Table of Contents

- Medical Disclaimer
- How to Use This Guide
- Combos
- Core Supplements
- Primary Options
- Secondary Options
- Unproven Supplements
- Inadvisable Supplements
- FAQ
- References
- Bios
Medical Disclaimer

This guide is a general-health document for adults 18 or over. Its aim is strictly educational. It does not constitute medical advice. Please consult a medical or health professional before you begin any exercise-, nutrition-, or supplementation-related program, or if you have questions about your health.

This guide is based on scientific studies, but individual results do vary. If you engage in any activity or take any product mentioned herein, you do so of your own free will, and you knowingly and voluntarily accept the risks. While we mention major known interactions, it is possible for any supplement to interact with other supplements, with foods and pharmaceuticals, and with particular health conditions.
How to Use This Guide

The Examine.com team has been publishing research on nutrition and supplementation since March 2011. Drawing from all we’ve learned, we’ve designed this Supplement Guide with two aims in mind: helping you decide which supplements are right for you, based on the scientific evidence, and helping you integrate these supplements into synergistic combos.

**Core supplements** have the best safety-efficacy profile. When used responsibly, they are the supplements most likely to help and not cause side effects.

**Primary options** may provide substantial benefit, but only in the right context. A primary option is not for everyone, but if you read the entry and find that you meet the criteria, consider adding the supplement to your combo.

**Secondary options** have less evidence for their effects. They could work or be a waste of money. Keep them in mind, but think twice before adding them to your combo.

**Unproven supplements** are backed by tradition or by mechanistic, animal, epidemiological, or anecdotal evidence, but not yet by convincing human trials. At this point, they are not good candidates for your combo.

**Inadvisable supplements** are either potentially dangerous or simply ineffective, marketing claims notwithstanding. Do not add them to your combo. At best, they’ll be a waste of money; at worst, they can cause you harm.

Now that you’ve learned of various supplements worthy of your consideration, you’ll learn to integrate them into synergistic combos. You’ll discover a core combo (composed of the core supplements) and several specialized combos (composed of primary and secondary options). Each specialized combo is optimized for a specific population. The simplest way to formulate your own combo is to combine the core combo with the specialized combo that best fits your situation, needs, and primary health goal.

Then comes the FAQ, in which we cover common questions that may arise when selecting and combining supplements. With all this, you should be able to identify and assemble the supplement combo best suited to your objective.
Combos

In this section you’ll learn to integrate various supplements into synergistic combos. You’ll discover a core combo (composed of the core supplements) and several specialized combos (composed of primary and secondary options). Each specialized combo is optimized for a specific population. The simplest way to formulate your own combo is to combine the core combo with the specialized combo that best fits your situation, needs, and primary health goal.

Core Combo

Each day, take 100–400 mcg of vitamin B₁₂.

Each day, take blueberries according to one of the following protocols:

- Blueberry anthocyanins: 0.5–1 gram (500–1,000 mg)
- Blueberry powder: 12 grams
- Freeze-dried blueberries: 24 grams
- Fresh blueberries: 60–120 grams
- Pure blueberry juice: 500 mL (17 oz)

Twice a day, take 250–500 mg of ALCAR (i.e., 500–1,000 mg/day).

Consume protein throughout the day (1.0–2.2 grams per kilogram of body weight, so 0.45–1.00 g/lb), with the help of a protein powder if necessary. Consult the protein entry to set the intake level best suited to your needs.

If your 25(OH)D levels are adequate or you don’t know your levels, 400 IU (10 mcg) of vitamin D₃ per day may help maintain your levels in the adequate range. If your 25(OH)D levels are low, 800–2,000 IU (20–50 mcg) of D₃ per day is likely to raise them to an adequate level, at which point 400–1,000 IU (20–25 mcg) per day should suffice for maintenance. In case of full-blown deficiency,
a medically supervised intervention will be needed.

💡 **Tip: Try the core combo alone for a few weeks**

The core supplements are recommended for most people; their efficacy and safety are backed by a significant body of evidence. Take them for a couple of weeks before you consider making any modification, such as adding one of the specialized combos.

---

**Specialized Combos**

**Bone health**

Each day, take 3–5 grams of creatine monohydrate, 200 mg of magnesium, and some vitamin K: 200 mcg (0.2 mg) of MK-7 and/or 45,000 mcg (45 mg) of MK-4.

Vitamins that increase bone mineralization
Cardiovascular health

Each day, take 3–5 grams of creatine monohydrate, 200 mg of magnesium, and some vitamin K: 200 mcg (0.2 mg) of MK-7 and/or 45,000 mcg (45 mg) of MK-4.

Each day, take L-carnitine. Have you suffered from cardiovascular complications?

• Yes: take 2–9 grams.
• No: take 0.5–2 grams (500–2,000 mg).

Cognition

Each day, take 3–5 grams of creatine monohydrate.
Twice a day, take 250–1,000 mg of CDP-choline (i.e., 500–2,000 mg/day) and 500 mg of ALCAR (i.e., 1,000 mg/day), preferably without food. This ALCAR dosage replaces the one in the [core combo].

**Energy and stamina**

Each day, take 3–5 grams of creatine monohydrate and 200 mg of magnesium.

If your DHEA-S levels are low, take 20–50 mg (males) or 10–30 mg (females) of DHEA per day. Ideally, supplement at the low end of the range for a month then get tested again.

**Immunity**

If you are underconsuming vitamin E or have low blood levels, take 200 IU (134 mg of natural α-tocopherol or 90 mg of synthetic α-tocopherol) per day. Since vitamin E has anticoagulant properties, make sure your diet contains at least your Adequate Intake (AI) of vitamin K (90 mcg/day for female; 120 mcg/day for males).

**Libido**

Take maca (2–3 g) at breakfast.

If your DHEA-S levels are low, take 20–50 mg (males) or 10–30 mg (females) of DHEA per day. Ideally, supplement at the low end of the range for a month then get tested again.

**Symptoms of menopause**

Take maca (2–3.5) at breakfast.
Core Supplements

Core supplements have the best safety-efficacy profile. When used responsibly, they are the supplements most likely to help and not cause side effects.

Blueberries

What makes blueberries a core supplement

The anthocyanins and pterostilbene in blueberries can help protect the brain and reduce cognitive decline. Episodic memory and executive function are most likely to benefit — the former especially in adults with mild cognitive impairment. Working memory might benefit too, but the evidence is mixed.

Anthocyanins are also the probable reason why blueberries can increase the activity of neuronal growth factor (NGF), a protein that acts as a neurotransmitter. NGF helps neurons grow, branch toward each other, and thus communicate better. In seniors, a diet high in blueberries can improve cognitive ability in as little as six weeks.

On average, 100 grams of fresh blueberries contains 200 mg of anthocyanins and 4 mcg (0.004 mg, or 4,000 ng) of pterostilbene, but actual contents depend on variety, soil, season, weather, farming method, shipping time, storage conditions, and storage duration.

Nanograms (ng) of pterostilbene per gram (g) of blueberry (dry mass)

<table>
<thead>
<tr>
<th>STUDY</th>
<th>SAMPLES</th>
<th>CULTIVARS</th>
<th>RANGE</th>
<th>AVERAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>6</td>
<td>1</td>
<td>—</td>
<td>11</td>
</tr>
<tr>
<td>STUDY</td>
<td>SAMPLES</td>
<td>CULTIVARS</td>
<td>RANGE</td>
<td>AVERAGE</td>
</tr>
<tr>
<td>-------</td>
<td>---------</td>
<td>-----------</td>
<td>----------</td>
<td>---------</td>
</tr>
<tr>
<td>2005</td>
<td>17</td>
<td>9</td>
<td>12–274</td>
<td>54</td>
</tr>
<tr>
<td>2004</td>
<td>3</td>
<td>2</td>
<td>9.9–52</td>
<td>26</td>
</tr>
</tbody>
</table>


Warnings about blueberries

Blueberries are not known to interact negatively with any supplements or pharmaceuticals. However, anthocyanins and pterostilbene are both mildly hypoglycemic, so it is theoretically possible (though not probable) for the blueberry doses listed below to cause low blood sugar (i.e., hypoglycemia) when taken with other supplements or pharmaceuticals that can lower blood sugar, such as most diabetes medicines.

How to take blueberries

Studies support the following protocols:

• Blueberry anthocyanins: 0.5–1 g/day
• Blueberry powder: 12 g/day
• Freeze-dried blueberries: 24 g/day
• Fresh blueberries: 60–120 g/day
• Pure blueberry juice: 500 mL/day (17 oz/day). Cheaper “blueberry juices” made with artificial flavoring and added sugar more than with actual blueberries will have little to no anthocyanins. Be sure to check the ingredients label.

💡 Tip: Why don’t you recommend specific supplement brands or companies?

We are 100% independent and extremely serious about being unbiased when it comes to
nutrition and supplement information. We only care about the science.

Our only goal is to break down and make sense of research. Not only do we not sell supplements, but we also don’t recommend any brands, nor do we do any consulting or accept advertisements, donations, or sponsorships.

Since we don’t sell or recommend supplement brands, we have less incentive to hype any of them or misrepresent any research.

All that being said, we are interested in keeping you safe. So here’s a list of steps you can take if a supplement has caught your interest.

## Carnitine

### What makes carnitine a core supplement

Carnitine plays a role in [cognition][11], [energy metabolism][12] and [cardiovascular health][13][14][15]. 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

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

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).[16]

Finally, a form of carnitine known as *acetyl-L-carnitine* (ALCAR) may benefit cognition by improving blood flow and promoting efficient energy use in brain cells.

Summary of carnitine’s benefits
Warnings about carnitine

Side 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

For neurological benefits, take acetyl-L-carnitine (ALCAR). Start with 250 mg twice a day (i.e., 500 mg/day). Over the course of a week, increase to 500 mg twice a day (i.e., 1 g/day). Taking ALCAR on an empty stomach will result in more potent cognitive benefits. This type of carnitine has a tart taste, but it can be dissolved in tea or coffee and still retain its effects.
For general non-neurological benefits, take 2 grams of **L-carnitine** per day, with carbohydrates if you wish to increase the rate of absorption by the muscles.

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 7,500–1,350 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.

**Protein**

**What makes protein a core supplement**

Dietary protein (the protein you ingest) plays important roles in your body, notably as a provider of **essential amino acids** (EAAs), the amino acids your body needs but cannot synthesize. In seniors, higher protein intakes are associated with greater **muscle mass**, and greater muscle mass with greater **longevity** and **bone mineral density**.[17][18][19]

Age-related muscle loss, also known as **sarcopenia**, affects about 50% of males and 70% of females past the age of sixty, but it can start as early as your twenties.[20]

Prevalence of sarcopenia by age and sex in the US
Fortunately, sarcopenia is neither inevitable nor irreversible — some seniors have built more muscle in their old age than they ever had in their youth. The older you get, however, the greater your muscles' anabolic resistance (i.e., their resistance to growth), and so the greater the exercise volume and protein intake you’ll need to stimulate muscle protein synthesis (MPS).

In other words, the older you get, the more exercise and protein you need in order to gain muscle. In fact, as you get older, aerobic exercise (aka “cardio”) may no longer suffice to ward off sarcopenia; you’ll need to include resistance training to your routine.

A basic resistance training program for seniors
As you get older, you may also need to increase your protein intake, as described below. Overall, whole foods are the healthier choice, but if your food intake does not cover your daily protein needs, you could add a supplement (preferably a powder, since the protein-to-calorie ratio of powders tends to be higher than that of other protein supplements, such as protein bars).

**Whey protein** and **casein** powders are both derived from **milk protein** (which is 20% whey and 80% casein). Whey protein digests faster and has a higher concentration of EAAs (notably of **leucine**, the most anabolic of the amino acids). It quickly increases EAA concentrations in the blood and is thus better able to stimulate MPS in anabolically resistant seniors.

**Whey protein concentrates** are the most common type of protein powder; they’re inexpensive and mix easily, and so are probably your best option if you are not vegan. Look at the food label: your powder should be close to 80% protein. A little lower is fine if the powder is flavored (any flavoring will use a percentage of the powder), but any big discrepancy should steer you away.

But what if you are vegan? Fortunately, you can still supplement with protein powders. For vegans,
two popular options are soy protein, which is a complete protein, and a 70:30 pea:rice protein blend, whose amino acid profile is similar to that of whey protein.

**Warnings about protein**

Very high doses (at least 3 grams of protein by kilogram of body weight per day, so ≥1.36 g/lb/day), may cause gastrointestinal issues and increase your levels of blood urea nitrogen (BUN), a measure of kidney function. High-protein diets also increase glomerular filtration rate (GFR), a marker for waste filtration in the kidneys, and it was once argued that increased GFR was a sign that undue stress was put on the kidneys, but later research has shown that kidney damage does not occur as a result of diets high in protein.

By raising BUN and GFR, however, high protein intakes may mask underlying issues. Consider having your BUN and GFR levels tested before you start consuming a diet very high in protein, so as to both get a baseline measurement and check up on your kidney function. If you are already consuming ≥3 g/kg/day yet plan to have your BUN or GFR tested, lower your protein intake to ≤1.8 g/kg/day for at least 1 week prior to testing so as to prevent a false positive.

If you have milk allergies, you should avoid supplements that contain whey protein or casein (the two proteins in milk). The most notable alternatives are egg protein and the vegan options described in the last paragraph of the previous section.

If you are lactose intolerant, you have the same options as people with milk allergies, but you may also be fine with a whey protein concentrate, since most of the lactose has been removed. Whey protein isolates contain even less lactose, but never zero (in the United States, a powder can be labeled as “lactose-free” if it contains less than 0.5 grams of lactose per serving). If you wish to try an isolate, look at the food label: your powder should be close to 90% protein. A little lower is fine if the powder is flavored (any flavoring will use a percentage of the powder), but any big discrepancy should steer you away.

**How to take protein**

In the United States, the Recommended Dietary Allowance RDA of 0.8 grams per kilogram of body weight (0.36 g/lb) is considered the minimum amount of protein a healthy adult must consume daily to prevent muscle wasting when total caloric intake is sufficient.

The current evidence suggests, however, that this amount has been underestimated. Recent studies point to 1.0–1.2 g/kg as the minimum daily intake before the body starts downregulating important non-essential processes, from immune function to muscle protein synthesis. Even a reanalysis of the data used to establish the above RDA suggests the minimum daily intake
should be at least 1.0 g/kg.\cite{33}

So, how much protein do you need daily?

- Sedentary but healthy seniors: 1.0–1.2 g/kg (0.45–0.54 g/lb)
- Sick or injured seniors: 1.2–1.5 g/kg (0.54–0.68 g/lb)
- Seniors wishing to lose weight: 1.5–2.2 g/kg (0.68–1.00 g/lb)
- Seniors wishing to build muscle: 1.7–2.0 g/kg (0.77–0.91 g/lb)

**Daily protein intake**

| BODY WEIGHT | BODY WEIGHT | 0.36 | 0.45 | 0.54 | 0.68 | 0.82 | 0.91 | 1.00 | 2.2 g/ | 2.0 g/ | 1.8 g/ | 1.5 g/ | 1.2 g/ | 1.0 g/ | 0.8 g/ |
|-------------|-------------|------|------|------|------|------|------|------|----|------|------|------|------|------|------|------|
| LB          | KG          |      |      |      |      |      |      |      | g/kg|      |      |      |      |      |      |      |
| 100         | 45          | 36   | 45   | 54   | 68   | 81   | 91   | 100  | g   |      |      |      |      |      |      |      |
| 125         | 57          | 45   | 57   | 68   | 85   | 103  | 113  | 125  | g   |      |      |      |      |      |      |      |
| 150         | 68          | 54   | 68   | 82   | 102  | 122  | 136  | 150  | g   |      |      |      |      |      |      |      |
| 175         | 79          | 64   | 79   | 95   | 119  | 142  | 159  | 175  | g   |      |      |      |      |      |      |      |
| 200         | 91          | 73   | 91   | 109  | 136  | 164  | 181  | 200  | g   |      |      |      |      |      |      |      |
| 225         | 102         | 82   | 102  | 122  | 153  | 184  | 204  | 225  | g   |      |      |      |      |      |      |      |
| 250         | 113         | 91   | 113  | 136  | 170  | 203  | 227  | 250  | g   |      |      |      |      |      |      |      |
| 275         | 125         | 100  | 125  | 150  | 187  | 225  | 249  | 275  | g   |      |      |      |      |      |      |      |


Unless you have a pre-existing condition that affects your liver or kidneys, the intakes in the above
table will not harm these organs.\textsuperscript{[27]} However, if you have a BMI of more than 30, you may want to calculate your protein requirements based on your goal body weight rather than your current body weight, so as to avoid overeating.

For maximal MPS stimulation, the minimal per-meal dose of quality protein (such as can be found in meat, eggs, dairy products, and soy) is 0.24–0.40 g/kg for adults in their twenties\textsuperscript{[23]}\textsuperscript{[37]} and 0.40–0.60 g/kg for adults aged sixty and older.\textsuperscript{[23]} Spreading your protein intake over a few meals, making sure this 0.40–0.60 g/kg threshold is met with each meal, will generally result in greater lean mass and strength.

Note that you don’t need to calculate your intake so that it falls within the 0.40–0.60 g/kg range. This range isn’t an ideal range — it is a range representing individual variations. In other words, some people can reach maximal MPS with just 0.40 g/kg, while others will need as much as 0.60 g/kg. Moreover, higher doses will not be wasted and are probably necessary when eating mixed meals that contain a variety of protein sources. You may have heard that if you eat more than 30 grams of protein in one sitting, the “excess” will pass undigested, but that’s just a myth.

### Desirable minimal protein intake range* per meal (g), by age for adults

<table>
<thead>
<tr>
<th>BODY WEIGHT (lb)</th>
<th>BODY WEIGHT (kg)</th>
<th>20s</th>
<th>30s, 40s, 50s</th>
<th>60</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>45</td>
<td>11–18</td>
<td>13–24</td>
<td>18–27</td>
</tr>
<tr>
<td>125</td>
<td>57</td>
<td>14–23</td>
<td>17–30</td>
<td>23–34</td>
</tr>
<tr>
<td>175</td>
<td>79</td>
<td>19–32</td>
<td>23–43</td>
<td>32–48</td>
</tr>
<tr>
<td>200</td>
<td>91</td>
<td>22–36</td>
<td>27–48</td>
<td>36–54</td>
</tr>
<tr>
<td>225</td>
<td>102</td>
<td>24–41</td>
<td>30–54</td>
<td>41–61</td>
</tr>
<tr>
<td>250</td>
<td>113</td>
<td>27–45</td>
<td>33–60</td>
<td>45–68</td>
</tr>
<tr>
<td>275</td>
<td>125</td>
<td>30–50</td>
<td>37–67</td>
<td>50–75</td>
</tr>
</tbody>
</table>

* The ranges in this table represent individual variations. The minimum protein requirements increase as you age, but to
what degree is uncertain because of the age gap left by the studies: most subjects were in their 20s (0.24–0.40 g/kg) or 60s/70s (0.40–0.60 g/kg). For people in their 30s, 40s, or 50s, the 0.29–0.53 g/kg range reflected in this table is an educated guess.


*Your mileage may vary.* The ranges in the paragraphs and table above cover the known extent of interindividual variations among healthy adults. However, as shown in the “Prevalence of sarcopenia based on sex and age” graphic, even people in their twenties can suffer from sarcopenia — in which case they would benefit from a protein intake closer to the one recommended in this table for adults over sixty.

After exercising, when your muscles are more sensitive to the anabolic effect of protein, take a dose in the range of your “desirable minimal protein intake per meal” (as shown in the table above). If you’ve been exercising on an empty stomach, you’ll be in negative protein balance, so take this dose as soon as possible. Otherwise, try to take it within a couple of hours — the exact size of your “window of opportunity” depends on how much protein you’re still digesting.[38]

💡 **Tip: Use our Protein Intake Calculator**

Your protein needs hinge on many factors — notably your weight, health goals, and level of physical activity. Based on our research and the data you input, we can calculate your optimal daily protein intake. Click on the image below to get started!

**YOUR OPTIMAL PROTEIN INTAKE:**

???

**Vitamin B₁₂ (cobalamin)**

**What makes vitamin B₁₂ a core supplement**

Suboptimal intake of vitamin B₁₂ (cobalamin) can cause anemia, cognitive impairment, mood disorders, nerve damage, and other health problems.[39]

B₁₂ is present naturally only in animal products, so suboptimal intake is more common in
vegetarians and vegans. Moreover, this protein-bound $B_{12}$ gets harder to digest as you age, so suboptimal intake is also more common in seniors. For those reasons, easily digestible $B_{12}$ is sometimes added to plant foods (which are said to be fortified with $B_{12}$).

Each vitamin has different forms, called vitamers. Four $B_{12}$ vitamers can be found in food.

- **Hydroxo**cobalamin
- **Aquac**obalamin
- **Methyl**cobalamin
- **Adenosyl**cobalamin

Most supplements and fortified foods use the synthetic **cyanoc**obalamin, which has the advantage of being particularly stable as long as it is kept away from bright light — ultraviolet (UV) rays in particular.

**Warnings about vitamin B$_{12}$**

People taking metformin may need to supplement $B_{12}$ or have their $B_{12}$ levels monitored, because this medicine may reduce $B_{12}$ absorption. However, people with kidney problems related to diabetes (i.e., diabetic nephropathy) should talk to their physician before supplementing $B_{12}$.

**How to take vitamin B$_{12}$**

All four commonly supplemented $B_{12}$ vitamers can degrade when exposed to UV rays, but cyanocobalamin and hydroxocobalamin are more stable (and widely available) than methylcobalamin and adenosylcobalamin.

Methylcobalamin and adenosylcobalamin can affect your body directly: they are *bioactive*. The other $B_{12}$ vitamers are not bioactive, but your body can transform them into methylcobalamin, which can be transformed into adenosylcobalamin. Adenosylcobalamin cannot be transformed into methylcobalamin, though, which is why it is seldom taken alone (it is usually paired with methylcobalamin).

Take **100–400 mcg/day** (all forms included). People on metformin or with absorption issues should aim toward the higher end of the range. People with swallowing difficulties or intestinal absorption issues can use sublingual $B_{12}$ supplements.

Fortunately, your body will not readily absorb more than it needs: doses as high as 1,000 mcg (1 mg) taken daily for 5 years have not been found to produce adverse effects. For that reason,
even the Institute of Medicine (now known as the Health and Medicine Division) did not set a Tolerable Upper Intake Level (UL) for B₁₂.[⁴⁷]

**Recommended Dietary Allowance (RDA) for vitamin B₁₂ (mcg)**

<table>
<thead>
<tr>
<th>AGE</th>
<th>MALE</th>
<th>FEMALE</th>
<th>PREGNANT</th>
<th>LACTATING</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–6 months</td>
<td>0.4*</td>
<td>0.4*</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>7–12 months</td>
<td>0.5*</td>
<td>0.5*</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>1–3 years</td>
<td>0.9</td>
<td>0.9</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>4–8 years</td>
<td>1.2</td>
<td>1.2</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>9–13 years</td>
<td>1.8</td>
<td>1.8</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>&gt;13 years</td>
<td>2.4</td>
<td>2.4</td>
<td>2.6</td>
<td>2.8</td>
</tr>
</tbody>
</table>

* Adequate Intake (AI)


**Vitamin D**

**What makes vitamin D a core supplement**

Suboptimal levels of vitamin D are common, especially in people whose skin exposure to sunlight (meaning without protection from clothes or sunscreen) is limited. Moreover, the darker your skin, the longer you need to expose yourself to sunlight to synthesize enough vitamin D, which is why people with darker skin are at an increased risk of suboptimal vitamin D levels.[⁴⁸]

The situation doesn’t improve as you age. The older you get, the less efficient your body becomes at synthesizing vitamin D, the less time you’re likely to spend outside, the less vitamin D you’re likely to get through food, and the more likely you become to carry extra fat (belly fat has been
Average yearly sunlight exposure in the US

Vitamin D is commonly available in two forms. Ergocalciferol (D$_2$) is available in a handful of plants and fungi, whose D$_2$ content can be increased dramatically when exposed to ultraviolet B (UVB) radiation, whereas cholecalciferol (D$_3$) is synthesized from the cholesterol in your skin when exposed to the sun’s UVB rays.

Before turning to supplementation, you should try incorporating some foods rich in vitamin D into your diet. Very few foods, alas, contain appreciable amounts of naturally occurring vitamin D, with fatty fish being a notable exception (cod liver oil, in particular). For that reason, milk is commonly fortified with either D$_2$ or, more recently, D$_3$. Why milk? Because milk is rich in calcium, which vitamin D helps your intestines absorb. For the same reason, yogurt, cheese, and breakfast cereal are also commonly fortified with D$_2$ or D$_3$. Other commonly fortified foods include bread, margarine, and fruit juice (orange juice, in particular). As usual, which foods get fortified, if any, vary by country, based on local laws and policies.

By helping your intestines absorb calcium, vitamin D can strengthen your bones. Consuming large doses regularly can also facilitate the calcification of your arteries, unfortunately, but this effect may be counteracted by vitamin K. Vitamins D and K may increase synergistically the rate at which...
minerals (notably calcium and magnesium) accumulate in bones, which is another reason to take them together.

Vitamin D supplementation might reduce the risk of falls and fractures in older people\textsuperscript{[56]} — though high single monthly doses (≥24,000 IU) taken for a year or more might increase the risk of falls.\textsuperscript{[57]} There is also observational evidence linking low levels of vitamin D with osteoporosis and other age-related diseases, such as cancer, hypertension, cardiovascular disease, type 2 diabetes, cognitive decline, and depression.\textsuperscript{[49]}

Vitamin D\textsubscript{3} is both more stable and more bioavailable than vitamin D\textsubscript{2}. As a supplement, it is usually derived from lanolin\textsuperscript{[58]}, a waxy substance secreted by the skin glands of woolly animals, but a vegan-friendly option (a lichen extract) is also available.

### Warnings about vitamin D

Keep in mind that, over months, daily doses of 10,000 IU (250 mcg) or more can become toxic as well as lead to hypercalcemia, a buildup of calcium in the soft tissues of the body (such as the arteries). The risk of hypercalcemia also increases when moderate doses of vitamin D (600–1,000 IU, so 15–25 mcg) are taken by people who also take high doses of supplemental calcium. Likewise, the risk of kidney stones can increase when even modest doses of vitamin D (400 IU, so 10 mcg) are taken by people who also take high doses of supplemental calcium.

If you supplement with more than 500 mg of calcium daily and this dose puts you over your RDA, consider reducing it before adding vitamin D. Of course, if the calcium supplement you are taking was prescribed to you, consult the prescriber before making any changes.

### Recommended Dietary Allowance (RDAs) for calcium

<table>
<thead>
<tr>
<th>AGE</th>
<th>MALE</th>
<th>FEMALE</th>
<th>PREGNANT</th>
<th>LACTATING</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–6 months</td>
<td>200*</td>
<td>200*</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>7–12 months</td>
<td>260*</td>
<td>260*</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>1–3 years</td>
<td>700</td>
<td>700</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>4–8 years</td>
<td>1,000</td>
<td>1,000</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>AGE</td>
<td>MALE</td>
<td>FEMALE</td>
<td>PREGNANT</td>
<td>LACTATING</td>
</tr>
<tr>
<td>----------------</td>
<td>------</td>
<td>--------</td>
<td>----------</td>
<td>-----------</td>
</tr>
<tr>
<td>9–13 years</td>
<td>1,300</td>
<td>1,300</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>14–18 years</td>
<td>1,300</td>
<td>1,300</td>
<td>1,300</td>
<td>1,300</td>
</tr>
<tr>
<td>19–30 years</td>
<td>1,000</td>
<td>1,000</td>
<td>1,000</td>
<td>1,000</td>
</tr>
<tr>
<td>31–50 years</td>
<td>1,000</td>
<td>1,000</td>
<td>1,000</td>
<td>1,000</td>
</tr>
<tr>
<td>51–70 years</td>
<td>1,000</td>
<td>1,200</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>&gt;70 years</td>
<td>1,200</td>
<td>1,200</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

* Adequate intake (AI)


If you take a multivitamin, check to see if it contains vitamin D. It may already contain sufficient amounts for your personal needs. Check the calcium dose as well, to ensure it is not too high.

A genetic mutation in the **CYP24A1** gene can cause idiopathic infantile hypercalcemia. This condition, usually identified in childhood, causes high levels of calcium in the blood and urine and leads to calcium deposits in the kidneys. This mutation can lead to vitamin D toxicity with daily intakes as low as 500 IU (12.5 mcg).

**Orlistat** (Alli, Xenical) reduces how much fat you absorb from the food you eat. As a result, it also reduces the absorption of fat-soluble vitamins. If you take this medicine, take your vitamin D supplement at least 2 hours before or after.

**How to take vitamin D**

First, you should determine if you really need to supplement vitamin D by checking your current vitamin D levels — your blood levels of 25-hydroxyvitamin D (25(OH)D).

**Serum 25(OH)D concentrations**
In case of deficiency, a medically supervised intervention will be needed. Do not begin any intervention without discussing it with your physician. Common medical interventions include taking 50,000 IU (1,250 mcg) of D$_2$ or D$_3$ at least three times a week for six to eight weeks, though people with a borderline deficiency may not need as high a dose. At the end of this intervention, if vitamin D levels are above 30 nmol/L (12 ng/mL), a daily dose of 400–1,000 IU (20–25 mcg) is commonly used for maintenance.

In case of inadequacy, 800–2,000 IU (20–50 mcg) of D$_3$ per day is likely to raise vitamin D levels to an adequate level, at which point 400–1,000 IU (20–25 mcg) per day should suffice for maintenance.

In case of adequate vitamin D levels, a vitamin D supplement may not be necessary, especially if you spend a lot of time outside and live near the equator. However, taking 400–600 IU (10–15 mcg) of D$_3$ per day may help maintain vitamin D levels in the adequate range, particularly during the colder, darker months, when you are least likely to synthesize enough vitamin D from sun exposure.

In case of high vitamin D levels (which can cause adverse effects), seek the help of a medical professional. Of course, stop taking any supplement containing vitamin D, unless otherwise instructed by a medical professional.

If you do not know your vitamin D levels and cannot get them tested but are still intent on taking a vitamin D supplement, it would be prudent to limit yourself to a maintenance dose of 400 IU (10 mcg) of D$_3$ per day. Alternatively, you could track your food intake for a week to determine your average vitamin D intake, then select a complementary dose to reach your RDA.
# Recommended Dietary Allowance (RDAs) for vitamin D (IU*)

<table>
<thead>
<tr>
<th>AGE</th>
<th>MALE</th>
<th>FEMALE</th>
<th>PREGNANT</th>
<th>LACTATING</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–12 months</td>
<td>400*</td>
<td>400*</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>1–13 years</td>
<td>600</td>
<td>600</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>14–18 years</td>
<td>600</td>
<td>600</td>
<td>600</td>
<td>600</td>
</tr>
<tr>
<td>19–50 years</td>
<td>600</td>
<td>600</td>
<td>600</td>
<td>600</td>
</tr>
<tr>
<td>51–70 years</td>
<td>600</td>
<td>600</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>&gt;70 years</td>
<td>800</td>
<td>800</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

* 40 IU = 1 mcg

** Adequate intake (AI)


If the maintenance doses in the paragraphs above prove insufficient, as could be the case notably if your BMI is over 30[^60] or if you suffer from poor vitamin D absorption or processing (due to a problem with your kidneys, liver, or gastrointestinal tract), you could switch to 1,000–2,000 IU (25–50 mcg) of D₃ per day.

Vitamin D being fat-soluble, it is better absorbed when taken with a fat-containing food or supplement (e.g., fish oil).
**Primary options** may provide substantial benefit, but only in the right context. A primary option is not for everyone, but if you read the entry and find that you meet the criteria, consider adding the supplement to your combo.

---

**Creatine**

**What makes creatine a primary option**

Supplementing with creatine monohydrate increases the body’s creatine stores, which are located primarily in the skeletal muscles. Your cells use creatine to regenerate *adenosine triphosphate* (ATP), life’s energy currency, before they turn to burning glucose.

Creatine can improve muscular strength and control, and thus fitness and mobility. In seniors, these improvements might help reduce the risk of falls, though many more studies are needed for confirmation. When paired with resistance training, creatine may also improve bone health. When creatine levels are suboptimal, as is often the case in seniors, vegans, and vegetarians, taking creatine might also enhance cognition.

---

**Seniors and the risk of falls**
Decades of research have demonstrated that creatine is generally well tolerated. The only recorded adverse effects are nausea, diarrhea, and stomach cramps in people taking more than 10 grams at once, and even at such high doses, these effects are rare. Still, should you find yourself particularly sensitive to creatine's digestive side-effects, split your daily dose, take it with some food, and drink more fluids. You could also try micronized creatine monohydrate, which dissolves more easily in liquids.

You may have heard that creatine can raise testosterone, the precursor to dihydrotestosterone (DHT), and can thereby accelerate or cause hair loss. To date, though, the overall body of evidence suggests that creatine doesn't affect testosterone or hair loss. Creatine can cause water retention, which may notably increase body weight. This side effect is largely harmless and is reversed when creatine supplementation is stopped. Theoretically, this water retention could harm people whose kidney disorder is being treated with diuretics, which cause water loss. This possible harm is based on known mechanisms rather than human trial data.

Blood levels of creatine (a byproduct of energy production) are used as an indicator of kidney function, but elevated levels caused by supplemental creatine are not a sign that your kidneys underperform. The current evidence does not support the persistent notion that creatine supplementation causes kidney damage. In both long- and short-term studies, daily doses up to 10 grams were found not to impair kidney function in people with healthy kidneys. Daily doses above 10 grams too were found not to impair kidney function in people with healthy kidneys, but there are fewer long-term trials on such high doses.
Creatine’s ability to raise creatinine levels may, however, mask underlying issues. Consider having your creatinine levels tested before you start taking creatine, so as to both get a baseline measurement and check up on your kidney function. If you are already taking creatine yet plan to have your creatinine tested, cease supplementation 3 weeks prior to testing so as to prevent a false positive.

Limited short-term evidence indicates that people with suboptimal kidney function may safely supplement with creatine. Long-term studies, however, are scarce.[89][90][91][92] If your kidney function is suboptimal, you might wish to forgo creatine, or otherwise take only a low daily dose (such as 3 grams[67]) after speaking with your physician. Out of caution, people taking medicines that increase the risk of harm or damage to the kidneys (i.e., nephrotoxic drugs) should skip creatine supplementation.

Finally, do not buy liquid creatine products — creatine breaks down into useless byproducts when left in liquids for too long.

How to take creatine

Take 3–5 grams of creatine monohydrate with food. Other forms of creatine may be more expensive, but studies have not found them to be more effective. People with more muscle mass may benefit from as much as 10 g/day, but this claim is not fully supported by the evidence. To supplement with 10 g/day, take 5 grams twice a day.

Loading creatine means taking a high daily dose for a few days (e.g., 25 g/day for 5 days) before moving down to a smaller maintenance dose, which can be taken indefinitely. This is not necessary for effective supplementation, however; benefits may be felt sooner through loading, but they normalize after a few weeks.

If you wish to load creatine, take 20–25 g/day for 7 days (you may help prevent intestinal discomfort by splitting your daily intake into smaller doses, taking them with some food, and drinking more fluids). Take 5 g/day thereafter.

Some people are creatine nonresponders: the creatine they ingest largely fails to reach their muscles.[93][94] Note that even if supplemental creatine fails to enter your muscles it can still benefit you in other ways, such as by improving your body’s methylation status (methylation being a way for your cells to help manage gene expression).

Alternate forms of creatine, such as creatine ethyl-ester, have been marketed to nonresponders, but they lack scientific support. Currently, the best way to lessen creatine nonresponse is to take 5 grams twice a day, each time with protein and carbs, preferably close to a time of muscle contraction (i.e., before or after your workout).
If you are not a creatine nonresponder, you need not worry about supplementation timing, though you should remember that taking your dose with food lowers the risk of an upset stomach.

Creatine can be added to any liquid, but it must be drunk within the day, because creatine in liquids degrades into creatinine over time (the higher the temperature and the lower the pH, the faster the degradation). If you add creatine to a hot liquid, increase your dose a little to compensate for potential degradation.

**DHEA**

**What makes DHEA a primary option**

The hormone dehydroepiandrosterone (DHEA) circulates throughout your body and can be called on to make other hormones, notably testosterone and estrogens. DHEA levels decrease with age, sometimes drastically; maintaining adequate DHEA levels can help support healthy testosterone levels, libido, and sexual function in seniors.

**Warnings about DHEA**

If your hormone levels are healthy, supplementing with DHEA is unlikely to benefit you — don’t play with your hormonal balance on a whim.

DHEA can mildly inhibit the activity of CYP3A4, an enzyme that helps in the metabolism of a wide range of pharmaceuticals — from antibiotics to blood pressure medicines. If you are currently on any medication, speak with your physician before taking DHEA.

A handful of trials reported an increase in acne, particularly in females. People with acne, or a history of acne, may be more prone to this side effect.

Observational and mechanistic evidence suggests that it may be prudent for people with a family history of prostate, ovarian, or breast cancer to avoid DHEA supplementation, since it affects androgenic (testosterone, DHT …) and estrogenic (estrogen, progesterone …) hormones.

In some sports leagues, DHEA and its derivatives (such as 7-keto DHEA) are banned substances; their use may result in suspension or expulsion from the sport. The legality of DHEA also differs by country and region: some regulate it as a supplement, others as a drug.
How to take DHEA

First, get tested. Your body synthesizes DHEA sulfate (DHEA-S) out of DHEA. Whereas blood levels of DHEA can change quickly, blood levels of DHEA-S are more stable. You want to know your DHEA-S levels.

### Typical normal DHEA-S ranges (µg/dL / µmol/L)

<table>
<thead>
<tr>
<th>AGE</th>
<th>MALES</th>
<th>FEMALES</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–29</td>
<td>280–640 / 7.56–17.28</td>
<td>65–380 / 1.75–10.26</td>
</tr>
<tr>
<td>40–49</td>
<td>95–530 / 2.56–14.31</td>
<td>32–240 / 0.86–6.48</td>
</tr>
<tr>
<td>50–59</td>
<td>70–310 / 1.89–8.37</td>
<td>26–200 / 0.70–5.40</td>
</tr>
<tr>
<td>60–69</td>
<td>42–290 / 1.13–7.83</td>
<td>13–130 / 0.35–3.51</td>
</tr>
<tr>
<td>&gt;69</td>
<td>28–175 / 0.76–4.72</td>
<td>17–90 / 0.46–2.43</td>
</tr>
</tbody>
</table>


- If they are normal, you don’t need to take DHEA.
- If they are above normal, do not take DHEA. Speak to your physician.
- If they are below normal, discuss taking DHEA with your physician.

If you decide to supplement, you can try taking DHEA once a day in the morning (with food) for a month, then get tested again.

- **Males** can take 20–50 mg/day.
- **Females** can take 10–30 mg/day.

These doses should suffice to maintain adequate circulating levels of DHEA. In cases of very low
DHEA, 50 mg/day may be needed by both sexes.

**Maca (for libido)**

**What makes maca a primary option**

Multiple studies show that maca, a root vegetable, enhances libido in older males and females. Libido may keep improving for up to 8 weeks before plateauing.\(^96\)\(^97\) It should be noted that maca has shown promise for postmenopausal females,\(^98\) an oft-overlooked population when it comes to libido enhancement.

Maca may serve to treat sexual dysfunction caused by selective serotonin reuptake inhibitors (SSRIs),\(^99\)\(^100\) a kind of antidepressant. It can also mildly benefit males with erectile dysfunction from other causes.\(^101\)

**Warnings about maca**

Maca is not known to interact with any major hormones (such as DHEA, estrogen, or testosterone) or any pharmaceuticals. To date, however, research into maca’s potential adverse effects is somewhat limited.

**How to take maca**

Take 2–3 grams of maca root powder at breakfast. For the purpose of improving libido, there is no difference between red, black, and yellow maca.\(^96\)

**Magnesium**

**What makes magnesium a primary option**

Like calcium, magnesium is one of the major mineral components of bone.\(^102\) Low levels in the blood are associated with bone loss; conversely, high levels are associated with greater bone mass in old age.

Hypomagnesemia (suboptimal magnesium levels in the blood) has been linked to neuromuscular and cardiovascular disorders,\(^103\) inflammatory diseases,\(^104\) and neurological disorders\(^105\)\(^106\) such as Alzheimer’s disease (actually, suboptimal levels in the blood aren’t associated with Alzheimer’s; but suboptimal levels in the hair and the cerebrospinal fluid are\(^107\)).
Hypomagnesemia can also result in abnormal nervous-system stimulation leading to anxiety and poor sleep. In older people with hypomagnesemia, supplemental magnesium has been shown to improve sleep quality.[108][109]

In people with low magnesium intakes, magnesium supplementation has been shown to raise slightly both total testosterone and the percentage of free testosterone (the percentage your body can use most easily).[110]

Who is more likely to have low magnesium levels?

- **Older people**, because they tend to have relatively low magnesium intakes[111] and may absorb less during digestion.[112]

- **People who sweat a lot**, because magnesium is lost through sweat. Athletes participating in sports requiring weight control may be especially vulnerable.

- **Type 2 diabetics**. It has been estimated that, over all adult ages in developed countries, hypomagnesemia affects less than 15% of healthy people but up to 50% of people with type 2 diabetes.[113]

In addition, certain diuretics, proton pump inhibitors, and the antifungal medicine amphotericin-b can cause significant magnesium loss.\[^{114}\]\^amiloride, eplerenone/Inspra, spironolactone/Aldactone, triamterene/Dyrenium) may not.\[^{114}\]

**Warnings about magnesium**

High doses of supplemental magnesium can cause diarrhea and general intestinal discomfort.\[^{115}\] Fortunately, magnesium obtained via food has not been seen to cause such problems.\[^{115}\]

### Tolerable Upper Intake Level (UL) for supplemental magnesium (mg)

<table>
<thead>
<tr>
<th>AGE</th>
<th>MALE</th>
<th>FEMALE</th>
<th>PREGNANT</th>
<th>LACTATING</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–12 months</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>1–3 years</td>
<td>65</td>
<td>65</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>4–8 years</td>
<td>110</td>
<td>110</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>&gt;8 years</td>
<td>350</td>
<td>350</td>
<td>350</td>
<td>350</td>
</tr>
</tbody>
</table>


Magnesium can lower blood sugar and may have additive effects when taken with other supplements or pharmaceuticals that can lower blood sugar, such as diabetes medicines.

Magnesium may impair the absorption of some pharmaceuticals, notably bisphosphonates and antibiotics — especially antibiotics in the tetracycline class (e.g., doxycycline) and quinolone class (e.g., ciprofloxacin).\[^{116}\] Take magnesium at least 6 hours before or after taking bisphosphonates or antibiotics.

Since calcium, iron, magnesium, and zinc compete for absorption, it is better to take them at least one hour apart.

Because magnesium might have a sedative effect, it is often supplemented before bed.
How to take magnesium

There is no single, agreed-upon, satisfactory method for assessing magnesium status\textsuperscript{[117]} (as we saw, suboptimal levels in the blood aren’t associated with Alzheimer’s, but suboptimal levels in the hair and the cerebrospinal fluid are\textsuperscript{[107]}).

We said that older people tend to have relatively low magnesium intakes, but to get a better sense of your typical magnesium intake, you should track what you eat for a week. If, on average, you are getting less than 80\% of your Recommended Dietary Allowance (RDA), supplementation becomes an option, though first you should try to eat more foods rich in magnesium.

### Recommended Dietary Allowance (RDA) for magnesium (mg)

<table>
<thead>
<tr>
<th>AGE</th>
<th>MALE</th>
<th>FEMALE</th>
<th>PREGNANT</th>
<th>LACTATING</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–6 months</td>
<td>30*</td>
<td>30*</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>7–12 months</td>
<td>75*</td>
<td>75*</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>1–3 years</td>
<td>80</td>
<td>80</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>4–8 years</td>
<td>130</td>
<td>130</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>9–13 years</td>
<td>240</td>
<td>240</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>14–18 years</td>
<td>410</td>
<td>360</td>
<td>400</td>
<td>360</td>
</tr>
<tr>
<td>19–30 years</td>
<td>400</td>
<td>310</td>
<td>350</td>
<td>310</td>
</tr>
<tr>
<td>31–50 years</td>
<td>420</td>
<td>320</td>
<td>360</td>
<td>320</td>
</tr>
<tr>
<td>&gt;50 years</td>
<td>420</td>
<td>320</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

* Adequate intake (AI)

If, for some reason, you cannot get enough magnesium through foods, start supplementing with **200 mg** once a day. Capsules with 400 mg are common, but keep in mind that the Tolerable Upper Intake Level (UL) for supplemental magnesium is 350 mg. The higher the dose, the higher the risk of gastrointestinal issues. Commonly supplemented forms include citrate, gluconate, and glycinate. To increase absorption, magnesium gluconate should be taken with food; other forms can also be taken on an empty stomach. **Avoid magnesium oxide:** it has poor bioavailability (rats absorbed only 15% in one study,[118] humans only 4% in another[119]) and is especially liable to cause intestinal discomfort and diarrhea.[119][120][121] Because magnesium might improve sleep quality, it is often supplemented before bed.

**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**
The accumulation of calcium in body tissues, notably bone, is called calcification. For bones, calcification is a good thing, but it can harden soft tissues, such as blood vessels — including coronary arteries, which supply oxygenated blood to the heart.

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. Hence, vitamin K can both strengthen the bones of older people (with more evidence in postmenopausal females) and reduce cardiovascular risk. However, there are notable differences between the different forms.

After being absorbed by your intestines, K₁ 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\textsubscript{1}. This should make K\textsubscript{1} better at supporting coagulation (i.e., blood clotting), and MK-4 better at preventing calcium from being deposited in the arteries.

Some K\textsubscript{1} converts indirectly to MK-4, but how much is unknown. Diets naturally rich in K\textsubscript{1} do not seem to reduce cardiovascular risk, but trials supplementing high K\textsubscript{1} doses have noted some reduction in coronary artery calcification. The reason may be that, in many plants, K\textsubscript{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, 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\textsubscript{1} to K\textsubscript{2}, or MK-4 to MK-7.

When it comes to bones, a few MK-4 trials looked at fracture risk and reported a decrease. One K\textsubscript{1} trial looked at fracture risk and reported a decrease, but without a concomitant increase in bone mineral density, so more research is needed to clarify the issue. Some MK-7 trials found an improvement in bone mineral density, but none have looked at fracture risk.

The vitamins K and D increase separately and synergistically the rate at which minerals (notably calcium and magnesium) accumulate in bones. MK-4 and MK-7 appear to do so more reliably than K\textsubscript{1}.

### Micrograms of vitamin K per 100 grams of food

<table>
<thead>
<tr>
<th>FOODS</th>
<th>K\textsubscript{1}</th>
<th>K\textsubscript{2} MK-4</th>
<th>K\textsubscript{2} MK-7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collards</td>
<td>440</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Spinach</td>
<td>360–380</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Broccoli</td>
<td>113–180</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Cabbage</td>
<td>98–145</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Natto</td>
<td>Not measured</td>
<td>0</td>
<td>939–998</td>
</tr>
</tbody>
</table>
## Warnings about vitamin K

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

K₁ is present mostly in leafy green vegetables, many of which are cruciferous. If you plan to increase your K₁ 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).

K₁ and K₂ are the only natural forms of vitamin K, but there exist several synthetic forms, the best known of which is K₃ (menadione). However, whereas the natural forms of vitamin K are safe, even

<table>
<thead>
<tr>
<th>FOODS</th>
<th>K₁</th>
<th>K₂ MK-4</th>
<th>K₂ MK-7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chicken</td>
<td>0–4.5</td>
<td>8.5–60</td>
<td>0</td>
</tr>
<tr>
<td>Pork</td>
<td>0–3.4</td>
<td>2.1–6</td>
<td>0.5–0.12</td>
</tr>
<tr>
<td>Beef</td>
<td>0.7–2.4</td>
<td>1.1–15</td>
<td>0–0.12</td>
</tr>
<tr>
<td>Beef liver</td>
<td>2.7</td>
<td>0.82</td>
<td>18.2</td>
</tr>
<tr>
<td>Egg</td>
<td>0.3–12</td>
<td>7–9</td>
<td>Not measured</td>
</tr>
<tr>
<td>Egg yolk</td>
<td>Not measured</td>
<td>15.5–64</td>
<td>0</td>
</tr>
<tr>
<td>Butter</td>
<td>7</td>
<td>15–21</td>
<td>0</td>
</tr>
<tr>
<td>Blue cheese</td>
<td>Not measured</td>
<td>Not measured</td>
<td>2.5–22</td>
</tr>
<tr>
<td>Cheddar</td>
<td>2.1</td>
<td>10.2</td>
<td>0–2.3</td>
</tr>
</tbody>
</table>

in high doses, K₃ can interfere with glutathione, your body’s main antioxidant. K₃ 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 K₃ gets converted into K₂ MK-4, which you can consume safely.[131]

**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) or 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.

Orlistat (Alli, Xenical) reduces how much fat you absorb from the food you eat. As a result, it also reduces the absorption of fat-soluble vitamins. If you take this medicine, take your vitamin K supplement at least 2 hours before or after.

**How to take vitamin K**

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.

For **bone health**, take 200 mcg (0.2 mg) of MK-7 and/or 45,000 mcg (45 mg) of MK-4. MK-4 is the form best supported by the evidence, but more studies are needed to determine if smaller doses are also beneficial.

For **cardiovascular health**, take 200 mcg (0.2 mg) of MK-7 and, optionally, 500–1,000 mcg (0.5–1 mg) of K₁.

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

The doses above 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)**

<table>
<thead>
<tr>
<th>AGE</th>
<th>MALE</th>
<th>FEMALE</th>
<th>PREGNANT</th>
<th>LACTATING</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–6 months</td>
<td>2.0</td>
<td>2.0</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>7–12 months</td>
<td>2.5</td>
<td>2.5</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>AGE</td>
<td>MALE</td>
<td>FEMALE</td>
<td>PREGNANT</td>
<td>LACTATING</td>
</tr>
<tr>
<td>----------</td>
<td>------</td>
<td>--------</td>
<td>----------</td>
<td>-----------</td>
</tr>
<tr>
<td>1–3 years</td>
<td>30</td>
<td>30</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>4–8 years</td>
<td>55</td>
<td>55</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>9–13 years</td>
<td>60</td>
<td>60</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>14–18 years</td>
<td>75</td>
<td>75</td>
<td>75</td>
<td>75</td>
</tr>
<tr>
<td>&gt;18 years</td>
<td>120</td>
<td>90</td>
<td>90</td>
<td>90</td>
</tr>
</tbody>
</table>

Secondary Options

Secondary options have less evidence for their effects. They could work or be a waste of money. Keep them in mind, but think twice before adding them to your combo.

Cholinergics

What makes cholinergics a secondary option

A supplement is said to be cholinergic when it increases the brain’s levels of acetylcholine, a major neurotransmitter associated with memory and attention span. Cholinergics may improve cognition in people experiencing cognitive decline, and very preliminary evidence indicates they might benefit people with dementia.[132]

CDP-choline (citicoline) can provide the brain with the choline it needs to produce more acetylcholine (choline bitartrate is much cheaper, but little of it seems to reach the brain[133]). CDP-choline is also a source of uridine, which has itself been hypothesized to improve cognition (though much more research is needed before it can be recommended for supplementation on its own). In addition, CDP-choline might improve vision in people suffering from glaucoma.

Warnings about cholinergics

Some temporary side effects, such as nausea and heartburn, have been documented in people taking CDP-choline. The interactions between CDP-choline and other supplements and pharmaceuticals are not well known.

The cholinergic Huperzine-A can inhibit acetylcholinesterase, an enzyme that breaks down the neurotransmitter acetylcholine; as a result, the brain’s levels of acetylcholine increase. Its half-life exceeds 24 hours (i.e., after 24 hours, more than half of the dose you took will still be in your system), so it accumulates in the body when taken daily, which is problematic since long-term studies are scarce. There is a possibility that, over time, the body could adapt by producing more acetylcholinesterase, which would lead to reduced acetylcholine levels and a withdrawal period after huperzine-A supplementation has ceased. While the doses used in the studies (0.2–0.99 mg)
were deemed safe in the short term, long-term supplementation cannot be recommended.

**How to take cholinergics**

To supplement with **CDP-choline** for cognitive improvements, take 500–2,000 mg/day.

To supplement with **CDP-choline** against glaucoma, take 1,600 mg/day.[134]

**Maca (for symptoms of menopause))**

**What makes Maca a secondary option**

The symptoms of menopause are vast and often troublesome, and there’s probably no single thing that can help with all or even most of them. In the case of Maca, several studies have been conducted and, overall, they mostly suggest a small but potentially meaningful improvement in general symptoms.[98][135][136][137][138][139]

Which symptoms they reduce are fairly inconsistent, with some studies suggesting a reduction in depression, headaches, and hot flashes, while some didn’t suggest effects. Decreases in anxiety and nervousness and improvements in sleep quality are the most consistent benefits.

**Warnings about maca**

Maca is not known to interact with any major hormones (such as DHEA, estrogen, or testosterone) or any pharmaceuticals. To date, however, research into maca’s potential adverse effects is somewhat limited.

**How to take maca**

Take 2–3.5 g of maca root powder at breakfast.

**Vitamin E**

**What makes vitamin E a secondary option**

As you age, your immune system weakens against invaders and stressors. Supplementation with vitamin E can improve markers of immune function, but this does not necessarily translate into a
reduced risk of catching infectious diseases. The evidence in this area is very mixed.[140][141]

Still, although more research is needed to better understand the effects of vitamin E on infection rates and illness severity, current evidence suggests that seniors can benefit from vitamin E supplementation.

**Warnings about vitamin E**

Vitamin E has both antiplatelet and anticoagulant properties — the latter because it interferes with the blood-clotting properties of vitamin K.[142] This could be a problem for people whose diet is poor in vitamin K or who take blood thinners, be they antiplatelet agents (such as aspirin) or anticoagulants (such as warfarin/Coumadin and acenocoumarol/Sintrom).

Moreover, because of these antiplatelet and anticoagulant properties, 200 IU of vitamin E (the dose recommended for daily supplementation) may lower systolic blood pressure.[143] Note that supplements and pharmaceuticals that lower blood pressure can have cumulative effects.

**Orlistat** (Alli, Xenical) reduces how much fat you absorb from the food you eat. As a result, it also reduces the absorption of fat-soluble vitamins. If you take this medicine, take your vitamin E supplement at least 2 hours before or after.

**How to take vitamin E**

Track what you eat for a week; if, on average, you are getting less than 80% of your Recommended Dietary Allowance, supplementation becomes an option, though first you should try eating more foods rich in vitamin E.

Alternatively, you could check your blood levels of vitamin E. Blood levels of alpha-tocopherol (α-tocopherol) under 0.5 mg/dL (<5 mcg/mL, or <11.5 μmol/L) are considered deficient.

**Recommended Dietary Allowance (RDA) for vitamin E (alpha-tocopherol) (mg / IU)**

<table>
<thead>
<tr>
<th>AGE</th>
<th>MALE</th>
<th>FEMALE</th>
<th>PREGNANT</th>
<th>LACTATING</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–6 months</td>
<td>4 / 6*</td>
<td>4 / 6*</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>AGE</td>
<td>MALE</td>
<td>FEMALE</td>
<td>PREGNANT</td>
<td>LACTATING</td>
</tr>
<tr>
<td>-----------</td>
<td>-------</td>
<td>--------</td>
<td>----------</td>
<td>-----------</td>
</tr>
<tr>
<td>7–12 months</td>
<td>5 / 7.5*</td>
<td>5 / 7.5*</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>1–3 years</td>
<td>6 / 9</td>
<td>6 / 9</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>4–8 years</td>
<td>7 / 10.4</td>
<td>7 / 10.4</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>9–13 years</td>
<td>11 / 16.4</td>
<td>11 / 16.4</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>&gt;13 years</td>
<td>15 / 22.4</td>
<td>15 / 22.4</td>
<td>15 / 22.4</td>
<td>19 / 28.4</td>
</tr>
</tbody>
</table>

* Adequate Intake (AI)


Take 200 IU of vitamin E (134 mg of natural α-tocopherol or 90 mg of synthetic α-tocopherol). Do not take more than 400 IU/day, and since vitamin E has anticoagulant properties, make sure your diet contains at least your Adequate Intake (AI) of vitamin K (90 mcg/day for females; 120 mcg/day for males).

Vitamin E being fat soluble, it is better absorbed when taken with a fat-containing food or supplement (e.g., fish oil)
Unproven Supplements are backed by tradition or by mechanistic, animal, epidemiological, or anecdotal evidence, but not yet by convincing human trials. At this point, they are not good candidates for your combo.

Vinegar

What makes vinegar an unproven supplement

Acetic acid is, after water, the main component of vinegar. It may slow the passage of food from the stomach to the small intestines, thus slowing the absorption of carbohydrates, thus reducing both insulin response and damage from hyperglycemia. It may also improve insulin signaling via various molecular mechanisms.[145]

The overall research suggests a smaller increase in post-meal blood glucose when vinegar is taken before or with a meal,[146] but this reduction is modest and doesn't last long (roughly 2 hours). Moreover, the studies are small and short-term, and their methodologies don't give us full confidence in their findings.

As for the reductions in HbA1c (a biomarker of glucose metabolism) and fasting blood glucose, they may not be strong enough to have a meaningful, long-term effect on health, and they're supported by scant evidence in the first place.[147][148][149][150][151][152]

Vinegar’s proposed mechanism of action
In short, vinegar’s ability to prevent or treat type 2 diabetes is uncertain, as is its long-term benefit for people with impaired glucose tolerance. You should wait for studies of higher quality, including long-term studies, before you go out of your way to take vinegar with all your meals.

However, if you want to give vinegar a try anyway, here is the dose best supported by current evidence:

- 2.8 g/day of acetic acid divided into 1.4 g doses taken right before breakfast and dinner

Alternatively, you can take the following.

- 2 tablespoons (29.6 mL) of apple cider vinegar right before breakfast and dinner (59.2 mL/day; which is approximately 3.6 grams of acetic acid per day)
Vitamin B<sub>7</sub> (biotin)

What makes biotin an unproven supplement

⚠️ Caution: Biotin can affect laboratory results

Biotin can interfere with many laboratory tests, from hormone tests to cardiovascular diagnostics. Cease supplement 3 to 7 days before getting any lab work done.

Biotin, also known as vitamin B<sub>7</sub>, partakes in the production of keratin, the protein at the core of hair and nails. For that reason, it is highly popular as a supplement to improve the appearance of hair and nails.[153][154]

As it stands, no randomized control trials (RCTs) have tested biotin’s effects on the hair or nails of healthy people,[155] but supplementation may promote healthy hair and nails in people with the following conditions:

- **Biotin deficiency** (which is rare, though maybe less so in people experiencing hair loss)[155][156]
- Genetic disorders affecting biotin metabolism (leading to a deficiency in two enzymes responsible for processing biotin: biotinidase and holocarboxylase synthetase)[155][157]
- Some nail medical conditions (brittle nails, triangular worn-down nails, trachyonychia, and habit-tic deformity)[158][159][160][161][162][163]
- **Uncombable hair syndrome**[153][164][165]
- Medication-induced hair loss (caused by valproic acid, for example)[166][167][168]

The studies on biotin supplementation for the above conditions are mostly case studies that provide preliminary, if encouraging, data. People who are biotin deficient or have inborn errors of biotin metabolism are the most likely to benefit from supplementation.

In cases of **genetic disorder affecting biotin metabolism**, larger biotin doses (10–30 mg/day) have helped.[155]

In cases of **biotin deficiency** or **medical condition** (brittle nails, uncombable hair syndrome, etc.), 0.3–3 mg/day may be beneficial.[155]
Inadvisable supplements are either potentially dangerous or simply ineffective, marketing claims notwithstanding. Do not add them to your combo. At best, they’ll be a waste of money; at worst, they can cause you harm.

Iron

What makes iron an inadvisable supplement

Data gathered between 2004 and 2013 show that, in the United States, three micronutrients are responsible for almost a third of all supplement-related emergency-room visits of adults aged 65 or older: calcium, potassium, and iron.\[169\] The study specifies that “swallowing problems caused most emergency department visits involving calcium products …, whereas abdominal symptoms (e.g., nausea, vomiting, and abdominal pain) were frequently associated with iron or potassium products”.[\[169\]

Supplement-related emergency-room visits in people aged 50+
More iron isn’t always better or even harmless. When too much iron builds up in your body (hemochromatosis), it becomes toxic and can lead to dysfunction in your heart, liver, and pancreas. In extreme cases, it can cause arrhythmia, heart failure, and death.

Postmenopausal females need less iron (8 mg/day, like males) than premenopausal females (18 mg/day). Although iron deficiency contributes substantially to the high prevalence of anemia seen in the elderly,[170][171] taking an iron supplement “just in case” (or because you look pale and feel tired) is ill-advised. If you think you might suffer from iron deficiency, see a physician and get tested.

Potassium
What makes potassium an inadvisable supplement

As mentioned above in the iron entry, potassium is one of the three micronutrients responsible for almost a third of all supplement-related emergency-room visits of adults aged 65 or more,\[^{169}\] mostly due to abdominal symptoms (e.g., nausea, vomiting, and abdominal pain).

Worse, too much potassium at once on an empty stomach can lead to hyperkalemia (very high levels of potassium in the blood) and thus to dangerous changes in heart rhythm (arrhythmia). For that reason, in the United States, supplemental potassium chloride (the most common form of supplemental potassium) in “solid oral” form (i.e., in tablets and capsules) is limited to 99 mg of elemental potassium per serving.

This is a very low amount, which makes it probable that the seniors who suffered from abdominal symptoms from potassium took more than one serving (or used a powder supplement, or took too much Nu-Salt®). It isn’t a risk you want to take. If you suspect you might have low potassium levels, see a physician and get tested.

Vitamin B\(_9\) (folate / folic acid)

What makes vitamin B\(_9\) an inadvisable supplement

Vitamin B\(_9\) comprises folate and its synthetic form, folic acid. The Recommended Dietary Allowance (RDA) for vitamin B\(_9\) is 400 mcg/day for males and most females; 600 mcg/day for pregnant females; and 500 mcg/day for lactating females. High doses of folic acid have been successfully used by pregnant females to prevent birth tube defects,\[^{47}\] which is why some foods, especially bread, are fortified with it.

Folate vs. folic acid
Unfortunately, preliminary research suggests that high doses of folic acid (>1,000 mcg/day) may increase the risk of colon cancer in seniors and may exacerbate pre-existing colon cancer. Neither folic acid supplements nor multivitamins, which most often contain too much folic acid, are recommended for seniors.

<table>
<thead>
<tr>
<th>Folate</th>
<th>Folic acid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naturally occurring form of the vitamin</td>
<td>Synthetic form of the vitamin</td>
</tr>
<tr>
<td>Good sources of folate include chickpeas and lentils</td>
<td>Used to fortify many foods</td>
</tr>
<tr>
<td>Mediocre absorption by the body</td>
<td>Good absorption by the body</td>
</tr>
</tbody>
</table>
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 to my combo not covered in this guide?

Supplement with your current combo for a few weeks before attempting any change. Talk to your physician and research each potential new addition in advance. 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., tiredness) 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 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 already 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 suffers 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 B\(_{12}\).

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 body fat and interindividual variability).

**Q. What’s the difference between elemental iron/magnesium/potassium and other kinds?**

“Elemental” refers to the weight of the mineral by itself, separately from the compound bound to it. For instance, ingesting 500 mg of magnesium gluconate means ingesting 27 mg of elemental
magnesium.

**Product labels display the elemental dosage.** On a label, “27 mg of magnesium (as magnesium gluconate)” means 27 mg of elemental magnesium (and 473 mg of gluconic acid).

**Q. Wait, where’s calcium?**

While calcium supplementation may promote bone health and reduce blood pressure, it may also increase the risk of hypercalcemia (dangerously high levels of calcium in the blood), potentially leading to heart disease, the leading cause of death among older adults in the United States. The evidence on bone and heart health is mixed and still developing; whether or not the potential benefits outweigh the potential harm is still to be determined.

**Q. What about multivitamins?**

You may be inclined to take a multivitamin as a sort of insurance against nutritional deficiencies. A multivitamin isn’t strictly necessary, but it can help if it is well formulated.

When buying a multivitamin, check on the label the content of each serving, the number of pills per serving, and the number of servings per day; don’t pay more for dubious bells and whistles; and stick to a company with a reputation for good manufacturing.

The form of the supplement can matter, too. Magnesium oxide, for instance, has very low bioavailability — not only will you absorb less elemental magnesium from it but it may also cause intestinal discomfort.

**Factors to consider when buying a multivitamin**
Q. What’s the difference between anthocyanins and anthocyanidins?

Anthocyanins contain anthocyanidins. To be more precise, an anthocyanidin is simply an anthocyanin without its sugar molecule(s).
## Phytochemical profiles of select berries
(mg per 100 grams of edible portion)

<table>
<thead>
<tr>
<th>FRUIT</th>
<th>TOTAL ANTHOCYANIDINS*</th>
<th>TOTAL FLAVAN-3-OLS**</th>
<th>TOTAL FLAVONOLS***</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chokeberry, raw</td>
<td>437.22</td>
<td>—</td>
<td>8.90</td>
</tr>
<tr>
<td>Bilberry</td>
<td>430.91</td>
<td>4.13</td>
<td>—</td>
</tr>
<tr>
<td>Black raspberry</td>
<td>324.02</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Currant, black, raw</td>
<td>272.44</td>
<td>1.17</td>
<td>12.69</td>
</tr>
<tr>
<td>Blueberry</td>
<td>163.52</td>
<td>51.71</td>
<td>9.72</td>
</tr>
<tr>
<td>Blackberry</td>
<td>90.46</td>
<td>42.50</td>
<td>2.49</td>
</tr>
<tr>
<td>Red raspberry, raw</td>
<td>38.68</td>
<td>6.63</td>
<td>1.32</td>
</tr>
<tr>
<td>Strawberry</td>
<td>33.63</td>
<td>4.51</td>
<td>1.60</td>
</tr>
<tr>
<td>Cranberry, dried, sweetened</td>
<td>0.72</td>
<td>—</td>
<td>6.91</td>
</tr>
<tr>
<td>Cranberry juice cocktail</td>
<td>0.46</td>
<td>0.19</td>
<td>1.79</td>
</tr>
<tr>
<td>Cranberry sauce, canned, sweetened</td>
<td>0.14</td>
<td>—</td>
<td>5.11</td>
</tr>
<tr>
<td>Cranberry juice, unsweetened</td>
<td>—</td>
<td>0.92</td>
<td>20.82</td>
</tr>
<tr>
<td>Mulberry, raw</td>
<td>—</td>
<td>—</td>
<td>2.47</td>
</tr>
</tbody>
</table>

* Total anthocyanidins (cyanidin, delphinidin, peonidin, petunidin)
** Total flavan-3-ols ((−)-epicatechin, (−)-epicatechin-3-gallate, (−)-epigallocatechin, (−)-epigallocatechin-3-gallate, (+)-
Q. Can I replace blueberries with other anthocyanin-rich foods?

Most studies are on blueberries, and the total amount of anthocyanins does not tell the whole story, because different types of anthocyanins can be found in different amounts in different berries. Studies on cognition have reported benefits from blue-purple anthocyanins, notably cyanidin and delphinidin, whereas red anthocyanins, such as pelargonidin, lack the same scientific backing.

So dark berries (blueberries, blackberries, elderberries …) might be interchangeable for the purpose of enhancing cognition, whereas red berries (strawberries, raspberries …), although also rich in anthocyanins, are likely not suitable alternatives.

Blue-purple anthocyanins can be found in foods other than dark berries, such as purple cauliflower, purple potatoes, and purple rice, but keep in mind that some blue-purple plants derive their color from betalains, not anthocyanins — for instance, beetroot.

Q. Are organic blueberries better?

In terms of anthocyanin content, not really: anthocyanin levels appear to be almost identical (within 5%) in organic and non-organic blueberries cultivated in the same area.[7] On the other hand, there appear to be large differences depending on the soil. For example, even within the United States, the anthocyanin content can range from 144 to 823 mg per 100 grams of blueberries, depending on the region where the bushes are grown.[7]

Q. Isn’t soy protein bad for males?

Phytoestrogens are plant compounds structurally similar to estradiol, the main estrogen in males and premenopausal females. Because soy contains isoflavones, a type of phytoestrogen, concern has been raised about soy affecting male health.

To this day, two case reports have documented adverse effects (gynecomastia, hypogonadism, reduced libido, and erectile dysfunction) from an estimated 360 mg of soy isoflavones per day for 6–12 months. However, a meta-analysis of 15 randomized controlled trials (RCTs, a much higher level of evidence than case reports) found that males’ levels of total and free testosterone were not notably affected by either 60–240 mg of isoflavones or 10–70 grams of soy protein per day.

Accordingly, a couple of scoops of soy protein powder are unlikely to have estrogenic effects in
males. If you’d like to take more, however, look for a soy protein concentrate or isolate produced through the alcohol-wash method, which dramatically lowers the isoflavone content.\textsuperscript{[173]}

Keep in mind that the isoflavone content of different soy products can vary depending on several factors, such as the variety of soybeans used, differences in growing and storage conditions, and differential food processing techniques employed.\textsuperscript{[174]} You can see how it varies below

\textbf{Isoflavone content of common soy foods}
<table>
<thead>
<tr>
<th>Food category</th>
<th>Food</th>
<th>Milligrams of isoflavones per 100 g of food</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Average</td>
</tr>
<tr>
<td>Traditional unfermented soy foods</td>
<td>Edamame</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>Soybeans (boiled)</td>
<td>65</td>
</tr>
<tr>
<td></td>
<td>Soybeans (raw)</td>
<td>155</td>
</tr>
<tr>
<td></td>
<td>Soybean sprouts</td>
<td>34</td>
</tr>
<tr>
<td></td>
<td>Soy milk (unsweetened)</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>Soy nuts</td>
<td>148</td>
</tr>
<tr>
<td></td>
<td>Tofu</td>
<td>30</td>
</tr>
<tr>
<td>Traditional fermented soy foods</td>
<td>Miso</td>
<td>41</td>
</tr>
<tr>
<td></td>
<td>Miso soup</td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td>Miso soup mix (powder)</td>
<td>70</td>
</tr>
<tr>
<td></td>
<td>Natto</td>
<td>82</td>
</tr>
<tr>
<td></td>
<td>Soy sauce</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Tempeh</td>
<td>61</td>
</tr>
<tr>
<td>Second-generation soy foods</td>
<td>Soy-based veggie “meats”</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>Soy cheeses</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>Soy yogurt</td>
<td>33</td>
</tr>
<tr>
<td>Soy flours and protein powders</td>
<td>Soy flour (defatted)</td>
<td>151</td>
</tr>
<tr>
<td></td>
<td>Soy flour (full-fat)</td>
<td>165</td>
</tr>
<tr>
<td></td>
<td>Soy infant formula (powder)</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>Soy protein concentrate (alcohol wash)</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>Soy protein concentrate (water wash)</td>
<td>95</td>
</tr>
<tr>
<td></td>
<td>Soy protein isolate</td>
<td>91</td>
</tr>
</tbody>
</table>

Q. Which dietary protein is best for bone health?

Most studies used dairy protein, yet the protein in our bones is mostly type 1 collagen. It follows that supplemental type 1 collagen should be optimal for bone health — and indeed, animal models appear to support this notion.

The few relevant human studies to date, however, had mixed results. Not only that, but they cumulated factors (they gave collagen with calcium, vitamin D, dietary changes …), making it impossible to determine which factor did what and to what extent. Until better human studies come along, collagen’s superiority over other proteins (for bone health) will stay hypothetical.

Q. Don’t dietary proteins reduce bone density?

More protein in the diet has been linked to more calcium in the urine. Two reasons have been suggested to explain this phenomenon:

- Your body draws from its calcium stores (in bones) to buffer the acid load caused by dietary protein. This has led researchers to suggest that higher protein intake could increase bone loss.\[175\]
- Most studies that looked at protein intake and calcium excretion list dairy products as a protein source,\[176\] so higher urinary calcium could simply be the result of higher calcium intake (i.e., more calcium in, more calcium out).

Therefore, looking only at calcium excretion wasn’t enough. Subsequent studies showed that dietary protein promotes dietary-calcium absorption\[177\] and that high protein intake “promotes bone growth and retards bone loss {whereas} low-protein diet is associated with higher risk of hip fractures.”\[17\] High-protein diets have also been shown to modestly suppress the decrease in bone mineral density caused by weight loss.\[178\]

What happens is that when you ingest more protein, you absorb more of the calcium in your food, so less calcium ends up in your feces. Later, your body gets rid of the calcium it doesn’t need, so more calcium ends up in your urine, but not as much as would have otherwise ended in your feces.\[18\] Therefore, an increase in protein intake leads to an overall decrease in calcium excretion, which points to an increase in calcium retention. High-protein diets also raise your insulin-like growth factor-1 (IGF-1),\[179\] which promotes notably bone growth.\[180\]

All in all, current evidence suggests that protein’s effect on bones is either neutral or beneficial.\[18\][19]
Q. I’ve heard that I should “load” creatine. What does that mean?

Loading creatine means taking a high daily dose for a few days before moving down to a smaller maintenance dose, which can be taken indefinitely. This is not necessary for effective supplementation, however; benefits may be felt sooner through loading, but they normalize after a few weeks.

If you wish to load creatine, take 20–25 g/day for 7 days (splitting your daily intake into smaller doses, taking them with some food, and drinking more fluids may help prevent intestinal discomfort). Take 5 g/day thereafter.

Q. Creatine doesn’t seem to work for me. What should I do?

Some people are creatine nonresponders: the creatine they ingest largely fails to reach their muscles. Alternate forms of creatine, such as creatine ethyl-ester, have been marketed to nonresponders, but they lack scientific support. Currently, the best way to lessen creatine nonresponse is to take 5 grams twice a day, each time with protein and carbs, preferably close to a time of muscle contraction (i.e., before or after your workout).

Note that even if supplemental creatine fails to enter your muscles it can still benefit you in other ways, such as by improving your body’s methylation status (methylation being a way for your cells to help manage gene expression).

Q. Can testosterone boosters bring my testosterone back to normal?

DHEA, vitamin D, magnesium, and zinc have been seen to raise low testosterone levels. Few other supplements seem to help at all.

A few trials back Coleus forskohlii, but its numerous potential adverse effects make it a risky proposition, especially for older people.

You might also have heard of D-aspartic acid, but its promising first trials were followed by several others that found that it didn’t increase testosterone.

Some other supplements, such as ginger and Eurycoma longifolia, might support testosterone levels only in infertile males (or in males with testicular damage).

Many other herbs, such as horny goat weed, have not even been studied in humans yet.

Finally, keep in mind that a supplement can benefit your libido (as do maca and, according to a small number of studies, Tribulus terrestris), your mood, or your energy levels, yet not affect your
testosterone.


14. ^ Serban MC, et al. Impact of L-carnitine on plasma lipoprotein(a) concentrations: A


22. ^ a b c Mcleod JC, Stokes T, Phillips SM. Resistance Exercise Training as a Primary Countermeasure to Age-Related Chronic Disease. Front Physiol. (2019)


28. ^ Poortmans JR, Dellalieux O. Do regular high protein diets have potential health risks on kidney function in athletes?. Int J Sport Nutr Exerc Metab. (2000)


33. ^a Elango R, et al. Evidence that protein requirements have been significantly underestimated. *Curr Opin Clin Nutr Metab Care.* (2010)


42. ^a Stover PJ. Vitamin B12 and older adults. *Curr Opin Clin Nutr Metab Care.* (2010)


58. Lanolin.


61. Farshidfar F, Pinder MA, Myrie SB. Creatine Supplementation and Skeletal Muscle Metabolism for Building Muscle Mass- Review of the Potential Mechanisms of


68. van der Merwe J, Brooks NE, Myburgh KH. Three weeks of creatine monohydrate supplementation affects dihydrotestosterone to testosterone ratio in college-aged rugby players. *Clin J Sport Med*. (2009)


76. Sheikholeslami D et al. The effects of creatine supplementation on performance


79. ^Rahimi R et al.. Creatine supplementation alters the hormonal response to resistance exercise. Kinesiology. (2011)


92. ^Shelmadine D et al.. The effects of supplementation of creatine on total homocysteine. JRN. (2013)


94. ^Hadjicharalambous M, Kilduff LP, Pitsiladis YP. Brain serotonin and dopamine


98. ^ a b Brooks NA, et al. Beneficial effects of Lepidium meyenii (Maca) on psychological symptoms and measures of sexual dysfunction in postmenopausal women are not related to estrogen or androgen content. Menopause. (2008)


109. ^ Nielsen FH, Johnson LK, Zeng H. Magnesium supplementation improves indicators
of low magnesium status and inflammatory stress in adults older than 51 years with poor quality sleep. Magnes Res. (2010)


120. ^ Walker AF, et al. Mg citrate found more bioavailable than other Mg preparations in a randomised, double-blind study. Magnes Res. (2003)


140. Pae M, Wu D. Nutritional modulation of age-related changes in the immune system


144. ^ a b Institute of Medicine (US) Panel on Dietary Antioxidants and Related Compounds. Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids.


174. Erdman JW Jr, et al. Not all soy products are created equal: caution needed in


Michael Hull
MSc in Human Nutrition

Michael received a BSc in exercise science with a minor in nutrition from George Mason University (where he mentored under GMU’s resident sports dietitian, Deanna Busteed, MS, RD, CSSD), then an MSc in human nutrition from McGill University. His master’s thesis examined how modifiable lifestyle factors can potentially predict vitamin D status. As a full-time senior research manager at Examine.com, he primarily writes and updates the Supplement Guides, maintains the company’s database of supplement studies, and blogs about various health topics. When not working for Examine.com, he enjoys finding ways of using technology to further science communication.

Wyatt Brown

Searching for ways to improve his health and frequently confused by the conflicting messages from publications and popular authors, Wyatt dove head first into the scientific research and became fascinated by its logic and methods. Contributing to his most respected website has only intensified his interest and motivated him to pursue an education in nutrition.
Kamal Patel
MBA, MPH, PhD(c) in Nutrition

Kamal Patel is cofounder and director of Examine.com. He holds two master’s degrees from the Johns Hopkins University, in business and in public health, and is on hiatus from a PhD in nutrition for which he’s investigated the link between diet and chronic pain. He’s published peer-reviewed articles on vitamin D and calcium, as well as on a variety of clinical research topics. He’s also been involved in research on fructose and liver health, on nutrition in low-income areas, and on mindfulness meditation.

Pierre-Alexandre Sicart
AA in English, Licentiate of Integrated European Studies, PhD in French Literature

Pierre-Alexandre holds graduate degrees from New York University, the University of Toulouse II, and the University of St Andrews. At NYU, he was MVP then captain of the Taekwondo Club, president of the Karate Club, and founder of the Martial Arts Club. After graduation, he wrote a grammar book, then found himself working as assistant professor of French in Taiwan. After some years enjoying the best foods in Asia, he moved back to France to freelance as a writer, translator, and copy editor. He’s Examine.com’s resident copy editor and has been overseeing our Supplement Guides since 2016.

... and the rest of the team!

With degrees in nutrition, exercise science, public health, pharmacology, toxicology, microbiology, biophysics, biomedical science, neuroscience, chemistry, and more, the members of our team are all accredited experts, but with very different backgrounds, so that when we review the evidence, we get the full picture.