



Table of contents

How this works

Introduction

Your Genetics

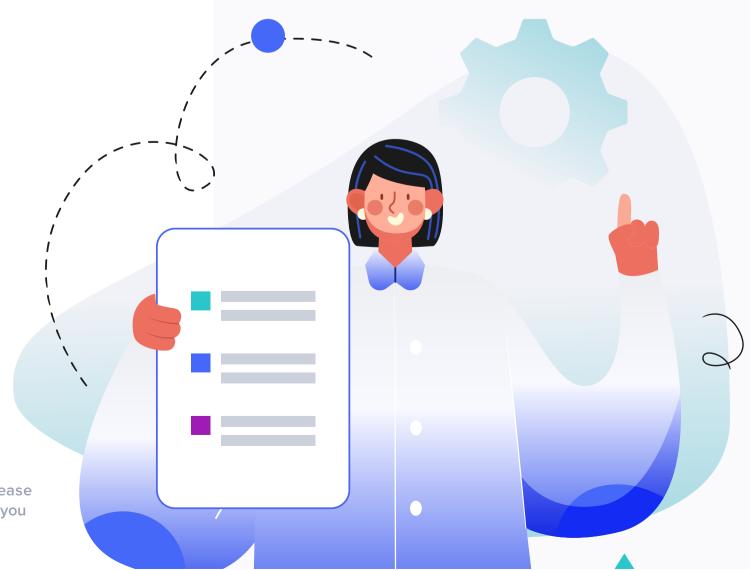
Your Recommendations

REPORT PROVIDED BY

Get Tested International AB

for Dummy Persson (EQMQH2-DNA)

https://gettested.io



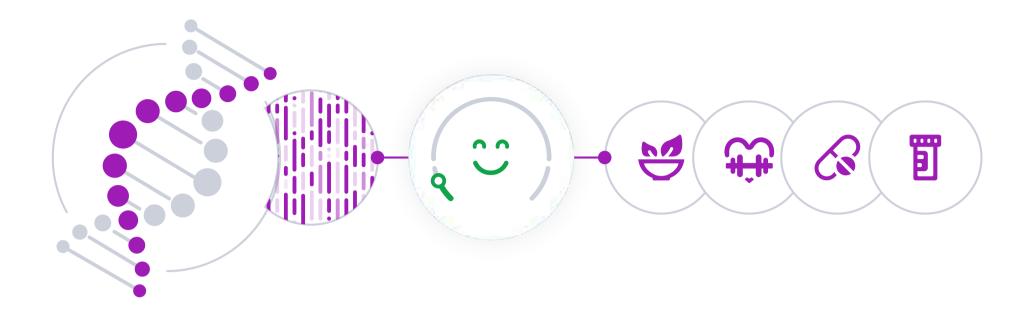
DISCLAIMER

This report does not diagnose this or any other health conditions. Please talk to a healthcare professional if this condition runs in your family, you think you might have this condition, or you have any concerns about your results.

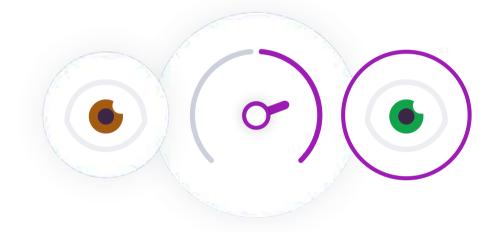
How this works

Our Health Reports analyze how your DNA influences your health.

We then use this analysis to give you personalized risk estimates and recommendations.



Similarly, our Trait Reports look at how your DNA influences your traits.



Your DNA is like an instruction manual — it contains a lot of information. You can think of it as a blueprint for your body.

Genetic variants are parts of DNA that differ from person to person. Some can make you more vulnerable to certain health issues, while others may influence traits such as eye color.



We use artificial intelligence and machine learning to analyze all this information. We then summarize your results as a risk score or display it on a gauge.

When we give a risk score, the risk icon tells you if you are at a higher or lower risk compared to other people:

In total, we analyze up to 83 million genetic variants.



Your risk is also displayed as a percentile. This will tell you how your risks compare to our sample population. The lower your percentile number, the lower your risk. The "50th percentile" would be an average risk.

Similarly, the gauge tells you your relative risk score compared to our sample population, or it indicates a specific trait or haplotype you are more likely to have based on your genetic variants.

When applicable, we also list top evidence-based recommendations that may help lower your risk. The focus is on recommendations that may be of benefit to you, based on your genetics.

Our recommendations come in four categories: diet, lifestyle, supplements, and drugs. The following icons tell you which category a recommendation falls into:









Our team of scientists also ranks each recommendation. We rank based on impact and strength of evidence.

Impact shows how strongly a recommendation will affect your health in a certain area. Evidence reflects how much scientific support there is for the recommendation in the medical literature. Rankings are from 1 to 5 (low to high):

■ ■ ■ ■ 3 / 5

EVIDENCE 4/

Impact

Impact scores range from 1-5. These scores reflect how much of an effect each recommendation can have. An impact score of 5 predicts the biggest effect.

When a recommendation affects something we can measure, we use those measurements to assign the impact score. For example, a recommendation that decreases cholesterol by 20% will have a higher impact score than one that decreases it by 5%.

Some recommendations affect things that we cannot directly measure, like stress or mood. For these, the impact score is based on how well they work relative to other recommendations and standard treatments. The best ones get the highest scores.

If there is a lot of research that shows a recommendation works especially well for your genotype, the impact score gets increased.

Recommendation Evidence

9 9 9 9 5 / 5

Recommendations that are considered effective and generally recommended by experts and medical bodies.

4/5

Recommendations that are considered likely effective and that have multiple independent meta-analyses and a great many studies supporting them.

3/5

Recommendations that are considered possibly effective and have many studies supporting them.

2/5

Recommendations that have insufficient evidence, with two or several clinical trials supporting them, or many studies but with ambiguous results.

---- 1/5

Recommendations that have insufficient evidence, with a single clinical trial, or with many studies most of which didn't find support for the recommendation.

---- 0/5

No evidence in humans.

Genotype-specific evidence

■ ■ ■ ■ High-quality

Direct evidence that a recommendation helps more in people with your gene variant (many clinical trials, a few large clinical trials, or a meta-analysis).

■ ■ ■ ■ Medium-quality

Direct evidence that a recommendation helps more in people with your gene variant (a few clinical trials or one large clinical trial).

Low-quality

Direct evidence that a recommendation helps more in people with your gene variant (a single clinical trial or more trials with inconsistent results).

Indirect

A recommendation may help more in people with your gene variant because it targets a specific gene or protein affected by your variant (e.g., MTHFR, dopamine).

■ ■ ■ ■ In theory

A recommendation may help more in people with your gene variant because it targets a specific mechanism affected by your variant (e.g., inflammation, oxidative stress).

Some things to keep in mind:

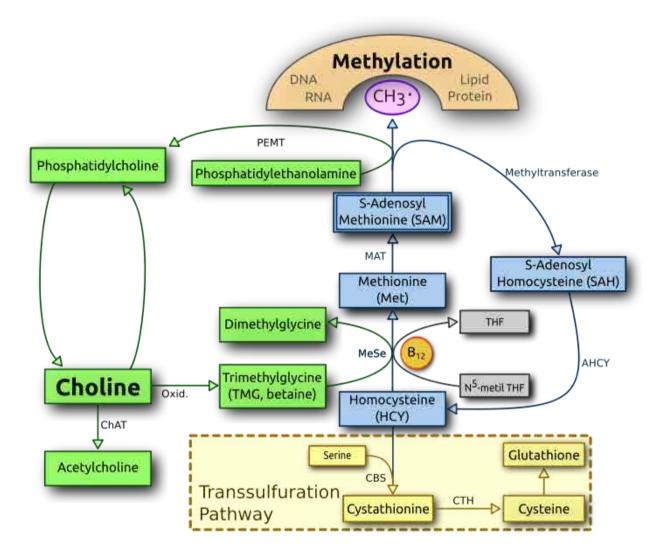
- The scores/gauges use the latest scientific studies. But they are not perfect and will change as the models improve.
- Not everyone with risk variants will develop a health condition.
- Genetics is not the whole story. Your health is most often a combination of genetics, lifestyle, and environmental factors. Great news, as this means that you can often change your lifestyle to lower your risk.
- Results might be more accurate for some ethnic groups than others. This depends on the studies used in each report.
- People without risk variants can also develop health conditions.
- It's important to work with your doctor to better understand your risks. Our reports do not diagnose or treat any health condition. They are not a substitute for medical advice. If you're diagnosed with a certain health condition, follow your doctor's advice.

About Methylation

On a chemical level, methylation is when a methyl group is transferred from one compound to another. Methyl groups are small backbones for organic compounds, the chemical compounds of all living beings that are found in every cell of your body.

Methyl groups are also switches that turn on or off genes based on environmental cues. This is called *epigenetics*. Additionally, methyl groups signal which hormones, brain chemicals, and amino acids need to be broken down and removed, maintaining a healthy balance in the body.

On a deeper level, the methylation cycle involves several steps outlined in the image below:



Starting from the **MTHFR** enzyme and folate you take in with food, the methylation cycle produces the active vitamin methylfolate that circulates in your bloodstream (5-methyl THF). This step is crucial for turning harmful homocysteine into methionine [R].

This pathway also relies on vitamin B12 and enzymes, including MTR and MTRR.

The other pathway for clearing homocysteine uses betaine derived from choline. It relies on the **CHDH** and **BHMT** enzymes.

In the next step, methionine obtained via these pathways creates SAM-e (S-adenosyl-methionine), a compound that provides a methyl group for methylation [R, R].

Methionine also helps produce phosphatidylcholine via the **PEMT** enzyme. This cycle reveals a close connection between the genes and enzymes involved in choline, folate & vitamin B12 metabolism [R, R].

The third pathway for clearing homocysteine, the so-called *transsulfuration pathway*, helps produce glutathione, a.k.a the "master" antioxidant. This pathway relies on vitamin B6 and the **CBS** enzyme.

These reactions — collectively known as the **one-carbon metabolism** — are vital for many aspects of physical and mental health. Issues with the methylation cycle play a role in heart health, mental health, fertility problems, birth defects, cancer, and more [R, R, R].

Methylation Genetics

The optimal function of the pathways discussed above depends on a number of enzymes that enable chemical reactions. Gene variants in some of those enzymes can alter their function and potentially compromise methylation.

Please note: Methylation is a complex process that goes way beyond the pathways and enzymes discussed in this report. There is insufficient evidence that any of the gene variants analyzed in this report impair methylation and its vital roles in the human body.

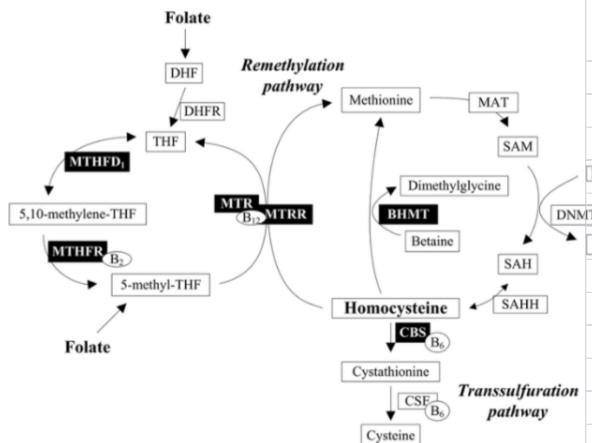


Image source: Huang, et al. 2020

MTHFR

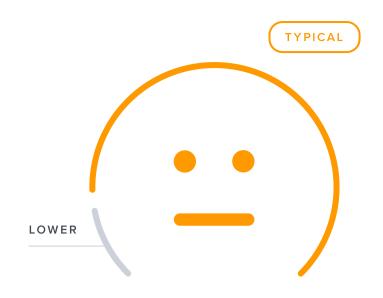
The <u>MTHFR</u> gene helps make an enzyme called methylenetetrahydrofolate reductase (MTHFR). It produces the active form of folate, methylfolate [R].

The whole methylation cycle depends on MTHFR, which is why it is called a "rate-limiting enzyme". Low MTHFR activity can make methylation as a whole much less productive [R].

Two of the most widely studied variants—rs1801133 and rs1801131—reduce MTHFR enzyme activity [\mathbb{R} , \mathbb{R}].

Studies found links between these variants, higher homocysteine, and [R, R, R, R, R]:

- Cognitive problems
- Heart disease and stroke
- Asthma and allergies



Likely typical methylation ability based on 30 genetic variants we looked at

	PREDISPOSITION	
GENE	SNP	GENOTYPE
MTHFR	rs1801131	TG
GNMT	rs9296404	ŢŢ
PEMT	rs7946	TT
NA MTHFD1	rs2236225	AA
SHMT1	rs1979277	AA
ONA meth@@iMiT	rs4680	GA
MTRR	rs1801394	GA
внмт	rs651852	СТ
DHFR	rs1643649	CC
TRDMT1	rs12780845	AA
CHDH	rs9001	II
MTR	rs1805087	AA
FOLH1	rs61886492	GG
MTRR	rs1532268	TC
ENOSF1	rs2853533	GC
PRXL2A	rs3851059	GA
BHMT2	rs625879	AC
PEMT	rs12936587	AG
PRXL2A	rs7087728	AG
MTHFR	rs1801133	GG

Read this blog post for more details about MTHFR variants and potential ways to reduce their impact.

Other Genes

The PEMT gene encodes an enzyme that produces phosphatidylcholine (PC) in the liver. This pathway supplies choline and thus plays a key role in the methylation cycle [R, R].

PEMT gene variants like rs7946 **and** rs12325817 are linked to:

- Choline deficiency
- Fatty liver
- Heart disease

The MTHFD1 gene encodes an enzyme that helps produce active folate and supports homocysteine methylation. A variant in this gene, rs2236225, is linked to increased choline and folate needs [R, R, R].

The MTRR gene encodes an enzyme that helps turn homocysteine into methionine, using vitamin B12 and riboflavin. MTRR variants like rs1801394 have been linked to [R, R]:

- Higher homocysteine levels
- Congenital disorders (mixed evidence) [R, R, R]
- Some types of cancer [R, R]
- Male fertility issues (mostly in Asians) [R, R]
- ADHD in children [R]

The CHDH gene codes for choline dehydrogenase, an enzyme that turns choline into betaine or TMG. Betaine then supplies a methyl group needed for homocysteine clearance. CHDH gene variants like rs9001 are linked to choline deficiency and may thus affect methylation [R, R].

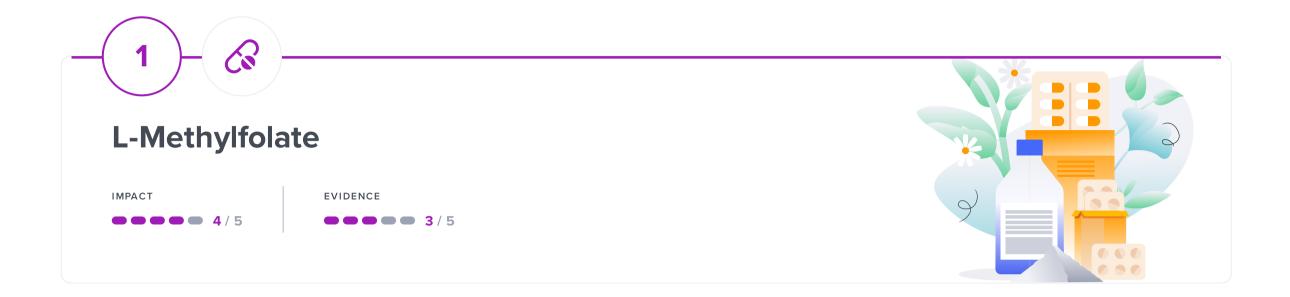
Variants in the following genes may also affect methylation and play a role in related health issues:

- CBS: a key component of the transsulfuration pathway [R, R, R]
- BHMT: helps turn homocysteine into methionine [R, R, R]
- COMT: methylates important chemicals by using SAM-e [R]
- SHMT1, DHFR, FOLH1: involved in folate metabolism [R, R, R, R]
- GNMT and DNMT3B: play a role in SAM-e metabolism [R, R]
- MTR: helps turn homocysteine into methionine [R]
- MAT1A: helps turn methionine into SAM-e [R]
- TRDMT1: plays a role in DNA methylation [R]
- PDXK: plays a role in vitamin B6 metabolism [R]
- AHCV involved in homogysteine and SAM-a

Your Recommendations

Your recommendations are prioritized according to the likelihood of it having an impact for you based on your genetics, along with the amount of scientific evidence supporting the recommendation.

You'll likely find common healthy recommendations at the top of the list because they are often the most impactful and most researched.



L-methylfolate is a biologically active form of folate, a B-vitamin that plays a crucial role in various bodily functions, including DNA synthesis and mood regulation. It is used as a supplement to support mental health and manage certain medical conditions.

L-methylfolate (5-MTHF or levomefolic acid) is the main "active" form of folate that helps build DNA, reduce homocysteine, and more [R].

It is also available as a supplement. Some resources claim L-methylfolate is superior to folic acid because it doesn't require activation, but the research is still ongoing [R].

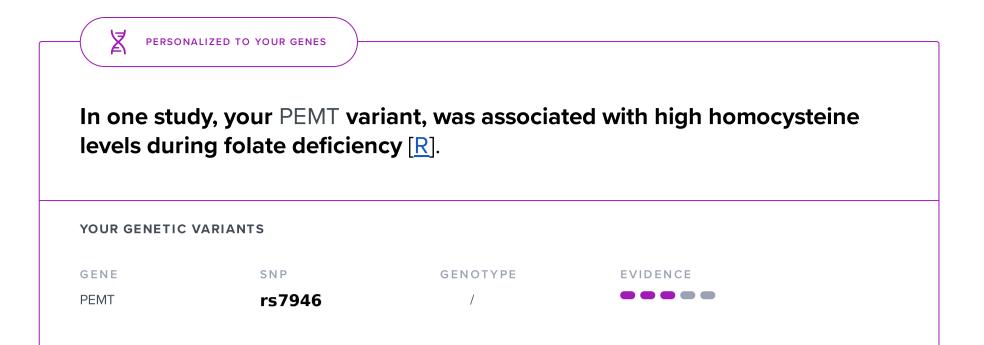
How L-Methylfolate helps with Methylation

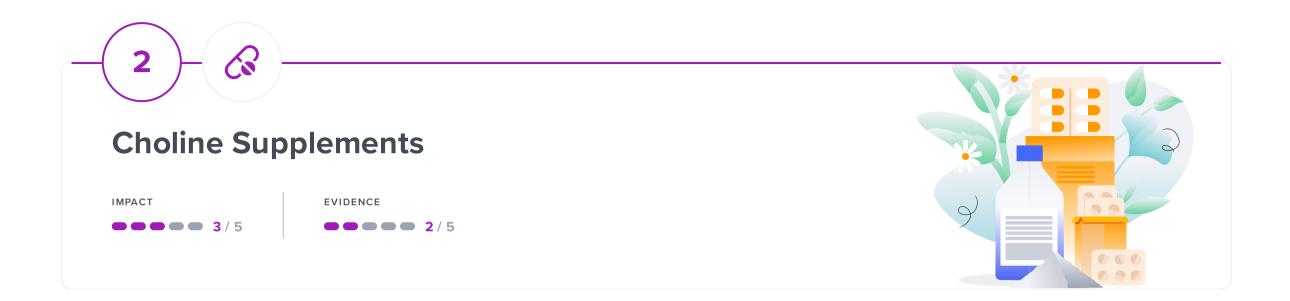
Folate supplements may help by providing more of this vitamin and enhancing homocysteine methylation, especially in pregnant women and those planning to conceive. Most supplements contain the recommended daily amount of 400 mcg [R].

People with methylation issues may not be able to produce enough methylfolate, which is the active form. Supplementing with active <u>L-methylfolate</u> should help bypass this issue, but the research is still limited [R, R].

Supplementation with folate (0.5-1 mg/day), both alone and combined with <u>vitamin B12</u>, may lower homocysteine levels in healthy people, those at risk of heart disease or cognitive decline, and patients with type 2 diabetes. A dose of 0.8 mg/day may be most effective [R, R, R, R, R, R].

The combination of folate, vitamin B12, vitamin B6, and omega-3 fatty acids may further lower homocysteine levels [R].





Choline is an essential nutrient that plays a crucial role in various bodily functions, including brain health, liver function, and metabolism. Incorporating choline-rich foods into your diet supports cognitive function and overall nutritional well-being.

<u>Choline</u> is a nutrient required for optimal health. Although the body makes some, we need to get choline from our diets to avoid deficiency [R].

It plays key roles in supporting [R, R]:

- DNA production
- Cell structure and function
- Brain, nerve, and heart health

Eggs and beef liver are the best sources of choline. If you can't meet your daily requirements with food, consider taking a choline supplement such as [R]:

- Phosphatidylcholine (PC)
- Citicoline (CDP-choline)
- Alpha-GPC
- Lecithin

They all supply choline, but each one has unique health perks you may prefer. Check out our posts on different choline-containing supplements to find out which one suits you best.

How Choline Supplements helps with Methylation

Choline is a crucial nutrient in the methylation cycle. It provides betaine (TMG), which helps clear homocysteine. Betaine donates methyl groups to homocysteine, converting it to methionine. This process is crucial for maintaining cellular function, gene expression, and neurological health [R].

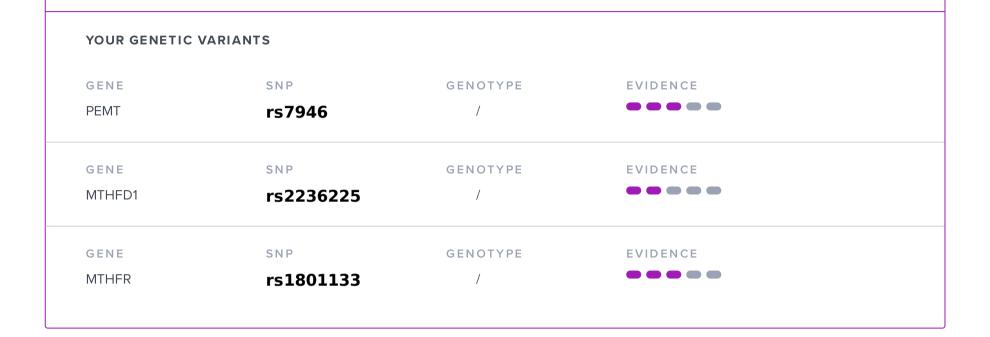
People with methylation issues may have increased choline needs. Insufficient choline can disrupt this cycle, leading to impaired methylation and associated health issues like liver dysfunction, neural tube defects, and more [R].

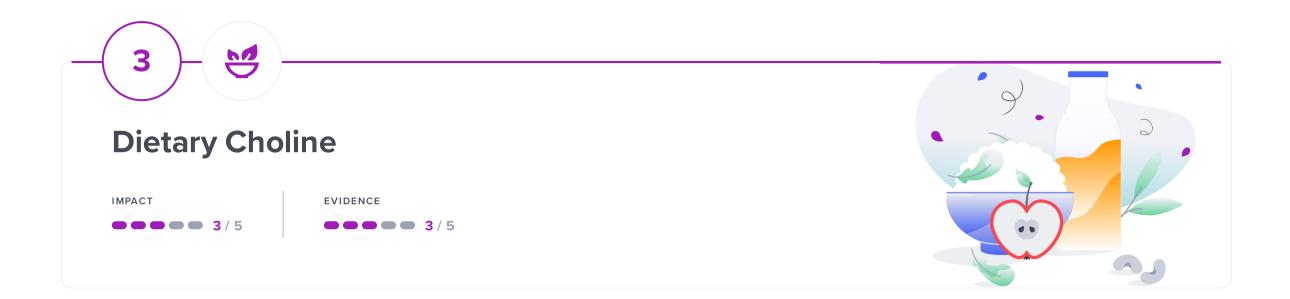


Your PEMT variant may be linked to higher homocysteine levels and fatty liver due to choline deficiency. Getting enough choline may cancel out the negative effects of this variant [R, R].

Your MTHFD1 gene variant is linked to choline deficiency, birth defects, and other methylation-related health problems. Getting enough choline may lessen the impact of this variant [R, R, R].

Choline supplementation may preserve DNA methylation more in people with your MTHFR gene variant [R].



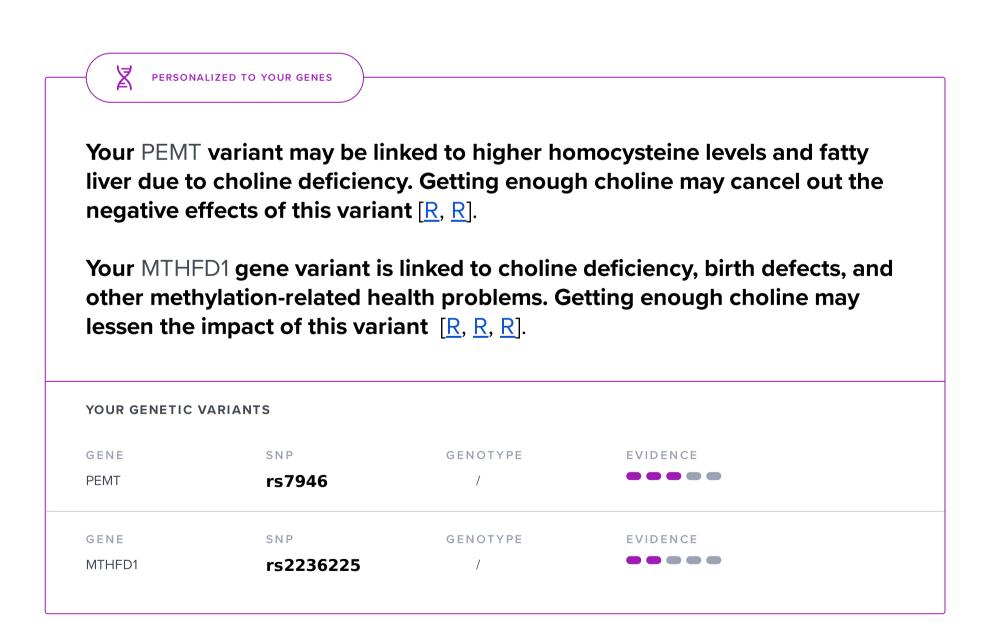


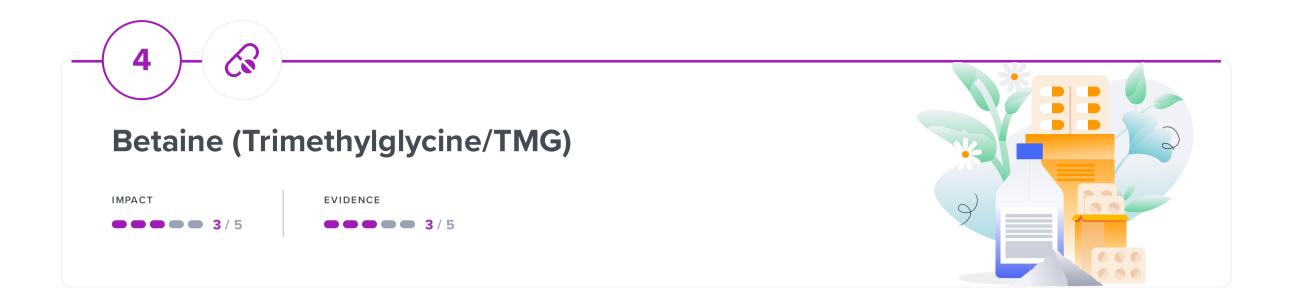
Choline is an essential nutrient that supports brain function, nerve signaling, and liver health. It is involved in neurotransmitter synthesis and cell membrane structure.

How Dietary Choline helps with Methylation

Choline is a crucial nutrient in the methylation cycle. It provides betaine (TMG), which helps clear homocysteine. Betaine donates methyl groups to homocysteine, converting it to methionine. This process is crucial for maintaining cellular function, gene expression, and neurological health [R].

People with methylation issues may have increased choline needs. Insufficient choline can disrupt this cycle, leading to impaired methylation and associated health issues like liver dysfunction, neural tube defects, and more [R].





Betaine is a compound found in various foods and used in dietary supplements for its potential to support liver health and contribute to healthy homocysteine levels.

Betaine (TMG) is a compound found in various foods and used in dietary supplements for its potential to support liver health and contribute to healthy homocysteine levels.

How Betaine (Trimethylglycine/TMG) helps with Methylation

TMG or betaine helps turn homocysteine into methionine. For this reason, it plays a key role in the methylation cycle.

People with poor methylation may have reduced betaine production. To make up for this effect, consume a variety of betaine-rich foods such as [R]:

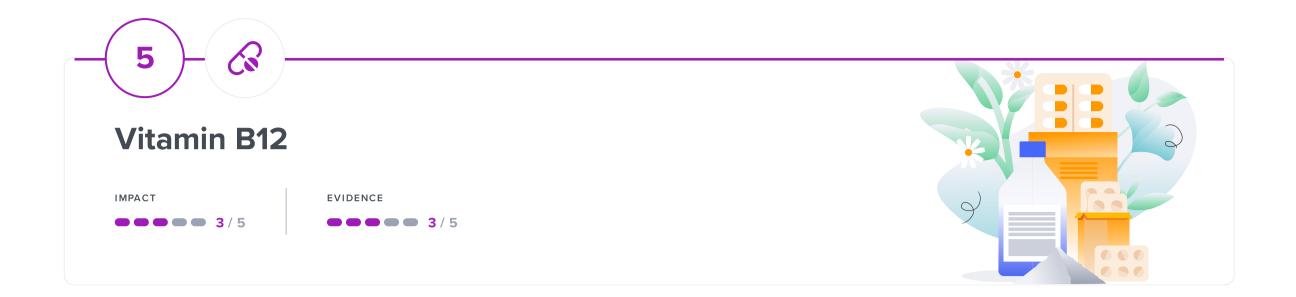
- Liver meats
- Quinoa
- Beets
- Wheat germ
- Spinach

A study of 860 mothers observed much lower neural tube defect rates for the highest vs. lowest dietary intakes of choline, betaine, and methionine [R].

Supplementing with TMG (1.5-4 g/day for 6-24 weeks) may lower homocysteine levels $[\underline{\mathbb{R}}, \underline{\mathbb{R}}]$.

Homocystinuria is a rare genetic disorder that results in elevated homocysteine levels in the urine. In people with this condition, TMG is approved by the FDA to lower urinary homocysteine [R].

Please note: doses above 4 g/day may increase LDL and triglyceride levels. TMG supplementation can cause a person's urine and sweat to smell fishy [R, R].



Vitamin B12 is a water-soluble vitamin primarily found in animal-based foods like meat, fish, and dairy products. It plays a crucial role in maintaining healthy nerve cells, DNA synthesis, and red blood cell formation. Vitamin B12 deficiency can lead to anemia, neurological issues, and fatigue.

Vitamin B12 is important for [R, R]:

- Building DNA
- Nervous system function
- Energy production

You can get vitamin B12 from [R]:

- Animal products (meat, fish, eggs, and dairy)
- Fortified foods
- Supplements

Adults should be getting **2.4 micrograms** of vitamin B12 every day [R].

How Vitamin B12 helps with Methylation

People with methylation issues may have higher homocysteine and increased needs for vitamin B12 [R].

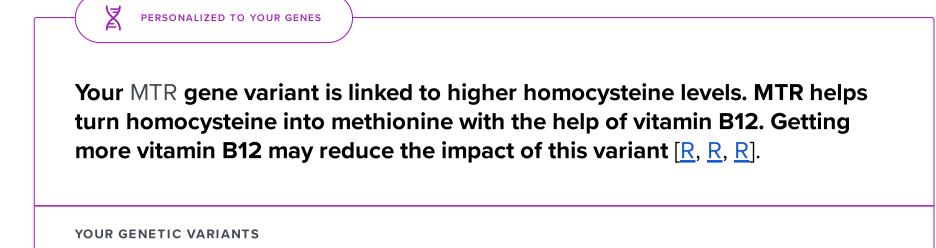
Supplementation with vitamin B12 (1 mg/day) may lower homocysteine levels in older people [R, R, R].

Methylcobalamin is the active form of vitamin B12 that might be more suitable for people with poor methylation [R].

In people supplementing with <u>folate</u>, taking vitamin B12 (0.5 mg/day), may further lower homocysteine levels. The combination may work in healthy people and those at risk of dementia or heart disease [R, R, R, R].

The combination of folate, vitamin B12, vitamin B6, and omega-3 fatty acids may further lower homocysteine levels [R].

B vitamins are required for the enzymes that break down homocysteine to work [R].



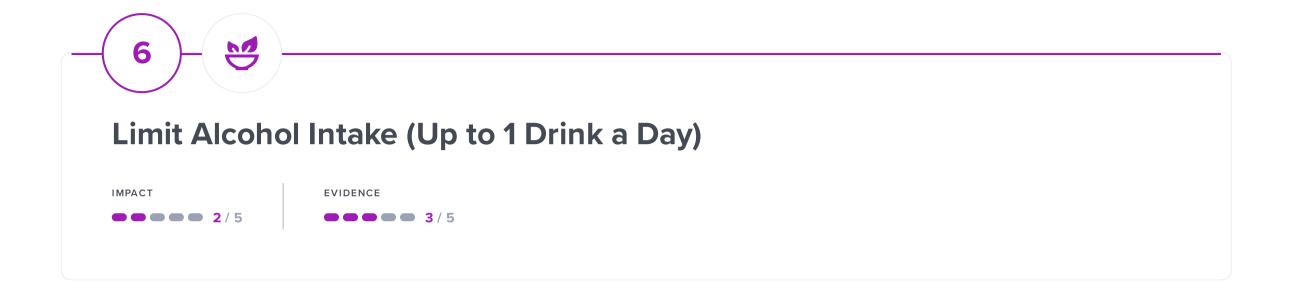
EVIDENCE

SNP GENOTYPE

rs1805087

GENE

MTR



Limiting alcohol intake is associated with numerous health benefits, including reduced risk of liver disease, cardiovascular problems, and certain types of cancer. However, experts agree that limiting alcohol intake to 1-2 drinks per day won't likely cause harm.

Many people drink alcohol in their free time. For some, alcohol can temporarily improve their mood and mental state [R].

Experts agree that having 1-2 drinks per day likely won't cause harm. However, heavy drinking is bad for your health [R].

How Limit Alcohol Intake (Up to 1 Drink a Day) helps with Methylation

Excess alcohol consumption depletes B vitamins and increases the risk of choline deficiency. Limit alcohol intake, especially if you are a poor methylator [R].

Alcohol can also worsen the impact of your genetics by blocking key enzymes like MTR and PEMT [R, R].

Chronic excessive alcohol consumption can wreak havoc on your liver. It causes fatty liver, inflammation, and scarring [R, R].

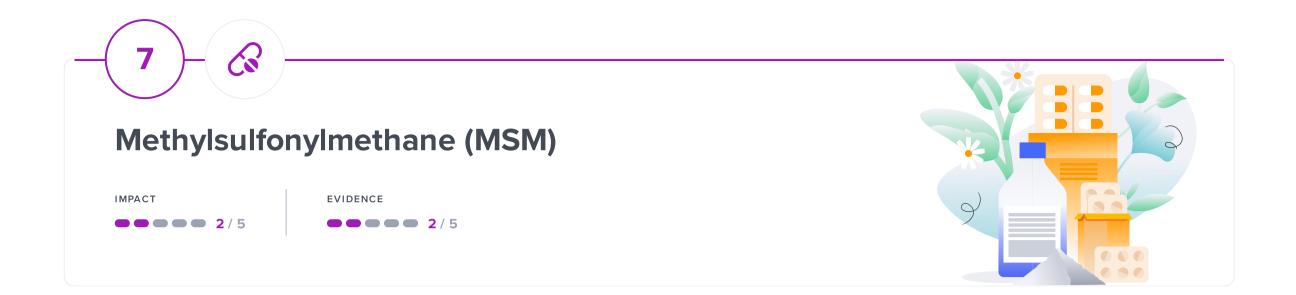
Adverse effects of excess alcohol on the methylation cycle can increase the risk of different congenital disorders, known as fetal alcohol spectrum disorders (FASD) [R].



Your MTHFD1 gene variant is linked to choline deficiency, birth defects, and other methylation-related health problems. Excess alcohol may contribute to choline deficiency and birth defects, worsening the impact of this variant $\boxed{\mathbb{R}}$.

Your PEMT variant may be linked to choline deficiency, high homocysteine levels, and fatty liver. Alcohol may worsen choline deficiency and fatty liver by blocking the PEMT enzyme [R, R, R].

YOUR GENETIC V	/ARIANTS			
GENE MTHFD1	snp rs2236225	GENOTYPE /	EVIDENCE	
G E N E PEMT	snp rs7946	GENOTYPE /	EVIDENCE •••••••••••••••••••••••••••••••••••	



MSM is a naturally occurring sulfur compound found in foods and used in dietary supplements. It has anti-inflammatory properties and may be used to support joint health and reduce exercise-related muscle soreness.

A molecule of MSM is broken down in the body into a sulfate (sulfur) group and two methyl groups.

The following may increase people's needs for sulfur and methyl groups: physical activity, recovery from injuries, inflammation, infections/sickness, toxins, etc.

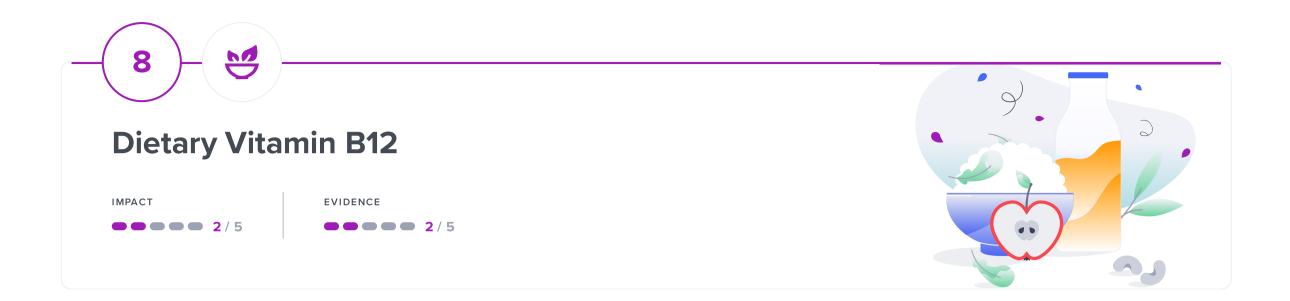
People also need more sulfur when taking hormones (DHEA, pregnenolone, etc.), drugs (Aspirin, Tylenol, NSAIDs, birth control, etc.) or supplements (flavonoids & polyphenols - resveratrol, quercetin, curcumin, etc.) that undergo sulfation.

How Methylsulfonylmethane (MSM) helps with Methylation

MSM can act as a methyl donor in the body. MSM contains sulfur and methyl groups (-CH3) in its molecular structure. The presence of these methyl groups allows MSM to participate in methylation processes.

As a source of sulfur, MSM contributes to the synthesis of sulfur-containing amino acids like methionine, which can help in methylation. MTHFR MSM may thus support MTHFR indirectly

Accordingly, it reduced homocysteine levels in some small trials [R, R].

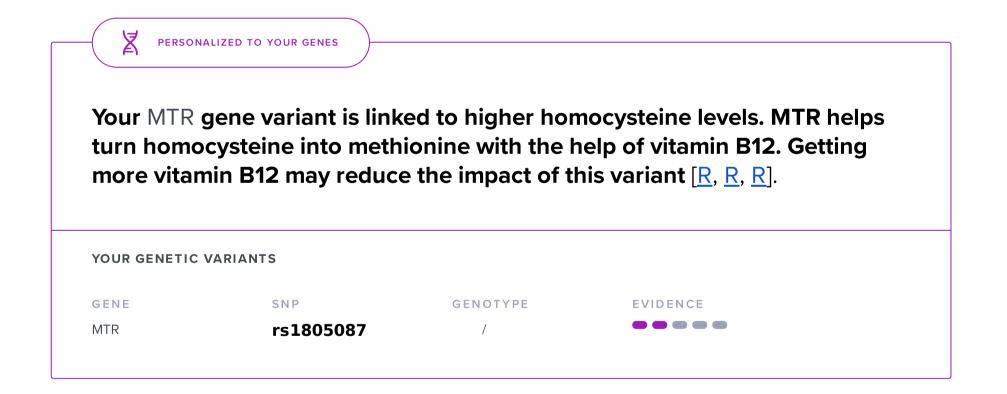


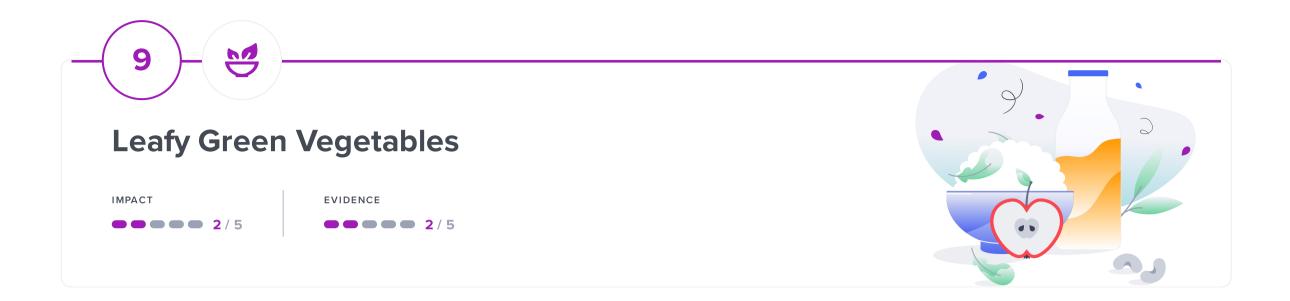
Vitamin B12 is important for nerve function, red blood cell production, and overall energy metabolism. It's crucial for preventing pernicious anemia and maintaining neurological health.

How Dietary Vitamin B12 helps with Methylation

People with methylation issues may have increased needs for B vitamins, especially B12 and folate. B12 is crucial for removing homocysteine, which tends to be higher in people with poor methylation [R].

High dietary intake of vitamin B12 is associated with lower homocysteine levels $[\mathbb{R}, \mathbb{R}]$.





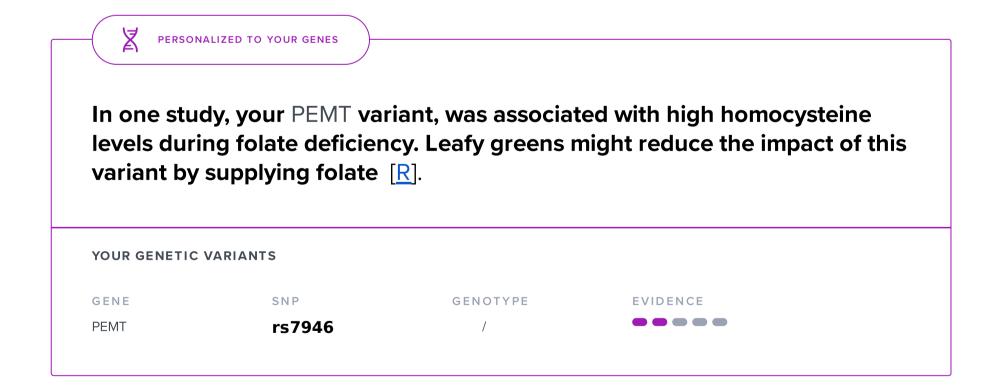
Leafy green vegetables like spinach and kale are packed with vitamins, minerals, and antioxidants. Incorporating them into your diet can promote overall health by providing essential nutrients, supporting digestion, and reducing the risk of chronic diseases like heart disease and certain cancers.

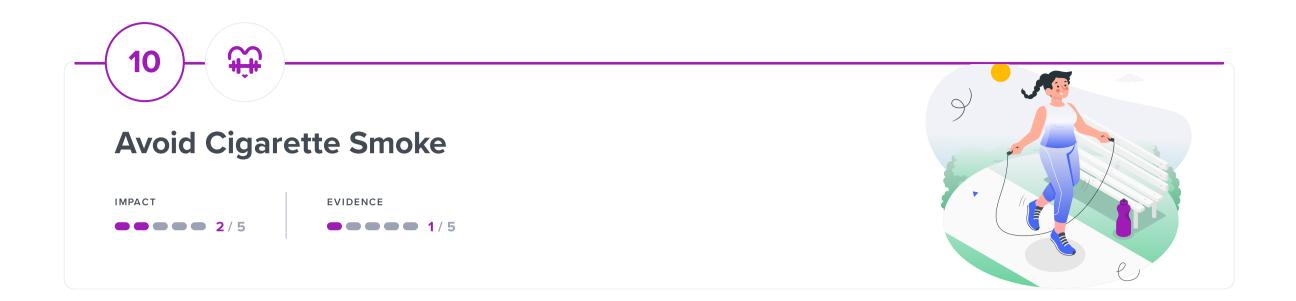
Leafy green vegetables, also called leafy greens, or greens, are edible plant leaves, which can include stalks and shoots as well. Common examples include: lettuce, spinach, kale, chard, endive, and fennel.

Leafy greens contain a host of vitamins and minerals, as well as fiber. Most of them are a particularly good source of vitamin K.

How Leafy Green Vegetables helps with Methylation

Leafy greens are rich in folate, which is critical for methylation pathways in the body. Regular consumption ensures a steady supply of this methyl-donor nutrient.





Avoiding exposure to cigarette smoke is crucial for protecting respiratory health and reducing the risk of serious diseases such as lung cancer and cardiovascular problems. It also helps create a smoke-free environment that benefits both smokers and non-smokers.

You already know that tobacco is not great for your health. **Smoking affects your entire body.** It can damage your brain, heart, lungs, and more [R].

Even if you're not a smoker, take care to avoid secondhand smoke. It can cause health issues similar to smoking [R, R].

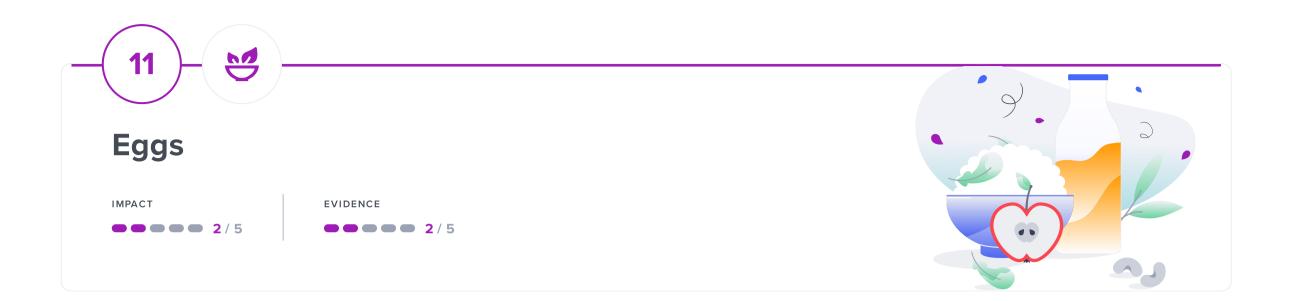
But, there's good news: avoiding cigarette smoke can reverse many of its negative effects. It's a great way to dramatically improve your health [R].

How Avoid Cigarette Smoke helps with Methylation

Cigarette smoke can impair methylation, through several mechanisms.

Smoke contains toxic compounds like arsenic, cadmium, and nickel, which can inhibit the activity of enzymes involved in the one-carbon cycle, such as methionine synthase and MTHFR. This disruption leads to decreased production of SAM-e, the primary methyl donor for DNA methylation.

Secondly, cigarette smoke increases oxidative stress in cells, producing reactive oxygen species (ROS) that can deplete folate and other B vitamins essential for the one-carbon cycle. Lower levels of these vitamins compromise the methylation process.

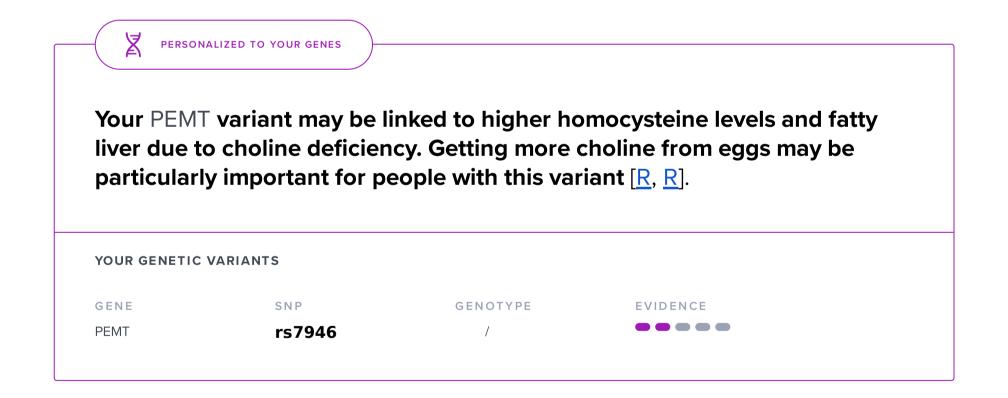


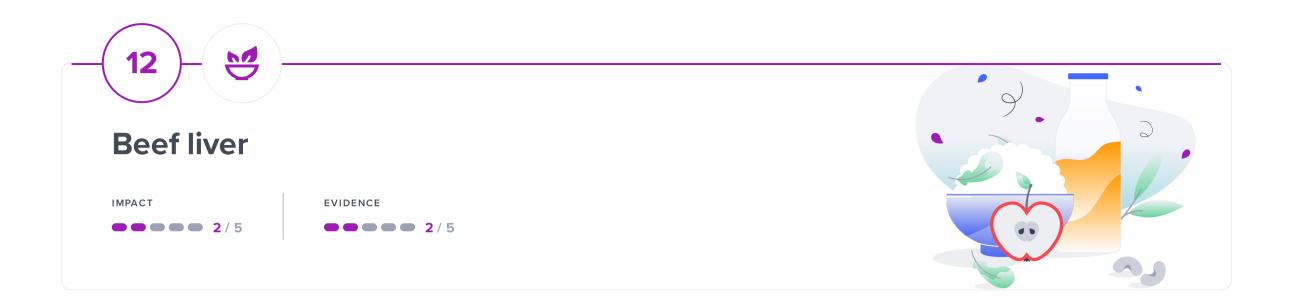
Eggs are a nutrient-dense food rich in protein, vitamins, and minerals. They support various aspects of health, including muscle development, brain function, and eye health.

Eggs are great nutrition sources, with protein, healthy fats, arachidonic acid, and numerous vitamins and minerals.

How Eggs helps with Methylation

Eggs are rich in choline and methionine, which are used in the body's methylation processes, especially in liver function and brain development.



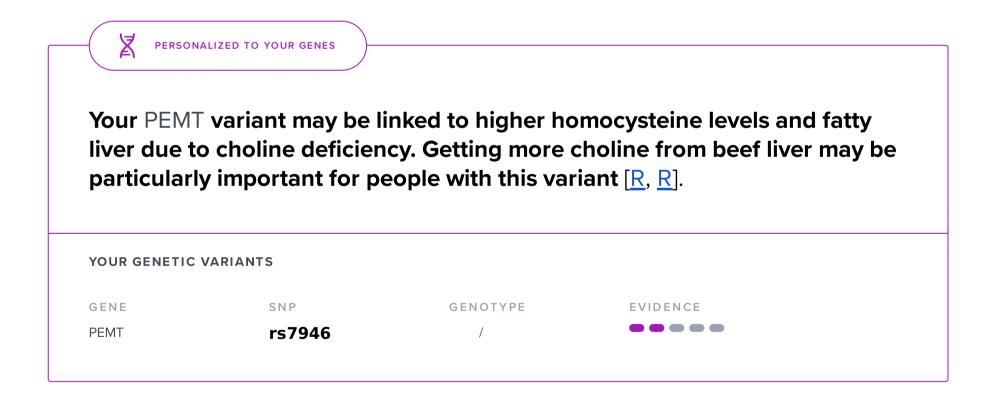


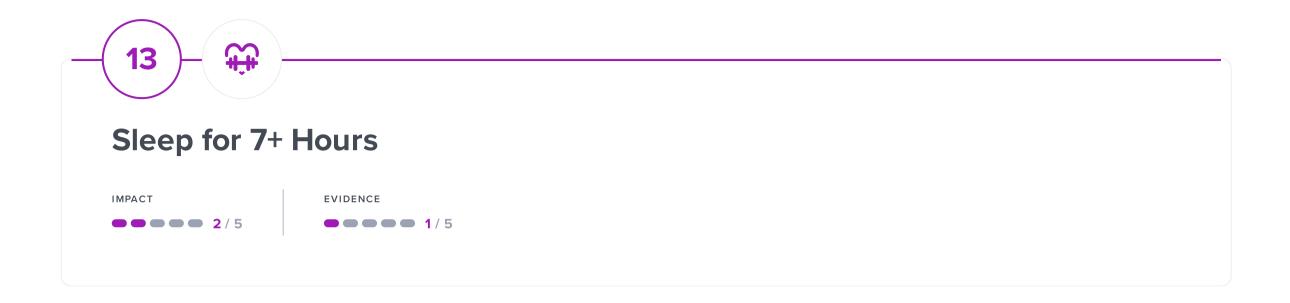
Beef liver is a commonly recommended organ meat due to its rich content of protein, B-vitamins, and minerals.

Chickpeas are a good source of vitamin B6, iron, folate, fiber, and rich in minerals like copper, zinc, and phosphorus. A $\frac{1}{2}$ cup serving provides 1.1 mg of vitamin B6 or 65%DV.

How Beef liver helps with Methylation

Beef liver is a nutrient-dense source of bioavailable choline, folate, and vitamins B12 and B6, which are necessary for effective methylation.





Optimizing sleep involves adopting healthy sleep habits and creating a sleep-conducive environment to ensure restorative and sufficient sleep duration. It supports cognitive function, mood stability, and overall physical health. Most experts recommend getting at least 7 hours of good-quality sleep each night.

Sleep supports your body and mind [R, R]. More precisely, sleep helps:

- Support brain health [R, R]
- Maintain a healthy weight and appetite [R, R, R]
- Regulate blood pressure [R, R]
- Balance blood sugar [R, R]

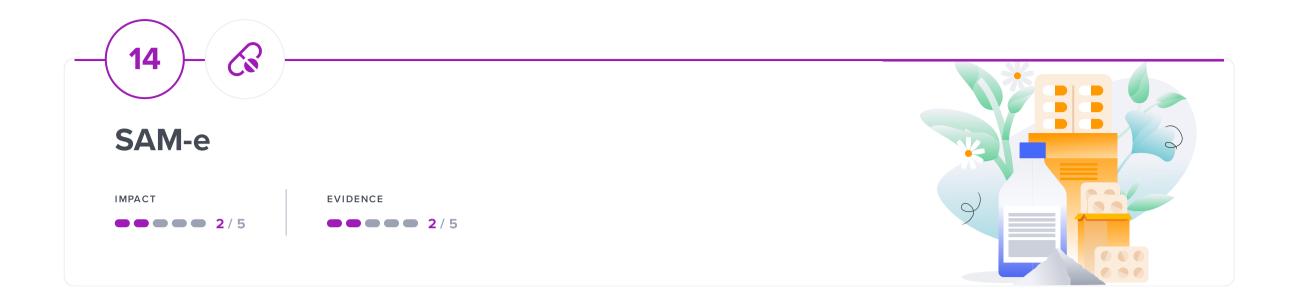
Ways to sleep better include [R]:

- Reducing your bright light exposure (screen time) in the evenings
- Sticking to a regular sleep schedule
- Avoiding hunger or large meals before bed
- · Avoiding nicotine, caffeine, and alcohol before bed
- Maintaining a sleep area that's cool, dark, and quiet

How Sleep for 7+ Hours helps with Methylation

Sleep plays a crucial role in regulating methylation processes in the body, impacting gene expression and overall health. Here's how adequate sleep can support methylation:

- **Cellular Repair and Regeneration**: Sleep is a time for the body to repair and regenerate. During sleep, methylation processes are involved in cell repair and the maintenance of DNA integrity. Adequate sleep ensures these processes occur efficiently.
- Stress Hormone Regulation: Sleep helps regulate cortisol, a stress hormone. Disrupted sleep patterns can lead to altered cortisol levels, impacting methylation patterns. Stress and cortisol are known to affect DNA methylation, particularly in genes related to the stress response.
- **Detoxification**: Sleep aids in the body's detoxification processes, partly mediated by methylation. This includes the clearance of metabolic byproducts and toxins that can interfere with methylation if accumulated.



SAM-e is a compound naturally produced by the body that plays a role in various biochemical processes. It is available as a dietary supplement and is used to potentially support mood, joint health, and liver function.

<u>SAM-e</u> is a chemical that helps maintain liver and brain health. Your body makes SAM-e from the amino acid *methionine*, but it's also available as a supplement [R].

SAM-e supplementation may help with:

- Joint pain [R]
- Liver disease [R]
- Depression [R]

Please note: SAM-e may not be safe for people with a bipolar disorder. It may also interact with 5-HTP, St. John's wort, and different medications. Combining it with antidepressants can be dangerous and even life-threatening. Never take SAM-e supplements without consulting your doctor [R, R, R].

How SAM-e helps with Methylation

S-adenosylmethionine or SAM-e provides methyl groups for methylation reactions and helps clear homocysteine [R, R].

It also boosts glutathione and may help support liver health, mood, and more [R].

Please note: SAM-e may not be safe for people with bipolar disorder. It may also interact with 5-HTP, St. John's wort, and different medications. Combining it with antidepressants can be dangerous and even life-threatening. Never take SAM-e supplements without consulting your doctor [R, R, R].



Your MAT1A gene variant may be linked to DNA damage and other methylation-related issues. The enzyme produced by this gene helps turn methionine to SAM-e. Supplementing with SAM-e may help reduce the impact of this variant [R, R].

YOUR GENETIC VARIANTS

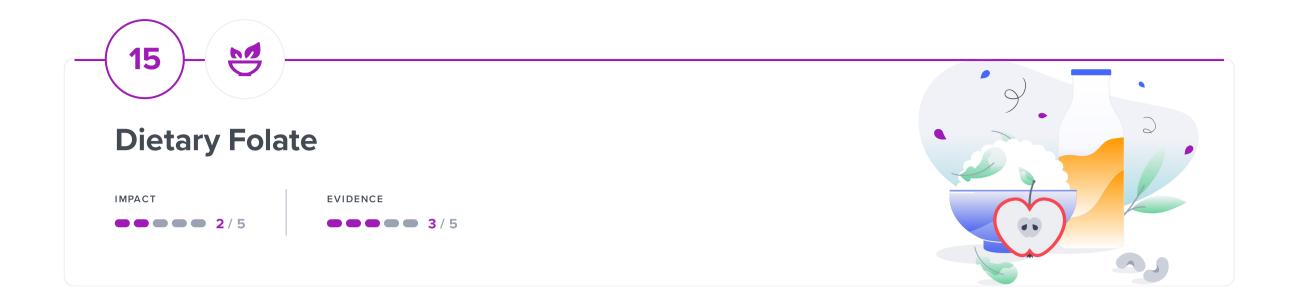
GENE

SNP

GENOTYPE

EVIDENCE

PRXL2A rs7087728



Vitamin B9 (folate) plays an essential role in [R, R, R]:

- Making DNA
- Metabolism
- Energy production

Rich sources of folate include [R, R]:

- Beef liver
- Spinach
- Black-eyed peas
- Asparagus
- Citrus fruits

While folate deficiency is rare, it can happen in people who don't eat enough fruits and vegetables. Alcoholics and lactating women may also be at increased risk [R].

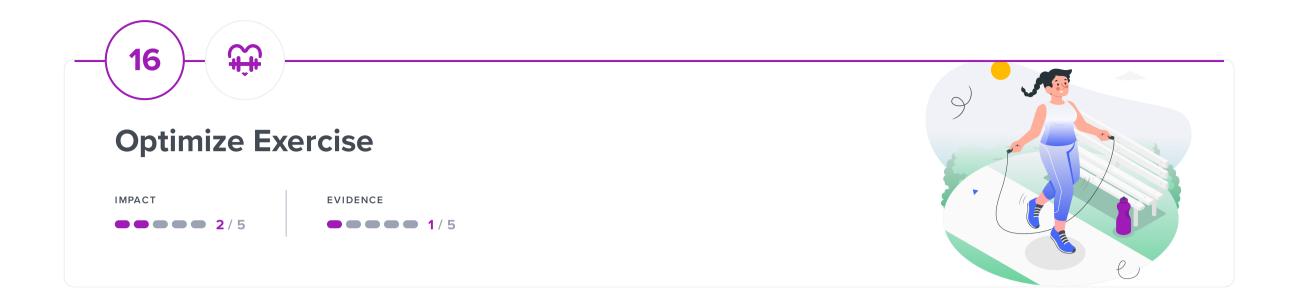
Adults should get **400 micrograms (mcg)** of folate per day. Pregnant or breastfeeding women should get **500-600 mcg per day**. Supplements are usually in the form of *folic acid* or L-methylfolate (5-MTHF) [R, R].

How Dietary Folate helps with Methylation

People with methylation issues may not be able to produce enough methylfolate, which is the active form $[\mathbb{R}]$.

Food sources of folate provide the active form of this vitamin. They include raw leafy greens, liver, eggs, nuts, seeds, kimchi, and nutritional yeast [R].

High dietary intake of folate is associated with lower homocysteine levels $[\mathbb{R}, \mathbb{R}]$.



Optimizing exercise involves tailoring physical activity to individual needs and goals, promoting fitness, muscle strength, and cardiovascular health while reducing the risk of injury. Properly structured exercise routines can lead to improved physical and mental health.

Exercise can do wonders for your health. It can help you lose weight, improve your heart health, boost your mood, and more [R].

There are many ways you can be active. You can walk, run, lift weights, dance, or play team sports. **Everything counts, and it's never too late to start!**

However, extreme exercise may contribute to heart rhythm problems, irregular periods, and more. It is important to get the right amount of physical activity to not stress your body [R, R, R].

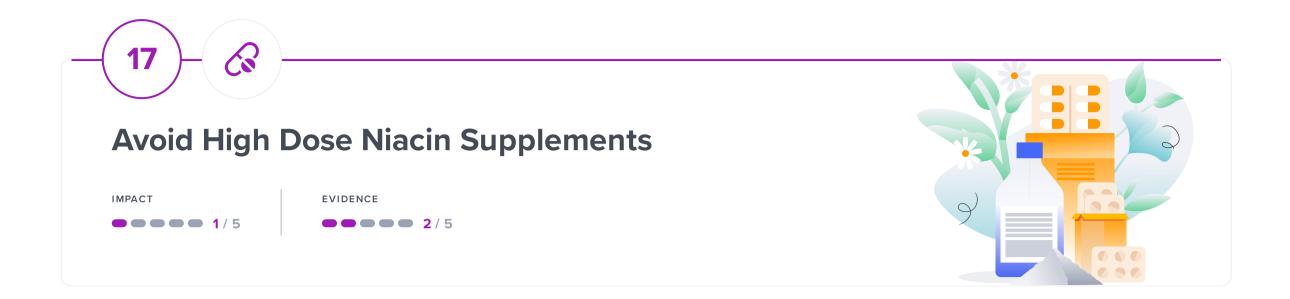
How Optimize Exercise helps with Methylation

Regular physical activity is known to influence DNA methylation and thus has an effect on gene expression and can promote health through epigenetic mechanisms.

However, excess exercise might increase methylation demand through several mechanisms:

- **Increased Energy Metabolism**: Physical activity boosts cellular metabolism, which relies on methylation reactions for energy production, repair, and recovery processes.
- **DNA Methylation Changes**: Exercise can induce alterations in DNA methylation patterns, particularly in genes involved in muscle growth, energy metabolism, and inflammation. These epigenetic changes are part of how the body adapts to exercise.
- **Stress Response**: Exercise, especially intense physical activity, is a form of stress that can temporarily increase oxidative stress and inflammation. The body responds to this by upregulating methylation processes to manage and counteract these effects.
- Muscle Repair and Growth: Exercise-induced muscle damage and subsequent repair processes involve methylation for protein synthesis and tissue remodeling.

If you are exercising a lot, make sure to get adequate methyl groups from your diet and supplements.



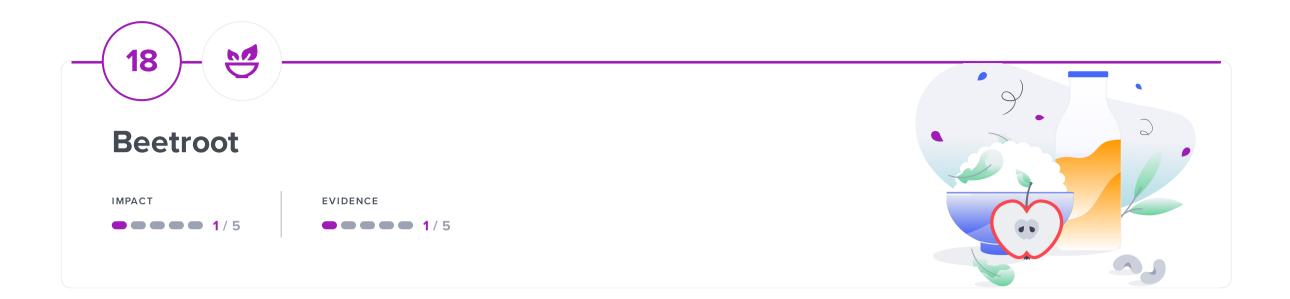
Please note: There is no evidence from controlled clinical trials to support this recommendation. It is included based on uncontrolled clinical trials, animal or cell studies, or non-scientific criteria. Please take this recommendation with a grain of salt until more research is available

High doses of Niacin (greater than 500mg) may reduce T4 levels. [R]

How Avoid High Dose Niacin Supplements helps with Methylation

Methylation is essential for converting homocysteine to methionine. High doses of niacin can exacerbate the accumulation of homocysteine in individuals with reduced MTHFR function.

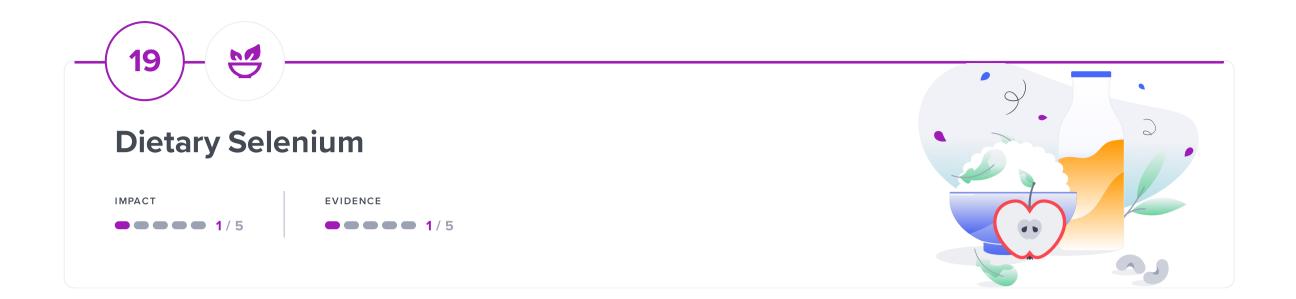
This is because niacin in large amounts can deplete methyl donors like SAMe (Sadenosylmethionine), which are needed for methylation [R].



Beetroot is a vegetable rich in dietary nitrates, which may help improve cardiovascular health and exercise performance.

How Beetroot helps with Methylation

Beetroot naturally contains betaine, also known as trimethylglycine, which acts as a methyl donor in the body, potentially aiding individuals with their methylation cycle.



Selenium is a trace mineral found in various foods, including nuts, seeds, and seafood. It is an essential nutrient that plays a crucial role in maintaining the body's antioxidant defenses and supporting thyroid function.

Selenium supports [R]:

- Reproduction
- Thyroid function
- DNA production
- Immune response

Adults should be getting **55 micrograms** of selenium per day. Good sources of selenium include [R]:

- Brazil nuts
- Fish
- Meat
- Eggs
- Rice
- Oatmeal

How Dietary Selenium helps with Methylation

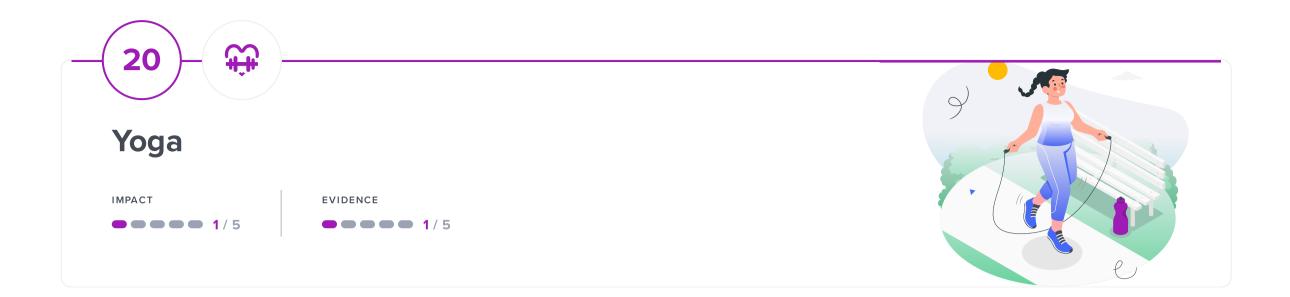
Selenium plays a role in protection against oxidative damage and affects selenoproteins which have been implicated in methylation pathways.

Positive effects:

- **Enzymatic cofactor**: Selenium is a crucial component of several enzymes involved in methylation pathways, particularly glutathione peroxidases. These enzymes contribute to antioxidant defense and protect against oxidative stress, which can disrupt methylation processes.
- **Gene expression modulation**: Selenium can influence the expression of genes involved in folate metabolism and other methylation-related pathways. This can potentially enhance overall methylation efficiency.
- **DNA methylation**: Some studies suggest selenium may influence global DNA methylation patterns, impacting gene expression and cell function. However, the exact mechanisms and long-term implications of this influence require further investigation.

Negative effects:

• **Excess selenium**: High selenium intake can inhibit the activity of certain methylation enzymes, potentially leading to impaired methylation processes. This can have negative consequences for various physiological functions, including DNA repair and gene expression.



Yoga is a mind-body practice that combines physical postures, breathing exercises, and meditation. It enhances flexibility, strength, and mental well-being and is used for stress reduction, relaxation, and overall health improvement.

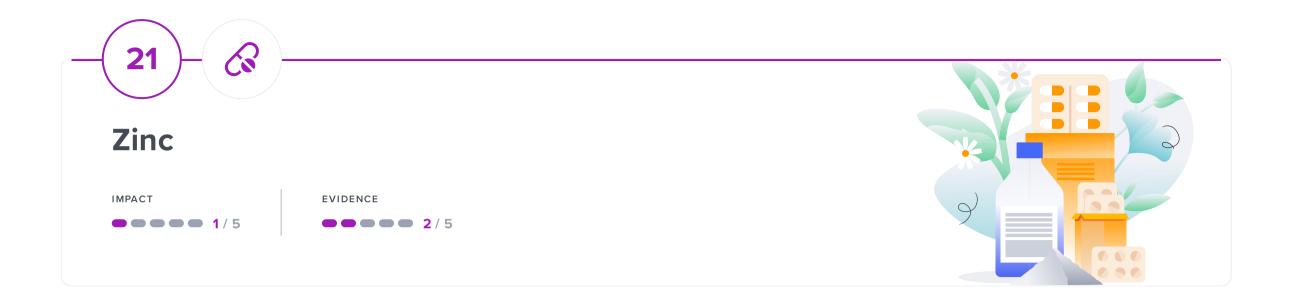
Yoga **combines breathing, stretching, and relaxation techniques.** Practicing yoga may help [R, R, R]:

- Reduce
- Improve fitness
- Lower blood pressure and heart rate
- Manage pain

How Yoga helps with Methylation

Yoga might modulate stress response systems by altering the methylation status of genes involved in the regulation of stress and inflammation. Detailed mechanisms include:

- 1. **Stress Reduction**: Yoga is known for its stress-reducing effects. Chronic stress can lead to changes in DNA methylation patterns, particularly in genes associated with the stress response. By reducing stress, yoga can help maintain balanced methylation in these genes.
- 2. **Anti-inflammatory Effects**: Regular yoga practice can reduce inflammation. Inflammation is linked to alterations in DNA methylation, especially in genes involved in the immune response. Yoga's anti-inflammatory benefits might therefore support healthier methylation patterns.
- 3. **Hormonal Balance**: Yoga can help regulate hormones, including cortisol, the stress hormone. Since hormonal balance is crucial for proper methylation processes, yoga may indirectly support efficient methylation through its regulatory effects on hormones.
- 4. **Improved Sleep Quality**: As yoga can enhance sleep quality, and adequate sleep is essential for optimal methylation processes, yoga indirectly supports methylation through its positive impact on sleep.



Zinc is an essential mineral found in various foods, including meat, dairy, and nuts. It is crucial for immune function, wound healing, DNA synthesis, and maintaining healthy skin and nails. Zinc supplements are sometimes used to support immune health and manage zinc deficiencies.

Zinc is an essential mineral. Your body needs it to [R, R]:

- Defend against disease
- Protect DNA from damage
- Heal wounds
- Control blood sugar

Some of the best sources of zinc include **shellfish**, **pork**, **beef**, **and beans**. It is also available as a supplement $[\mathbb{R}]$.

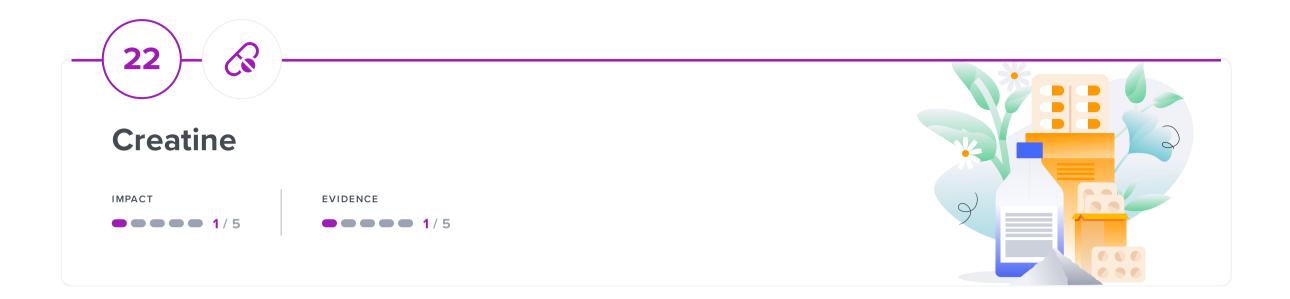
Adults should get 8-11 mg of zinc per day [R].

How Zinc helps with Methylation

Zinc is important for folate absorption and healthy methylation. Ensure that your zinc levels are optimal [R].

If you are deficient in zinc, your gut enzymes can't break down folate into the form you can absorb [R, R].

Zinc also helps folate carry out its role in the body [R].



Creatine is a popular dietary supplement among athletes and bodybuilders, known to enhance muscle performance during short bursts of high-intensity activities. It may help improve exercise performance and support muscle growth when used as directed.

<u>Creatine</u> is a compound naturally produced by the body. It's stored in the muscles and brain [R].

During exercise, creatine is released to boost performance and help build muscles. For this reason, it's a popular supplement among athletes [R, R].

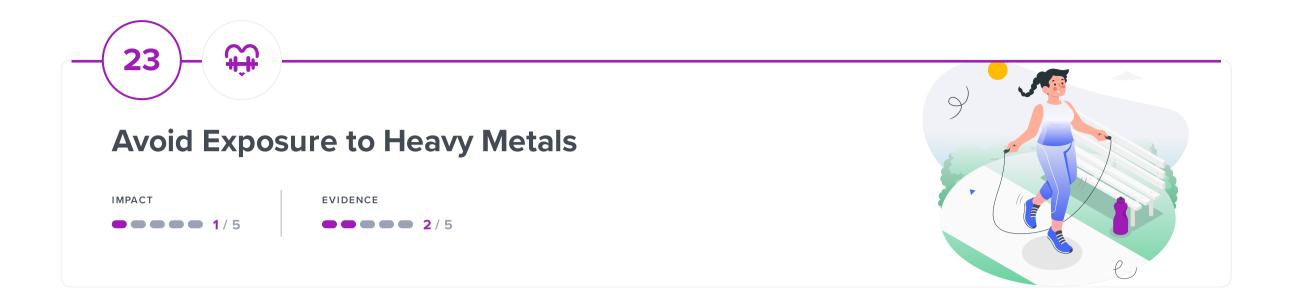
Sources of creatine include [R]:

- Red meat
- Seafood
- Supplements

How Creatine helps with Methylation

Creatine may help reduce your requirements for methylation, especially if you have high homocysteine [R].

Approximately half of your body's methylation efforts are used to make creatine, which muscles require to quickly produce energy (ATP). Creatine might thus lower the body's need for methylation.



Heavy metals are elements naturally found in the environment. They are also used for agricultural, industrial, and medicinal purposes. Some can even be found in small amounts in your body [R, R].

Long-term exposure to high amounts of heavy metals can be harmful to your health $[\mathbb{R}, \mathbb{R}]$.

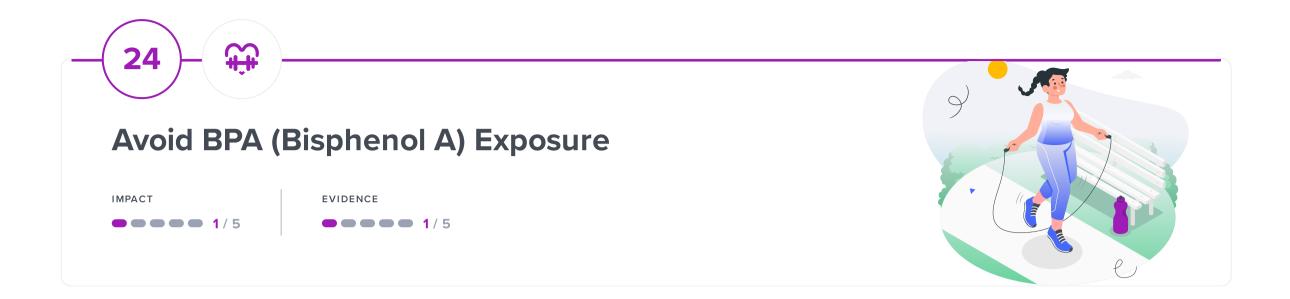
Heavy metals that are most often linked to health problems include [R, R]:

- Lead
- Cadmium
- Arsenic
- Chromium
- Mercury

How Avoid Exposure to Heavy Metals helps with Methylation

Heavy metals can interfere with the activity of enzymes involved in methylation, potentially leading to impaired methylation of essential molecules like DNA and proteins. This can have negative consequences for various physiological functions.

Some heavy metals, like mercury and arsenic, can be methylated by the body as a way to facilitate their excretion. This process further increases methylation demand.



Avoiding BPA (Bisphenol A) exposure involves minimizing contact with products or containers containing this chemical, which is commonly found in plastics and can potentially disrupt hormone regulation.

BPA (bisphenol A) is a chemical used to make certain plastics and resins. BPA-containing plastics are often used in containers that store food and beverages. Plastics marked with **recycling code 3 or 7** may contain BPA [R].

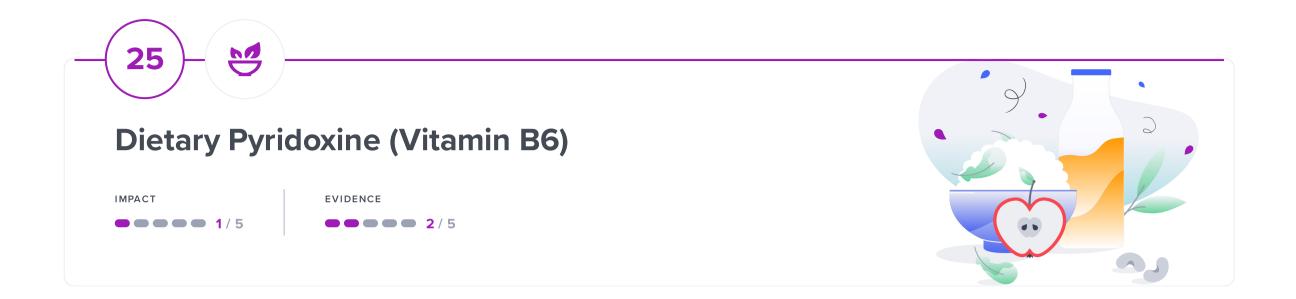
BPA is a well-known hormone disruptor. Research has linked BPA exposure to diabetes, heart disease, altered behavior, and more [R].

How Avoid BPA (Bisphenol A) Exposure helps with Methylation

Industrial toxins like bisphenol A (BPA) inhibit methylation enzymes. BPA is mostly found in plastics, but it can also sneak into cosmetics.

All the while, toxins increase the body's methylation demands, since methylation eliminates them. Methylation also creates the antioxidant glutathione, which you need more of to neutralize BPA and other toxins [R].

Be mindful of your exposure to chemicals and substances that increase your need for detoxification. Consider switching to toxin-free household and cosmetic products, eating organic foods, filtering your water, and avoiding polluted areas.



Vitamin B6 is involved in over 100 enzyme reactions in the body and plays a role in brain development, immune function, and hormone regulation. It is found in foods like poultry, fish, potatoes, and bananas.

Vitamin B6 (pyridoxine) is important for nervous and immune system health [R].

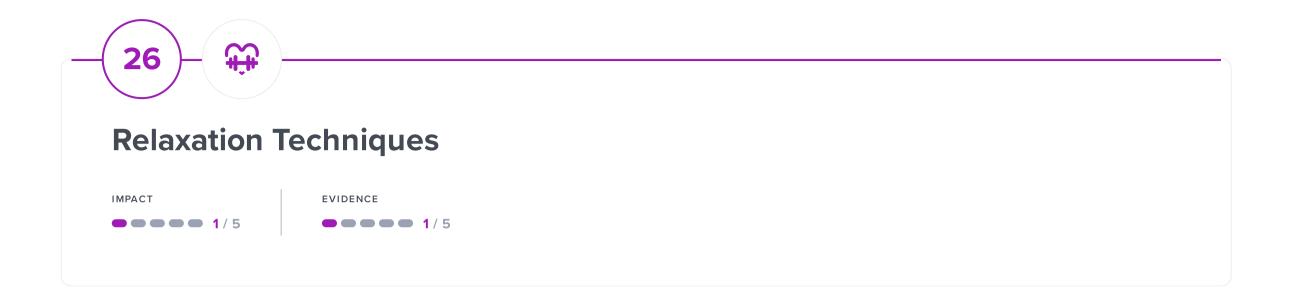
Good sources of vitamin B6 include [R]:

- Poultry
- Fish
- Potatoes
- Chickpeas
- Bananas
- Fortified cereals

How Dietary Pyridoxine (Vitamin B6) helps with Methylation

People with methylation issues may have increased needs for B vitamins, especially folate, B12, and B6 [R].

Vitamin B6 helps support methylation. It's crucial for the **transsulfuration pathway** that clears homocysteine and produces glutathione [R].



Relaxation techniques encompass various methods like deep breathing, yoga, meditation, and progressive muscle relaxation, aimed at reducing stress and promoting mental and physical relaxation. Practicing these techniques regularly can help manage stress, improve mental clarity, and enhance overall emotional well-being.

We all get stressed from time to time.

Stress can help you deal with a challenge or avoid danger. However, it's not healthy to be stressed for a long time [R, R].

Relaxation techniques such as yoga and meditation can relieve stress in different ways. Most of them focus on breathing and help you get rid of negative thoughts and emotions [R].

People use relaxation techniques to improve conditions like [R, R, R]:

- Anxiety
- Depression
- Chronic pain

Progressive muscle relaxation is another relaxation technique. In this technique, you focus on tensing and relaxing different parts of your body. It is common to start with the toes and slowly work your way up to the neck and head [R, R].

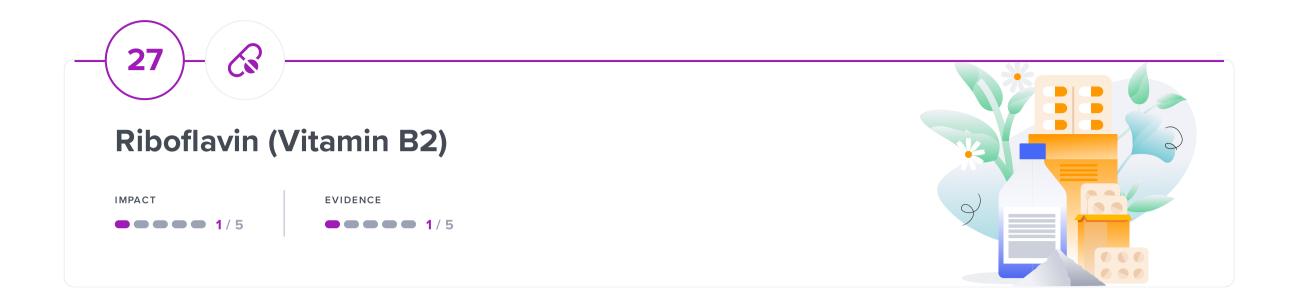
Autogenic training is a relaxation technique that a person may carry out on their own. It uses exercises that take the mind's attention to bodily sensations such as warmth and heaviness [R, R].

How Relaxation Techniques helps with Methylation

Stress demands more out of your methylation cycle. If you are going through a stressful period, you may have a higher need for folate and other B vitamins. Make sure you get enough and manage your stress levels.

Stress requires your body to have more methyl donors to produce and break down catecholamine neurotransmitters (such as epinephrine, norepinephrine, and dopamine). In balanced amounts, these neurotransmitters enhance motivation, focus, and feelings of pleasure. In excess, they trigger anxiety, high blood pressure, addiction, and aggression.

Psychological stress temporarily increases homocysteine levels, which return to normal levels after the stress resolves. If you are constantly under stress, your homocysteine may remain high [R].



Riboflavin is a water-soluble B vitamin found in various foods like dairy products, leafy greens, and lean meats. It plays a crucial role in energy production, metabolism, building red blood cells, and maintaining healthy skin and eyes.

Vitamin B2 helps our cells create energy. It's also known as riboflavin [R, R].

This vitamin is important for [R, R]:

- Brain, liver, and gut health
- Building red blood cells

Riboflavin deficiency is rare in the US. People with gut, eating, or hormonal disorders may be at a higher risk. Alcohol abuse and certain medications can also deplete this vitamin [R, R].

Good sources of riboflavin include [R, R]:

- Eggs
- Dairy
- Lean and organ meats
- Green vegetables
- Fortified cereals

How Riboflavin (Vitamin B2) helps with Methylation

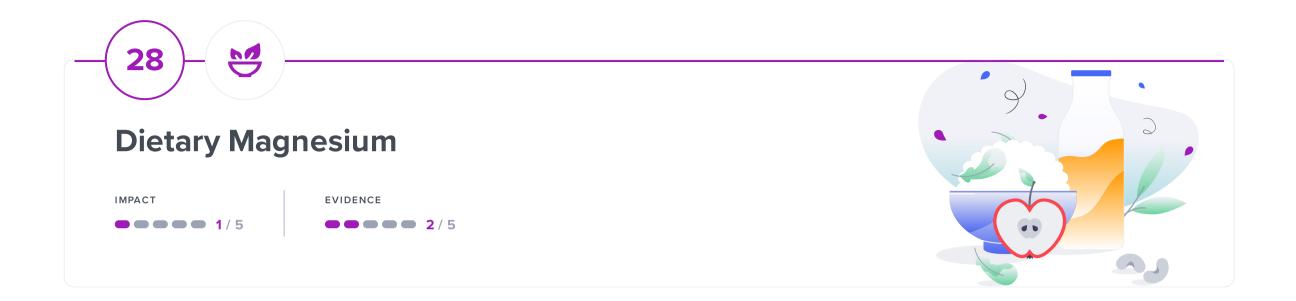
Riboflavin helps in the activation of vitamin B6, which is essential for methylation and homocysteine removal.

In a <u>placebo-controlled trial of 42 older participants</u>, supplementation with riboflavin (10 mg/day) for 28 days **significantly decreased blood homocysteine** [R].

However, supplementation with riboflavin (8.4 mg/day) for 2 weeks **failed to lower homocysteine and blunted the effects of folic acid supplementation** in a <u>placebocontrolled trial of 32 healthy men</u> [R].

Riboflavin (1.6 mg/day for 12 weeks) also **failed to lower homocysteine** in a <u>placebocontrolled trial of 52 elderly participants with sub-optimal riboflavin status</u> [R].

The beneficial effects of riboflavin on methylation and homocysteine removal might be limited to people with **lower MTHFR activity** [R, R, R].



Magnesium is a vital mineral involved in over 300 biochemical reactions in the body. It supports various functions, including muscle and nerve function, bone health, and blood sugar regulation.

Magnesium is an essential mineral. Your body needs it for [R, R, R]:

- Muscle, nerve, and bone function
- Blood sugar and blood pressure control
- DNA and protein production
- Strong immunity

Women need 310-320 mg of magnesium per day, while men need 400-420 mg [R].

Foods rich in magnesium include **nuts, seeds, and leafy greens**. Magnesium is also available as a supplement [R].

How Dietary Magnesium helps with Methylation

Magnesium acts as a cofactor in many enzymatic reactions in the methylation cycle, and inclusion in the diet may support those with MTHFR mutations. It helps with the following enzymes:

- **S-adenosylmethionine (SAM) synthase**: This enzyme catalyzes the synthesis of SAM, the major methyl donor in the body. Magnesium binds to the active site of SAM synthase, stabilizing its structure and facilitating the reaction between methionine and ATP to produce SAM.
- Methionine adenosyltransferase (MAT): This enzyme plays a role in the regeneration of SAM from S-adenosylhomocysteine (SAH), which is formed when SAM donates its methyl group. Magnesium acts as a cofactor for MAT, enhancing its activity and ensuring efficient SAM production.
- **Methyltransferases**: These enzymes directly transfer methyl groups from SAM to various acceptor molecules, including DNA, proteins, and other metabolites. Magnesium is essential for the proper folding and activity of these enzymes, ensuring accurate and efficient methylation processes throughout the body.
- Other enzymes: Magnesium may also play a role in the activity of other enzymes involved in related pathways, such as folate metabolism and one-carbon metabolism, which indirectly contribute to the methylation cycle.

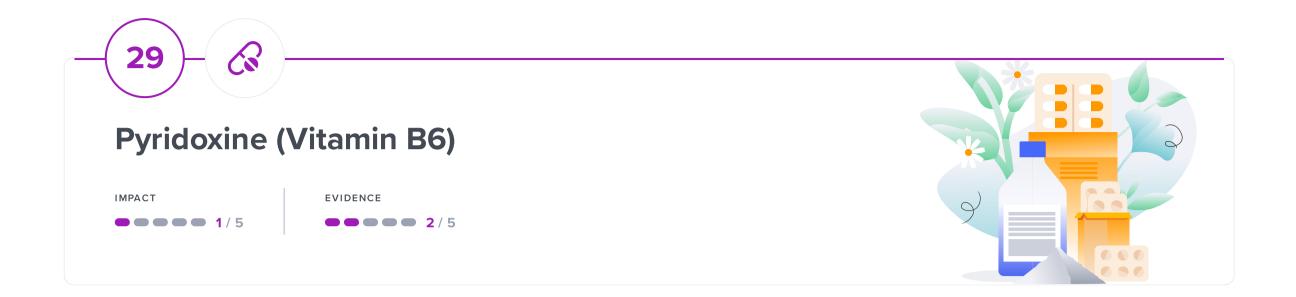


Your MTHFD1 gene variant is linked to choline deficiency, birth defects, and other methylation-related health problems. This variant makes the MTHFD1 enzyme less stable, but magnesium might reduce this effect $[\underline{R}, \underline{R}, \underline{R}]$.

YOUR GENETIC VARIANTS

GENE

SNP GENOTYPE EVIDENCE

MTHFD1 rs2236225 

A **vitamin B6 supplement** of up to 1.3-1.7 mg per day can be taken to meet needs not achieved through diet. Long term supplementation of vitamin B6 can be problematic, so talk to your doctor before using.

How Pyridoxine (Vitamin B6) helps with Methylation

People with methylation issues may have increased needs for B vitamins, especially folate, B12, and B6 [R].

Vitamin B6 helps support methylation. It's crucial for the **transsulfuration pathway** that clears homocysteine and produces glutathione [R].

Next Steps

Remember, your genes only tell one important part of your health story!

These next steps will teach you how to get the most complete picture of your health.





Your Lifestyle

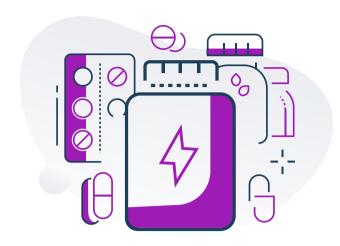
Answer questions to understand the health impacts of your lifestyle.





Your Labs

Labwork is how you discover the true impact of your lifestyle and genetics on your current health.





Your Supplements

Discover key supplements that you can introduce to your body to achieve optimal health.