GlycanAge report for medical professionals

# Holistic Longevity London

 Test ID:
 Date of sampling:
 Date of birth:

 GA-RW-016991
 15 Feb 2024
 15 Jan 1984

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

Report v2.0

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#### <u>Glycan insights (Beta)</u>

How to interpret glycan insights Increased risk of hypertension Pre-hypertension Hypertension MI & CVA Atherosclerosis Coronary artery disease Type 2 diabetes Dyslipidemia Rheumatoid arthritis Ulcerative colitis Crohn's disease SLE COPD Perimenopause

#### **Influencing factors**

Diet Stress Insufficient sleep Exercise Overexercising Weight loss Supplements Metformin Irregular cycles Pregnancy Post-pregnancy Perimenopause Hormone replacement therapy **Hint:** You can click on this icon from any page to return here. 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 <u>ScienceDirect</u>.

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	0/1 🔮 No significant overlap
	Hypertension	1/3 嫯 No significant overlap
	MI & CVA	0/1 蓉 No significant overlap
	Atherosclerosis	1/5 🤹 No significant overlap
	Coronary artery disease	0/2 嫯 No significant overlap
Metabolic	Type 2 diabetes	1/5 🔮 No significant overlap
	Dyslipidemia	0/4 🔮 No significant overlap
Autoimmune	Rheumatoid arthritis	1/4 🔮 No significant overlap
	Ulcerative colitis	2/4 嫯 No significant overlap
	Crohn's disease	1/5 嫯 No significant overlap
	SLE	1/4 🔮 No significant overlap
Respiratory	COPD	1/2 🕂 Minor overlap
Female	Perimenopause	0/4 🔮 No significant overlap

**Result breakdown** 

# Glycans regulate **pro-** and **antiinflammatory** functions of the immune system.

### GlycanAge result



# **10 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



#### Lower biological age Lower 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



#### Higher biological age Higher chronic inflammation

#### 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



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



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### 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 (especially in peri- and menopausal women)

#### How to optimise the index:

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





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

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## 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?

- Assess hormonal health (estrogen, progesterone)
- Check for symptoms of menopause if age indicates
- Consider checking other hormones thyroid hormones, cortisol, etc.
- Check body composition

#### How to optimise the index:

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







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# 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:



# 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







Glycan insights Beta

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

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# 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 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.

#### Rheumatoid arthritis



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 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**

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.

#### Rheumatoid arthritis research papers All research papers

# Increased risk of hypertension

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



 $\rightarrow$  Direction of change in a condition

**Glycan Lifestyle** Below average



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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 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.

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# **Pre-hypertension**

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



→ Direction of change in a condition

**Glycan Youth** Around average



#### 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.

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# Hypertension

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



 $\rightarrow$  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

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



 $\rightarrow$  Direction of change in a condition

Glycan Glycan 22 Around average

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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.

# Atherosclerosis

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



 $\rightarrow$  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
- Signs of coronary artery disease (e.g., self-resolving chest pain, breathlessness)
- Signs of peripheral artery disease (e.g., leg pain during activity)

#### 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., coronary artery calcium score)

#### **Related research papers**

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

In a study involving 2,970 women aged 40–79 from the TwinsUK cohort, IgG glycosylation was examined in relation to the estimated 10-year risk of atherosclerotic cardiovascular disease and the presence of carotid and femoral plaque. A decrease in G1, G2 and S was observed, alongside an increase in G0 and B. These findings were replicated in 967 women from the ORCADES cohort (Orkney Complex Disease Study). Additionally, some of these glycan changes were also associated with 845 men in the study.

# Coronary artery 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 cardiovascular diseases
- BMI above 25

#### Signs and symptoms

- Self-limiting chest pain ± radiation into jaw/left arm/back
- Breathlessness
- Other (syncope, palpitations, leg edema, orthopnea, etc.)

#### 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., stress echocardiogram)

#### **Related research papers**

#### IgG N-Glycosylation Is Altered in Coronary Artery Disease

In the CAPIRE study, male and female participants aged 45 to 75 years without prior clinical manifestations of coronary artery disease (CAD) were assessed using coronary computed tomography angiography (CCTA). They were categorized into CAD-negative (clean coronaries) and CAD-positive (significant coronary atherosclerosis) based on CCTA findings, aligning with the AHA classification. This research paper aimed to explore the association between the N-glycome profile of immunoglobulin G (IgG) and CAD presence. Among the 198 women in the study, with an average age of 59.9 years, significant glycan alterations were noted, specifically an increase in G0 and a decrease in S.

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# Type 2 diabetes

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



 $\rightarrow$  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

- 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**

#### IgG glycan patterns are associated with type 2 diabetes in independent 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.



 $\rightarrow$  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> <u>dyslipidaemia</u>

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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#### 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**

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

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.

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# **Ulcerative colitis**

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
- 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**

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

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.

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# **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**

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

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.



 $\rightarrow$  Direction of change in a condition



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#### 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**

#### Association of Systemic Lupus Erythematosus With Decreased Immunosuppressive Potential of the IgG Glycome

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 **minor overlap** of glycan metrics between current results and this condition.

#### $\rightarrow$ Direction of change in a condition

**Glycan Median** Below average

**Glycan Lifestyle** Below average



# Signs and symptomsDifficulty breathing

- Chronic cough (± productive)
- Fatigue

#### Possible follow-up

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

#### **Related research papers**

#### <u>N-glycosylation patterns of plasma proteins and immunoglobulin G in chronic</u> <u>obstructive pulmonary disease</u>

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.

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## Perimenopause

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



 $\rightarrow$  Direction of change in a condition



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#### Other factors to consider

• Age between 40 and 55

#### Signs and symptoms

- Irregular menstrual cycle
- Vasomotor symptoms (e.g., hot flushes)
- Other (e.g., mood swings, cognitive difficulties, sleep disturbance)

#### Possible follow-up

- Blood tests (incl. FSH, oestradiol, progesterone, testosterone, AMH)
- Blood pressure check
- Referral to (peri)menopause specialist/gynaecologist

#### **Related research papers**

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

In a comprehensive study examining IgG galactosylation only, 713 healthy adults from two cohorts representing White, Hispanic, and African American back grounds, along with 159 subjects from four randomized controlled trials on endocrine manipulation, were assessed, totaling 872 participants with an equal gender distribution. The study found that menopause was linked to an increase in agalactosylated IgG glycans, particularly the fucosylated nonbisected (GOF) glycoform. Treatment effects were noted, where conjugated estrogens and raloxifene reduced GOF glycans in postmenopausal women, and in premenopausal women, leuprolide increased GOF glycans, an effect that was reversed by estradiol. **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 shortterm 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.



**Biological age** Chronic inflammation

#### **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**

#### <u>Not-So-Sweet Dreams: Plasma and IgG N-Glycome in the Severe Form of the</u> <u>Obstructive Sleep Apnea</u>

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:

## Exercise

Regular physical activity and exercise have positive effects on biological age and glycan indexes.

However, individuals who engage in exercise after a long period of inactivity and sedentary lifestyle may initially experience an increase in chronic inflammation and their biological age, especially if they are overweight.

Exercise is also crucial for cardiovascular health and studies in women show that exercise has positive effects on a specific glycan that has a cardio protective role.



### **Cardio health**

Cardio protective alvcan

Physical Exercise Induces Significant Changes in Immunoglobulin G N-Glycan **Composition in a Previously Inactive, Overweight Population** 

The study investigated the impact of regular exercise on IgG glycans in previously inactive, middle-aged, overweight population. 397 participants were subjected to one of the following exercise programs for 12 weeks:

- circular exercise program
- cardio exercise program
- Nordic walking program

After completing the program, the participants showed an increase in some proinflammatory glycans, which was somewhat expected as they were previously inactive.

The main result of the study was an increase in a specific glycan structure (GP9) which is reported to have a protective role in cardiovascular health in women.

# 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 lowgrade 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**

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

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 lowcalorie 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.



Indeterminate effect No clear outcome from the study 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 IqG 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.

### Irregular cycles

During a woman's menstrual cycle, hormones fluctuate cyclically, and IgG glycans also change in a cyclic pattern. However, these changes are typically not significant enough to affect the overall GlycanAge score, so the menstrual cycle phase generally does not influence the results.

However, for women with irregular menstrual cycles or conditions like polycystic ovary syndrome (PCOS) or endometriosis, which are characterized by hormonal imbalances and increased inflammation, the GlycanAge score may be higher.



#### **Biological age** Chronic inflammation

#### Related research papers

#### <u>Periodic Changes in the N-Glycosylation of Immunoglobulin G During the</u> <u>Menstrual Cycle</u>

The study examined longitudinal changes in IgG glycans during the menstrual cycle in a cohort of healthy premenopausal women with regular cycles (n=70). The women were sampled at 12 time points during their cycle—every 7 days for 3 months. Although the average variation in Glycan indexes was only up to 1.1%, the changes exhibited a cyclic pattern.

The folicular phase was characterized by the highest abundance of Glycan Mature, Glycan Median, and Glycan Lifestyle indexes, which are known to have proinflammatory properties. After ovulation, we saw an increase in anti-inflammatory Glycan Youth and Glycan Shield indexes.

These variations were associated with female sex hormones and menstrual cycle phases, however, the changes in Glycan indexes didn't overlap with the highest concentrations of sex hormones but appeared as menstrual cycle phase-specific events. Despite the observed changes in IgG glycans, they weren't significant enough to affect the overall GlycanAge score.

#### **Additional notes**

If the patient has irregular cycles due to entering peri-menopause, you can refer to the <u>perimenopause</u> page for more information.

### Pregnancy

During pregnancy, estrogen levels increase significantly, with a specific form of estrogen being predominantly produced by the placenta (estradiol E2).

Estrogen has known anti-inflammatory properties, similar to the effects seen with IgG glycans. During pregnancy, women can experience a reduction in their GlycanAge score, along with improvements in antiinflammatory indexes (Glycan Youth, Glycan Shield).



↑ Glycan Youth Anti-inflammatory Immunoglobulin G galactosylation and sialylation are associated with pregnancyinduced improvement of rheumatoid arthritis and the postpartum flare: results from a large prospective cohort study

We investigated changes in IgG glycans in Caucasian women diagnosed with rheumatoid arthritis (RA) from pre-pregnancy until six months postpartum. The study included 148 RA patients and 32 healthy controls. We observed an increase in the anti-inflammatory Glycan Youth and Glycan Shield indexes from preconception until the end of pregnancy, which was associated with remission of RA symptoms during pregnancy. After pregnancy, we observed a significant decrease in both Glycan Youth and Glycan Shield indexes, reaching their lowest levels at six months postpartum. This decrease was associated with a flare-up in RA severity.

#### **Additional notes**

Pregnancy has been observed to improve chronic conditions like rheumatoid arthritis, which often flare up again postpartum. These changes are likely due to the pregnancy-induced increase in estrogen and are also reflected in glycan levels and indexes.

## **Post-pregnancy**

After giving birth, woman's body undergoes significant changes as hormone levels gradually return to their pre-pregnancy state.

The marked increase in estrogen observed during pregnancy diminishes, often leading to an increase in the GlycanAge score. This is often reflected by a reduction in anti-inflammatory indexes (Glycan Shield, Glycan Youth).



Glycan Youth Anti-inflammatory

#### **Related research papers**

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

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# Perimenopause

Perimenopause is a phase preceding menopause in which estrogen levels start to drop.

Before perimenopause, women exhibit a similar aging pace to men. However, upon entering perimenopause, their GlycanAge score rises abruptly, reflecting the increase in inflammation due to a large drop in estrogen levels.

Perimenopause is predominantly characterized by an increase in the pro-inflammatory Glycan Mature index and a decrease in the anti-inflammatory Glycan Youth index. Studies also observe an increase in Glycan Lifestlye index.



**Biological age** Chronic inflammation



**Glycan Shield** Anti-inflammatory



Glycan Youth Anti-inflammatory

#### **Related research papers**

# Immunoglobulin G glycome composition in transition from premenopause to postmenopause

The study analyzed the IgG glycome in 5080 samples from 1940 females multiple times during their transition from pre-menopause to menopause. The most prominent changes associated with entering menopause were an increase in the Glycan Mature and Glycan Lifestyle indexes and a subsequent decrease in Glycan Youth and Glycan Shield. These changes are known to occur with aging in general, however, they were more pronounced in peri-menopausal women compared to women of other age groups and to men.

#### **Additional notes**

During their transition from pre- to peri-menopause, women can experience an increase in their GlycanAge score by over a decade.

# Hormone replacement therapy

Hormone replacement therapy (HRT) is often used in managing symptoms of peri- and menopausal women to restore hormonal balance, especially estrogen.

Estrogen is a known modulator of IgG glycans that has anti-inflammatory properties.

Women who undergo HRT often experience a reduction in their GlycanAge score and a reduction in the proinflammatory Glycan Mature index.



**Glycan Mature** 

Pro-inflammatory

#### **Related research papers**

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

Postmenopausal women (n=58) with low estrogen levels were randomized to receive estrogen, raloxifene (medication used to relieve some symptoms of menopause) or placebo. Those on estrogen and raloxifene showed positive changes such as a reduction in the pro-inflammatory Glycan Mature index.

To confirm the effects of estrogen even further, pre-menopausal healthy women (n=21) were treated with leuprolide, which lowered estrogen production, mimicking symptoms of menopause. Some women received transdermal estrogen and others were on placebo.

The placebo group experienced an increase in the pro-inflammatory Glycan Mature index and showed an average increase in their GlycanAge score by 9,1 years. This effect was prevented by transdermal estrogen therapy. After recovery, GlycanAge scores of women returned to baseline.

#### Additional notes

HRT in women isn't just about optimizing estrogen - it's about finding the right balance between all female sex hormones, including progesterone.

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# **Research papers**

#### **Biological age**

<u>Glycans Are a Novel Biomarker of Chronological and Biological Ages</u> <u>Immunoglobulin G glycans – Biomarkers and molecular effectors of aging</u> <u>Heritability of the glycan clock of biological age</u> <u>Immunoglobulin G glycosylation in aging and diseases</u> 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 The use of a systems approach to increase NAD+ in human participants Extensive weight loss reduces glycan age by altering IgG N-glycosylation Effects of testosterone and metformin on the GlycanAge index of biological age and the composition of the IqG glycome Regular moderate physical exercise decreases Glycan Age index of biological age and reduces inflammatory potential of Immunoglobulin G N-glycosylation profiling of plasma provides evidence for accelerated physiological aging in post-traumatic stress disorder Not-So-Sweet Dreams: Plasma and IqG N-Glycome in the Severe Form of the Obstructive Sleep Apnea Intense Physical Exercise Induces an Anti-inflammatory Change in IqG N-Glycosylation Profile Physical Exercise Induces Significant Changes in Immunoglobulin G N-Glycan Composition in a Previously Inactive, Overweight Population

#### Diseases

N-glycosylation of immunoglobulin G predicts incident hypertension The Association Between Glycosylation of Immunoqlobulin G and Hypertension: A Multiple Ethnic Cross-Sectional Study Immunoglobulin G N-Glycosylation Signatures in Incident Type 2 Diabetes and Cardiovascular Disease Glycosylation Profile of Immunoalobulin G Is Cross-Sectionally Associated With Cardiovascular Disease Risk Score and Subclinical Atherosclerosis in Two Independent Cohorts IgG N-Glycosylation Is Altered in Coronary Artery Disease IqG qlycan 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 IqG Fc galactosylation predicts response to methotrexate in early rheumatoid arthritis Low galactosylation of IgG associates with higher risk for future diagnosis of rheumatoid arthritis during 10 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 A unique serum IgG glycosylation signature predicts development of Crohn's disease and is associated with pathogenic antibodies to mannose glycan Association of Systemic Lupus Erythematosus With Decreased Immunosuppressive Potential of the IgG Glycome N-glycosylation patterns of plasma proteins and immunoglobulin G in chronic obstructive pulmonary disease Estrogens regulate alycosylation of IgG in women and men Immunoglobulin G glycome composition in transition from premenopause to postmenopause