Examine®

Allergies & Immunity Supplement Guide

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Introduction

In times of good health, we're barely aware that our immune system even exists. Yet at any given time, we're battling an invading horde that is invisible to the naked eye and can evolve much faster than we can.

Fortunately, we have a dedicated defense system against these germs, and it's on call 24-7, fighting several threats at a time while readying for the next. But even so, we can still get sick, and when this happens, we become aware of the war taking place inside us.

From the latest pandemic down to those bothersome colds and allergy symptoms that somehow surprise us every year, we must face occasional reminders of the thin line we constantly walk between health and illness. Unsurprisingly, that's when we start wondering how we can help our immune system keep us healthy — or how we can reduce the duration and severity of an illness, should one strike.

Supplementation is a controversial topic, especially when its purpose is to avoid or mitigate illness. The field is full of scammers eager to exploit people's fear to make a quick buck. And even when we have the best intentions, we seldom have a good understanding of the science and are too eager to latch onto any potential cure. As we'll see, though, the immune system is complex and multifaceted, making it tough to predict the effects a promising supplement will have in real life.

As it stands, ravaging viral pandemics aren't just a threat to overall health; they can also cause economies to come to a screeching halt. Our health is our greatest asset, but still, when money becomes scarce, we need to make especially sure it isn't wasted on useless (or even dangerous supplements).

Ironically maybe, the main goal of this guide is to help you make good decisions about what *not* to take. As we're about to learn, attempts to "boost" or "enhance" the immune system through supplementation with herbs or excessively large doses of a vitamin or mineral can end up doing more harm than good.

Immunology 101

The innate immune system

From a historical standpoint, the field of immunology was launched when doctors observed that during periods of pandemic disease, individuals who became infected and didn't die couldn't be infected again; they were *immune*. Somehow, after the infection, the body was able to fight back, not only by killing off the initial infection but by protecting against future infections of the same type. This, of course, would be the goal of any immune-boosting agent: to enhance this *adaptive* immune response. But there are two major parts to the immune system that work together, and the ability to fight off infections depends on their coordinated function.

Think of the innate arm of the immune system as the first responder to insult, injury, or infection. It consists of multiple parts. Epithelial cells, such as those in the skin, provide a physical barrier to pathogens, preventing their entry; those that line the airway also secrete antimicrobial substances. An array of specialized proteins are also present in our blood and are designed to bind to foreign invaders, tagging them for destruction by effector cells called macrophages or neutrophils, which rush in to gobble up bacteria or kill virus-infected cells.

The effector cells themselves express proteins called *pattern recognition receptors* (PRRs), which act as sensors to microbial infection. PRRs work by binding to specific molecules present on pathogens and

triggering the release of specialized proteins called cytokines. The type of cytokines released during an infection promote inflammation, which calls in additional immune cells to help.

One example of a PRR is *toll-like receptor 4* (TLR4), which recognizes endotoxins (aka lipopolysaccharides, or LPS), molecules present on the cell walls of many bacteria. When present during a bacterial infection, LPS binds to TLR4 and stimulates the release of pro-inflammatory cytokines, such as *interleukin-6* (IL-6), *tumor necrosis factor alpha* (TNFα), and others, which send a "danger signal", mobilizing the immune system to fight off the foreign invaders.

The innate immune response to viral infection

Some PRRs are also designed to detect viral infection by sensing DNA or RNA from viruses, triggering antiviral responses. Let's say you were exposed to a virus. As with other infectious agents, the innate immune system is again the first line of defense. Viruses make their entrance into host cells through specialized vesicles (membrane pouches) called endosomes. Within these are PRRs, such as TLR7 or TLR8,[1] that bind to and sense the presence of viral RNA, triggering the innate antiviral response. Should the virus escape from the endosomes and make it into the cytosol of the cell (i.e., the liquid inside of cells) — a likely event during an active viral infection — additional virus sensors, such as *retinoic acid-inducible gene I* (RIG-I)[2] and others, detect the infection and sound the alarm.

The "alarm" consists of inflammatory cytokines and *type I interferons* (IFN), such as IFNα and IFNβ, that trigger the innate antiviral response. When initiated, the antiviral response deploys a number of countermeasures to slow down the infection and induce an antiviral state in neighboring cells that haven't been infected.[3][3] These measures brought on by the interferon response include cell death by apoptosis (programmed cell death), cell cycle arrest (to keep virus-infected cells from dividing), and mobilization of the adaptive immune system to fight the infection (more on that later).[4][5][6]

Although the innate antiviral system evolved over thousands of years to help stop viral infections, the viruses aren't helpless. They, too, have evolved a number of tricks to circumvent our antiviral defenses — by evading detection by the endosomal or cytosolic PRR sensors, for example.[7]

Adaptive immune system

Although the innate immune system is capable of stopping a virus on its own, some infections can't be defeated by the innate response alone, particularly if that pesky virus has some tricks up its sleeve to evade detection. (The inability of the innate system to stop the virus is much more likely when we are sleep deprived, malnourished, or stressed). In these situations, the innate response continues to do its best to slow the rate of infection as much as possible while calling on the slower-acting, but much more targeted, adaptive immune system for help.

Adaptive immune system cells are called lymphocytes and include B cells and T cells. Unlike innate immune system cells, which recognize general parts of microbes through PRRs, lymphocytes detect and deal with infections in a much more precise way. Each lymphocytic cell expresses a receptor unique to a certain type of pathogen. When it encounters the pathogen that it binds to, a lymphocyte produces a large amount of pathogen-specific effector cells. After massive cell cloning and then the elimination of the infection, some of the pathogen-specific cells stick around to provide long-term immunity.

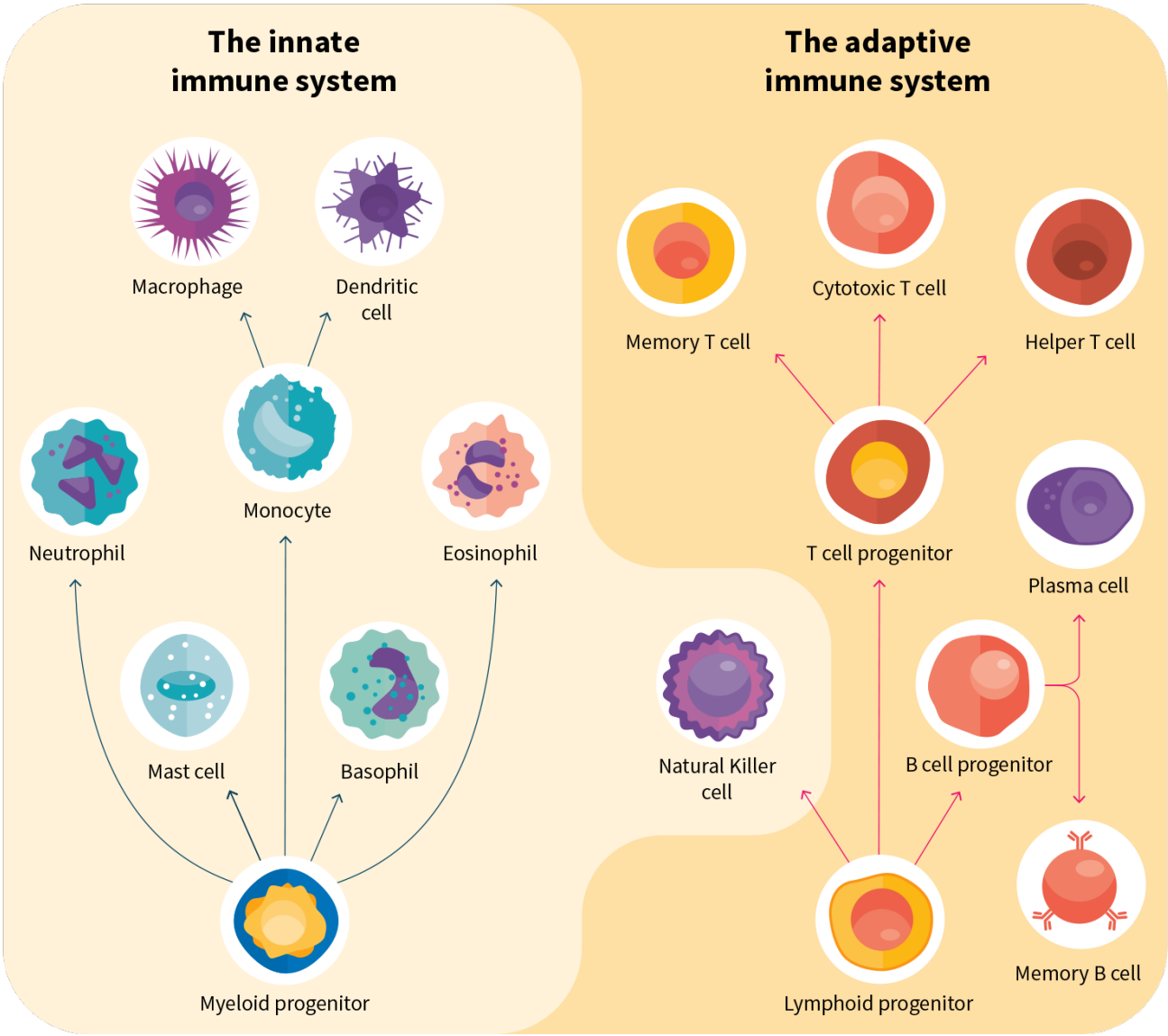
In this way, the adaptive immune system has a type of memory. If you are exposed to the same infection down the road, you wouldn't get sick, because your body would rapidly recognize and fight off microbes

before the infection could ever take hold. In other words, you would be immune. For some pathogens — the measles virus[8] is a good example — immunity can last for years or even decades. For others, such as influenza, immunity is much shorter lived, because the virus mutates and changes form yearly.[9]

The innate and adaptive immune systems work together

Although the innate immune system is the first line of defense and the adaptive system develops slower and is more targeted, this doesn't mean that they function independently. Their activity is highly coordinated.

Cells of the immune system



To visualize how this works, we can look at an overview of the process after the pathogen — a virus, for example — makes its way into the body. Let's say you were unlucky enough to be exposed to a virus for which you have no immunity. It will likely enter through a mucosal surface (eyes, mouth, or throat) and infect the epithelial cells in the area. This will cause some cell death and an inflammatory response, which will change the endothelial lining of blood vessels in the area.

Not only will they express different surface proteins, causing them to become "stickier", but the spacing

between cells will increase. This allows immune cells to adhere to the area and squeeze their way past the endothelial layer into the infected tissue. Specialized *antigen presenting cells* (APC) in the innate immune system, such as dendritic cells, gobble up cell debris and the virus at the infection site, grinding them up and presenting parts of them (i.e., antigens) on their cell surface on *major histocompatibility complexes* (MHC).

Loaded with antigen, the dendritic cells travel through the lymphatic system to a local lymph node, where they help trigger the adaptive immune response. (This is why the lymph nodes in your throat or elsewhere become swollen during an infection; APCs are accumulating to set off an adaptive immune response against the microbes expressing that particular antigen.)

Once in the lymphoid tissue, the dendritic cell will activate the naive T cells that happen to bind to that same antigen. The activated naive T cell then undergoes multiple rounds of cell division to increase in number and mature. There are three main types of effector T cells: cytotoxic T cells, helper T cells, and memory T cells.

Cytotoxic T cells (aka CD8 T cells) are the foot soldiers of the immune system.[10] After being activated in lymphoid tissue, they travel back to the infected area to attack and destroy infected cells.

Helper T cells come in a couple of varieties. T_H1 cells travel back to the infected tissue, where they help activate innate immune cells, such as macrophages. In contrast, T_H2 cells remain in the lymphoid tissues, where they interact with antigen-specific B cells and induce them to produce antibodies.

B cells bind to antigens through their *B cell receptor* (BCR). When one encounters an activated T_H2 cell in the lymph node that also happens to bind to parts of the same pathogen, the B cell activates undergoing multiple rounds of cell division and mutation to select those cells with the best antibodies. Ultimately, they differentiate into the two main types of B effector cells: plasma cells and memory B cells.

Plasma cells are professional antibody producers, purposely built to make and secrete large numbers of antibodies. These antibodies operate at the business end of adaptive immunity, binding to and neutralizing pathogens as well as flagging them for destruction by other immune cells.

Finally, after an active infection, a subset of antigen-specific B and T cells stop short of differentiating into effector cells and remain in a preactivated state, ready to spring into action at the slightest sign of infection. These memory cells give us long-term immunity, also called immunological memory.

Vaccines are a great example of immunological memory. They protect us by artificially introducing parts of a bacterium or virus. By injecting part of the microbe (or whole microbes that have been killed and are not capable of infection), the body generates an adaptive immune response against that pathogen. After immunological memory is established, if you were exposed to the live virus or bacteria in the future, you wouldn't get sick, because you'd be immune.

Why immune boosters don't make sense, even on paper

As we've learned, the immune system is complex and multifaceted, consisting of an early-acting, always-on innate system and a potent and precise but slower-developing adaptive system. They work together, and much of the cross-talk is controlled by the release of inflammatory cytokines and inflammation. Given this, if we were to consider what boosting the immune system might look like and how we would accomplish it,

all of a sudden immune boosters don't look so promising.

Supplements to target inflammation?

A double-edged sword

There are certainly plenty of supplements for inflammation out there, and they work … to a point. But do we really want to suppress inflammation, when the timely release of pro-inflammatory cytokines during an initial infection is key to slowing the infection *and* activating the adaptive immune system? Probably not. And attempts to do so could be the difference between prolonged illness and good health — or even life and death with new pathogens that have jumped from animals to humans, such as COVID-19.

Increasing inflammation is also a nonstarter, because too much is not a good thing at all in this case. Many deaths from respiratory viruses such as influenza or COVID-19 are caused by a so-called "cytokine storm",[11] which is an overreaction of the immune system that creates massive amounts of inflammation that can lead to organ failure and death.

What about antioxidants?

Antioxidants are certainly important during an active infection, but immune cells also tend to attack pathogens via an oxidative mechanism[12]. While there are some links between vitamin C intake and resistance to upper respiratory viruses — vitamin C is included as a primary option for this reason — it is important not to overdo it, which could interfere with the mechanism. But we are talking about immune *boosters* here, and antioxidants are not that.

Do we really want to boost the immune system?

There's a fine line between immunity and autoimmunity, and the latter occurs when the adaptive immune system becomes overactivated and begins attacking our own cells, tissues, and proteins. A hallmark of adaptive immunity, when it is working properly, is that it turns off after the infection is defeated. If allowed to persist, immunity can be developed against our own cells and tissues. This happens in autoimmune conditions such as lupus,[13][14] rheumatoid arthritis,[14] and Sjogren's syndrome,[15] where the adaptive immune system is inappropriately keyed up on "self" proteins. There may be a fine line between autoimmunity and a "boosted" immune system.

In summary

To stay healthy and infection free, the innate and adaptive immune systems need to be robust enough to fight off invading microbes but regulated enough that they don't do too much damage to our own cells, proteins, and tissues. We don't accomplish this by taking buckets of supplements, clumsily targeting inflammation or any other signaling process. Instead, this is accomplished by taking care of yourself.

That means being well nourished, sleeping enough, staying properly hydrated, and controlling stress the

best we can. There are certain micronutrients and supplements that can *support* a high-functioning immune system, and we've included them in this guide. But without taking care of yourself, the supplements amount to a drop of water in the ocean.

Bill Willis, senior researcher *PhD in Biomedical Science*

Combos

Core Combo

Three times a day, with food, take garlic (either 1–2 cloves or 200–400 mg of an extract) and vitamin C (500 mg). Those supplements can only help if taken regularly (i.e., before the first symptoms).

If your blood levels of vitamin D (25(OH)D) are adequate or you don't know your levels, 400 IU (10 mcg) of vitamin D_3 per day may help maintain levels in the adequate range. If your 25(OH)D levels are low, 800–2,000 IU (20–50 mcg) of D_3 per day is likely to raise them to an adequate level, at which point 800–1,000 IU (20–25 mcg) per day should suffice for maintenance. In case of full-blown deficiency, consult your physician as a medically supervised intervention may be needed.

> 💡 ***Tip:*** **Try one combo alone for a few weeks**
>
> Taking too many supplements at once may prevent you from determining which ones are truly working. Start with just one of the combos suggested here for a couple of weeks before you consider making any modification, such as adding another supplement, altering a supplements dosage, or incorporating the supplements from an additional combo.
>
> When adding another supplement to your regimen, be methodical. For example, you may wish to take all the supplements from two combos. Select the combo that you wish to try first and take this for a couple of weeks. Then, add one supplement from the second combo and wait another week to see how it affects you. Continue this process until you've added all the supplements you wish to.
>
> If a supplement appears in two combos you wish to combine, don't stack the doses; instead, combine the ranges. For instance, if the range is 2–4 mg in one combo and 3–6 mg in the other, your new range becomes 2–6 mg. Always start with the lower end of the range — especially in this case, since the reason why one of the ranges has a lower ceiling in one combo may be due to a synergy with another supplement in the same combo. Reading through the full supplement entry may help you decide which dose to aim for, but if you're not sure, lower is usually safer.

Specialized Combos

For people who easily get sick

Thrice a day, in addition to the core supplements, take *Echinacea purpurea* in the form of a powder (300–500 mg) or tincture (2.5–10 mL / 0.5–2 teaspoons).

For people at the onset of a sickness characterized by flu-like symptoms

In addition to the core supplements, take *Pelargonium sidoides* until the symptoms disappear. Thrice a day before eating, take either the raw powder (720 mg), an EPs 7630 syrup (1 mL, so about ¼ teaspoon), or an EPs 7630 hydroalcoholic extract (1.5 mL, so about 1 teaspoon or 30 drops).

Additionally, take 700–900 mg of elderberry extract per day, as a *lozenge* or *capsule*, split into 3 or 4 doses. Alternatively, take 1 teaspoon (5 mL) of elderberry *syrup*, four times a day. Continue until the symptoms disappear.

You can also suck zinc acetate lozenges throughout the day (75–95 mg/day) for one week or until the symptoms disappear, whichever comes first.

For people with chronic stuffy nose

In addition to the core supplements, take spirulina (2 g/day).

For people with COPD

In addition to the core supplements, take NAC (600 mg twice a day) year-round.

For seniors

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 females; 120 mcg/day for males).

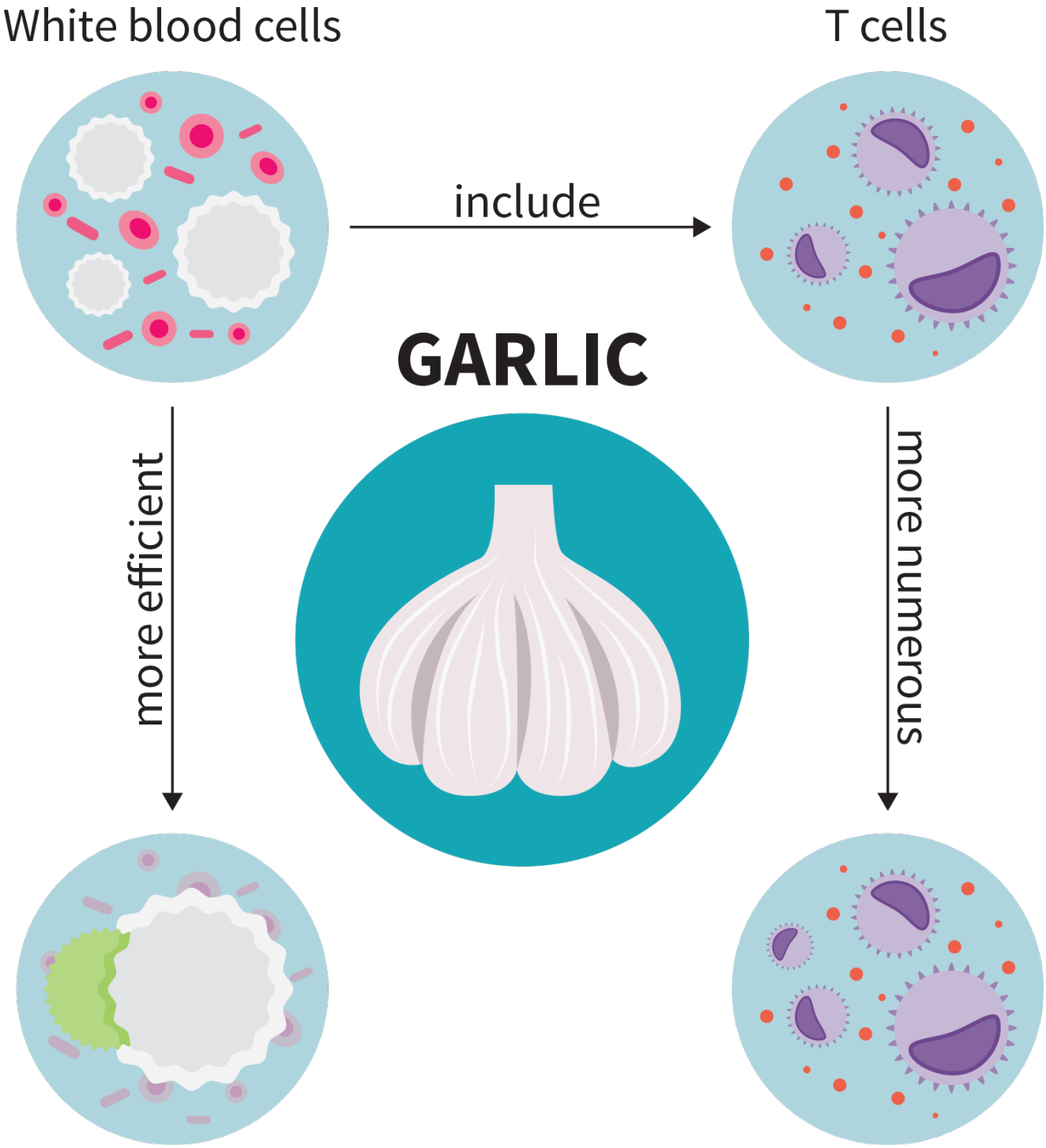
Primary Supplements

Garlic

What makes *garlic* a core supplement

By improving the ability of white blood cells (lymphocytes) to fight invaders and by increasing the production of T cells (T lymphocytes), garlic can enhance the immune system and thus reduce the risk of colds and other infections. Garlic will not, however, reduce the duration of a disease or the severity of the symptoms; it is a preventive supplement.

Effects of garlic on white blood cells



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

Taking too much garlic, or taking garlic with other hypotensive agents, could cause low blood pressure. Hypotensive agents can be pharmaceuticals but also supplements, such as nitrate, cocoa extract, grape seed extract, or pycnogenol, to mention a few.

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

How to take *garlic*

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

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

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

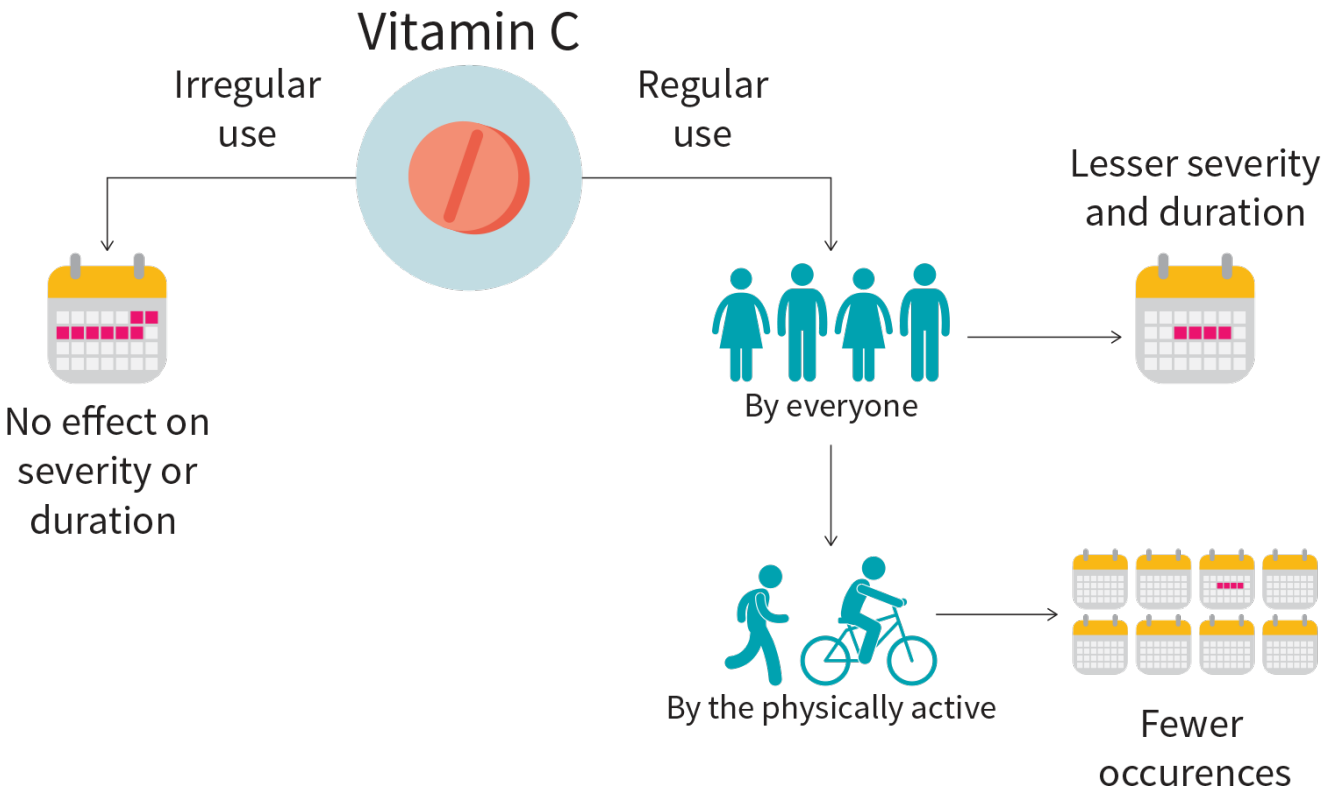
> 💡 ***Tip:*** **Why don't you recommend brands or specific products?**
>
> For two reasons:
>
> - We don't test physical products. What our researchers do — all day, every day — is analyze peer-reviewed studies on supplements and nutrition.
> - We go to great lengths to protect our integrity. As you've probably noticed, we don't sell supplements, or even show ads from supplement companies, even though either option would generate a lot more money than our Supplement Guides ever will — and for a lot less work, too.
>
> If we recommended any brands or specific products, our integrity would be called into question, so … we can't do it. That being said, in the interest of keeping you safe, we drew a short list of steps you should take if a product has caught your interest.

Vitamin C

What makes *vitamin C* a core supplement

Vitamin C is unique in that it can be either an antioxidant or a pro-oxidant, depending on physiological context. Vitamin C is researched mostly for its effects on colds. It might help reduce the duration and severity of colds, but only when taken regularly (so before the first symptoms).[16] In people who are physically very active, and thus more likely to get sick, it can also reduce the occurrence of colds.[16]

Effects of vitamin C on colds



Like garlic, vitamin C may reduce the effectiveness of some HIV medications. Moreover, since it can increase the absorption of iron and aluminum, it should not be supplemented within several hours of aluminum-based antacids (Amphojel, AlternaGEL, Alu-Cap, Alu-Tab, Dialume).

Ascorbic acid is the most commonly studied and commercially available form of vitamin C. Other forms (calcium ascorbate, potassium ascorbate, sodium ascorbate ...) may be more *expensive*, but they haven't been shown to be more *effective*.

How to take *vitamin C*

Take 1–2 grams of vitamin C in the form of *ascorbic acid* in divided doses throughout the day. Further research is needed to determine whether vitamin C is better absorbed with food.

Do not exceed 2 grams of vitamin C per day. For adults, the Tolerable Upper Intake Level (UL) for vitamin C is 2 g/day.

Tolerable Upper Intake Level (UL) for vitamin C (mg)

AGE	MALE	FEMALE	PREGNANT	LACTATING
0–12 months	*	*	—	—
1–3 years	400	400	—	—
4–8 years	650	650	—	—
9–13 years	1,200	1,200	—	—
14–18 years	1,800	1,800	1,800	1,800
>18 years	2,000	2,000	2,000	2,000

* Formula and food should be the only sources of vitamin C for infants.

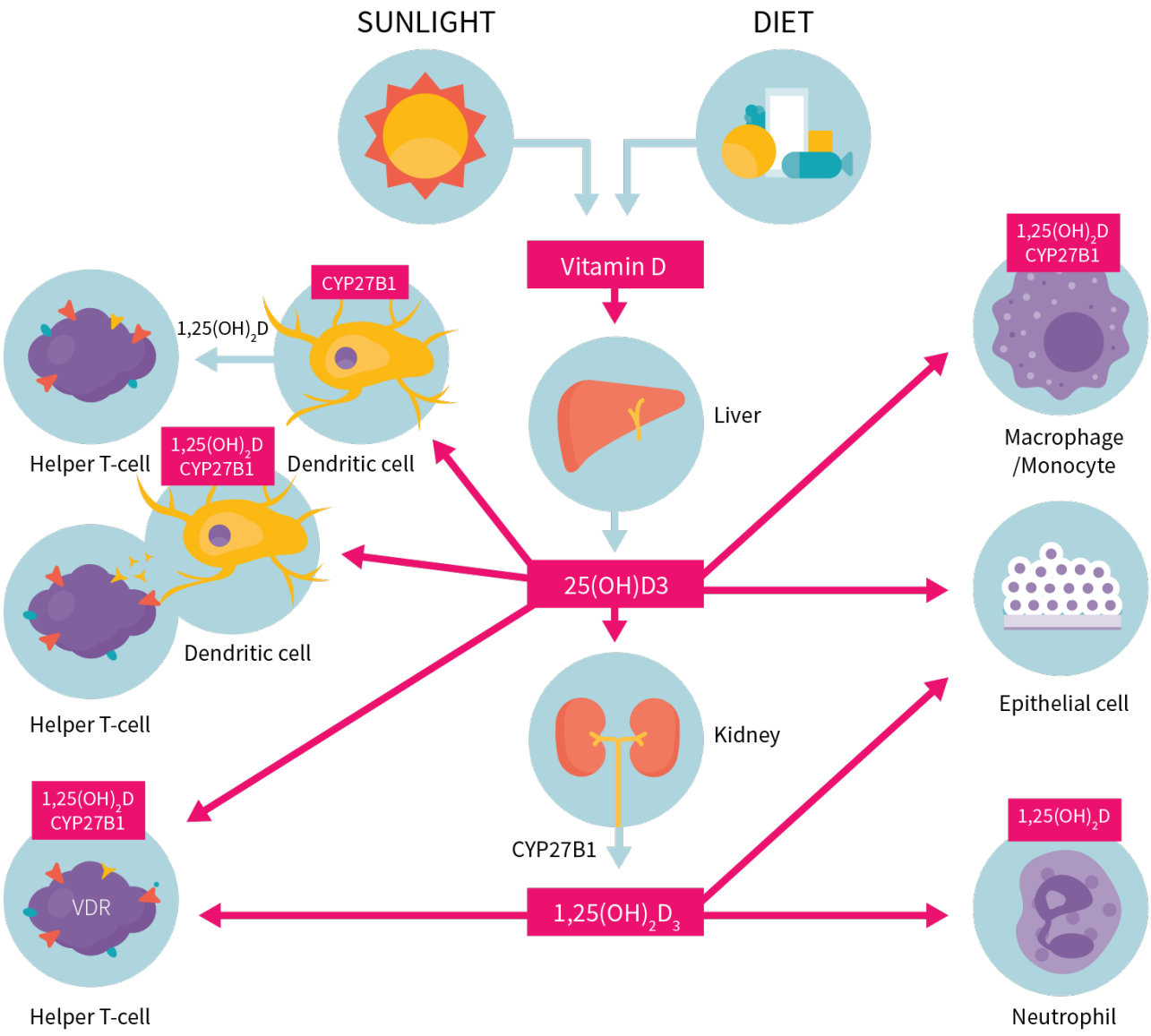
Reference: Institute of Medicine. Vitamin C (chapter 5 in *Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids*. The National Academies Press. 2000. DOI:10.17226/9810)

Vitamin D

What makes *vitamin D* a core option

Low levels of vitamin D have been associated with worse immune function[17] and increased rates[18] of acute respiratory infection, possibly due to its role in regulating the immune system as outlined below.[19] For example, it has been well documented that low levels of vitamin D in countries with suboptimal sunlight (about 32-42° N or S of the equator[20]) as well as a genetic predisposition for low vitamin D status[21] are both associated with increased rates of acute respiratory tract infections. This observation has also been seen in the United States, specifically.[22] These data suggest that adequate vitamin D status might be a protective factor against acute respiratory tract infections.

The immunomodulatory effects of vitamin D



Reference: Lang et al. *Osteoporos Int.* 2013.[23]

A recent individual patient data (IPD) meta-analyses of randomized, double-blind, placebo controlled trials examined the effect of supplementation with vitamin D_3 or vitamin D_2. The included trials recorded the incidence of acute respiratory tract infections in 11,321 participants.[24]

The participant pool was diverse, ranging in age from newborn babies (less than six months of age) to elderly individuals (over 90 years old) and spanning across a number of racial and ethnic backgrounds (e.g., Afghani, American, Australian, Canadian, Finnish, Indian, Israeli, Japanese, and Polish).

The primary outcome was the incidence of acute respiratory tract infections (i.e., upper respiratory tract infectionhttps://examine.com/conditions/upper-respiratory-tract-infection/), lower respiratory tract infection, and acute respiratory tract infection of unclassified location).

In people who had deficient levels of vitamin D (<25 nmol/L / <10ng/mL) when they began supplementation, they saw a 18–60% reduction in the odds of experiencing an acute respiratory tract infection compared to people who were vitamin D deficient but took a placebo.

On the flip side, people with sufficient levels of vitamin D experienced a lesser benefit — a 0–23% reduction in the odds of acute respiratory tract infections.

Importantly, daily or weekly doses of vitamin D exerted the protective effect but larger, less frequent doses taken every one to three months did not — not even among participants with deficient vitamin D levels.

🔍 ***Digging Deeper:*** **The benefits of individual patient data meta-analyses**

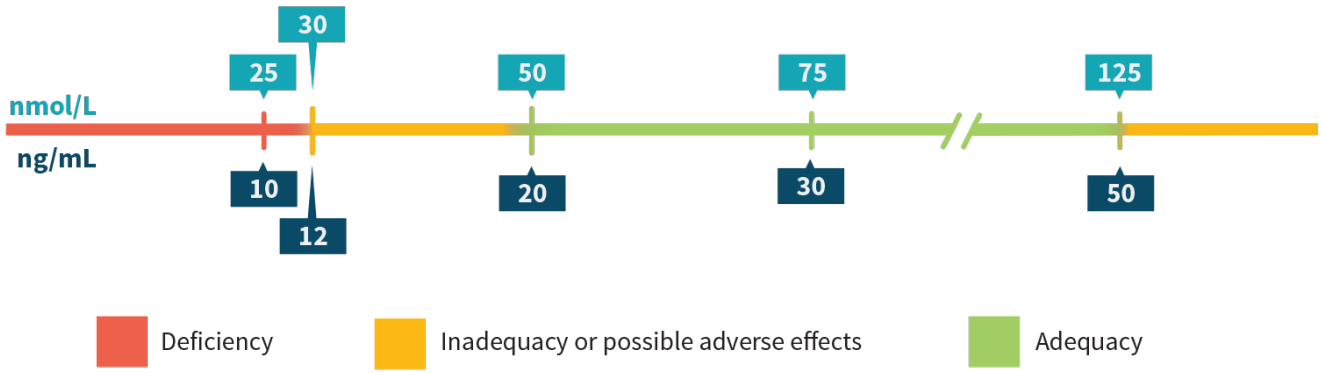
By using individual patient data (IPD), it may be possible to overcome some of the limitations of conducting meta-analyses at the trial level. IPD can be used to more specifically determine whether certain treatments are effective for what kinds of people and under which circumstances.

In addition to allowing for conducting subgroup analysis on consistently defined criteria, utilizing IPD data overcomes several key issues with trial-level meta-analyses that use aggregate data. Trial-level meta-analyses ignore the effect of missing data and omit important correlational structures, which are overcomed by IPD analyses.[25]

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



Reference: Institute of Medicine. Overview of Vitamin D (chapter 3 in *Dietary Reference Intakes for Calcium and Vitamin D*. The National Academies Press. 2011. DOI:10.17226/13050)

In case of *deficiency*, a medically supervised intervention may 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*)

AGE	MALE	FEMALE	PREGNANT	LACTATING
0–12 months	400**	400**	—	—
1–13 years	600	600	—	—
14–18 years	600	600	600	600
19–50 years	600	600	600	600
51–70 years	600	600	—	—
>70 years	800	800	—	—

* 40 IU = 1 mcg | ** Adequate intake (AI)

Reference: Institute of Medicine. Dietary Reference Intakes for Adequacy: Calcium and Vitamin D (chapter 5 in *Dietary Reference*

If the maintenance doses in the paragraphs above prove insufficient, as could be the case notably if your BMI is over 30 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 D_3 per day.

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

Secondary Supplements

Pelargonium Sidoides

What makes *Pelargonium sidoides* a primary option

Pelargonium sidoides, a plant also known as umckaloabo or South African geranium, contains compounds called prodelphinidins that can prevent bacteria from attaching to the throat and lungs.

Taken at the beginning of an illness characterized by dry and hoarse coughing, *Pelargonium sidoides* can reduce the severity of the symptoms and the duration of the disease. However, it does not seem to prevent infections from occurring in the first place.

Pelargonium sidoides is used primarily to treat acute bronchitis. It has less evidence for treating the common cold.

How to take *Pelargonium sidoides*

Most studies on *Pelargonium sidoides* used EPs 7630 (a patented 8–10:1 extract), but you could also supplement the raw powder.

To supplement an *EPs 7630 syrup*, take 1 mL (about ¼ teaspoon) thrice a day before eating, so 3 mL per day.

To supplement an *EPs 7630 hydroalcoholic extract*, take 1.5 mL (about 1 teaspoon or 30 drops) thrice a day before eating, so 4.5 mL per day.

To supplement the *raw powder*, take 720 mg thrice a day before eating, so 2,160 mg per day.

Supplementation of *Pelargonium sidoides* should begin at the onset of dry respiratory symptoms and continue until the symptoms have disappeared.

Zinc

What makes *zinc* a primary option

Zinc is a dietary mineral that can bolster the immune system and thus protect against the common cold and other infectious diseases. As a first line of defense, you should make sure your diet provides you with enough (but not too much) zinc.

Tolerable Upper Intake Level (UL) for zinc (mg)

AGE	MALE	FEMALE	PREGNANT	LACTATING
0–6 months	4	4	—	—
7–12 months	5	5	—	—
1–3 years	7	7	—	—
4–8 years	12	12	—	—
9–13 years	23	23	—	—
>13 years	15 / 22.4	15 / 22.4	15 / 22.4	19 / 28.4

Reference: Institute of Medicine. Zinc (chapter 12 in *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*. The National Academies Press. 2001. DOI:10.17226/10026)

Zinc lozenges can limit virus replication at the nasal epithelium and may reduce respiratory-tract inflammation. Taken within a day of the first symptoms, zinc lozenges may prevent them from worsening; they can also reduce the duration of the disease by 2–4 days, though symptoms may persist for a few days thereafter. Lozenges with zinc acetate may be more effective than lozenges with zinc gluconate (a more common form), but the evidence is mixed.

Lozenges are meant to be sucked, so that the zinc can better reach the throat tissues. This supplementation method can cause minor nausea and a temporarily disrupted sense of taste. To offset the nausea, eat some food prior to taking a lozenge. *Zinc nasal sprays, swabs, and gels carry a risk of temporary or permanent loss of smell and possibly taste; they should be avoided.*

How to take *zinc*

Suck *zinc acetate* lozenges every 1.5–3 hours (75–95 mg of zinc per day). Ideally, start within 24 hours of experiencing the first symptoms of a cold — if you start later, the lozenges may still help, but they may be less effective.

Stop after two weeks or as soon as the symptoms disappear, whichever comes first. Over time, such high doses of zinc can irritate the gastrointestinal tract. They can also cause a copper deficiency, since zinc kick-starts the process of creating metallothionein, a protein that binds zinc but also other metals, notably copper; the bound metals then leave the body as waste products.[26][27] Even higher doses of zinc can damage the liver and kidneys, too, so be careful not to cumulate zinc supplements (the lozenges mentioned in this guide and the zinc in a multivitamin, for instance).

If you start suffering from headaches, nausea, vomiting, loss of appetite, stomach cramps, or diarrhea, all signs that you may be taking more zinc than your body can stand, just stop supplementing with zinc. (Of course, if those symptoms persist after you've stopped supplementation, then the culprit is probably your cold, not the zinc.)

Since calcium, iron, magnesium, and zinc compete for absorption, it is better to take them at least one hour apart. Although to a lesser extent than magnesium, zinc may also impair the absorption of antibiotics, notably the tetracycline (e.g., doxycycline) and quinolone (e.g., ciprofloxacin) classes, so consider taking zinc and antibiotics at least 6 hours apart. Zinc can also impair the absorption of penicillamine, a drug used

to treat rheumatoid arthritis, so these should be taken at least 2 hours apart. Thiazide diuretics may increase zinc excretion, thus causing zinc deficiency if taken in the long term.[28]

Zinc can lower blood sugar and may have additive effects when taken with other supplements or pharmaceuticals that can lower blood sugar, such as antidiabetic drugs.

Promising Supplements

Echinacea

What makes *Echinacea purpurea* a secondary option

Echinacea purpurea was one of the first herbs marketed as an immune system booster. It contains a variety of bioactive compounds called alkylamides, but more research is needed to determine how they interact and what effects they have on the immune system.

Taken year round or during periods of likely illness, *Echinacea purpurea* can reduce the risk of catching a cold. It probably will not reduce the *duration* of a cold, but it might reduce the risk of complications (such as pneumonia).

Echinacea may interact with many pharmaceuticals. If you are currently taking medication, talk to your physician before supplementing *Echinacea*. Do not supplement *Echinacea* if you are taking immunosuppressive drugs.

How to take *Echinacea purpurea*

Echinacea purpurea is sold as a powder (usually in capsules) and as a tincture. Three times a day, take 300–500 mg of the powder (i.e., 900–1,500 mg/day) or 2.5–10 mL (0.5–2 teaspoons) of the tincture (i.e., 7.5–30 mL/day / 1.5–6 teaspoons/day).

More research is needed to determine the optimal dose of *Echinacea* and if it is more effective when taken with food or on an empty stomach.

Elderberries

What makes *elderberries* a secondary option

Berries from the elder (*Sambucus nigra*) have a long history of medicinal use in Native American, Mediterranean, and ancient Egyptian cultures. They have also been used traditionally for protection against witches, but no randomized controlled trials have been performed to test this hypothesis.🤦‍♀️

In vitro and animal studies suggest that elderberries have antiviral properties and may notably inhibit influenza. Most human trials had small sample sizes and all suffered from methodological limitations, but their results were consistent: supplementation within a day of the first symptoms led to a mild to moderate reduction of the infection's severity and duration.

If you choose to prepare elderberries yourself rather than purchasing a supplement, *you must properly cook them*. Uncooked, they can cause cyanide toxicity and thus nausea, vomiting, and worse. The bark, root, and leaves of the elder tree, being even richer in cyanide than the berry, should never enter in the preparation of supplements such as elderberry juice.

How to take *elderberries*

Begin supplementation within one day of the first symptoms and continue until they disappear (which typically takes about 5 days).

To supplement *lozenges* or *capsules*, take 700–900 mg of elderberry extract per day, split into 3 or 4 doses.

To supplement *a syrup*, take 1 teaspoon (5 mL) four times a day. In one study of Sambucol, an elderberry syrup brand, 12 teaspoons (60 mL) were taken daily for 5 days with no adverse effects noted, but this higher dosage was not shown to be more effective.

Using elderberry as a short-term prophylactic (e.g., supplementing for a week before a trip) *might* reduce your chance of catching a cold, but research here is still preliminary.

> 🔍 ***Digging Deeper:*** **Elderberry and cytokine storms**
>
> Some people on the Web have warned that elderberry could initiate or exacerbate a cytokine storm, based on a study that shows increased cytokine production from elderberry intake.[29] The authors say that "in addition to its antiviral properties, Sambucol Elderberry Extract and its formulations activate the healthy immune system by increasing inflammatory cytokine production" (cytokines being a natural and critical part of your immune system's response to pathogens).
>
> A cytokine storm isn't a mere bump in cytokine production, however, but a severe immune overreaction to a pathogen. In cases of severe flu, cytokine storms are associated with outcomes ranging from lung inflammation to death.[30]
>
> Although it appears unlikely that a low-to-moderate dose of elderberry would initiate a cytokine storm, nobody knows if taking elderberry (especially in large amounts) when symptoms are severe has any adverse effects. Discuss supplementation thoroughly with your physician before using it.

N-Acetylcysteine (NAC)

What makes *NAC* a secondary option

NAC (N-acetylcysteine) is a mucolytic: it reduces the viscosity of mucus, making it easier to cough out. Also, by replenishing the cells' stores of the antioxidant glutathione, NAC can further hinder some chronic lung diseases. For instance, NAC can reduce the number of *chronic obstructive pulmonary disease* (COPD) exacerbations, though only in people suffering from frequent exacerbations, and even then, only to a very

small extent.

NAC does not have sufficient evidence for the treatment of other chronic respiratory conditions, such as cystic fibrosis, chronic bronchitis, or chronic cough.

How to take *NAC*

Take 600 mg of NAC twice a day, with or without food. Higher doses do not seem to be more effective, whereas lower doses do not seem to be effective at all.

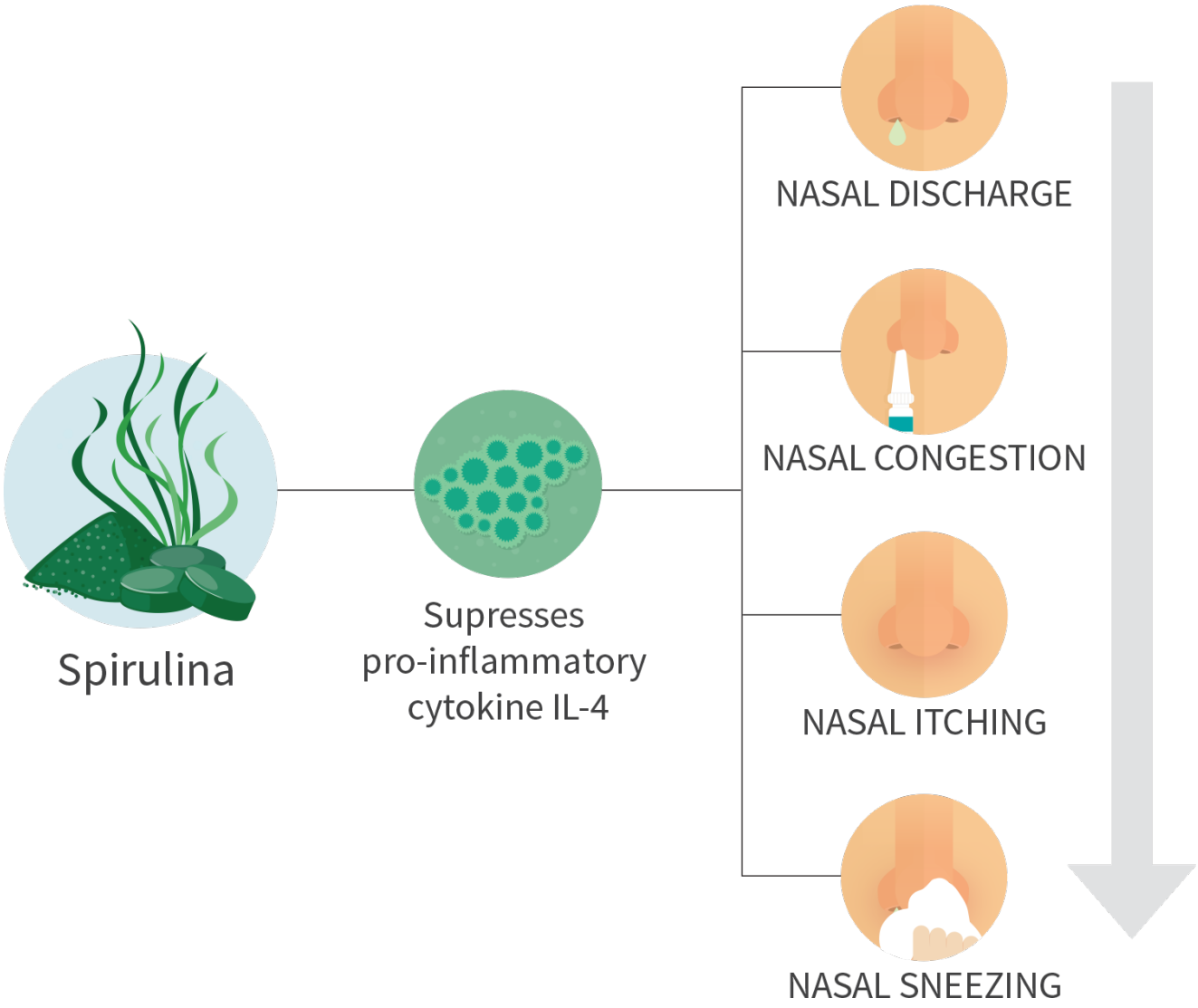
To lower a high frequency of COPD exacerbations, NAC should be taken year-round.

Spirulina

What makes *spirulina* a secondary option

Spirulina is a protein-rich algae that contains anti-inflammatory compounds. Limited evidence suggests that it can reduce symptoms of nasal allergies, such as sneezing or a stuffy nose. Further research is needed to confirm this benefit and determine whether spirulina can ward off sickness.

Effects of spirulina on nasal allergies



How to take *spirulina*

To supplement spirulina, take 2 g/day for at least 12 weeks, with or without food. Spirulina is available as bulk powder, as powder in capsules, and in tablet form.

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.[31][32]

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.

Vitamin E has both antiplatelet and anticoagulant properties — the latter because it interferes with the

blood-clotting properties of vitamin K.[33] 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.[34] 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)

AGE	MALE	FEMALE	PREGNANT	LACTATING
0–12 months	4 / 6*	4 / 6*	—	—
7–12 months	5 / 7.5*	5 / 7.5*	—	—
1–3 years	6 / 9	6 / 9	—	—
4–8 years	7 / 10.4	7 / 10.4	—	—
9–13 years	11 / 16.4	11 / 16.4	—	—
>13 years	15 / 22.4	15 / 22.4	15 / 22.4	19 / 28.4

* Adequate Intake (AI)

Reference: Institute of Medicine. Vitamin E (chapter 6 in *Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids.* The National Academies Press. 2000. DOI:10.17226/9810)

Take 200 IU of vitamin E (134 mg of natural α-tocopherol or 90 mg of synthetic α-tocopherol).[35] 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

Synbiotics

What makes *synbiotics* an unproven option

The gut microbiome is involved in physiological functions that relate to immunity and protection from pathogens. Considering that there is "crosstalk" between the gut microbiota and the lungs (termed the gut-lung axis),[36] it's no surprise that gut dysbiosis (i.e., the disturbance of the gut microbiota balance) has been associated[37] with *respiratory tract infections* (RTIs)[38] — infectious diseases of the upper or lower respiratory tract.

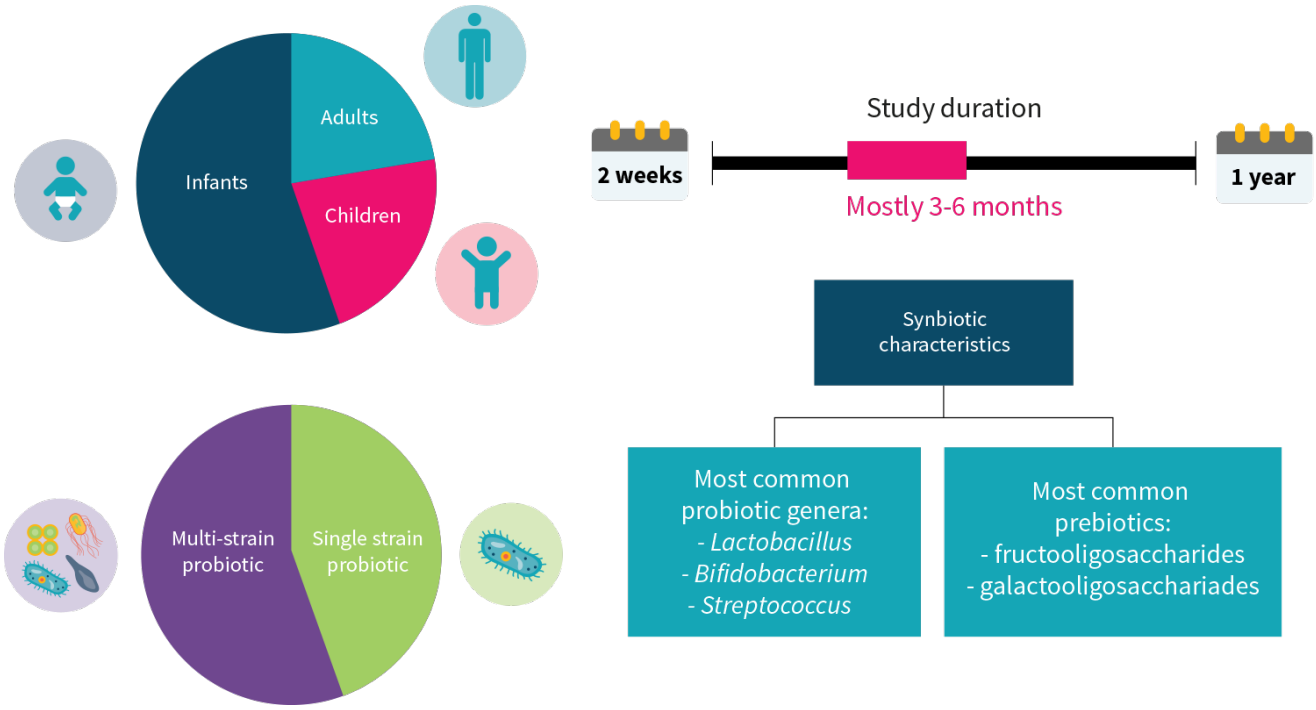
Types of respiratory tract infections

UPPER RESPIRATORY TRACT INFECTIONS (URTIs)	LOWER RESPIRATORY TRACT INFECTIONS (LRTIs)
Common cold	Bronchiolitis
Laryngitis	Bronchitis (acute and chronic)
Otitis media	Pneumonia
Pharyngitis and tonsillitis	Tracheitis
Rhinitis	
Rhinosinusitis, sinusitis	

Since probiotics (live microorganisms that may provide health benefits when used in adequate amounts) and prebiotics (compounds that provide nutrition for the growth of beneficial microorganisms) may have independent beneficial effects on the immune system, it has been suggested that the appropriate combination of both could have synergistic effects.[39] These combinations, called synbiotics, are one potential strategy to help prevent RTIs.[40]

A meta-analysis of 18 randomized controlled and/or placebo-controlled trials involving 10,443 participants examined the overall impact of synbiotic use on RTI prevention.[41] As you can see in the image below, the study characteristics were quite diverse. Additionally, various types of pre- and probiotics were used in different combinations.

Study characteristics



Reference: Chan et al. *Adv Nutr.* 2020.[41]

Compared to the control, synbiotics may reduce the incidence of RTI by 4–27% and the proportion of participants who experienced at least one RTI episode by 5–26%. The wide ranges seen in the results means that the true effect of synbiotic supplementation on RTI prevention may be anywhere from negligible to relatively impressive.

Because of the many differences in the studies currently available, it limits our ability to make specific conclusions about:

- The populations more likely to benefit from synbiotic supplementation
- The minimum and/or optimal treatment duration
- The most effective pre- and probiotic combinations
- The optimal dosing protocols.

More specific and targeted research in future trials may help narrow down some of these variables.

Inadvisable Supplements

Tinospora crispa

What makes *Tinospora crispa* an inadvisable option

> ⚠ ***Caution:*** **This supplement has the potential to harm your health**
>
> Please read the following section carefully. The available evidence indicates this supplement may have harmful effects. It should not be added to your supplement regimen.

Tinospora crispa, not to be confused with Tinospora cordifolia,[42] is an herb traditionally used in Ayurvedic medicine.

Limited evidence suggests that it can alleviate the symptoms of allergies, such as a stuffy nose. Similarly to garlic, it may also prevent infections by improving the ability of white blood cells to fight invaders. Further research is needed to determine whether garlic and *Tinospora crispa* are synergistic.

Data on the toxicity of *Tinospora crispa* in humans are limited. However, in five clinical trials and one case report, enzymes used as indicators of potential liver damage (AST and ALT) were elevated in some of the participants taking *Tinospora crispa*.[43][44][45][46][47] These markers returned to normal after treatment stopped. Such elevations have been seen in animal studies as well. Additionally, there are open questions about the effects *Tinospora crispa* may have on cholesterol, as it *might* cause an increase.[44]

Because current evidence has not shown a benefit of *Tinospora crispa* for immune function and there is some evidence it may be harmful to the liver or cholesterol levels, this herb should not be supplemented.

FAQ

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

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

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

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

Q. Can I modify the recommended doses?

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

Q. At what time should I take my supplements?

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

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

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

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

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

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

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

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

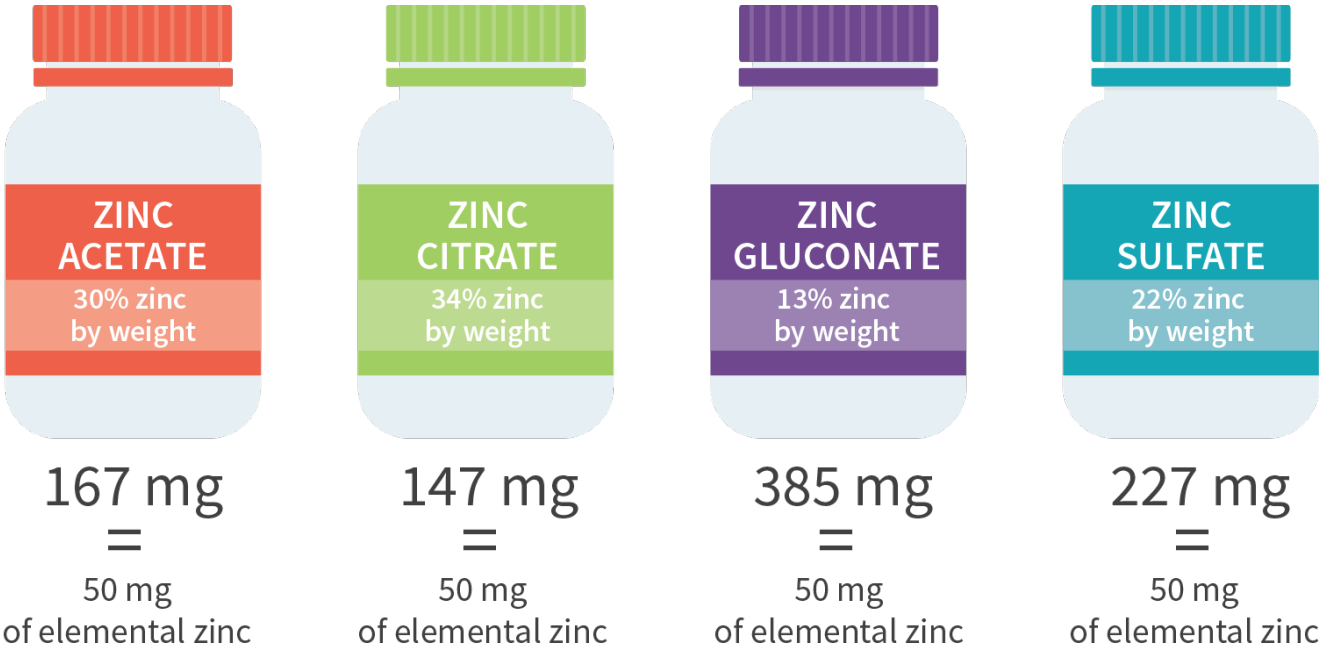
Q. Can I take garlic and vitamin C in one dose instead of three?

Water-soluble vitamins taken in excess are readily excreted. Smaller doses of vitamin C are more easily assimilated and stored (for a few days). Similarly, frequent dosing allows the bioactive compounds in garlic to remain longer in your body. This makes splitting your daily dose more effective, but not to a very great extent in either case, so if you can only manage a single dose per day, you'll still benefit.

Q. What's the difference between elemental zinc and other kinds of zinc?

"Elemental" refers to the weight of the mineral by itself, separately from the compound bound to it. For instance, consuming 50 mg of zinc acetate means consuming 15 mg of elemental zinc. *Product labels display the elemental dosage.* On a label, "15 mg of zinc (as zinc acetate)" means 15 mg of elemental zinc (and 35 mg of acetic acid).

Four different compounds of zinc



Q. A lot of spirulina is farm-grown and harvested. How do I know it is safe?

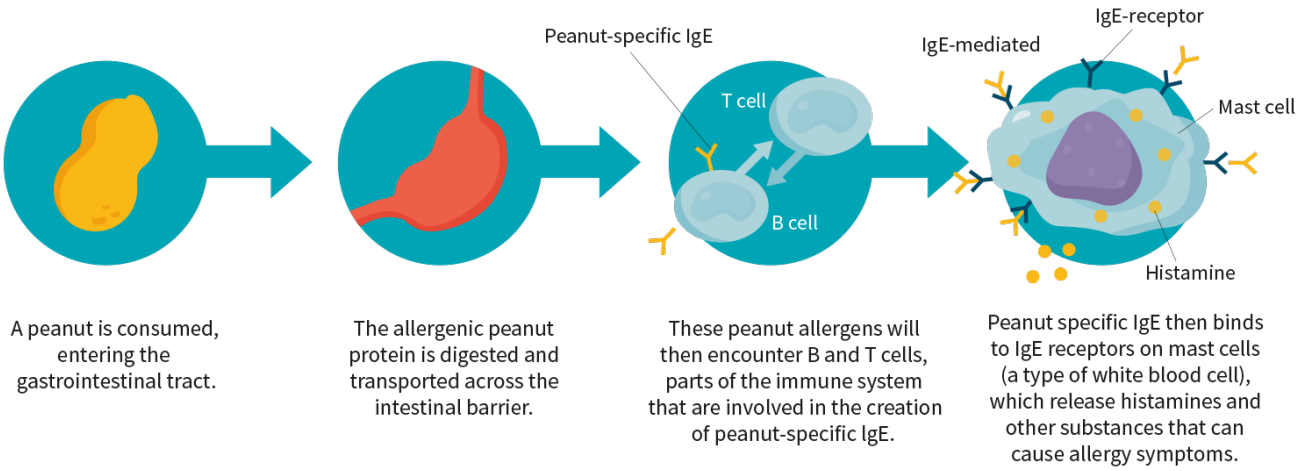
Spirulina is considered a food grade product and is generally rigorously tested. For example, it undergoes microbiological and chemical composition tests as well as tests for contaminants like heavy metals, pesticides, and extraneous materials.

That being said, here's a list of steps you can take to find a high quality spirulina supplement.

Q. Is there anything to help with peanut allergies?

Despite an increase in the number of mothers avoiding peanuts and other common allergy triggers during pregnancy and breastfeeding, the prevalence of peanut allergies actually increased since 1997.[48] About 4.4 million people in the U.S. now have allergies to peanuts,[48] and peanut allergies remain one of the deadliest food allergies.[49]

How peanuts cause allergic reactions



Reference: Burks. *J Clin Invest*. 2003.[50]

There is evidence that introducing infant-safe forms of peanuts (e.g., pureed into a smoothie) can reduce the risk of peanuts allergies. Timing depends on the risk level of the infant, with the highest-risk infants being introduced to peanuts at 4–6 months, with later introduction for lower risk infants.[51][52][53][54][55]

In short: infants at risk for developing peanut allergies who avoided peanut consumption were five times as likely to actually develop the allergy, compared to infants who consumed a peanut product at least three times per week through age 5.[52][53]

But what if you're not an infant?

Fortunately, a medication recently approved in the United States can help temper the consequences of accidental peanut exposure in this group of children. The drug's brand name is Palforzia. It's the first drug approved by the United States Food and Drug Administration for any food allergy, and is indicated for children with peanut allergy aged 4 to 17. However, it can also continue to be taken into adulthood if started in childhood. It doesn't cure peanut allergy; instead, it mitigates the allergic reaction to peanuts upon accidental exposure. However, children taking Palforzia should still avoid peanuts.

Palforzia is made of pharmaceutical-grade powdered peanut allergens that can be sprinkled into semi-solid foods like applesauce and yogurt. However, you can't just pick it up in your local drug store, take it home, and use it. It's only available in specific, licenced locations and patients have to enroll in a special program in order to get the drug. That's because, while it's effective, it does run the risk of inducing a serious allergic reaction.

While Palforzia treatment requires some monitoring in order to maximize safety and not all children can tolerate it, there's good evidence to suggest that it's effective in those children who can tolerate it.[56] Around 66% of children who were highly allergic to peanuts and who reached the maintenance phase after escalating their Palforzia dose could tolerate eating 600 mg of peanut protein (roughly equal to a couple of peanuts), compared to only 4% of children in the placebo group.

The study also included some adults, but there was no statistically significant effect in this age group, which is why Palforzia is only currently approved in children, with the option to continue it into adulthood.

While Palforzia isn't a cure for peanut allergies, and children on the drug still have to avoid peanuts, it's a major step forward in lowering the risk of a serious allergic reaction to accidental peanut exposure.

Q. Do any supplements protect against COVID-19?

Some supplements have evidence for prevention or symptom reduction for the flu or the common cold — nobody knows how well this evidence applies to COVID-19 (if at all). If you opt to supplement with any supplements, including the ones mentioned in this guide, remember that *none* of them have proven efficacy against COVID-19. Harm from supplementation is especially possible with COVID-19 due to unknowns surrounding this virus and its manifestations.

Supplements are not strictly necessary, and they pale in comparison to established preventative measures.[57] *Maintaining proper hygiene should be your primary focus*, as it is the proven option for reducing the risk of spreading or contracting SARS-CoV-2.

Don't let supplements lure you into a false sense of security. If you suspect you have COVID-19, do not rely on supplements as a cure or treatment — contact a healthcare professional.

That being said, The International Society for Immunonutrition (ISIN) has published a position statement on nutrition, immunity, and COVID-19. *For the elderly specifically*, it recommends increasing the daily intake of the following nutrients:

- Vitamin C: 200–2,000 mg
- Vitamin D: 400–4,000 IU (10–100 mcg) if low blood levels
- Vitamin E: 134–800 mg
- Zinc acetate: 30–220 mg

Importantly, they make the following disclaimer:

> *"There is no specific evidence these nutritional measures can help protect against, or even lessen the effects of, COVID-19 infection."*

Let's add that the higher end of their zinc intake range (220 mg) far exceeds the established Tolerable Upper Intake Level (UL) of 40 mg/day.[58] Taking too much zinc for too long can be toxic and cause copper deficiency.[26][27] *Do not exceed the UL for zinc for more than 2 weeks unless under the direction and supervision of a physician.*

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