

Acetaminophen and Liver Damage

Biohacker Report

REPORT CATEGORIES —



DETOX



LIVER HEALTH

Sample Client

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omicsedge

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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.

Personal information

NAME

Sample Client

SEX AT BIRTH

Male

HEIGHT

5ft 5" 165cm

WEIGHT

137lb 62kg



How this works

Our Wellness 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.

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

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



Genotype color info:

AA

You don't have any risk alleles

AA

You have 1 risk allele

AA

You have 2 risk alleles

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: lifestyle, diet, 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 the strength of evidence in the medical literature.

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



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

- 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:

- Genetics doesn’t play a considerable role in a condition or a trait.
- There is not enough research available to estimate a genetic predisposition.
- There are technical limitations to estimating or presenting a genetic predisposition.
- The topic is sensitive, and a genetic predisposition should only be estimated and presented by a healthcare professional.

Introduction

Acetaminophen, commonly known as Tylenol (in the US) or paracetamol (in Europe) is a widely used painkiller and antipyretic that is available over-the-counter. While generally safe when used within recommended dosages, acetaminophen is a leading cause of drug-induced liver injury, particularly when taken in overdose [\[R\]](#).

The liver metabolizes acetaminophen primarily via conjugation with sulfate and glucuronide, which are non-toxic and easily excreted. SULT and UGT enzymes are primarily responsible for this process. However, about 10-15% of acetaminophen is metabolized by [CYP2E1](#). This leads to the accumulation of the toxic metabolite N-acetyl-p-benzoquinone imine (NAPQI) [\[R\]](#), [\[R\]](#)

Under normal circumstances, NAPQI is detoxified by conjugation with glutathione and subsequently excreted. However, glutathione stores are depleted in case of overdose, allowing NAPQI to accumulate and bind to cellular proteins within the liver. This leads to oxidative stress, lipid peroxidation, DNA damage, and ultimately, cell death [\[R\]](#), [\[R\]](#).

The following factors increase the risk of acetaminophen-induced liver damage:

- **Overdose:** consuming amounts exceeding 4,000 milligrams per day (the maximum recommended daily limit) significantly increases the risk of liver damage [\[R\]](#).
- **Chronic use:** regular, long-term use, even at therapeutic doses, may cause cumulative liver damage, particularly in individuals with underlying liver conditions [\[R\]](#).
- **Alcohol use:** concurrent alcohol consumption increases the activity of CYP2E1, enhancing the production of NAPQI. Alcohol abuse also depletes glutathione, reducing the liver’s capacity to neutralize toxins [\[R\]](#).
- **Fasting or poor nutrition:** low levels of hepatic glutathione, common in malnourished individuals, can diminish the liver's ability to detoxify NAPQI [\[R\]](#).
- **Genetics**

Genetics of Acetaminophen-Induced Liver Damage

UDP-glucuronosyltransferase (UGT) is a family of enzymes responsible for performing a chemical reaction called [glucuronidation](#), which is an important step in the body's [detox process](#). Glucuronidation is one of the main pathways for acetaminophen breakdown [\[R\]](#).

The ‘A’ allele of the [UGT2B15](#) polymorphism [rs1902023](#) encodes a UGT enzyme with decreased activity. This reduces acetaminophen clearance and potentially increases the risk of liver damage [\[R\]](#), [\[R\]](#)

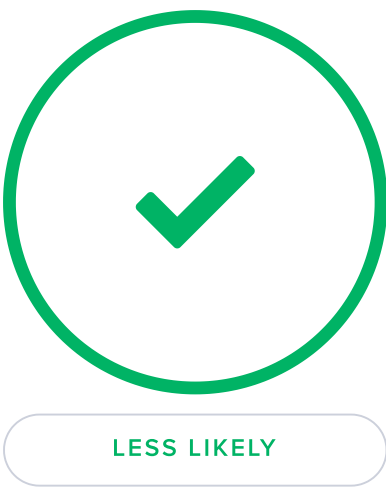
In contrast, the ‘G’ allele of [rs8330](#) encodes a version of the [UGT1A1](#) enzyme with increased activity and has been associated with a decreased risk of acetaminophen-induced liver damage [\[R\]](#).

Similarly, three [UGT1A6](#) variants (‘G’ of [rs6759892](#), ‘G’ of [rs2070959](#), and ‘C’ of [rs1105879](#)) encode a form of the protein with a 2-fold higher acetaminophen clearance activity commonly known as UGT1A6*2. These variants may reduce the risk of liver damage [\[R\]](#).

The [CD44](#) gene encodes a cell-surface glycoprotein involved in cell-cell interactions, cell attachment, and migration. This protein is involved in multiple cellular processes, including cell differentiation, recruitment of immune system cells, and as a receptor for hyaluronic acid. Importantly, CD44 contributes to liver damage by regulating the activation and infiltration of immune cells (macrophages) [\[R\]](#), [\[R\]](#).

The ‘T’ allele of [rs1467558](#) has been associated with increased liver damage in response to acetaminophen. People with the ‘TT’ genotype may be at a 4-fold higher risk of liver failure with chronic acetaminophen use [\[R\]](#).

The [AVP](#) gene encodes vasopressin, a hormone that helps control water balance by directing the kidneys to reabsorb



Less likely to have acetaminophen-induced liver damage based on 12 genetic variants we looked at



Your top variants that most likely impact your genetic predisposition:

GENE	SNP	GENOTYPE
MROH2A	rs8330	CG
UGT1A6	rs6759892	TT
UGT1A6	rs2070959	AA
UGT1A6	rs1105879	AA
AVP	rs2282018	CT
CYP1A2	rs28399424	CC
UGT2B15	rs1902023	AC
CYP2E1	rs2515641	CT
CYP3A5	rs776746	CC
CD44	rs1467558	CC
AVPR1A	rs11174811	AA
CYP2D6	rs1065852	GG

The number of "risk" variants in this table doesn't necessarily reflect your overall result.

more water and to make less urine. Vasopressin is also involved in cognition, cardiovascular functions, and sexual and maternal behavior. In turn, the [AVPR1A](#) encodes a receptor activated by this hormone [\[R, R\]](#).

A study of 229 patients with acute acetaminophen-induced liver failure found that the ‘T’ allele of the *AVP* [rs2282018](#) polymorphism and the ‘C’ allele of the *AVPR1A* [rs11174811](#) polymorphism were more common in cases than in controls [\[R\]](#).

[CYP1A2](#) and [CYP2D6](#) are critical enzymes in the cytochrome P450 family, responsible for metabolizing various substances in the liver. They play central roles in the detoxification of both endogenous compounds, such as hormones and neurotransmitters, and exogenous substances, including drugs, caffeine, and environmental toxins. Importantly, they are among the main enzymes involved in acetaminophen metabolism [\[R, R\]](#).

A study of 150 participants identified the ‘CC’ genotype of [rs28399424](#) (*CYP1A2**6) and the ‘AA’ genotype of [rs1065852](#) (*CYP2D6**10) as decreasing acetaminophen breakdown [\[R\]](#).

The [CYP2E1](#) gene encodes an important detox enzyme involved in the metabolism of alcohol and acetaminophen. In people who drink a lot of alcohol, the expression of this gene is increased. This contributes to 20% of alcohol breakdown in the brain. Unfortunately, this also means increased production of the toxic metabolite NAPQI [\[R, R, R\]](#).

The ‘T’ allele of [rs2515641](#) significantly reduces *CYP2E1* expression, potentially reducing the risk of acetaminophen-induced liver damage [\[R\]](#).

The [CYP3A5](#) gene encodes a member of the cytochrome P450 superfamily of enzymes. These proteins eliminate most drugs from the body. In the liver, this enzyme oxidizes a variety of structurally unrelated compounds, including steroids, fatty acids, and xenobiotics. This enzyme can metabolize acetaminophen, although to a lesser degree than *CYP2E15*. Interestingly, most people carry a non-functional version of the enzyme [\[R, R, R\]](#).

The ‘T’ allele of [rs776746](#) encodes a functional version of *CYP3A5* that increases the risk of acetaminophen-induced liver damage [\[R\]](#).

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.

DOSAGE		DOSAGE	
1	Limit Substance Use	2	N-acetylcysteine (NAC)1200 mg
3	Methionine200 mg	4	Milk Thistle (Silymarin)300 mg
5	Glutathione supplements	6	Betaine (TMG)500 mg

1



Limit Substance Use

IMPACT

1 / 5

EVIDENCE

1 / 5

How to implement

Reduce the frequency and quantity of alcohol, tobacco, and any non-prescribed drugs you consume. For alcohol, aim to have no more than one drink per day if you're female and two if you're male. Avoid tobacco and non-prescribed drugs entirely whenever possible.

Description

Limiting substance use, particularly the misuse of alcohol, tobacco, and illicit drugs, is essential for preserving physical and mental health. Responsible and controlled use of these substances, or abstaining from them, supports a safer and healthier lifestyle.

Substances include alcohol and drugs. In some cases, substances can be used responsibly. For example, having 1-2 alcoholic drinks per day likely won't cause harm. Likewise, cannabis can be used for medical purposes in some countries or states [\[R\]](#), [\[R\]](#), [\[R\]](#).

However, these substances can also be misused. Substance misuse can lead to dependence on a substance. This can have long-term health and social consequences [\[R\]](#), [\[R\]](#), [\[R\]](#), [\[R\]](#).

Even at low or prescribed doses, alcohol and some drugs can have side effects like palpitations [\[R\]](#), [\[R\]](#).

How it helps

Limiting substance use, particularly alcohol, reduces the risk of liver damage by minimizing the burden on hepatic metabolism, which is crucial for processing acetaminophen. This protective measure enhances liver function and decreases the likelihood of toxicity associated with acetaminophen overdose.

2



N-acetylcysteine (NAC)

IMPACT1 / 5

EVIDENCE1 / 5

How to implement

Take 600 mg of N-Acetylcysteine (NAC) supplement daily with water. It can be taken at any time of the day, but try to take it at the same time each day for best results.

TYPICAL STARTING DOSE
1200 mg

Description

NAC is a supplement that contains a form of the amino acid cysteine, a protein building block that your body uses to make the antioxidant glutathione. It is used for its potential antioxidant properties and its ability to support lung, gut, and mental health.

[N-acetylcysteine](#) (NAC) is converted to cysteine in the body. Cysteine is a protein building block (amino acid) that helps make the antioxidant glutathione [\[R\]](#).

People take NAC to potentially support [\[R\]](#), [\[R\]](#):

- Mental health
- Ovarian health and pregnancy outcomes
- Lung health
- Gut health

How it helps

N-acetylcysteine (NAC) helps protect against acetaminophen-induced liver damage by replenishing glutathione levels, a critical antioxidant that detoxifies harmful metabolites, thereby safeguarding liver cells from oxidative stress.

3



Methionine

IMPACT

1 / 5

EVIDENCE

1 / 5

How to implement

Take a methionine supplement in the form of SAME at 200-400mg daily, with water, preferably on an empty stomach to enhance absorption. It's recommended to start with a lower dose and gradually increase as needed. Consult with a healthcare provider for personalized advice, especially if you have other medical conditions or are taking medications.

TYPICAL STARTING DOSE

200 mg

Description

Methionine is an essential amino acid found in various protein-rich foods. It plays a crucial role in protein synthesis and liver function and is important for overall health.

1. A **methionine supplement** can vary depending on which source is utilized to boost methionine levels. One or more of the following options can be taken to boost methionine levels:
- a. SAME or S-Adenosyl-Methionine can be taken in doses starting at 200 mg/day. It is sometimes recommended to take with the other two supplements to promote absorption.

b. TMG (Betaine) or trimethylglycine supplements are made from the byproducts of sugar beet processing. Typically, it is offered in 500-1000 mg capsules.

c. Methylfolate is the biologically active form of folate (vitamin B9) and typically offered in dosages of 7.5-15 mg.

Note: excessive levels of methylfolate can cause adverse reactions like anxiety and sore joints and muscles. Speak with your doctor before using a methionine supplement.

How it helps

Methionine aids in the synthesis of glutathione, a critical antioxidant that protects liver cells from damage. Supplementing with methionine may enhance liver function and reduce the risk of acetaminophen-induced liver injury.

4



Milk Thistle (Silymarin)

IMPACT

1 / 5

EVIDENCE

1 / 5

How to implement

Take a 300 mg milk thistle (silymarin) supplement daily with water, preferably with a meal for better absorption. Continue this regimen as advised by your healthcare provider.

TYPICAL STARTING DOSE

300 mg

Description

Silymarin is a natural plant extract derived from the milk thistle plant (*Silybum marianum*). It has been traditionally used for its potential anti-inflammatory and liver-protective properties. Silymarin consists of several flavonolignans, including silybin, silydianin, and silychristin.

Milk thistle (*Silybum marianum*) is a purple flowering plant in the daisy family. Traditionally, it has been used for liver problems. Some people also eat the leaves in salads [\[R\]](#), [\[R\]](#).

The extract of milk thistle is called *silymarin* [\[R\]](#), [\[R\]](#), [\[R\]](#).

People use milk thistle to help with [\[R\]](#), [\[R\]](#), [\[R\]](#):

- Liver problems
- Blood sugar control
- Indigestion
- Skin problems

How it helps

Milk thistle, containing silymarin, enhances liver regeneration and provides antioxidant protection against oxidative stress induced by acetaminophen, thereby mitigating potential liver damage.

5



Glutathione supplements

IMPACT

1 / 5

EVIDENCE

1 / 5

How to implement

Take glutathione supplements orally, usually in pill or powder form, with a recommended dose ranging from 500mg to 1000mg daily, divided into two doses. It's best taken on an empty stomach or as directed by a healthcare professional. Continuous use is advised for sustained benefits, but consulting with a healthcare provider for personalized advice and duration is important.

Description

Glutathione (GSH) is your body’s strongest antioxidant. It has an enormous capacity to combat [oxidative stress](#) and neutralize harmful free radicals. Chemically speaking, glutathione is a tripeptide made up of 3 amino acids [\[R\]](#):

- [Glutamate](#)
- **Cysteine**
- [Glycine](#)

Low glutathione levels have been linked to cognitive decline, age-related disease, and general mortality among the elderly [\[R, R\]](#).

People take glutathione supplements to help with:

- Oxidative stress and detox
- Immune system support
- Skin aging and damage
- Exercise recovery
- Chronic diseases such as type 2 diabetes, Alzheimer's disease, Parkinson's disease, or COPD

How it helps

Glutathione supplements aid in replenishing reduced levels of this critical antioxidant in the liver, promoting detoxification and protecting against oxidative stress induced by acetaminophen metabolism. This helps mitigate the risk of liver damage following acetaminophen exposure.

6



Betaine (TMG)

IMPACT

1 / 5

EVIDENCE

1 / 5

How to implement

To take Betaine (TMG) as a supplement, consume 500-2000 mg daily, preferably with a meal to enhance absorption. It is recommended to start at the lower end of the dosage range and adjust based on personal tolerance and effectiveness. This supplement can be taken indefinitely for ongoing support of heart health and liver function.

TYPICAL STARTING DOSE

500 mg

Description

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.

How it helps

Betaine supplementation may enhance liver function by promoting the metabolism of homocysteine and aiding in the detoxification processes, potentially mitigating the hepatotoxic effects of acetaminophen and supporting overall liver health.