

Patient/Clinician Information Sheet

What is Age Related Macular Degeneration?

Age-related macular degeneration (called 'AMD' in the rest of this document) is an eye condition that affects the macula, the central part of the retina responsible for sharp, central vision. AMD results in progressive loss, or blurring, of central vision without affecting the peripheral, or side, vision. AMD doesn't result in complete black blindness, but losing your central vision can make it harder to see faces, read or drive. For some people, AMD progresses very slowly and may not impact vision. For others, AMD may progress faster and lead to vision loss in one or both eyes. You can have early signs of AMD without knowing.

AMD is a leading cause of vision loss in older adults, responsible for half of all blindness and severe vision loss in Australia. In Australia, 1.4 million people, or 1 in 7 people, aged 50 years or older have AMD, and 17% of those people will experience vision impairment.¹

Vision lost to AMD is unfortunately irreversible once it has occurred. However, once diagnosed, there are things you and your health practitioner can do to keep your macular healthy. This could delay the onset or progression of AMD.

More information about AMD and the risk factors for AMD can be found at the Macular Disease Foundation Australia. Visit mdfoundation.com.au.

What are the main risk factors for AMD?

The risk that a person will develop AMD in the future, or that someone with early signs of AMD will develop vision loss, depends on a wide range of factors.² These include:

- Risk factors such as an age over 50, a family history of AMD, or being of European descent.
- Currently smoking, overweight, high blood pressure or history of heart disease.
- Variations in genes that influence the risk of AMD.

More information about AMD and risk factors can be found at the Macular Disease Foundation Australia. Visit mdfoundation.com.au.

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 many of these genetic variants to estimate the overall risk of a person developing a particular health condition, such as AMD. 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-AMD?

SightScore-AMD is a DNA test that looks at 70 genetic variants in a person's genome to create a personalised polygenic risk score for AMD. It estimates a person's genetic risk of developing AMD in future or, if they already have AMD, the risk their AMD might get worse, relative to others in the community with similar ancestry.

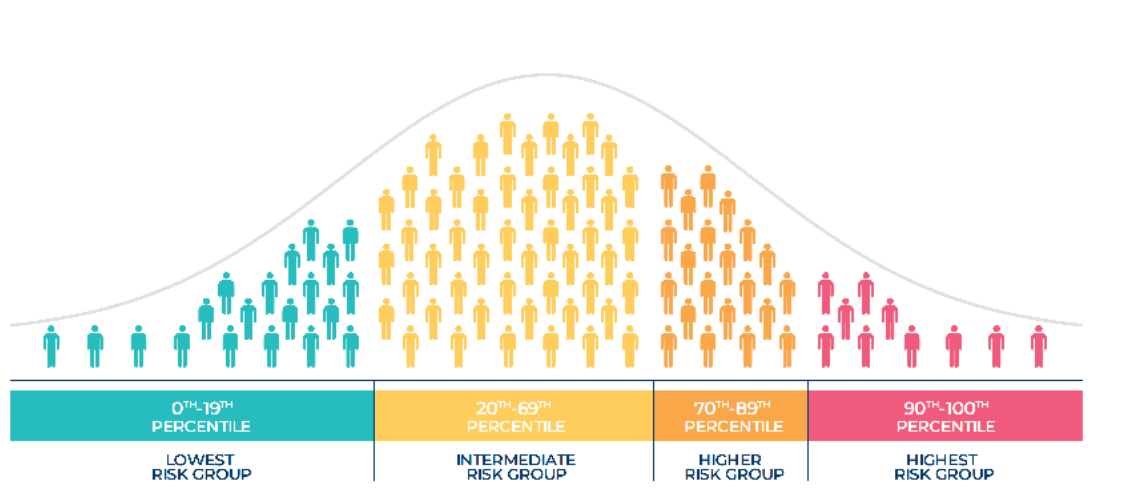
SightScore is a number between 0 and 100 (called a 'percentile score') that places a person's AMD risk within the spread of AMD risks for the community as a whole. For example, a 90th percentile SightScore means that 90 out of 100 people in the community have a lower genetic risk than the person being tested, and only 10 out of 100

¹ Keel S, Xie J, Foreman J, et al. Prevalence of age-related macular degeneration in Australia. The Australian National Eye Health Survey. *JAMA Ophthalmol.* 2017; 135(11):1242-9.

² Heesterbeek TJ, et al. Risk factors for progression of age-related macular degeneration. *Ophthalmic Physiol Opt.* 2020 Mar;40(2):140-170.

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 AMD; 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 AMD at the present time will develop AMD in the future.
- A person who has suspicious, but not definite, features of AMD will develop AMD in the future.
- A close blood relative of someone with AMD will develop AMD in the future (parent, brother/sister, adult child).
- A person with an AMD diagnosis will experience their AMD 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 an AMD diagnosis and a 90th percentile SightScore may be at higher risk of their AMD becoming worse, compared to an average AMD patient. Alternatively, someone with no evidence of AMD and a 90th percentile SightScore may be at higher risk of developing AMD over their lifetime.

It is important to remember that a high SightScore does not mean a person will definitely develop AMD in the future or, if they already have AMD, that it will definitely worsen. Equally, a low-risk score does not rule out developing AMD or AMD 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 AMD, it may be relevant to compare their SightScore with other people who have diagnosed AMD. This enables a risk to be calculated that specifically takes

their diagnosed AMD 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 AMD check
- How often a person should be checked for AMD
- Lifestyle modifications
- How to best care for a person with AMD, including some treatment decisions; and
- Whether blood relatives (parents, brothers/sisters, children) should be checked for AMD

What can be done about AMD risk?

The most important thing is to follow the advice of a healthcare practitioner and particularly, to attend regular eye health check-ups. A healthy lifestyle, including avoidance of smoking, a good diet, exercise and managing your weight is also recommended.³

How does SightScore relate to family history?

Blood relatives (e.g. parents, brothers/sisters, 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 AMD, 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 AMD without a family history of the condition. It is also possible to have a family history of AMD 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 AMD.

SightScore is a personalised genetic test which uses your own DNA to assess your individual risk of developing AMD. 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, siblings, 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 AMD.

Does SightScore test every aspect of genetic risk?

SightScore is a polygenic risk score that tests for 70 common genetic variants that contribute to AMD disease risk, including in the Complement Factor H and Age-Related Maculopathy Susceptibility 2 (ARMS2) genes. These each have an accumulative effect on disease risk.

Occasionally, a person will have a very rare single variant in a key AMD gene that has a large impact on the risk of developing AMD. SightScore does not test for these rare variants and only provides an overall polygenic risk

³ Saigal K, Salama JE, Pardo AA, Lopez SE, Gregori NZ. Modifiable Lifestyle Risk Factors and Strategies for Slowing the Progression of Age-Related Macular Degeneration. Vision (Basel). 2025 Feb 23;9(1):16

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 for AMD was derived and clinically validated using studies of large numbers of people with and without AMD. Data on 64,885 AMD cases and 568,740 controls, drawn from several major ancestry groups were used.

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