# GlycanAge report for medical professionals

# HackingBiology.com

Test ID:

Date of sampling:

Date of birth:

GA-RW-020372

05 Feb 2025

31 Aug 1980

This report does not constitute medical advice. Results should be interpreted by a medical professional in context of medical history, clinical signs and symptoms.



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# **Executive summary**

GlycanAge measures **inflammaging**, which indicates the levels of chronic inflammation driven by the immune system as it ages.

# **Results**

We analyse 29 different glycan structures gathered from the blood sample. We group related structures into 5 different indexes.

**Primary indexes** (Shield, Youth, Mature) have either a pro- or anti- inflammatory function. By looking at the ratio between these indexes, we're able to determine biological age of a person.

Supportive indexes (Median, Lifestyle) can help narrow down associations with specific disease types, genetic traits, and/or some lifestyle habits. They don't influence the overall biological age.





# Glycan insights Beta

We've extracted data from over 300 scientific papers to understand how glycan indexes vary in individuals with specific diseases. Full study available on **ScienceDirect**.

We've cross-referenced the most research-supported diseases with your patient's glycan profile.

Overlaps indicate how many of your patient's glycan metrics overlap with disease-specific glycan changes. Diseases have a different number of max overlapping metrics. Refer to disease-specific pages for more info.

**Please note:** This part of the report is still in Beta version; Glycan insights should be triangulated with other clinical data; Glycan changes may reflect progression of pathological changes into disease, and thus occur up to 10 years before the onset of any symptoms.



Area	Condition	Overlaps
Cardiovascular	Inc. risk of hypertension	<b>0/1</b> No significant overlap
	Pre-hypertension	<b>0/1</b> No significant overlap
	Hypertension	0/3 🌺 No significant overlap
	MI & CVA	0/4 🔖 No significant overlap
Metabolic	Type 2 diabetes	0/5 💮 No significant overlap
	Dyslipidemia	0/4 No significant overlap
Autoimmune	Rheumatoid arthritis	0/4 😵 No significant overlap
	Ulcerative colitis	0/4 🐼 No significant overlap
	Crohn's disease	0/5 No significant overlap
	SLE	0/4 No significant overlap
Respiratory	COPD	0/2 No significant overlap

# Result breakdown

Glycans regulate **pro-** and **anti- inflammatory** functions of the immune system.

# GlycanAge result





16 years younger than chronological age



# What does this mean?

GlycanAge measures inflammaging, which indicates the levels of chronic inflammation driven by the immune system as it ages. It is not a diagnostic tool but can provide valuable insights into potential health risks and areas for intervention.

A lower biological age compared to chronological age may indicate a reduced risk of age-related diseases and a healthier aging trajectory. Conversely, a higher biological age may suggest accelerated aging and increased susceptibility to chronic conditions.

Understanding a patient's biological age can help identify potential areas for targeted interventions and assist in developing personalized treatment plans to optimize health and well-being.



# GlycanAge reflects chronic inflammation



### **Optimised lifestyle**

Optimised lifestyle is one of several domains which reduces chronic inflammation. This could include:

- Personalised diet
- Better quality sleep
- Suitable exercise routine
- Better stress management

### Genetic advantage

Some individuals have a favourable genetic make-up when it comes to glycans and/or may have a family history of (super)centenarians.

- Centenarian genes
- Good glycan genes

### **Effect of therapies**

Certain therapies and medications may on their own contribute to a reduction in chronic inflammation. Examples include:

- Hormone replacement therapy
- Prolonged use of steroids
- Biologics

### Other factors

Other less common causes include:

- Current pregnancy
- Bariatric surgery followed by extensive weight loss
- IVIG



### **Unoptimised lifestyle**

Unoptimised lifestyle often associates with higher levels of chronic inflammation. It could include one or several of the following factors:

- Poor diet
- Sleep deprivation
- Over/under exercising
- Poor stress management

### Poor health

Most chronic disease are precipitated or lead to raised chronic inflammation levels. Other factors and conditions that may lead to raised inflammation:

- Existing chronic condition(s)
- Hormone imbalance (post-pregnancy, menopause, testosterone deficiency)

### **Future health**

Individuals at risk of a disease, particularly those with strong family history of certain diseases, may present with raised chronic inflammation levels:

• Family history of chronic diseases



### **Future investigation**

You may investigate further for signs of chronic inflammation:

- Check for lack of nutrition
- Check hormone levels
- Assess cardiovascular risk
- Blood tests
- Check of unusual symptoms

# Biological age over time

Tracking biological age over time provides valuable insights into a patient's aging trajectory. Monitoring changes in biological age can help to:

- Assess the effectiveness of interventions:

  Evaluate the impact of lifestyle modifications,

  treatments, or medications on aging biomarkers.
- Identify early warning signs: Detect potential health issues before they become symptomatic.
- Personalize care plans: Tailor treatment and prevention strategies based on individual aging patterns.



We currently have only one data point for this patient. Additional data points over time are required to create a graph of biological age over time.



# Glycan Shield (S)

This index represents glycans with sialic acid.

Sialylated glycans help reduce inflammation and are more abundant in younger people, so having a **higher** score in this index is better.

### What to look into?

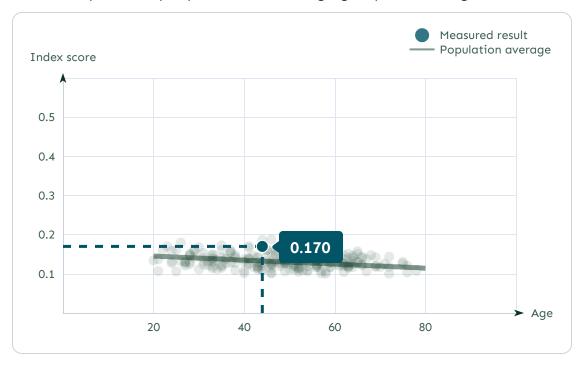
- Check your patient's diet (exclusion diets such as vegan, carnivore, keto, etc.)
- Check patient's eating habits (fasting windows, meal timing)
- Check which supplements your patient is taking
- Consider simple blood tests for nutrient deficiencies

### How to optimise the index:

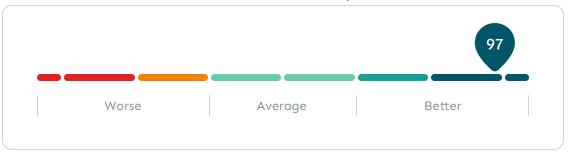
- Optimize patient's diet and eating habits (fasting windows/frequency)
- Consider supplementation (Mg, Omega-3, Vit D)
- Optimize their workouts (ensure proper rest and recovery)
- Experimental data: NAD+ supplementation and vitamins



### Compared to people in the same age group and biological sex:



### This result ranks in the 97<sup>th</sup> percentile:



# Glycan Youth (G2)

This index groups glycans that contain two galactoses.

Glycans with galactoses help reduce inflammation and are more abundant in younger people, so having a higher score in this index is better.

### What to look into?

- Check body composition
- Check for autoimmune conditions (metabolic diseases, skin conditions, etc.)
- Check levels of sex hormones (testosterone)

### How to optimise the index:

- Weight loss if needed (caloric restriction, adequate exercise)
- Sex hormone optimization (experimental data shows that testosterone replacement therapy improves this index)
- Management of autoimmune conditions



### Compared to people in the same age group and biological sex:



### This result ranks in the 47<sup>th</sup> percentile:



# Glycan Mature (G0)

This index groups glycans that are missing both of their galactoses.

Glycans without galactoses promote inflammation and are more abundant in older people, so having a **lower** score in this index is better.

### What to look into?

- Check levels of sex hormones (testosterone)
- Consider checking other hormones thyroid hormones, cortisol, etc.
- Check body composition

### How to optimise the index:

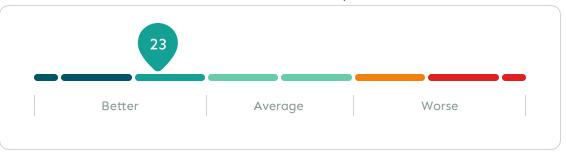
- Sex hormone optimization (experimental data shows that testosterone replacement therapy improves this index)
- Weight loss if applicable



### Compared to people in the same age group and biological sex:



### This result ranks in the 23<sup>rd</sup> percentile:



# Glycan Median (G1)

This index groups glycans that contain one galactose making them more protective compared to those without one but not more than those containing two of them.

These glycans have a prominent genetic component and neither too much nor too little of them is optimal.

### What to look into?

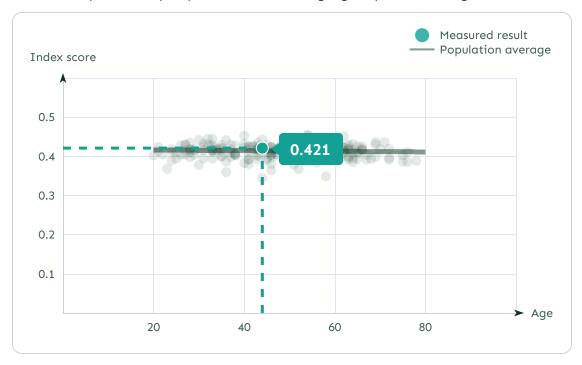
- Check their Glycan Mature and Glycan Youth indexes
- Assess cardiovascular health (family history, blood pressure, lipid profile, etc.)
- Check for autoimmune conditions

### How to optimise the index:

- Cardiovascular risk management
- Autoimmune disease management
- Focus on optimizing Glycan Youth and Glycan Mature indexes



### Compared to people in the same age group and biological sex:



### This result ranks in the 66<sup>th</sup> percentile:



# Glycan Lifestyle (B)

This index groups glycans that have a bisecting GlcNAc.

Glycans with this modification promote inflammation, so having a lower score in this index is better.

### What to look into?

- Patient's smoking status
- Environmental conditions (e.g., air quality, toxin check)
- Assess stress levels and sleep quality
- Check body composition
- Check diet quality (particularly intake and frequency of ultra-processed foods)

### How to optimise the index:

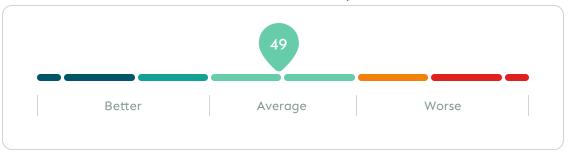
- Quitting smoking
- Manage stress and ensure proper sleeping pattern
- Weight loss if applicable



### Compared to people in the same age group and biological sex:



### This result ranks in the 49<sup>th</sup> percentile:





# Glycan insights Beta

# Specific diseases have their own unique **glycan fingerprint** that can provide valuable insights into a person's health.

**Please note:** This part of the report is still in Beta version; Glycan insights should be triangulated with other clinical data; Glycan changes may reflect progression of pathological changes into disease, and thus occur up to 10 years before the onset of any symptoms.



# How to interpret glycan insights

Patient's glycan fingerprint compared to disease-specific patient profiles

Disease-specific changes in glycan indexes are represented by arrows. Your patient's results are shown above arrow.

2 At-a-glance summary

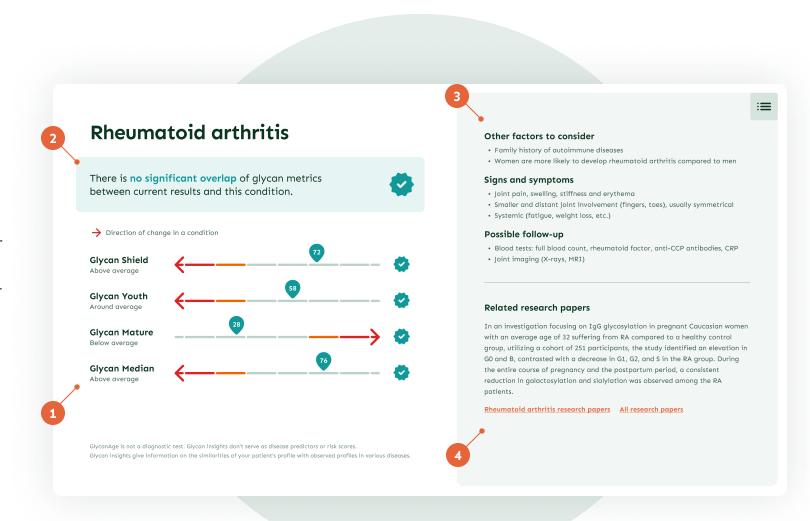
Here you can find a summary of glycan metrics. However, it is important to take your patient's full medical history into account, as well as observe the amount of overlap of their glycan fingerprint.

3 Follow-up hints

Useful follow-up tests and symptoms to check for when assessing the risk of a disease.

4 Related research papers

Research that was done to observe glycosylation patterns within a specific disease or condition.



# Increased risk of hypertension

There is **no significant overlap** of glycan metrics between current results and this condition.



→ Direction of change in a condition

Glycan Lifestyle

Around average





GlycanAge is not a diagnostic test. Glycan insights don't serve as disease predictors or risk scores.

Glycan insights give information on the similarities of your patient's profile with observed profiles in various diseases.



### Other factors to consider

- Family history of cardiovascular diseases
- BMI above 25

### Signs and symptoms

• Usually asymptomatic

### Possible follow-up

- Serial blood pressure (BP) measurements ± 24-hour BP monitoring
- BMI and/or body composition check
- Basic bloods (lipid profile, renal and liver function)

### Related research papers

### N-glycosylation of immunoglobulin G predicts incident hypertension

In a study investigating the relationship between IgG glycosylation and hypertension, 989 unrelated incident hypertension cases and 1,628 controls from the TwinsUK cohort, with a mean follow-up of 6.3 years, were examined. The average age of the participants was 56. The findings, which included an observed increase in B, were validated in additional cohorts from the "10,001 Dalmatians" (106 individuals) and KORA S4 (729 individuals). A predictive model incorporating age, BMI, mean arterial pressure (MAP), and specific glycan peaks with B modifications demonstrated robust predictive accuracy, achieving a very high AUC of 0.983.

# **Pre-hypertension**

There is **no significant overlap** of glycan metrics between current results and this condition.



→ Direction of change in a condition









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### Other factors to consider

- Family history of cardiovascular diseases
- BMI above 25

### Signs and symptoms

• Usually asymptomatic

### Possible follow-up

- Serial BP measurements and/or 24-hour BP monitoring
- BMI and/or body composition check
- Basic bloods (lipid profile, renal and liver function)

### Related research papers

<u>The Association Between Glycosylation of Immunoglobulin G and Hypertension:</u>

<u>A Multiple Ethnic Cross-Sectional Study</u>

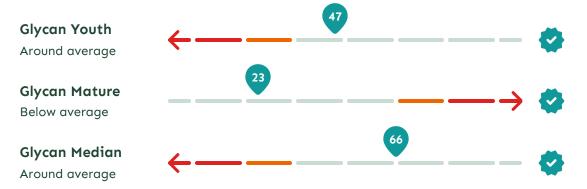
In an extensive study with 4,757 participants, including 913 from the Chinese Han Beijing population, 985 from Croatian Korčula, 896 from Croatian Vis, and 1,963 from Scottish Orkney, researchers investigated changes in IgG glycans associated with prehypertension and hypertension. The demographic composition of the study was approximately 40% female and 60% male participants. A notable observation was the decrease in G2 in the cohort with prehypertension.

# Hypertension

There is **no significant overlap** of glycan metrics between current results and this condition.



→ Direction of change in a condition



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### Other factors to consider

- Family history of cardiovascular diseases
- BMI above 25

### Signs and symptoms

- Usually asymptomatic
- BP consistently >140/90 mmHg
- Signs of malignant hypertension (headache, dizziness, breathlessness, etc.)

### Possible follow-up

- Serial BP measurements and/or 24-hour BP monitoring
- BMI and/or body composition check
- Basic blood tests (lipid profile, renal and liver function)

### Related research papers

<u>The Association Between Glycosylation of Immunoglobulin G and Hypertension:</u>

<u>A Multiple Ethnic Cross-Sectional Study</u>

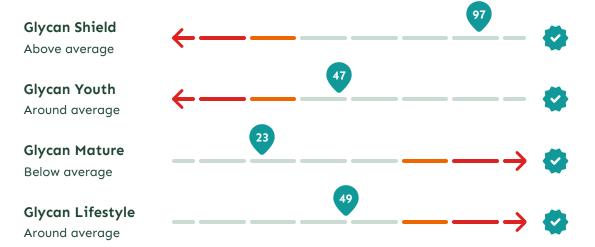
In an extensive study with 4,757 participants, including 913 from the Chinese Han Beijing population, 985 from Croatian Korčula, 896 from Croatian Vis, and 1963 from Scottish Orkney, researchers investigated changes in IgG glycans associated with prehypertension and hypertension. The demographic composition of the study was approximately 40% female and 60% male participants. Among hypertension patients, there was a noted decrease in G2 and S, alongside an increase in G0.

MI & CVA Myocardial infarction and cerebrovascular accident

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→ Direction of change in a condition



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### Other factors to consider

- Family history of cardiovascular diseases
- BMI above 25

### Signs and symptoms

- Past medical history (cardiometabolic syndrome, autoimmune disease)
- Medication history (e.g., statins, blood thinners)
- Current/previous smoking history

### Possible follow-up

- Blood tests: basic and extended lipid profile (e.g., Lp(a), ApoB), hsCRP, homocysteine, renal and liver function, HbA1c
- BP check
- ECG
- Cardiology referral for other tests (e.g., cardiac echo, coronary CT)

### Related research papers

Immunoglobulin G N-Glycosylation Signatures in Incident Type 2 Diabetes and **Cardiovascular Disease** 

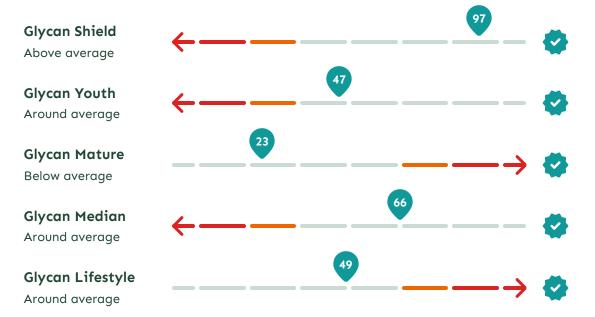
In the EPIC-Potsdam cohort, involving 2,175 participants in the cardiovascular disease (CVD) subcohort, which includes 417 cases of MI and CVA, changes in IgG glycosylation were analysed. This cohort comprised 61% females and 39% males, with an average age of 49. For female participants, a significant association was found with a single glycan peak (peak 22), identified as a predictive marker for future MI and CVA, exhibiting a hazard ratio (HR) of 0.74.

# Type 2 diabetes

There is **no significant overlap** of glycan metrics between current results and this condition.



→ Direction of change in a condition



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Glycan insights give information on the similarities of your patient's profile with observed profiles in various diseases.



### Other factors to consider

- Family history of cardiovascular diseases
- BMI above 25

### Signs and symptoms

- Fatigue
- Increased thirst and frequent urination
- Slow wound healing, blurred vision, frequent thrush

### Possible follow-up

- Blood tests: full blood count, renal and liver function, fasting glucose and insulin, HbA1c, HOMA-IR
- BP check
- BMI and/or body composition check

### Related research papers

<u>IgG glycan patterns are associated with type 2 diabetes in independent</u> European populations

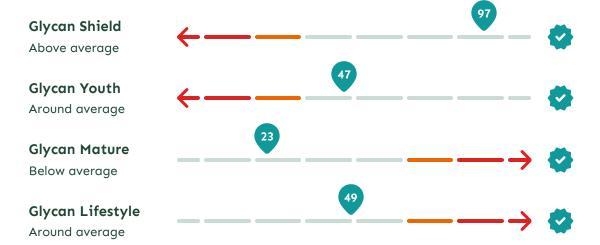
In the DiaGene study, a population-based case-control study with 1,886 cases and 854 controls, 58 IgG glycan traits were analyzed. The findings were then replicated and meta-analyzed in the combined population-based studies of CROATIA-Korcula, CROATIA-Vis, and ORCADES, involving 162 cases and 3,162 controls. Within this research, 46% of cases and 60% of controls were female, with an average participant age of 65. The analysis revealed a decrease in G1, G2, and S glycans, alongside an increase in G0 and B. A predictive model incorporating four specific glycan peaks achieved an AUC of 0.729. When IgG glycans were added to a model containing only age and sex, the AUC improved from 0.542 to 0.734, although incorporating them into a more comprehensive model did not significantly enhance the AUC.

# **Dyslipidemia**

There is **no significant overlap** of glycan metrics between current results and this condition.



→ Direction of change in a condition



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### Other factors to consider

- Family history of cardiovascular diseases
- BMI above 25

### Signs and symptoms

• Usually asymptomatic

### Possible follow-up

- Lipid profile blood tests: basic and extended (incl. oxLDL, VLDL, LDL-P, Lp-PLA2, Lp(a), ApoB)
- Other blood tests: hsCRP, homocysteine, renal and liver function, HbA1c
- BP check

### Related research papers

# <u>The changes of immunoglobulin G N-glycosylation in blood lipids and</u> dyslipidaemia

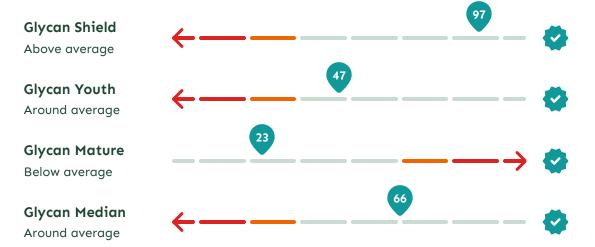
In a study focusing on IgG glycome changes related to dyslipidemia, 598 participants (67% female participants) were selected from a larger observational cross-sectional study conducted in 2012, which initially involved 913 participants of Chinese Han ancestry from Beijing. The glycomic analysis revealed a decrease in G2 and S, coupled with an increase in G0 and B. A predictive model incorporating six specific glycan structures was developed from these findings, resulting in an AUC of 0.692.

# Rheumatoid arthritis

There is **no significant overlap** of glycan metrics between current results and this condition.



→ Direction of change in a condition



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Glycan insights give information on the similarities of your patient's profile with observed profiles in various diseases.



### Other factors to consider

- Family history of autoimmune diseases
- Women are more likely to develop rheumatoid arthritis compared to men

### Signs and symptoms

- Joint pain, swelling, stiffness and erythema
- Smaller and distant joint involvement (fingers, toes), usually symmetrical
- Systemic (fatigue, weight loss, etc.)

### Possible follow-up

- Blood tests: full blood count, rheumatoid factor, anti-CCP antibodies, CRP
- Joint imaging (X-rays, MRI)

### Related research papers

<u>Association between galactosylation of immunoglobulin G and improvement of rheumatoid arthritis during pregnancy is independent of sialylation</u>

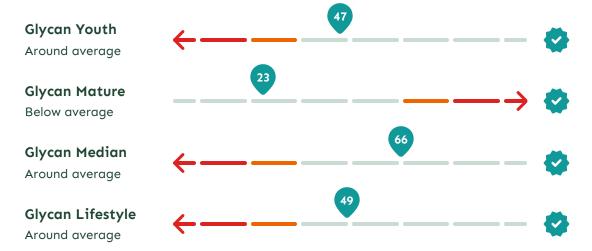
In an investigation focusing on IgG glycosylation in pregnant Caucasian women with an average age of 32 suffering from RA compared to a healthy control group, utilizing a cohort of 251 participants, the study identified an elevation in G0 and B, contrasted with a decrease in G1, G2, and S in the RA group. During the entire course of pregnancy and the postpartum period, a consistent reduction in galactosylation and sialylation was observed among the RA patients.

# Ulcerative colitis

There is **no significant overlap** of glycan metrics between current results and this condition.



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Glycan insights give information on the similarities of your patient's profile with observed profiles in various diseases.



### Other factors to consider

• Family history of autoimmune diseases

### Signs and symptoms

- Abdominal pain and cramping
- Urgency to defecate
- Recurring diarrhea (± blood)

### Possible follow-up

- Blood tests: full blood count, renal and liver function, CRP
- Stool tests: faecal immunochemical test (FIT), fecal calprotectin
- Referral for CT colonoscopy

### Related research papers

<u>Inflammatory bowel disease associates with proinflammatory potential of the immunoglobulin G glycome</u>

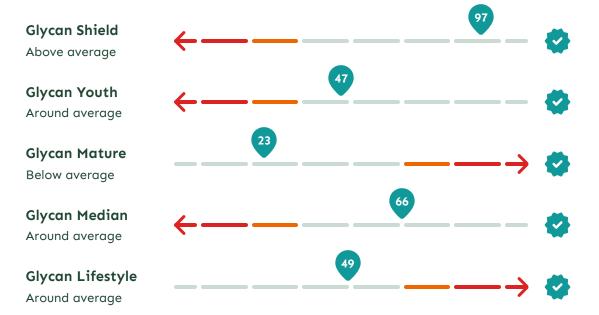
In a Scottish study examining IgG glycosylation in IBS, focusing on the ulcerative colitis (UC) segment, a cohort of 507 UC patients and 320 controls, all with an average age of 45, was evaluated. The analysis revealed a significant increase in G0 and a decrease in G1 in the UC patients compared to the controls. Observed alterations of specific glycan peaks demonstrated predictive power, with an area under the curve (AUC) of 0.72, indicating their potential utility in distinguishing between UC patients and healthy individuals.

# Crohn's disease

There is **no significant overlap** of glycan metrics between current results and this condition.



→ Direction of change in a condition



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### Other factors to consider

• Family history of autoimmune diseases

### Signs and symptoms

- Abdominal pain and cramping
- Recurring diarrhea (± blood)
- Weight loss

### Possible follow-up

- Blood tests: full blood count, renal and liver function, CRP
- Stool tests: faecal immunochemical test (FIT), faecal calprotectin
- Referral for CT colonoscopy

### Related research papers

<u>Inflammatory bowel disease associates with proinflammatory potential of the immunoglobulin G glycome</u>

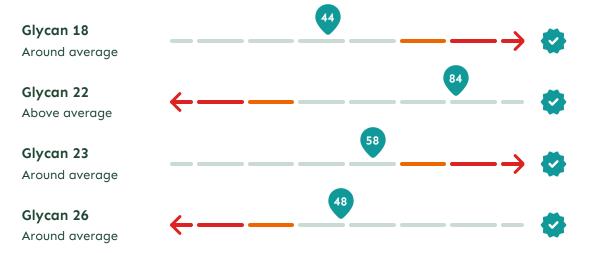
In a Scottish study examining IgG glycosylation changes in IBS, a cohort of 287 CD patients and 320 controls, all with an average age of 42, was evaluated. The analysis indicated a significant increase in G0 and B glycan traits and a decrease in G1, G2, and S in CD patients compared to controls. The changes in specific glycan peaks showed predictive value, with an AUC of 0.77.

# **SLE** Systemic lupus erythematosus

There is **no significant overlap** of glycan metrics between current results and this condition.



→ Direction of change in a condition



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Glycan insights give information on the similarities of your patient's profile with observed profiles in various diseases.



### Other factors to consider

- Family history of autoimmune diseases
- Women are more likely to develop SLE compared to men

### Signs and symptoms

- Systemic (e.g., fatigue, weight loss, mouth ulcers, butterfly skin rash)
- Organ-specific (chest pain, difficulty breathing, leg swelling, anaemia, etc.)
- Joint pain and swelling

### Possible follow-up

- Blood tests: full blood count, renal and liver function, CRP, ESR, autoantibodies (e.g., ANA, anti-dsDNA)
- Urinalysis
- Organ-targeted imaging (e.g., CT thorax, CT abdomen)

### Related research papers

<u>Association of Systemic Lupus Erythematosus With Decreased</u> <u>Immunosuppressive Potential of the IgG Glycome</u>

In an analysis focusing on SLE, a discovery cohort consisting of 261 predominantly female SLE patients and 247 matched controls of Latin American Mestizo origin was studied for changes in IgG glycome, alongside two independent replication cohorts from Trinidad (108 SLE patients and 193 controls) and China (106 SLE patients and 105 controls). The study identified specific alterations in glycan traits, including a decrease in G2 and S, and notable changes in glycan peaks, with increases in peaks 18 and 23 and decreases in peaks 22 and 26. Utilizing these peak variations, a predictive model was developed, achieving an AUC of up to 0.882.



COPD Chronic obstructive pulmonary disease

There is **no significant overlap** of glycan metrics between current results and this condition.



→ Direction of change in a condition



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### Signs and symptoms

- Difficulty breathing
- Chronic cough (± productive)
- Fatigue

### Possible follow-up

- Blood tests: full blood count
- Spirometry
- ECG, chest X-ray

### Related research papers

N-glycosylation patterns of plasma proteins and immunoglobulin G in chronic obstructive pulmonary disease

In a Croatian study focusing on COPD, researchers analyzed IgG glycosylation in 137 COPD patients and 95 controls in the discovery cohort, and 61 COPD patients and 148 controls in a replication cohort from another medical center. The discovery cohort included 97 female participants (42%), while the replication cohort had 116 females (56%). The study observed a decrease in G1 and an increase in B glycan structures in COPD patients.

# **Influencing factors**

Lifestyle, life stages, as well as pharmacological interventions can have a significant impact on chronic inflammation, which will likely reflect on GlycanAge results.

# Diet

Dietary habits shape inflammation levels and affect the GlycanAge score. While short-term lapses in diet, such as an occasional indulgence, won't impact the GlycanAge score, long term changes in diet will most likely affect the results.

There is no one-size-fits-all diet, as each person's metabolism is unique and finding the optimal diet for an individual is a difficult task. This makes GlycanAge a valuable tool that can help you understand whether your patient's diet is good for them or if it fuels inflammation.

Our research found that in overweight individuals, only caloric restriction has an overall anti-inflammatory effect in most people whereas other types of diets show different effects depending on a individual.





### Related research papers

# Effects of low-calorie and different weight-maintenance diets on IgG glycome composition

The study investigated the effects of different diets on IgG glycans, analyzing 1,850 samples from the Diogenes study, one of the largest dietary intervention studies. A total of 938 participants who were overweight underwent an 8-week low-calorie diet (800 kcal/day), followed by one of the weight maintenance diets for 6 months:

- Low protein / low glycemic index
- Low protein / high glycemic index
- High protein / low glycemic index
- High protein / high glycemic index

Only caloric restriction (CR) resulting in weight loss showed anti-inflammatory effects. After 8 weeks of CR, a decrease was observed in the pro-inflammatory Glycan Mature index and an increase in the anti-inflammatory Glycan Shield index. These changes returned to baseline after some of the weight was gained back on maintenance diets.

While no statistically significant changes in IgG glycans were observed on the maintenance diets, individual responses varied—some participants showed improvement, while others experienced worsening results. This variability underscores the importance of a personalized approach to nutrition showing there is no one-size-fits-all diet.

## **Stress**

When the body experiences stress, it activates the fight-or-flight response, which is beneficial in short-term situations. However, chronic stress disrupts the hormonal balance, keeping hormones like adrenaline and cortisol high, which leads to disruption of the immune system and fuels inflammation.

Therefore, individuals who are under a lot of stress can have higher GlycanAge scores. Both individuals under constant stress, such as work-related pressure, and those who encounter sudden, intense stress, like major life events, may experience an increase in their GlycanAge due to the body's sustained inflammatory response.





### Related research papers

N-glycosylation profiling of plasma provides evidence for accelerated physiological aging in post-traumatic stress disorder

The study aimed to explore whether traumatic stress accelerates the aging process by analyzing glycan profiles in individuals experiencing varying levels of stress. A total of 32 participants were included: 13 individuals with post-traumatic stress disorder (PTSD), 9 trauma-exposed individuals without PTSD, and 10 low-stress control subjects. The researchers used the GlycoAge test, a biomarker for physiological aging, and found that, on average, individuals with PTSD and those exposed to trauma showed signs of accelerated aging by 15 years compared to the low-stress controls./day), followed by one of the weight maintenance diets for 6 months:

# Insufficient sleep

Insufficient sleep has been shown to raise inflammatory markers in the body. Both acute sleep deprivation (e.g., being awake for 24 hours) and chronic insufficient sleep can increase inflammation.

While short-term sleep deprivation does not affect the GlycanAge score, long-term insufficient sleep can cause elevated GlycanAge score.

Additionally, individuals with sleep disorders such as sleep apnea, which disrupts normal breathing during sleep, may also have higher scores due to the inflammatory nature of this condition. Our research indicates that people with severe obstructive sleep apnea (OSA) are, on average, 6.9 years older biologically than their chronological age.





### Related research papers

Not-So-Sweet Dreams: Plasma and IgG N-Glycome in the Severe Form of the Obstructive Sleep Apnea

The aim of the study was to explore whether IgG glycans can be used as biomarkers for severe obstructive sleep apnea (OSA). IgG and total plasma glycans were analyzed in 70 subjects with severe OSA and 23 controls. Significant changes were observed in both IgG and total plasma glycans. Furthermore, patients with severe OSA exhibited accelerated biological aging, with GlycanAge score on average being 6.9 years higher than their chronological age. This study suggests that both IgG and total plasma glycans might be considered biomarkers for severe OSA./day), followed by one of the weight maintenance diets for 6 months:

# Overexercising

Although exercise and regular physical activity are crucial for good health, overexercising can have negative impacts on levels of inflammation.

The acute inflammation caused by a workout is beneficial. However, constant overexercise without proper recovery period can cause an increase in low-grade systemic inflammation and may increase the GlycanAge score.

Professional athletes and individuals with extreme exercise regimens generally have a higher GlycanAge score compared to those who engage in moderate and balanced exercise.





### Related research papers

Regular moderate physical exercise decreases Glycan Age index of biological age and reduces inflammatory potential of Immunoglobulin G

The study included 276 healthy participants divided into 4 groups based on their activity level:

- inactive group
- newly involved recreational group
- regularly moderate active group
- professionally competing athlete group

On average, those who exercise regularly had the lowest GlycanAge score when compared to other groups. It was found that those who exercises regularly had on average a lower GlycanAge score by 7.4 years when compared to inactive individuals (around 10 years for women and 6 for men). Professional athletes showed an increased GlycanAge score by 7.6 years on average compared to those who exercise regularly, however, this trend was observed in women only.

### **Additional notes**

Some forms of intense exercise, such as repeated sprint training (RST), show positive effects on glycans and lead to a reduction in biological age.

# Weight loss

Excess body weight significantly influences IgG glycans and is associated with a higher GlycanAge score and poor index scores.

Weight loss, whether through dieting, exercise, or bariatric surgery, generally leads to a reduction in the GlycanAge score and improvements in nearly all indexes.

However, extreme weight loss can temporarily increase the GlycanAge score. Upon fat tissue reduction, inflammatory molecules stored in the fat are released into the bloodstream, causing increased inflammation.











### Related research papers

### Extensive weight loss reduces glycan age by altering IgG N-glycosylation

Individuals scheduled for bariatric surgery (n=37) were subjected to 3 weeks of low-calorie diet (900 kcal/daily). In the short period while under caloric restriction, an improvement in the Glycan Lifestyle index was observed, indicating a reduced proinflammatory potential of IgG glycans.

Following the bariatric surgery, additional improvements such as a decrease in the pro-inflammatory Glycan Mature index and an increase in anti-inflammatory indexes Glycan Youth and Glycan Mature were observed.

The results were further validated on 1680 individuals from the TwinsUK cohort followed for 20 years where it was observed that reduction of BMI through weight loss was associated with a reduced GlycanAge score and improvements in the Glycan Mature and Glycan Youth indexes.

### **Additional notes**

In another <u>study</u>, we investigated the effects of different diet types on IgG glycans and found that caloric restriction, rather than a specific type of diet, is the main driver of positive changes.

# **Supplements**

Supplements can affect the GlycanAge score both positively and negatively, as individuals have different responses to them.

Our studies looking at the effects of omega-3s and NAD+ precursor supplements, show positive effects on the GlycanAge score and indexes.

Experimentally we know various other supplements affect the GlycanAge score, especially if the supplements target common deficiencies (e.g. vitamin D) or have anti-inflammatory properties.

However, not all supplements are suitable for everyone and GlycanAge can help you understand how your patient is responding to them.





### Related research papers

The effect of n-3 polyunsaturated fatty acids-enriched hen eggs consumption on IgG and total plasma protein N-glycosylation in healthy individuals and cardiovascular patients

The study investigated the effects of omega-3 PUFAs-enriched hen eggs consumption on IgG glycans and other inflammatory biomarkers in healthy people and in cardiovascular (CV) patients. In healthy individuals who consumed omega-3 enriched eggs, we saw a decrease in the Glycan Lifestyle index and in those consuming normal eggs we saw an increase in the Glycan Mature index. In CV patients, we saw a switch towards a less-inflammatory profile of the total blood plasma glycans.

### The use of a systems approach to increase NAD+ in human participants

This double-blinded, placebo-controlled crossover trial investigated the efficacy of the NAD+ supplement Nuchido TIME+. Healthy participants (n=26) aged 21-72 were randomized to receive either the supplement or a placebo for 28 days, followed by a one-week washout period, after which the groups switched treatments. Participants taking the NAD+ supplement experienced an average decrease in their GlycanAge score by 1.26 years after only 28 days, a change not observed in those receiving the placebo.

# Metformin

Metformin is a prescription drug commonly used for treating type 2 diabetes and insulin resistance. Due to its supposed benefits, it is also being used in nondiabetics.

The effects of metformin are still being researched, especially for non-diabetics. Our studies show that metformin generally does not significantly influence GlycanAge in non-diabetics. However, some individuals do experience changes in their GlycanAge scores while on metformin, reflecting their unique response to the treatment.





### Related research papers

Effects of testosterone and metformin on the GlycanAge index of biological age and the composition of the IgG glycome

This clinical trial investigated the effects of metformin and testosterone replacement therapy (TRT) in 82 male participants dealing with obesity and low testosterone levels. They were randomized into receiving:

- metformin
- TRT
- metformin+TRT
- placebo

Samples were taken at 3 timepoints - before starting the treatment, at the 6-month mark, and again one year into the treatment. Significant changes in IgG glycans were observed only in the groups receiving TRT, whether alone or combined with metformin, indicating that these changes were attributed to TRT rather than metformin. In the metformin group, there was no consistent trend in GlycanAge scores - some individuals experienced a minor increase, while others experienced a minor decrease. The exception was one participant who showed a significant decrease in their GlycanAge score after taking metformin.

### Additional notes

Preliminary data shows that metformin has some positive effects on IgG glycans in diabetics.

# **Andropause**

Andropause, or male menopause, is characterized by a gradual decline in testosterone levels.

While testosterone is the primary male sex hormone, it also serves as a precursor for estrogen production, which has anti-inflammatory properties, as seen from its effects on IgG glycans.

Estrogen regulates IgG glycans in both men and women. Therefore, men who are going through andropause, with lower levels of testosterone and estrogen, tend to have higher GlycanAge scores and a higher Glycan Mature index.







### Related research papers

### Estrogens regulate glycosylation of IgG in women and men

The study examined the effects of sex hormones on IgG glycosylation in both men and women. A group of men were given goserelin, a synthetic hormone that inhibits the production of testosterone. Those who received testosterone replacement via gel maintained healthy levels of both testosterone and estrogen, whereas those on placebo did not, resulting in an increase in the pro-inflammatory Glycan Mature index.

To evaluate whether the negative effects were due to the depletion of testosterone or estrogen, another group of men received an aromatase inhibitor, which prevents the conversion of testosterone to estrogen, while a control group did not. The men who were unable to produce estrogen showed an increase in pro-inflammatory glycans, confirming that it is testosterone-derived estrogen that modulates IgG glycosylation.

### Additional notes

Reduction in testosterone levels in younger men can also result in an increase in the GlycanAge score, considering the big role sex hormones play in regulating IgG glycans.

# Testosterone replacement therapy

Testosterone replacement therapy (TRT) is used to treat testosterone deficiencies in men.

TRT can have anti-inflammatory effects in men with lower testosterone levels, leading to a reduction in the GlycanAge score and improvements in multiple indexes, including Glycan Shield, Glycan Youth, and Glycan Mature.



**Biological age**Chronic inflammation





### Related research papers

### Estrogens regulate glycosylation of IgG in women and men

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### Additional notes

There are different types and methods of administering TRT, and not every type is suitable for everyone. GlycanAge responds to different types of TRT and can be used as a valuable tool for tailoring individual treatment plans.

# Help us enhance our report

Share your insights

We strive for continuous improvement and your feedback is invaluable to us. As we seek to refine the quality and relevance of our report, we invite you to contribute your perspectives and suggestions.

Your insights will ensure that our future reports are even more aligned with your needs and interests, providing you with the most valuable and actionable information.

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# Research papers

### **Biological** age

Glycans Are a Novel Biomarker of Chronological and Biological Ages

Immunoglobulin G glycans - Biomarkers and molecular effectors of aging

Heritability of the glycan clock of biological age

Immunoglobulin G glycosylation in aging and diseases

IgG glycans in health and disease: Prediction, intervention, prognosis, and therapy

### **Influencing factors**

Immunoglobulin G galactosylation and sialylation are associated with pregnancy-induced improvement of rheumatoid arthritis and the postpartum flare: results from a large prospective cohort study

Periodic Changes in the N-Glycosylation of Immunoglobulin G During the Menstrual Cycle

Immunoglobulin G glycome composition in transition from premenopause to postmenopause

Effects of estradiol on biological age measured using the glycan age index

Estrogens regulate glycosylation of IgG in women and men

The effect of n-3 polyunsaturated fatty acids-enriched hen eggs consumption on IgG and total plasma protein N-glycosylation in healthy individuals and cardiovascular patients

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Effects of testosterone and metformin on the GlycanAge index of biological age and the composition of the IaG alycome

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N-glycosylation profiling of plasma provides evidence for accelerated physiological aging in post-traumatic stress disorder

Not-So-Sweet Dreams: Plasma and IgG N-Glycome in the Severe Form of the Obstructive Sleep Apnea

Intense Physical Exercise Induces an Anti-inflammatory Change in IgG N-Glycosylation Profile

<u>Physical Exercise Induces Significant Changes in Immunoglobulin G N-Glycan Composition in a Previously</u> Inactive, Overweight Population

### Diseases

N-glycosylation of immunoglobulin G predicts incident hypertension

The Association Between Glycosylation of Immunoglobulin G and Hypertension: A Multiple Ethnic Cross-Sectional Study

Immunoglobulin G N-Glycosylation Signatures in Incident Type 2 Diabetes and Cardiovascular Disease

<u>Glycosylation Profile of Immunoglobulin G Is Cross-Sectionally Associated With Cardiovascular Disease Risk</u>
Score and Subclinical Atherosclerosis in Two Independent Cohorts

<u>IgG N-Glycosylation Is Altered in Coronary Artery Disease</u>

IgG glycan patterns are associated with type 2 diabetes in independent European populations

The changes of immunoglobulin G N-glycosylation in blood lipids and dyslipidaemia

Association between galactosylation of immunoglobulin G and improvement of rheumatoid arthritis during pregnancy is independent of sialylation

IgG Fc galactosylation predicts response to methotrexate in early rheumatoid arthritis

<u>Low galactosylation of IgG associates with higher risk for future diagnosis of rheumatoid arthritis during 10</u> years of follow-up

Inflammatory bowel disease associates with proinflammatory potential of the immunoglobulin G glycome

Glycosylation of Immunoglobulin G Associates With Clinical Features of Inflammatory Bowel Diseases

<u>A unique serum IgG glycosylation signature predicts development of Crohn's disease and is associated with pathogenic antibodies to mannose glycan</u>

<u>Association of Systemic Lupus Erythematosus With Decreased Immunosuppressive Potential of the IgG</u> Glycome

N-glycosylation patterns of plasma proteins and immunoglobulin G in chronic obstructive pulmonary disease

Estrogens regulate glycosylation of IgG in women and men

Immunoglobulin G glycome composition in transition from premenopause to postmenopause