



# ATLAS LITERATURE REVIEW

Issue 6 • Summer

2022-2023



Welcome to the sixth issue of Centre for Eye Health's **ATLAS Literature Review**. Each quarter we'll be bringing you reviews from our pick of the latest literature as part of your ATLAS subscription.

## Heavy smoking increases risk of glaucoma progression

Prepared by Elisa Wang and Sharon Ho

**Clinical applications:** A theoretical link between smoking and glaucoma has been known to exist for many years. Proving a link however has been complicated as the majority of previous studies to date have been cross sectional rather longitudinal and didn't include a dose dependent effect (amount of smoking). This study however addressed both of these factors and suggests that heavy smoking can increase the risk of the progression of visual field defects in patients with primary open-angle glaucoma (POAG).

As well as the many other benefits of smoking cessation, this study assist clinicians with an evidence base to direct patients with POAG who smoke to appropriate smoking cessation health services to help reduce their risk of glaucoma progression, and emphasise that stopping smoking will help to save their vision.

**Summary:** This retrospective cohort study recruited patients with POAG, and assessed if different levels of smoking intensity were associated with visual field progression. Patients recruited needed to have a minimum of 3 years of follow-up and 5 visual field tests.

**Key findings:** In total, 511 eyes of 354 patients with POAG were evaluated. Heavy smokers ( $\geq 20$  pack-years) were 2.2 times more likely to develop visual field progression compared to patients with no smoking history. While it is difficult to account for all variables in case-control studies, higher smoking intensity was associated with faster visual field loss (-0.05 dB/year per 10 pack-years) after adjusting for current alcohol assumption and body mass index in patients with POAG.

**Reference:** Mahmoudinezhad G, Nishida T, Weinreb RN, et al. Impact of Smoking on Visual Field Progression in a Long-term Clinical Follow-up. *Ophthalmology*. 2022;129(11):1235-1244.

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### In this issue:

Prepared by Sharon Ho and Elisa Wang

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## New drugs found to increase the risk of acute angle closure

Prepared by Sharon Ho and Elisa Wang

**Clinical applications:** Acute angle closure (AAC) can be caused by either pupillary block, which is often related to mydriasis, or non-pupillary block more commonly related to anterior displacement of the peripheral iris due to lens position of ciliary body oedema. The use of a wide range of prescription drugs are known to increase the risk of AAC through an effect on these mechanisms. Clinicians should be aware of the increased risk of AAC in patients who take these drugs and adopt appropriate precautionary measures, particularly when other risk factors for ACC (e.g. older age, female sex, Asian ancestry, shallow anterior chamber) are present.

**Summary:** This study analysed 949 drugs that were newly prescribed to 13,531 patients within 30 days prior to having an AAC attack. Drugs associated with AAC occurrence were identified along with the risk of AAC associated with each drug.

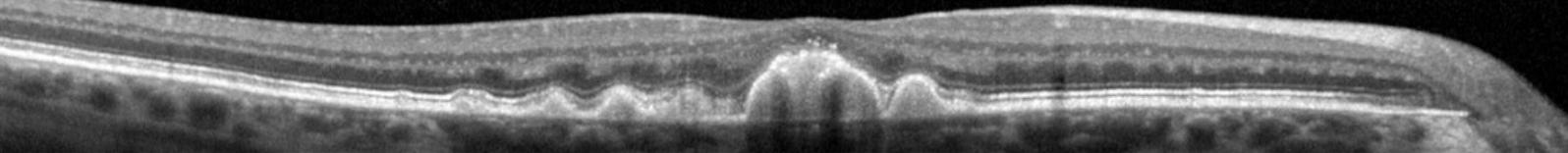
**Key findings:** Sixty-one drugs were significantly associated with AAC. Sumatriptan had the highest odds of AAC development (over 12 times higher than for those who did not take the drug), followed by topiramate and duloxetine. Drugs for the respiratory system, alimentary tract and metabolism, genitourinary system and sex hormones, and musculoskeletal system were also identified, among others. The median period from prescription of the drug to the onset of AAC for the 61 drugs was 11.9 days.

**Reference:** Na KI, Park SP. Association of Drugs With Acute Angle Closure. JAMA Ophthalmol. 2022 Sep 22:e223723. Online ahead of print.

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DRUG CATEGORY	DRUG NAME	ODDS RATIO (95% CONFIDENCE INTERVAL)
Antimigraine preparation	Sumatriptan	12.60 (4.13-38.44)
Antiepileptic	Topiramate	5.10 (2.22-11.70)
Antidepressant	Duloxetine	4.04 (2.95-5.54)
Non-steroidal anti-inflammatory	Naproxen	3.49 (2.28-5.34)
Drug for urinary frequency and incontinence	Propiverine	3.22 (2.53-4.10)
Antidepressant	Escitalopram	2.93 (2.13-4.04)
Constipation drug	Lactulose	2.81 (1.72-4.61)
Antidepressant	Nortriptyline	2.61 (1.82-3.75)
Antivertigo preparation	Flunarizine	2.56 (1.98-3.31)
Drug for gastrointestinal disorders	Metoclopramide	2.52 (1.95-3.25)
Drug for urinary frequency and incontinence	Solifenacin	2.50 (1.93-3.24)
Obstructive airway disease drugs	Aminophylline	2.23 (1.62-3.06)
Systemic antihistamines	Mequitazine	2.02 (1.62-2.52)

ABOVE: Table summarising the drugs with the highest associated risk of acute angle closure (odds ratio over 2)



## Extramacular drusen do not increase the risk of progression to late AMD

Prepared by Sharon Ho and Elisa Wang

**Clinical applications:** Extramacular drusen in this paper refers to drusen in the posterior pole located outside the ETDRS grid but not including midperipheral or peripheral drusen. Reticular pseudodrusen and cuticular drusen were included unless they presented on their own (without typical drusen).

Extramacular drusen are commonly seen in eyes with age-related macular degeneration (AMD) and are more frequent with increasing drusen burden within the macula. Clinicians should be aware that in eyes with intermediate AMD, while associated with larger macular drusen, extramacular drusen do not confer additional risk for progression to late AMD (both geographic atrophy and neovascular AMD).

**Summary:** This study investigated the prevalence of extramacular drusen and their role in the progression of AMD. Retrospective analysis was performed of 4,168 eyes with intermediate AMD from the AREDS 2 study using colour fundus photographs. The characteristics of extramacular drusen were compared to drusen within the macula, and progression rate to late AMD was measured.

**Key findings:** Extramacular drusen were present in 86.9% of eyes, of which 80% were a continuation of macular drusen (i.e. most likely representing a larger area of involvement rather than a discrete or different mechanism or entity). Eyes with extramacular drusen were significantly associated with larger macular drusen size and larger macular drusen area compared to eyes without extramacular drusen. Progression to late AMD was seen in 35.8% of eyes with extramacular drusen and 34.1% of eyes without extramacular drusen. After adjusting for baseline age, gender, smoking, AMD severity and reticular pseudodrusen, the risk of developing late AMD over 5 years was similar in eyes with and without extramacular drusen.

**Reference:** Domalpally A, Xing B, Pak JW, et al. Extramacular Drusen and Progression of Age-related Macular Degeneration (AMD); Age-related Eye Disease Study 2 Report 30. *Ophthalmol Retina*. 2022 Aug 5:S2468-6530(22)00374-8.

[Click here for abstract](#)

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## Ask your patients with age-related macular degeneration... "Are you okay?"

Prepared by Sharon Ho and Elisa Wang

**Clinical applications:** In a holistic approach to eye care, clinicians should be mindful of the mental health status of patients with age-related macular degeneration (AMD) as these patients have been shown to generally present with lower mental health scores. If symptoms of depression, worry or frustration are observed, it is important for patients to be appropriately referred for screening and treatment of potential mental health problems.

**Summary:** Patients with AMD were administered the National Eye Institute-Visual Function Questionnaire (NEI-VFQ-25); a validated questionnaire designed to measure a patient's subjective assessment of visual function. The study's analysis assessed the relationship between visual acuity and mental health subscale scores on the NEI-VFQ-25, across different AMD classifications (early, intermediate, and late - geographic atrophy and neovascular).

**Key findings:** A total of 875 patients were included in the study. There was a significant association between mental health scores and AMD classification, as well as visual acuity. Patients with bilateral late AMD had the lowest mental health scores. A step-wise decline in mental health scores was demonstrated as visual acuity worsened in both the better- and worse-seeing eyes. Older age and an unmarried status also played a role in predicting lower mental health scores. Of note, while there was overall a significant association with decreased VA and mental health, there was a marked range of mental health scores within each group. As a result, clinicians should consider the mental health of ALL patients with a diagnosis of AMD, regardless of the stage and effect of the disease.

**Reference:** Fonteh CN, Mathias MT, Mandava N, et al. Mental health and visual acuity in patients with age-related macular degeneration. *BMC Ophthalmol*. 2022 Oct 2:22(1):391.

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## Beware of vigorous exercise as a risk factor for central serous chorioretinopathy

Prepared by Elisa Wang and Sharon Ho

**Clinical applications:** The role of the choroidal blood supply in central serous chorioretinopathy (CSCR) is becoming clearer thanks to a combination of a better understanding of the mechanism of the condition, in particular through ICG Angiography and OCT imaging. In particular, problems with regulation of the choroidal vasculature have been shown to be potentially impaired in patients who develop CSCR.

This study suggests that patients that regularly perform vigorous physical activity have an increased risk of developing central serous chorioretinopathy (CSCR) in comparison to matched controls that do not perform the same level of exercise. It is hypothesized that an increase in blood pressure from the exercise may contribute to the causative underlying choroidal leakage.

As a result, clinicians should consider pro-actively advising patients that have had previous CSCR or have other risk factors for developing CSCR (e.g. corticosteroid use, hypertension, thick choroid, Serous Pigment Epithelial Detachments etc.) on the symptoms of and how to self-monitor for active CSCR.

While it may be implied, this paper does not provide any evidence that ceasing vigorous activity during an active episode of CSCR is beneficial.

**Summary:** This study compared patients who had active CSCR and healthy patients (i.e. no history of ocular pathology). Both groups completed a survey about the amount of vigorous physical activity they did per week. Vigorous physical activity was defined as "that activity which requires hard physical exertion and that makes you breathe at a much more frequent rate than normal." The energy expended for each physical activity was calculated and expressed in metabolic equivalent of task. Moderate/high vigorous physical activities were compared to an absent/low amount of physical activity for each of the groups.

**Key findings:** There was a significant association between vigorous physical activity and CSCR, with a 5.58 times risk of having the disease. There were 63.5% of CSCR participants who did moderate/high vigorous physical activity compared to 26% in the control group. Weightlifting and bicycling had a significantly higher frequency in the CSCR group compared to the control group.

**Reference:** Piccolino FC, Fruttini D, Eandi C, et al. Vigorous Physical Activity as a Risk Factor for Central Serous Chorioretinopathy. American Journal of Ophthalmology. 2022; 244:30-37.

[Click here for abstract](#)



Thank you for taking the time to read the CFEH Summer 2022-2023 ATLAS Literature Review.

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@cfefh.com.au](mailto:education@cfefh.com.au).

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