.e., high blood pressure), but has no effect on heart rate. In short, its effects are similar to cocoa's, though less potent and with less supportive evidence.

Trials on Pycnogenol and blood flow

Source	Sample	Duration	Dose	Result
Enseleit et al. *Eur Heart J.* (2012)	23 elderly, overweight men and women with coronary artery disease	8 weeks	200 milligrams of Pycnogenol daily	Improved blood flow independent of changes in blood pressure
Nishioka et al. *Hypertens Res.* (2007)	16 healthy young male adults	2 weeks	180 milligrams of Pycnogenol daily	Improved relaxation response in blood vessels
Liu et al. *Life Sci.* (2004)	58 middle-age to elderly healthy men and women	8 weeks	100 milligrams of Pycnogenol daily	Improved blood flow and a trend toward higher NO levels

References: Enseleit et al. *Eur Heart J.* 2012.[75] ● Nishioka et al. *Hypertens Res.* 2007.[76] ● Liu et al. *Life Sci.* 2004.[77]

Judging from a study on a grape seed extract, the improvement in blood flow from pine bark extracts might be negated by the flavonoid quercetin, whose concurrent supplementation should therefore be avoided.

Taking a pine bark extract with other hypotensive agents could cause low blood pressure. Hypotensive

agents can be pharmaceuticals but also supplements — garlic, notably, but also nitrates, cocoa, or grape seed extracts, to mention only the supplements presented in this guide.

How to take *Pycnogenol*

Take 100–200 mg of Pycnogenol once a day with a meal.

Unproven Supplements

Arjuna

What makes *arjuna* an unproven supplement

Water extracts from the bark of the arjuna (*Terminalia arjuna*) have long been used in Ayurvedic medicine to improve cardiovascular health. Preliminary studies support this traditional use, but more research is needed to confirm the benefit they reported and determine both its magnitude and its mechanism of action.

In rodent studies, arjuna prevented abnormal heart rates and protected cardiac tissue from damaging stressors. Should these effects extend to humans, arjuna might also benefit healthy people by increasing cardiovascular capability during exercise.

Until more human studies confirm its benefits, however, arjuna can only rank as an unproven supplement.

Inadvisable Supplements

Stimulants

What makes *stimulants* an inadvisable supplement

People with heart problems are more likely to suffer from the adverse effects of stimulants, which include increased blood pressure, abnormal heartbeats (i.e., arrhythmia), and a greater risk of traumatic cardiovascular injuries, such as heart attacks.

If you choose to take a stimulant, respect the recommended dosage. Should tolerance develop, do not increase the dosage, but stop using the stimulant long enough for sensitivity to return.

Be aware that most fat burners and pre-workout supplements contain stimulants, such as caffeine or synephrine. Be especially careful if you take several such products, as their effects (including adverse effects) can cumulate or even synergize.

You might be consuming more caffeine than you think. When you calculate your daily intake, consider all your beverages, foods, and supplements. Bear in mind that caffeine can be "hidden" in a product — for instance, if you read "guarana seeds" on a label, remember that those are richer in caffeine than coffee beans.

Caffeine upper limit (400 mg) in number of drinks

References: McCusker et al. *J Anal Toxicol*. 2006.[78] ● Desbrow et al. *Nutr Health*. 2019.[79] ● Ludwig et al. *Food Funct*. 2014.[80] ● Fox et al. *J Agric Food Chem*. 2013.[81] ● McCusker et al. *J Anal Toxicol*. 2003.[82] ● Angeloni et al. Food Res Int. 2019.[83]

FAQ

Q. What about the supplements not covered in this guide?

Our guides are regularly updated, often with new supplements. We prioritize assessing (and reassessing) the most popular of them and those most likely to work. However, if there is a specific supplement you'd like to see covered in a future update, please let us know by filling out this survey.

Q. Can I add a supplement not covered in this guide to my combo?

Supplement with your current combo for a few weeks before attempting any change. Talk to your physician and research each potential addition. Check for known negative interactions with other supplements and pharmaceuticals in your current combo, but also for synergies. If two supplements are synergistic or additive in their effects, you might want to use lower doses of each.

Q. Can I modify the recommended doses?

If a supplement has a recommended dose range, stay within that range. If a supplement has a precise recommended dose, stay within 10% of that dose. Taking more than recommended could be counterproductive or even dangerous. Taking less could render the supplement ineffective, yet starting with half the regular dose could be prudent — especially if you know you tend to react strongly to supplements or pharmaceuticals.

Q. At what time should I take my supplements?

The answer is provided in the "How to take" section of a supplement entry whenever the evidence permits. Too often, however, the evidence is either mixed or absent. Starting with half the regular dose can help minimize the harm a supplement may cause when taken during the day (e.g., fatigue) or in the evening (e.g., insomnia).

Q. Should I take my supplements with or without food?

The answer is provided in the "How to take" section of a supplement entry whenever the evidence permits. Too often, however, the evidence is either mixed or absent. Besides, a supplement's digestion, absorption, and metabolism can be affected differently by different foods. Fat-soluble vitamins (A, D, E, K), for instance, are better absorbed with a small meal containing fat than with a large meal containing little to no fat.

Q. What are DRI, RDA, AI, and UL?

The Dietary Reference Intakes (DRIs) is a system of nutrition recommendations designed by the Institute of Medicine (a US institution now known as the Health and Medicine Division). RDA, AI, and UL are part of this system.

- Contrary to what the name suggests, a *Recommended Dietary Allowance* (RDA) doesn't represent an *ideal* amount; it represents the *minimum* you need in order to avoid deficiency-related health issues. More precisely, it represents an amount just large enough to meet the minimum requirements of 97.5% of healthy males and females over all ages — which implies that the RDA is too low for 2.5% of healthy people.
- The *Adequate Intake* (AI) is like the RDA, except that the number is more uncertain.
- The *Tolerable Upper Intake Level* (UL) is the maximum safe amount. More precisely, it is the maximum daily amount deemed to be safe for 97.5% of healthy males and females over all ages — which implies that the UL is too high for 2.5% of healthy people.

As a general rule, a healthy diet should include at least the RDA of each nutrient — but less than this nutrient's UL. This rule has many exceptions, though. For instance, people who sweat more need more salt (i.e., sodium), whereas people who take metformin (a diabetes medicine) need more vitamin B12.

Moreover, the DRIs are based on the median weight of adults and children in the United States. Everything else being equal (notably age, sex, and percentage of body fat), you likely need a lesser amount of nutrients if you weigh less, and vice versa if you weigh more. The numbers, however, are not proportional — if only because the brains of two people of very different weights have very similar needs. So you can't just double your RDIs for each nutrient if you weigh twice as much as the median adult of your age and sex (even if we overlook that people weighing the same can differ in many respects, notably body fat).

Q. Why don't you mention vitamin K_3?

K_1 and K_2 are the only natural forms of vitamin K, but there exist several synthetic forms, the best known of which is K_3. However, whereas the natural forms of vitamin K are safe, even in high doses, K_3 can interfere with glutathione, your body's main antioxidant.

K_3 was once used to treat vitamin K deficiency in infants, but it caused liver toxicity, jaundice, and hemolytic anemia. Nowadays, it is used only in animal feed, in small doses. In animals, vitamin K_3 gets converted into K_2 MK-4, which you can consume safely.

Q. Can *nitric oxide* (NO) supplements be combined?

Yes, they can. Rather than being mutually redundant, the three types of NO supplement in this guide are synergistic. Each has a different mechanism of action. The flavonoids in cocoa, grape seeds, or pine bark can increase the rate of NO production, whereas nitrates bring raw material your body can turn into NO without help from the *nitric oxide synthase* (NOS) enzyme. As for garlic, it enhances NO signaling, but its lowering action on blood pressure is mostly due to its enhancing hydrogen sulfide (H_2S) signaling.

Q. Can I get enough nitrates from fruit?

In short, no. Even “nitrate-rich” fruits, such as melons and strawberries, pale in comparison to most vegetables. Compare, for instance, 100 g of beetroot (199.2 mg of nitrates) with 100 g of melon (32.5 mg), strawberries (17.2 mg), banana (7.6 mg), apple (2 mg), or orange (0.9 mg).

Q. What can I do to help prevent my fish oils from oxidizing?

Since fish oil is primarily polyunsaturated fat, it is prone to becoming rancid and oxidizing. Oxidation largely depends on exposure to heat, light, and oxygen. The addition of antioxidants to the final product can reduce the rate of oxidation during storage. Vitamin E is typically used, but there’s a lot of research on other antioxidants like carnosic acid suggesting they might be superior.[84]

Part of the responsibility for ensuring fish oil remains unoxidized is on the buyer. Exposure of fish oil to light, heat, and oxygen accelerates the oxidation of the oil, with the magnitude of damage depending on the length and degree of exposure. Once you buy the supplement, it is prudent to store it in a cool place away from light, such as the fridge.

If you buy oil in a bottle, the bottle should be tinted to prevent light from getting through and small enough that you can work through it in a month or two. After all, oxygen gets in the bottle every time you open it. Some fish oil bottles come with a pump, which can help reduce oxygen exposure. Buying capsules instead of bottles can also help prevent oxidation.

Q. Wait, where’s calcium?

While calcium supplementation may promote cardiovascular health and reduce blood pressure, it may also increase the risk of hypercalcemia (dangerously high levels of calcium in the blood), potentially contributing to heart disease, the leading cause of death among older adults in the United States. When paired with vitamin D, there is a possible increased risk of stroke.[85] The evidence on heart health is mixed and still developing; whether or not the potential benefits outweigh the potential harm is still to be determined.

Q. If I have a heart condition, can I still have caffeine?

In healthy adults, caffeine intake of up to 400 mg/day has not been linked to increases in cardiovascular disease risk.[86][87] However, if you have high blood pressure or pre-existing heart conditions (in other words, in people for whom stimulants in general are contraindicated), the long-term effects of regular caffeine intake are uncertain[86][88]. Low to moderate intake may be OK, but this should be assessed on a case-by-case basis in consultation with a physician.

Q. How is hypertension (i.e., high blood pressure) defined?

Blood pressure is usually reported in two numbers. For example, a reading of 120/80 mmHg. The first number, systolic blood pressure, tells us how much pressure your blood is exerting against the arterial walls when your heart contracts. The second number, diastolic blood pressure, signifies how much pressure your blood is exerting when the heart is relaxed and being refilled with blood. Blood pressure measures are generally divided into the four categories seen below.

Blood pressure category cutoffs (mmHg)

CATEGORY	SYSTOLIC	DIASTOLIC
Normal blood pressure	<120	<80
Elevated blood pressure	120–129	<80
Stage 1 hypertension	130–139	80–89
Stage 2 hypertension	≥140	≥90

Adapted from Whelton et al. *Hypertension*. 2018.[89]

Q. What are the effects of lifestyle interventions on blood pressure?

Clinically, even a small 2 to 5 mmHg decrease in systolic blood pressure (SBP) can noticeably reduce cardiovascular disease and total mortality.[90] Hypertension (i.e., high blood pressure) can be handled using a multitude of approaches, which are often better in combination than they are in isolation. However, here are how individual treatments alone can affect your blood pressure.[91][92][93][94][95]

Effects of lifestyle interventions on systolic blood pressure* (mmHg)

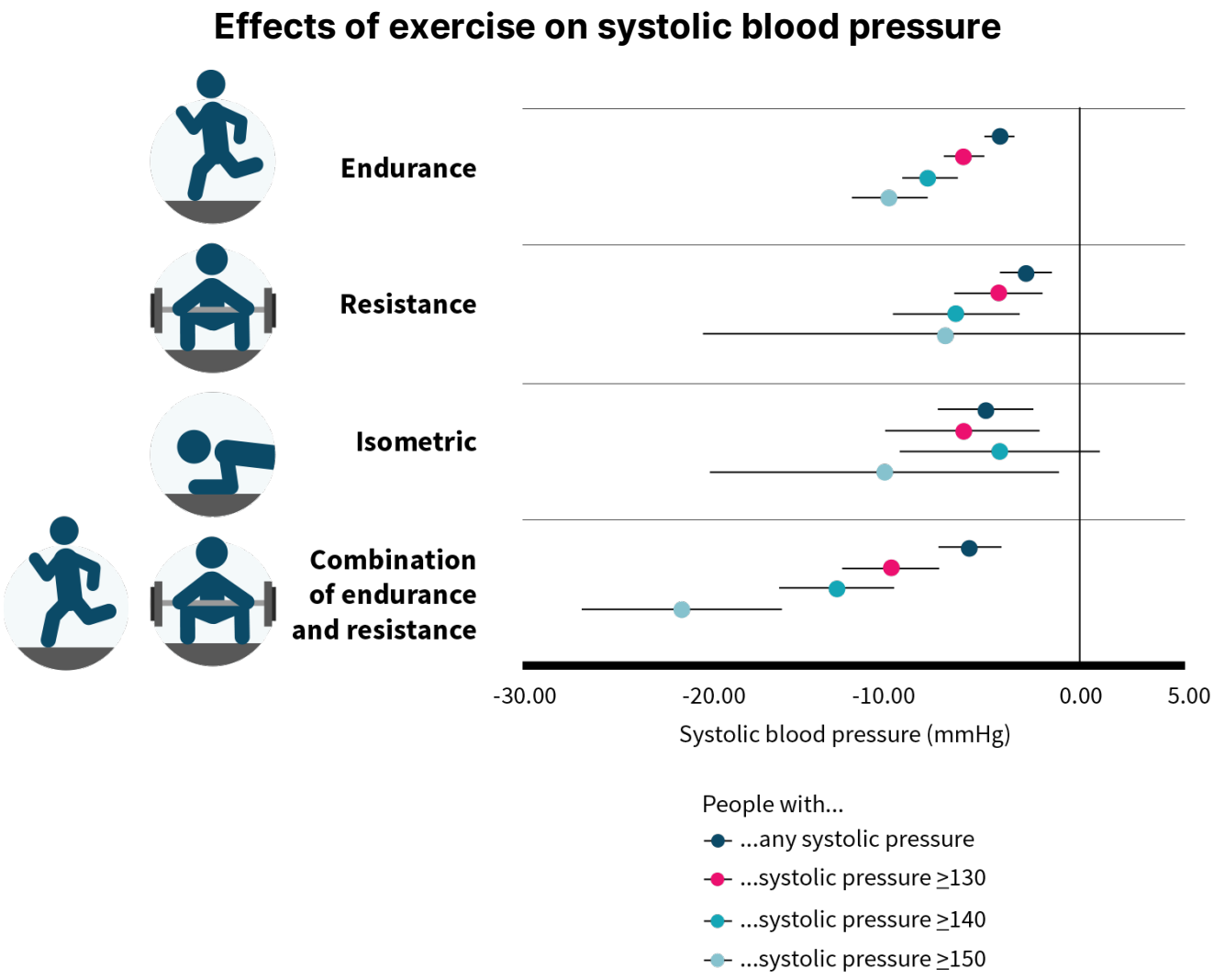
INTERVENTION	SBP REDUCTION	CAVEAT
Protein intake	2–3	Depends on baseline protein intake. Minimum effective dose unknown.
Weight loss	5–20	About 1 mmHg for every 1 kg (2.2 lb) reduction in body weight.The effect eventually plateaus as body weight normalizes.
DASH diet	8–14	Depends on the baseline diet pattern. The DASH diet tested was rich in fruits and vegetables and low in fat and saturated fat.
Salt intake reduction	2–8	Depends on baseline salt intake. Aim for at least a 1,000 mg (1 g) reduction.
Potassium intake increase	4–5	With an intake of 3,500–5,000 mg (3.5–5 g) per day, particularly from potassium rich foods.
Increased physical activity	4–9	A mix of endurance and resistance may be more effective than either alone.
Alcohol intake reduction	2–4	Depends on baseline alcohol intake.

* Greater improvements will be seen in those with higher starting systolic blood pressure

Q. Is there a best type of exercise to reduce blood pressure?

As we mentioned above, increasing physical activity can reduce your systolic blood pressure by 4–9 mmHg. However, it's not as clear if there's a dose-response effect of exercise or what types of exercise might impact blood pressure the most. Luckly, a recent network meta-analysis aimed to answer these questions.[96]

Exercise becomes more effective for lowering blood pressure the higher the starting systolic pressure is — in other words, people with higher starting blood pressures tend to benefit more from exercise. You can also see from the figure below that a combination of resistance and endurance training looks to be more effective, although there's no clear winner between isometric, endurance, and resistance training taken on their own.



Reference: Naci et al. *Br J Sports Med*. 2019.[96]

However, the authors of the paper caution that more research is needed to explore whether one type of exercise is indeed better than another due to the relative lack of research into this topic. There are also some other key takeaways from this research that aren't apparent from the figure.

- Due to reporting issues and lack of relevant data, the authors were not able to explore whether some frequencies or durations of exercise improved blood pressure more than others.
- The authors didn't see a clear relationship between exercise intensity and blood pressure reduction, mainly due to not having enough data. There is much more room for future research to explore the relationship between exercise intensity and blood pressure reduction.
- There's some concern about the generalizability of the exercise results to people with hypertension (i.e., high blood pressure), since most of the exercise trials involved people with normal or mildly elevated blood pressure. Future research focused on exercise's effect on people with hypertension would be useful.

In short: all types of exercise seem to reduce systolic blood pressure, especially in people with

hypertension. However, how much exercise is best, whether intensity matters, and exactly what kinds of exercise have the biggest impact are still unclear.

Q. Should I modify how I exercise based on my cardiovascular disease risk factors?

Different types of cardiovascular disease (CVD risk) may require different amounts, types, or doses of exercise, and major guidelines don't provide such tailored advice. Recently, a team of experts created a system called the *EX*ercise *P*rescription in *E*veryday practice & *R*ehabilitative *T*raining (EXPERT) tool to help guide clinicians to give patients tailored exercise advice based on their needs.

The team released a consensus statement that gives specific exercise recommendations for several cardiovascular risk states based on the evidence they considered.[97] Some of the team's recommendations are summarized below.

Each recommendation is accompanied by a grade denoting the level of the recommendation.

"*A*" means the recommendation is supported by high-quality systematic reviews or randomized controlled trials that are directly relevant for the population at hand.

"*B*" means high-quality observational evidence or inference from randomized trials supports the recommendation.

"*C*" means the recommendation is supported by well-conducted case-control or cohort studies with overall consistent results could be applicable to the target population.

"*D*" means the recommendation is supported by poorer-quality observational evidence, inference from higher-quality observational evidence, or expert opinion.

Exercise recommendations by CVD risk factors

Cardiovascular risk factor	**Obesity**	**Dyslipidemia** (LDL-C > 100 mg/dL in high-risk people or > 70 mg/dL in very high risk people)	**Type 2 diabetes**
Goal of the exercise intervention	To lower fat mass	To lower LDL-C	To improve glycemic control
Recommendations	**A:** Aerobic exercise for more than 250 minutes per week for at least six months **B:** Permanently increase daily physical activity **B:** Use moderate-intensity exercises that involve large muscle groups **A:** Start with three days a week, and build up to five **B:** Resistance training is generally not recommended as an addon if the goal is solely to maximally reduce fat mass	**A:** Exercise lowers LDL-C **D:** Moderate-intensity aerobic exercise is preferred to high intensity since most of the evidence concerns the former **A:** Use aerobic sessions greater than 40 minutes that burn more than 900 kcal/week for at least 40 weeks to see the greatest effect **D:** Choose exercises that burn more calories per unit time **A:** Resistance training may be added for additional impact, although much of the impact is on HDL-C	**A:** Walk more than 30 minutes a day for 5-7 days a week **A:** In addition, more than 150 minutes of moderate-intensity or 90 minutes of vigorous-intensity exercise broken up into sessions of at least 30 minutes each is recommended **A:** High-intensity training works. **A:** A minimum of 12 weeks is needed to see an effect. **A:** Resistance training involving all muscle groups for three sets of 8-12 reps should be added 2-3 times a week for additional benefit
Safety Considerations	Overuse injuries are common in this population. Their risk can be reduced by alternating exercise type, using low-impact exercises, and starting low and slowly progressing to the desired exercise dose.	None	People with diabetes should talk to a physician before undertaking an exercise program, as there are several possible complications that could arise from starting an exercise program unsupervised.

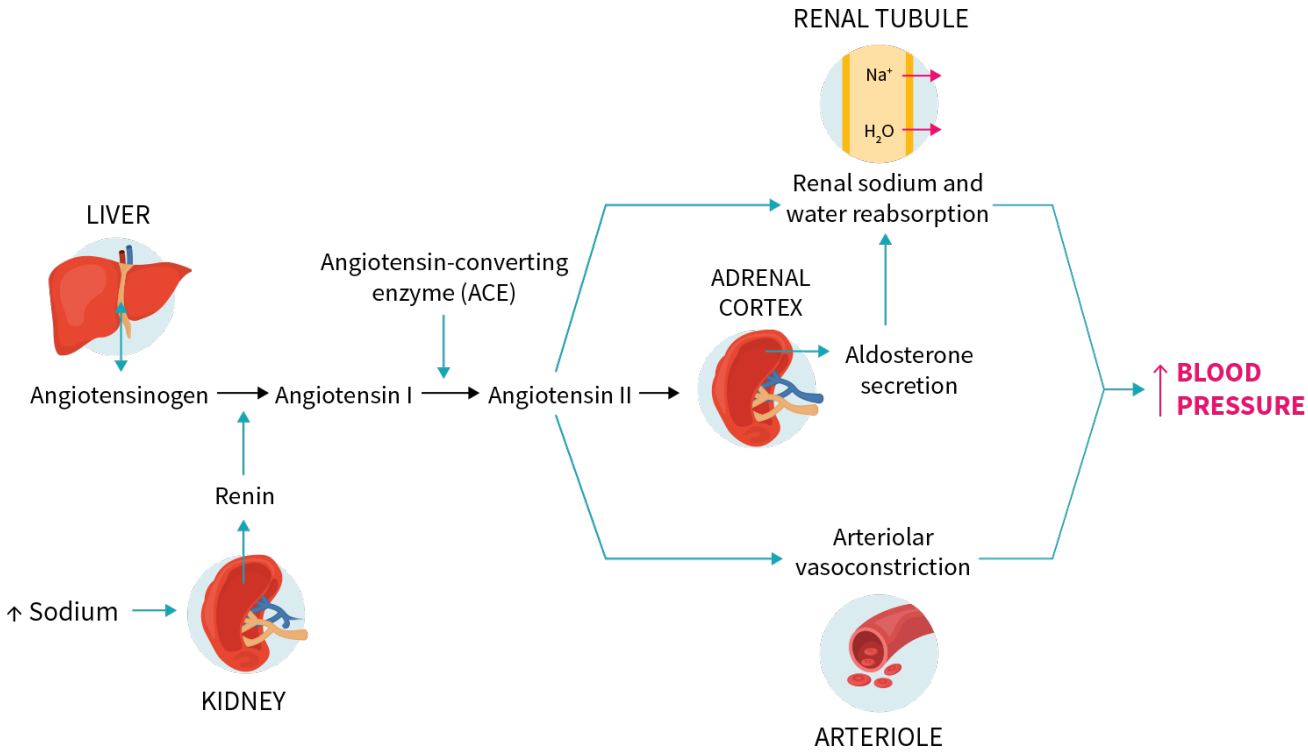
Reference: Hansen et al. *Sports Med.* 2018.[97]

Q. How does salt increase blood pressure?

Sodium is a known regulator of blood pressure. Sodium concentrations are sensed by macula densa cells in the kidneys.[98] When the blood sodium concentration increases, these cells activate the renin-angiotensin-aldosterone system, as shown below.

In short, increased salt intake causes your body to hold onto more water, which increases blood pressure. This extra pressure places a strain on your cardiovascular system which can eventually lead to worse cardiovascular disease outcomes over time.

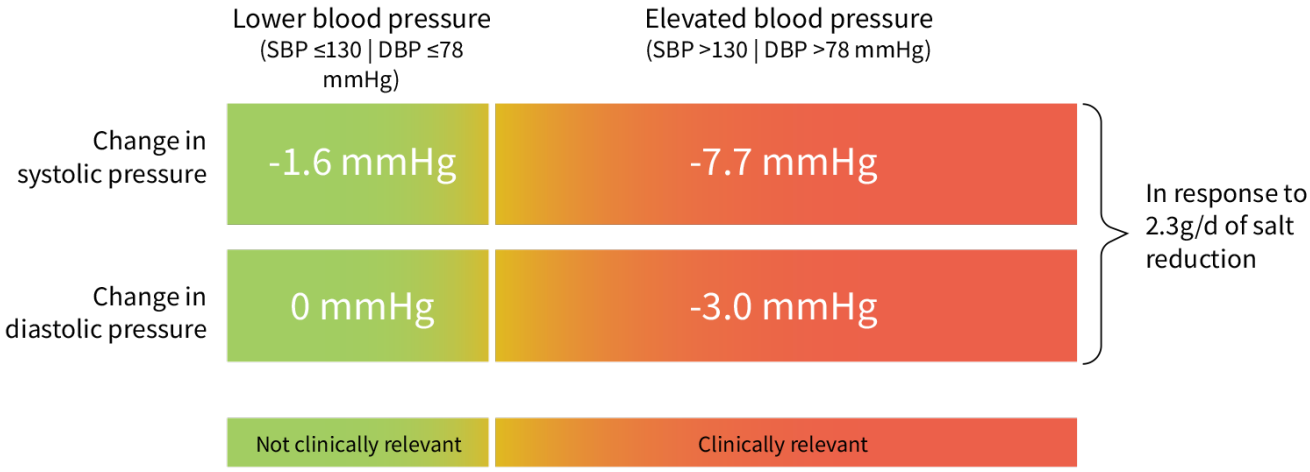
Sodium's role in blood pressure



Q. How does baseline blood pressure modify the effects of salt reduction?

Sodium restriction may reduce both systolic and diastolic blood pressure, primarily among people starting out with higher blood pressure. Although there can be small benefits among people with lower blood pressure, these effects are either not clinically relevant (and possibly non-existent). The effects of a reduction in salt intake of 2,300 milligrams (2.3 g) stratified by blood pressure are summarized below.

Changes in blood pressure to salt reduction, by baseline status



Q. Can red meat cause heart disease?

There is some evidence that eating a lot of red meat or processed meat might increase the risk of cardiovascular diseases, but that evidence tends to be of lower certainty.[99][100][101] Yet, given the difficult nature of conducting long-term nutrition trials, we aren't likely to get any truly high-quality evidence

anytime soon. So, what are we to make of the studies we have, low-quality though they may be?

Remember that red and processed meat consumption is just a small part of the overall lifestyle factors that will influence your heart health. If you moderate your red meat intake, exercise regularly, eat your fruits and veggies, consume adequate fiber, don't smoke, and drink alcohol only in moderation, red meat's effect on your heart health isn't something to worry *too* much about.

Still, if you wish to be cautious, you can limit your intake to three servings per week (1 serving of meat = 3 oz = 85 grams). Prioritize limiting the kind of meat that has been cured, smoked, or highly processed.

Q. Why take NAC to make glutathione? Why not take glutathione directly?

Oral glutathione gets digested into its constituent amino acids: cysteine, glycine, and glutamic acid. Of those three, cysteine is the rate-limiting factor in endogenous glutathione production. Oral N-Acetylcysteine (NAC) is simply a more efficient (and cheaper) way of providing your body with cysteine. Multiple studies have reported greater increases in circulating glutathione from oral NAC than from (an equal dose of) oral glutathione.

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