Patient/Clinician Information Sheet

What is Primary Open Angle Glaucoma?

Primary Open Angle Glaucoma (called `glaucoma' in the rest of this document) is an eye condition in which loss of vision results from optic nerve damage, most often due to increased pressure within the eye. It mainly occurs when the eye's drainage canals become clogged over time and the correct amount of fluid can't drain out of the eye. Loss of vision in glaucoma is usually gradual and affects peripheral (side) vision first. There can be significant loss of vision before there is an awareness of any problem.

Glaucoma is a leading cause of irreversible vision loss worldwide. In Australia, 300,000 people have glaucoma; about 1 in 200 people have glaucoma by age 40, increasing to 1 in 8 by age 80[a].

Vision lost to glaucoma is unfortunately irreversible once it has occurred. However, once diagnosed, glaucoma can usually be managed successfully with eye drops, laser therapy, or surgery.

Glaucoma has a strong genetic component. Family members of people with glaucoma have a higher risk of the condition.

What are the main risk factors for glaucoma?

The risk that a person will develop glaucoma in the future, or that already-diagnosed glaucoma will get worse, depends on a wide range of factors[b]. These include:

- Risk factors such as an age over 50, a family history of glaucoma, or being of African descent
- Clinical features such as high eye pressure, certain types of vision loss, or signs of optic nerve damage
- Variations in genes that influence the risk of glaucoma

Go to Glaucoma Australia to learn more about glaucoma and the risk factors for glaucoma.

What is a Polygenic Risk Score?

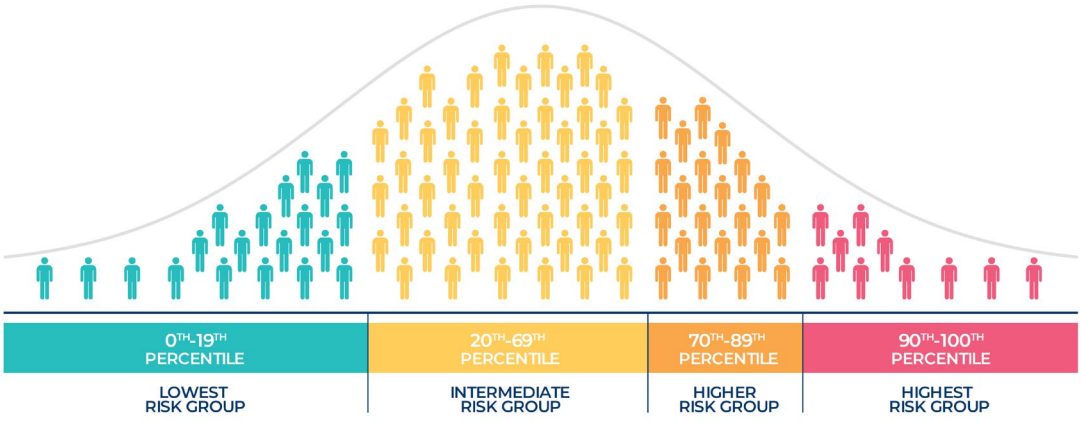
Humans share the same genetic code apart from some differences, called genetic variants, that make each of us unique. Some of these variants are known to increase the risk of developing certain health conditions, while others reduce the risk. It is possible to combine the risks from thousands of these genetic variants to estimate the overall risk of a person developing a particular health condition, such as glaucoma. This overall risk is known as a polygenic risk score. In some cases, a polygenic risk score may also be linked to the potential severity of the health condition and the way it might develop over time.

What is SightScore?

SightScore is a DNA test that looks at millions of genetic variants in a person's genome to create a personalised polygenic risk score for glaucoma. It estimates a person's genetic risk of developing glaucoma in future or, if they already have glaucoma, the risk their glaucoma might get worse, relative to others in the community with similar ancestry.

SightScore is a number between 0 and 100 (called a 'percentile score') that places a person's glaucoma risk within the spread of glaucoma risks for the community as a whole. For example, a 90th percentile SightScore means that 90 out of 100 people in the community have a lower genetic risk than the person being tested, and only 10 out of 100 people have an equal or higher risk. A 90th percentile score therefore indicates a person has a higher risk than most people in the community. However, it **does not** mean that individual has a 90 percent chance of developing glaucoma; only that the risk is higher than for most people.

The spread of percentile scores in a population is represented by a 'bell-shaped' curve, with most people in the middle (with intermediate risk), and fewer people at the upper (higher and highest risk) and lower (lowest risk) ends.



Risk increases gradually from the lowest risk individuals on the left, to the highest risk individuals on the right.

The range of percentile scores has been divided into the following risk groups to help healthcare practitioners manage their patients:

- 0th - 19th percentile: Lowest genetic risk group (shown in green). Lower risk than many others in the community.
- 20th - 69th percentile: Intermediate genetic risk group (shown in yellow). Fairly normal risk compared to others in the community.
- 70th – 89th percentile: Higher genetic risk group (shown in orange). Higher risk than many others in the community.
- 90th - 100th percentile: Highest genetic risk group (shown in red). Higher risk than most others in the community.

SightScore can be used to estimate the risk that:

- A person who doesn't have any features of glaucoma at the present time will develop glaucoma in the future.
- A person who has suspicious, but not definite, features of glaucoma will develop glaucoma in the future.
- A close blood relative of someone with glaucoma will develop glaucoma in the future (parent, brother/sister, adult child).
- A person with a glaucoma diagnosis will experience their glaucoma getting worse in future.

A person's SightScore remains constant throughout their life, as their DNA does not change over time*. However, the meaning of a given SightScore depends on the reason the healthcare practitioner ordered the SightScore test. For example, someone with a glaucoma diagnosis and a 90th percentile SightScore may be at higher risk of their glaucoma becoming worse over the next 3 years, compared to an average glaucoma patient. Alternatively, someone with no evidence of glaucoma and a 90th percentile SightScore may be at higher risk of developing glaucoma over their lifetime.

* v2.1

It is important to remember that a high SightScore does not mean a person will definitely develop glaucoma in the future or, if they already have glaucoma, that it will definitely worsen. Equally, a low-risk score does not rule out developing glaucoma or glaucoma worsening in the future.

In some situations, someone's SightScore may be compared with others in the community who share similar clinical features. For example, if someone already has diagnosed glaucoma, it may be relevant to compare their SightScore with other people who have diagnosed glaucoma. This enables a risk to be calculated that specifically takes their diagnosed glaucoma into account. This risk may also be divided into Lowest, Intermediate, Higher, and Highest risk groups to help healthcare practitioners make informed decisions.

How might SightScore be used by a healthcare practitioner?

Together with other clinical features and medical history, a healthcare practitioner may use SightScore to consider:

- The age for a person's first glaucoma check,
- How often a person should be checked for glaucoma,
- Whether a person is best monitored in optometry or ophthalmology,
- How best to care for a person with glaucoma, including some treatment decisions; and
- Whether blood relatives (parents, brothers/sisters, adult children) should be checked for glaucoma.

What can be done about glaucoma risk?

The most important thing is to follow the advice of a healthcare practitioner and particularly, to attend regular eye health check-ups. The National Health and Medical Research Council recommends regular eye health checks for everyone over the age of 50, and for people of African descent over the age of 40. A healthy lifestyle, including avoidance of smoking, moderate exercise and a balanced diet, is also recommended[c].

How does SightScore relate to family history?

Blood relatives (e.g. parents, brothers/sisters, adult children) share parts of their genetic code and will have some of the same genetic variants. Thus, for conditions with a strong genetic contribution, such as glaucoma, a healthcare practitioner will take account of a person's family history when assessing their risk.

However, a family history is not the same as a person's individual genetic risk. It is possible to have a high genetic risk of glaucoma without a family history of the condition. It is also possible to have a family history of glaucoma and have a low individual genetic risk. This is because a family history does not mean a person has **personally** inherited the genetic variants that increase the risk of glaucoma.

SightScore is a personalised test which uses a person's own DNA to assess their **individual** genetic risk of developing glaucoma. It is important to understand that SightScore does not replace an accurate family history. Instead, it provides useful information about whether someone is at higher or lower risk than would be expected from their family history alone.

What are the implications for family members?

Close blood relatives (e.g. parents, brothers/sisters, adult children) of someone with a high SightScore are more likely than average to have an elevated SightScore and to be at increased risk of developing glaucoma.

Does SightScore take into account things like eye pressure, age, family history or environmental factors?

SightScore only estimates genetic risk based on the provided patient sample. It does not take these other factors into account. However, a healthcare practitioner will consider them when advising about future health care.

Does SightScore test every aspect of genetic risk?

Rarely, a person will have a single variant in a key glaucoma gene (e.g.Myocilin) that has a large impact on glaucoma risk. SightScore does not test for these rare variants, and only provides an overall polygenic risk score. A healthcare practitioner may order separate testing of these variants in the fairly rare cases it is warranted, based on family history and other clinical considerations.

What is the evidence behind SightScore?

The SightScore polygenic risk score was derived and clinically validated using studies of large numbers of people with and without glaucoma. Data on 296,757 open angle glaucoma (OAG) cases and 6,240,939 controls, drawn from several major ancestry groups were used. These were supplemented with glaucoma related traits (intraocular pressure, optic disc parameters, ocular hypertension; N=320,296), enabling construction of a glaucoma polygenic risk score (PRS).

References

a. Glaucoma Australia. What is Glaucoma? https://glaucoma.org.au/what-is-glaucoma
b. Grzybowski A, et al., 2020. Primary Open Angle Glaucoma and Vascular Risk Factors: A Review of Population Based Studies from 1990 to 2019. J Clin Med. 9(3):761.
c. Pasquale LR, Kang JH., 2009. Lifestyle, nutrition, and glaucoma. J Glaucoma. 18(6):423-8.

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