

# Literature Update



Centre for Eye Health

Issue12 Winter 2024

Welcome to the new-look Centre for Eye Health ATLAS Literature update. Each quarter we will continue to bring you summaries of key peer-reviewed papers that add to the existing knowledge-base as part of your Centre for Eye Health ATLAS subscription.

## What's new this quarter?

We have searched the literature for the most clinically-relevant articles, and come up with some really interesting papers this quarter. Topics covered in this review include the below (click on the title to jump to the article summary):

- [1. Update to the AREDS Simplified Severity Scale for AMD released](#)
- [2. Are patients with glaucoma at an increased risk of dementia and Alzheimer's Disease?](#)
- [3. Should the 10-2 visual field test be used for patients with early glaucoma?](#)
- [4. Differential diagnosis: Late onset Stargardt Disease or geographic AMD?](#)



# Update to the AREDS Simplified Severity Scale for AMD released

## What was already known

The AREDS Simplified Severity Scale, developed over two decades ago, is a clinical tool used to categorise the risk of developing advanced age-related macular degeneration (AMD). This scale estimates the risk of progression to late AMD by assessing both eyes.

Patients receive a score from 0 to 4 based on the presence or absence of large drusen and AMD pigmentary abnormalities in the macula, with one point assigned for each feature in each eye. If neither eye has large drusen, one point is still assigned if both eyes have medium-sized drusen. Based on these scores, the five-year risk of progression to late AMD is approximately 0.3%, 12%, 25%, and 50%, respectively. However, the scale has limitations, such as not considering reticular pseudodrusen (RPD), an independent risk factor for AMD progression.

## What this study adds

A post hoc analysis was conducted on two clinical trial cohorts: AREDS and AREDS2. The presence or absence of RPD was determined using validated deep learning grading of colour fundus photographs and incorporated into the calculation of five-year rates of progression to late AMD. The updated AREDS Simplified Severity Scale is stratified by the presence and absence of RPD (table 1).

Score	AREDS SSS (no RPD)	AREDS SSS (with RPD)
0	~0.5%	3%
1	~4%	8%
2	12%	~30%
3	~25%	~60%
4	50%	~70%

Table 1: Updated AREDS Simplified Severity Scale, incorporating the presence/absence of RPD

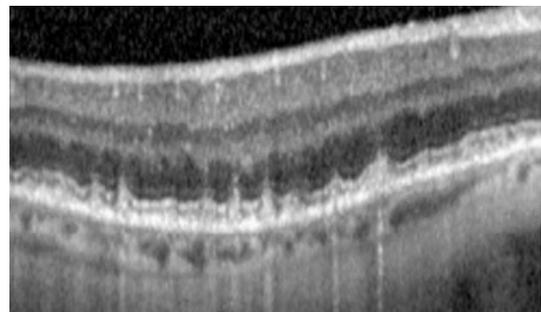


Image 1: Spectralis OCT line scan showing RPD which appear as deposits above the RPE in contrast to typical drusen which are located below the RPE.

## How this study might impact clinical practice

The presence of RPD significantly increases the risk of progression to late AMD according to the new scale. Clinicians should proactively incorporate the detection of RPD in the evaluation of their AMD patients. Additionally, AMD patients with RPD may require more vigilant observation compared to those without RPD.

## Reference

Agrón E, Domalpally A, Chen Q, Lu Z, Chew EY, Keenan TDL, for the AREDS and AREDS2 Research Groups, An Updated Simplified Severity Scale for Age-Related Macular Degeneration, Incorporating Reticular Pseudodrusen: Age-Related Eye Disease Study Report No. 42, Ophthalmology (2024), doi: <https://doi.org/10.1016/j.ophtha.2024.04.011>

# Are patients with glaucoma at increased risk of Dementia and Alzheimer's disease?

## What was already known

Glaucoma and Alzheimer's disease (AD) are both neurodegenerative diseases that share pathophysiological features, including optic nerve degeneration, loss of retinal ganglion cells, and thinning of the retinal nerve fiber layers. Studies investigating whether glaucoma is associated with an increased risk of dementia have often been underpowered and have yielded conflicting results.

## What this study adds

This large-cohort study calculated hazard ratios for AD, vascular dementia (VaD), and all-cause dementia in 324,730 patients diagnosed with glaucoma over a 22-year period. These patients were compared with 3,247,300 age- and sex-matched control subjects who did not have a prior diagnosis of dementia.

The study found that persons diagnosed with glaucoma had a 35% increased risk of AD, a 65% increased risk of VaD, and a 55% increased risk of all-cause dementia compared to controls, after adjusting for sociodemographic factors and comorbidities. When risk was analysed based on age at diagnosis, the highest risk for AD and dementia was observed in those diagnosed at age 70 or above, with no elevated risk for those diagnosed with glaucoma before the age of 60.

## How this study might impact clinical practice

Care must be taken when applying these results in practice. While there is an elevated risk of AD or dementia, this does not mean that every glaucoma patient will develop these conditions. However, if an elderly patient with glaucoma attends your practice and exhibits or reports symptoms suggestive of dementia, such as changes in cognitive function and memory, it may be worthwhile to refer the patient to their general practitioner for further investigation.

Early detection and treatment of AD can enable earlier lifestyle and therapeutic interventions, greatly benefiting patients and their families.

A self-administered dementia screening questionnaire is available on the Dementia Australia website: <https://www.alz.org/media/Documents/ad8-dementia-screening.pdf>.

## Reference

Casey Crump, Jan Sundquist, Weiva Sieh, Kristina Sundquist, Risk of Alzheimer's Disease and Related Dementias in Persons with Glaucoma: A National Cohort Study, *Ophthalmology*, Volume 131, Issue 3, 2024, Pages 302-309, ISSN 0161-6420, <https://doi.org/10.1016/j.ophtha.2023.10.014>.

# Should the 10-2 Visual Field Test Be Used for Patients with Early Glaucoma?

## What was already known

The 24-2 visual field test grid is routinely used for patients with early-stage glaucoma. In contrast, the 10-2 test grid provides more detailed information about the central visual field and is typically employed in later stages when significant central field damage is present. However, recent studies have shown that thinning within the macular ganglion cell complex often occurs early, raising the question of whether the 10-2 test should be used as an additional testing strategy for early glaucoma. The key considerations are: (1) whether the 10-2 test improves the detection of field defects, and (2) if this improvement justifies the additional cost, time, and effort required from both the clinician and the patient.

## What this study adds

This literature review and report by the American Academy of Ophthalmology examined peer-reviewed papers investigating the utility of central visual field testing for patients with early glaucoma and rated them for strength of evidence. Data from 21 papers were extracted and reviewed.

The diagnostic abilities of the 24-2 and 10-2 strategies are comparable. If abnormal points are found in the central 12 inner locations of the 24-2 test strategy (within the central 10 degrees), most will show a defect on the 10-2 visual field test. While defects on the 10-2 grid might be missed using the 24-2 test grid, this issue is mitigated by using a modified 24-2 test that includes additional test locations within the central 10 degrees, such as the HFA 24-2C. However, this modification does not necessarily improve the detection of early glaucoma compared to the 24-2 alone. The review also found that the 10-2 testing grid has a better correlation with results from the OCT macular ganglion cell analysis.

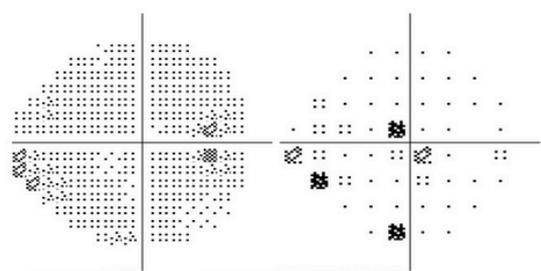


Figure 2: 24-2 SITA Fast visual field test results from a patient with early glaucoma and abnormal points centrally.

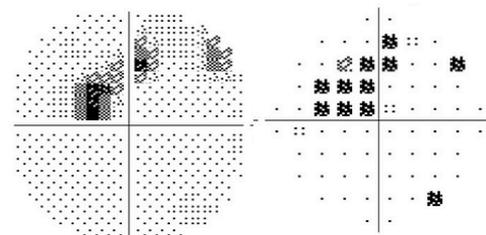


Figure 3: 10-2 SITA Fast visual field test results from the same patient above, on the same day.

## How this study might impact clinical practice

The authors concluded that routinely performing the 10-2 test for patients with early glaucoma is not supported, as it does not provide sufficient additional information compared to the 24-2 test. Scrutinizing the 12 inner points of the 24-2 test strategy is critical for detecting central defects. However, the 10-2 test grid may offer additional insights for patients with repeatable defects in the pattern deviation plot among the central 12 points of the 24-2 or 24-2C, and/or those with thinning of the ganglion cell complex on OCT. To effectively monitor the progression of defects on the 10-2 test, serial 10-2 testing should be conducted in future follow-ups

## Reference

Darrell WuDunn, Hana L. Takusagawa, Jullia A. Rosdahl, Arthur J. Sit, Vikas Chopra, Yvonne Ou, Grace M. Richter, O'Rese J. Knight, David Solá-Del Valle, Stephen J. Kim, Central Visual Field Testing in Early Glaucoma: A Report by the American Academy of Ophthalmology, Ophthalmology, Volume 131, Issue 2, 2024, Pages 240-248,

# Differential Diagnosis: Late onset Stargardt Disease or Geographic AMD?

## What was already known

Late onset Stargardt disease is a milder subset of Stargardt Disease type (STGD1), defined by an age of onset of 45 years or older. It is often misdiagnosed as late AMD with geographic atrophy, with previous studies cited in this paper showing this occurs in up to 22% of cases.

## What this study adds

The authors of this paper aim to raise awareness by describing the characteristics, genetics and progression of Late-onset STGD1 and highlight their differences from AMD. As foveal involvement is more likely in AMD than STGD1, AMD is typically associated with a lower baseline VA. Foveal sparing is more typical in late-onset STGD1. Key clinical differences between these two conditions using multimodal imaging are also presented below.

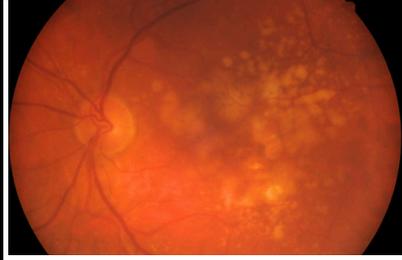
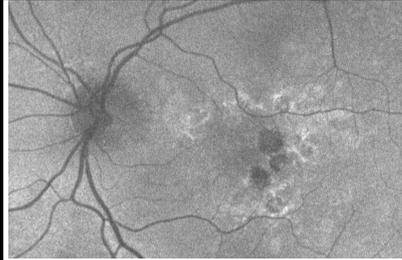
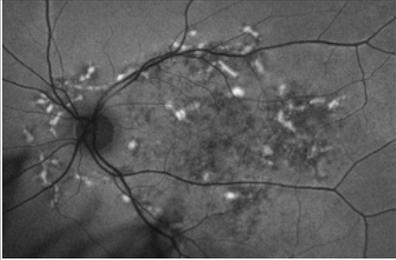
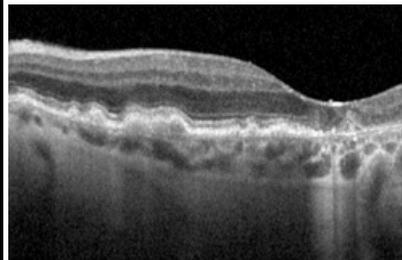
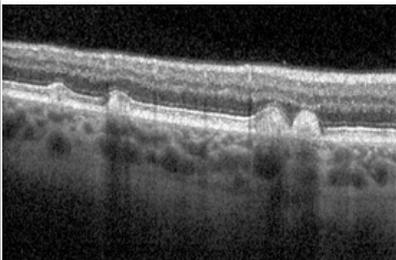
AMD with Geographic atrophy	Late-onset STGD1	Description of differences
		<p><u>Fundus Photography:</u> Drusen (AMD) are round and distinctly yellow in colour and concentrated at the macula, while the flecks associated with STGD1 are irregular in shape, more difficult to see, only slightly yellow in colour and typically scattered across the posterior pole/mid-periphery.</p>
		<p><u>Fundus Autofluorescence (FAF):</u> STGD1 flecks are strongly hyper-AF while drusen may have variable auto fluorescent properties.</p>
		<p><u>OCT:</u> STGD1 flecks are located within the photoreceptor layers. Typical drusen are located beneath the RPE.</p>

Table 2: Key differences between AMD with Geographic atrophy and Late-onset Stargardt disease using commonly available multimodal imaging modalities. Images shown in this table are from patients referred to CFEH,

# Differential Diagnosis: Late onset Stargardt Disease or Geographic AMD?

## How this study might impact clinical practice

This paper aims to help prevent the misdiagnosis of late onset STGD1 as geographic atrophy. Misdiagnosis can result in a patient receiving unnecessary treatment for AMD - treatment that is unlikely to have benefit for late-onset STGD1 - whilst also potentially missing out on therapeutic clinical trials specific to their condition. An improved understanding of the differences between these conditions may lead to better patient outcomes.

## Reference

Li CHZ, Pas JAAH, Corradi Z, Hitti-Malin RJ, Hoogstede A, Runhart EH, Dhooge PPA, Collin RWJ, Cremers FPM, Hoyng CB. Study of Late-Onset Stargardt Type 1 Disease: Characteristics, Genetics, and Progression. *Ophthalmology*. 2024 Jan;131(1):87-97. doi: 10.1016/j.ophtha.2023.08.011. Epub 2023 Aug 19. PMID: 37598860.

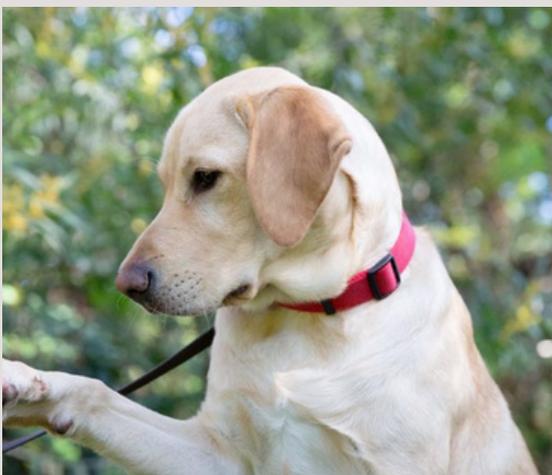
[Full paper](#)



## A special update from the CFEH team

The CFEH team have been working on a new platform to support telehealth consultations, due to be launched in the coming months.

This new initiative will allow you to discuss your own cases remotely, one-on-one with our experienced optometrists. Get personalised advice on disease diagnosis and management for your patients, and log these consultations as interactive CPD. Further updates to follow!



## Guide Dogs.

Thank you for taking the time to read the CFEH Winter 2024 ATLAS Literature Review. The CFEH team wanted to acknowledge Guide Dogs NSW/ACT whose support makes all of our work possible.

We appreciate any feedback you may have about our educational resources, particularly the CFEH Atlas. This resource will undergo continuous review and improvement and more cases will be added over time. If you have any feedback or suggestions, we would love to hear them! Please send us an email: [education@cfeh.com.au](mailto:education@cfeh.com.au).