## The Research Issue

## TARRGET Pilot Study Research Update

The Targeting At Risk Relatives of Glaucoma patients for Early diagnosis and Treatment (TARRGET) study is a partnership project between Glaucoma Australia and the Australian and New Zealand Registry of Advanced Glaucoma (ANZRAG), based at Flinders University, Adelaide.

TARRGET aimed to investigate the feasibility of offering free glaucoma screening to immediate relatives of people who have been diagnosed with advanced glaucoma. Researchers hypothesised that relatives of those people severely affected by glaucoma would have higher rates of glaucoma diagnosis than relatives of less severely affected glaucoma patients.

The pilot study has revealed that if you have advanced glaucoma your first degree relatives have up to a $54 \%$ chance of developing the disease, which is simply staggering.


Here we have summarised some of the key findings:

- The pilot study recruited 177 first degree relatives, with 131 completing the eye examination.
- 72 of the 131 first degree relatives screened either had glaucoma or had early signs that need to be monitored carefully.
- This indicates that if a person has a family member with advanced glaucoma they have up to a $54 \%$ chance of developing the disease.
- $93 \%$ of participants were aware of their family history, however $17 \%$ stated they had not been screened for glaucoma before, with an additional 14\% having had an eye health check but unsure if they had been screened for glaucoma.
- One third of first degree relatives did not understand how their family history of glaucoma related to their own personal risk of developing glaucoma.
- Newly detected cases of glaucoma tended to have intra-ocular pressure in the normal tension range, mild visual field defects and cup-to-disc ratio below 0.7 with a similar trend found in new suspects.

As the project transforms to a national study, we will look to advocate for better screening pathways for these individuals. This may involve lobbying for altered Medicare structures for nerve fibre layer testing and ongoing screening of family members. An important part of this process has been to realise that family members often feel that after one "normal" test they are cleared of the risk of glaucoma. In fact, as an ageing disease, ongoing, lifetime monitoring is required at least every 2 years.

If you have glaucoma - one way you can help reduce vision loss from glaucoma is to make sure your first degree relatives understand that they are also at risk and should have a regular eye exam.

To read the full report visit
www.glaucoma.org.au/news/research-articles

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Dear Friends and Supporters
The past three months have been a hive of activity at Glaucoma Australia as we continue with our vital mission to boost the detection of glaucoma.

Our team led by CEO Annie Gibbins have been very busy developing and trialing a new patient support journey to ensure every person diagnosed with glaucoma is actively being supported by Glaucoma Australia through personalised education and support when they need it most.

A recent trial of the new patient support journey with 200 patients recently referred to us has indicated where intervention and education is most required. Ideally, contact from Glaucoma Australia pre and post consultation and at 5 months post diagnosis, is aimed at increasing appointment and treatment adherence rates. Strategic interventions, both by phone and email, are now targeted toward improving education and support from the point of diagnosis and throughout the patient journey. Very importantly, we encourage people with glaucoma to alert their family members to the risk they also face and the urgent need to have a check for glaucoma

We're confident that this ground-breaking work will impact early detection rates, patient knowledge, reduce anxiety and improve treatment participation.

New Resources
In addition, new patient centered support resources are being developed and are now mapped to the four specific stages of the patient journey - diagnosis, starting treatment adherence and ongoing management.

Some of our new resources include:

- Glaucoma Risk Calculator - assess your potential risk of developing glaucoma based on age, gender, ethnicity, family history of glaucoma and other health issues such as diabetes and myopia.
- Glaucoma in Perspective - watch glaucoma in action in a new series of videos
- How to prepare for your ophthalmic appointment including a list of questions you might like to ask your specialist
Visit www.glaucoma.org.au/resources to access new and existing resources
Glaucoma Research: A Year of Progress
As custom dictates, the July issue of Glaucoma News is dedicated to glaucoma research and the achievements and
progress made over the past year. I'd like to thank Dr Simon Skalicky \& Clinical Associate Professor Andrew White fo providing a very comprehensive year in review. I am pleased research, which will ultimately provide better care and outcomes for people with glaucoma.

In addition we have recently received the latest report on the TARRGET Pilot Study and the results are staggering. If you have advanced glaucoma your first degree relatives have up o a $54 \%$ chance of developing the disease. I encourag everyone to read the summary of results on page 1 .

Glaucoma Australia Research Framework
Over the past 6 months, your Council has formulated a longerm research strategy for the next 5-10 years to ensure a more hopeful future for people with glaucoma.

As part of this strategic process we have identified four research domains that centre on the practical challenges of managing glaucoma by:

- Improving the treatment experience for people with glaucoma.
- Improving the quality and experience of monitoring the condition progression for individual people and maintaining better population wide statistics.
Increasing the rate and reliability of detection. That is, detect more people earlier in their progression.
Providing management tools to improve the quality of life for people with glaucoma.
ram pleased to advise you that Glaucoma Australia will soon be seeking expressions of interest from leading research organisations interested in collaborating with Glaucoma Australia to fund research projects that deliver on these research domains and our mission: to eliminate glaucoma blindness.
Kathleen Holmes Scholarships
Congratulations to the following young doctors on being awarded a 2018 Glaucoma Australia 'Kathleen Holmes Scholarship: Ellie Bowditch, Lukas Sahhar, Kay Lam and Joobin Hooshmand.
Miss Kathleen Holmes was the co-founder of Glaucoma Australia 30 years ago and was awarded an OAM in 1996 in recognition of her dedication to the glaucoma cause.
These scholarships enable ophthalmology trainees to attend the annual Australian and New Zealand Glaucoma Society ANZGS Scientic Meeting. We hope the $\$ 125$ youreceiv an be used to progress your know blindness

It was a delight for Glaucoma Australia CEO Annie Gibbins to meet Mr Marcus Quinlivan OAM in Canberra recently.

Mr Quinlivan is the founder of The William A Quinlivan Glaucoma Australia Research and Scholarship Fund, set up in honour of his late father. Mr Quinlivan proposed and financed the establishment of this special fund with the cooperation of Glaucoma Australia to fund research into laucoma including its causes, treatments and eventual cure.

The TARRGET study has been an excellent example of how genetic research can influence future campaigns aimed at finding the $50 \%$ of people currently undiagnosed with glaucoma. Data from this research indicates that first degree relatives of people with advanced glaucoma appear to have a higher than $54 \%$ chance of showing a east the early signs of glaucoma. This has resulted in a massive shift in focus towards early detection of glaucoma, specifically for first degree relatives of those with advanced glaucoma.
Further research is now being planned for more socia research which will improve communications that influence

behavioural changes related to early detection and treatment adherence.
Our focus is to take glaucoma seriously and act at the earliest opportunity.
If you would like to donate to the The William A Quinlivan Glaucoma Australia Research and Scholarship Fund lease call 0294117722

## My Story: My Glaucoma

Sydney resident Bob Corben shares his glaucoma story. My dear Mum had had no idea I had glaucoma until I changed optometrist in 2001. That very observant man did a regular eye examination and discovered a problem there and immediately referred me to an ophthalmologist.
When I was first diagnosed with glaucoma I really didn't have a clue what it was all about. I thought oh well it's another problem to deal with in life. I really underestimated what glaucoma was all about. Now I find glaucoma is one of the most frightening diseases I could ever know about - but 's not going to win it case. it's being treated by the best people I know. I have a great specialist who I visit every three months.

I would have been about 52 or 53 when I was first diagnosed with glaucoma. Interestingly enough my ophthalmologist told me if I had gone another 5 or 6 years l'd probably be blind by now.
couldn't picture being blind, just the thought of it is frightening. So I do everything I possibly can to look after my eyes. My glaucoma is in an advanced stage - but I still have very good eyesight in both eyes and I have an unrestricted driving license.
glaucoma. I knew that she had glaucoma when I was a teenager, but I didn't
 know it was hereditary. was never told it could be passed on by my optometrists or anyone else for that matter; or my mum, she wasn't aware of it either. I just wish there would have been a glaucoma and its effects then, as there is now.
have a brother and two sisters, and I make sure they get have a brother and two sisters, and I make sure they get have been found to have glaucoma and neither have my children, but they all get checked regularly.

I urge people to get tested for glaucoma. When you go for your next regular eye test ask specifically for a test for glaucoma. It's a hidden disease, so you don't know if you've got it, and if there is a history in the family please get tested very quickly

Greater knowledge of disease risk factors, new conjunction with cataract pproaches to detection and monitoring, and nnovative treatments are positively impacting glaucoma outcomes.

Over the past year we've seen a continued shift toward urgical/laser management of glaucoma, coupled with depot preparation medication trials rather than drop therapy. A major prospective trial looking at the efficacy of depot bimatoprost intracamerally has just finished ecruiting (ARTEMIS 1) and two more are still underway ARTEMIS 2 and ATHENA). Other similar trials are underway as well as assessment of an ocular ring releasing bimatoprost. 1 .,

Should we add Vitamin B3 to the Water? The paper with the biggest potential therapeutic impact this year described the potentially protective role of Vitamin B3 in glaucoma. A team from the Jackson Labs in the US fed vitamin B3 to mice prone to ocular hypertension, resulting in a significant reduction in the risk f ganglion cell death. This effect was even greater than targeted gene therapy treating the proposed metabolic/inflammatory pathway implicated in the disease process. ${ }^{3}$ Small scale clinical trials have already started. Much like the findings from the Nurses Health Study and nitrates, there seems to be an increasing role or dietary and nutritional supplementation in preventing glaucoma and/or halting progression. ${ }^{4}$

Minimally Invasive Glaucoma Surgery
Undoubtedly in 2017, glaucoma clinical practice focused on minimally invasive glaucoma surgery (MIGS).

MIGS represents a broad group of small surgical devices characterised by minimal conjunctival dissection, short operating times, rapid recovery and a good safety profile. This is a rapidly expanding field with trans-trabecula devices (eg iStent, Glaukos), increasingly performed in a growing body of supportive data, such as the Cypass (Alcon), which creates a cyclodialysis cleft and drains to the suprachoroidal space and the Hydrus microstent (Ivantis), a fenestrated curved tube that enters, passes through and dilates Schlemm's canal.

Currently, Medicare restricts the use of these devices to only at the time of cataract surgery, although work is underway to expand the availability for the procedure to a wider body of glaucoma patients, and potentially allow stand-alone MIGS procedures.

There is still a scarcity of robust MIGS scientific data. A meta-analysis of all MIGS papers released up until 2016 found that while overall safety data from MIGS is reassuring, good head-to-head random clinical trials comparing MIGS devices to one another or to traditional glaucoma surgery is lacking. ${ }^{5}$ As clinicians in this field, it is imperative we collect quality local data that evaluates MIGS in real-world clinical practice, and audit through communal software platforms such as the Save Sigh Registry.

Hydrus was compared head-to-head with selective lase trabeculoplasty (SLT) in a small ( $n=56$ ) case series. Hydrus resulted in a greater reduction in medication dependence than SLT at 12 months. ${ }^{6}$

## Filtration Surgery

Glaucoma filtration surgery (eg. trabeculectomy, tube surgery) involves creating an aqueous drainage pathwa from inside the eye to the subconjunctival space. Some preliminary results have been released for the Primary Trab vs. Tube Study (PTVT) that attempts to settle the question as to whether a primary drainage tube may be better than trabeculectomy as a first surgical procedure for glaucoma. In a word, no., ${ }^{7,8}$ IOP control was better in the trabeculectomy group, especially in those with lowe starting IOP. The complication rate was similar despite more early complications/interventions in the trabeculectomy group

The Xen Gel Implant (Allergan) is a soft collagen implan hat is inserted, ab interno, from the anterior chamber into the subconjunctival space creating a bleb. In many ways it is more similar to traditional filtration surgery than to other MIGS devices. It is increasingly used as an alternative to trabeculectomy, although quality head-tohead studies comparing Xen to trabeculectomy are few.

The Xen was shown to be effective in uveitic glaucoma, despite the potential for sight-threatening complications of hypotony, bleb infection ${ }^{9}$ or suprachoroidal haemorrhage ${ }^{10}$ (ie similar complications to a trabeculectomy).


Xen Gel Implant

## Lasers in Glaucoma

The efficacy and safety of SLT in the treatment of open angle glaucoma (OAG) continues to be supported by the iterature. SLT was evaluated in Afro-Carribeans with primary OAG (POAG) and found to have a 12 month success rate of 78 per cent. ${ }^{11}$ In Belgium, SLT was evaluated as replacement therapy for medically controlled OAG; it was able to completely replace medical therapy in 77 per cent of eyes after 18 months ${ }^{12}$ and improved treatment related quality-of-life (QoL) ${ }^{13}$ with similar efficacy between phakic and pseudophakic eyes. ${ }^{14}$ However, when 24- hour IOP rhythm was evaluated by the contact lens sensor Triggerfish, SLT was not shown to alter the amplitude or pattern of the IOP rhythm. ${ }^{15}$

Angle Closure and Glaucoma
Angle closure is frequently missed, both among patients referred for cataract surgery who are often dilated without prior gonioscopy, and among patients with Primary Open Angle Glaucoma (POAG) who can develop phacomorphic angle closure with age. Two studies from Canada elegantly demonstrated this; of patients referred for cataract surgery, 1.5 per cent were found to have undetected narrow angles, ${ }^{16}$ and one in 11 patients, with a diagnosis of OAG referred to a tertiary glaucoma centre, were found to in fact have angle closure. ${ }^{17}$

Dysphotopsia is a rare but debilitating complication of aser peripheral iridotomy (LPI). Previous data suggested the frequency of this can be reduced by tempora placement of the LPI. ${ }^{18}$ However, a larger ( $n=595$ ) ndian/US RCT found that location, LPI size, and amoun of laser energy used did not affect the frequency of dysphotopsia reported. ${ }^{19}$

Another large Indian study confirmed that LPI hastens the development of cataract. ${ }^{20}$ These findings support the landmark EAGLE study that compared early clear lens extraction (CLE) to laser iridotomy in the management of primary angle closure glaucoma (PACG). CLE showed greater efficacy and was more cost-effective than lase ridotomy. ${ }^{21}$

Externally applied micropulse cyclophotocoagulation (M CPC) is an alternative mode of laser delivery continuous wave cyclophotocoagulation (CW-CPC) Micropulse has a high post- treatment inflammation rate (46 per cent after three months) and a similar but potentially lower complication profile than CW-CPC. ${ }^{22}$ More head-to-head studies are required comparing micropulse to continuous wavelength and to endoscopic CPC to better elucidate this rapidly developing technology.

Monitoring and Detection
We have yet to improve the 50 per cent undiagnosed glaucoma rate in Australia. However, new advances in diagnostic technology, a greater drive for optometry-led detection, and an emphasis on first-degree relative screening such as through the TARRGET study may improve the detection rate.

Australian-developed tablet-based perimetry has the potential to revolutionise glaucomatous monitoring, allowing home or waiting-room self-screening for glaucoma. It is easy to use and sensitive to glaucomatous progression. ${ }^{23,24}$

Three separate studies have confirmed the importance of central (eg 10-2) visual fields in glaucoma diagnosis to complement 24-2 fields; the latter might miss early glaucomatous defects. This trend persisted irrespective of the type of field machine used. ${ }^{25-27}$ Furthermore 10-2 changes had a greater impact on vision-related quality of life (QoL) than 24-2 changes. ${ }^{28}$

The frequency of monitoring for glaucoma patients continues to vex strained clinics. One study found twice yearly visual field testing had similar sensitivity to thrice yearly for detecting glaucoma progression, provided two quality baseline tests were available for reference. ${ }^{29}$ Thes
findings support the UK Glaucoma Treatment Study, in Further prospective study needs to be done to better which a few early visual fields established a firm baseline; understand the pathophysiology behind this finding. this allowed sensitive detection despite greater intervals between later field tests. ${ }^{30}$

OCT-angiography (OCT-A) continues to be explored in glaucoma. Adding to vascular loss previously described at the optic nerve head, new studies have found macular vascular density declines in glaucoma. ${ }^{31,32}$ However this finding was not consistent; one study found the macular vessels were spared in glaucoma. ${ }^{33}$ In addition, the diagnostic sensitivity of OCT-A is lower than traditional OCT metrics (RNFL and MGC complex thickness). ${ }^{33}$

One drawback of OCT analysis glaucoma is a floor effect of the peripapillary RNFL (sensitivity is lost in advanced disease). In agreement with prior studies, the ganglion cell nner plexiform layer metric was again shown to be more sensitive for advanced glaucoma than the peripapillary RNFL and continued to demonstrate progression once the RNFL had reached its floor effect. ${ }^{34,35}$

More data has supported the water-drinking test, finding IOP spikes induced by the water-imbibed challenge were predictive of future glaucomatous progression. ${ }^{36}$

## The Genetics of Glaucoma

The last few years have seen an explosion of genes dentified in glaucoma pathogenesis. Novel loci include: for POAG (ABCA1, AFAP1, GMDS, PMM2, TGFBR3, FNDC3B, ARHGEF12, GAS7, FOXC1, ATXN2, TXNRD2); PACG (EPDR1, CHAT, GLIS3, FERMT2, DPM2-FAM102) and pseudoexfoliation syndrome glaucoma (CACNA1A). ${ }^{37}$ There are so many genes implicated that work is beginning to move towards better phenotyping of glaucoma for targeted gene studies, and studies looking at the functionality of these genes and interactions with each other (ie. is it combinations of gene anomalies rather than a single gene that is causative?). Stay tuned.
ealth, Socioeconomic and Lifestyle Factors Smoking was the smoking gun for glaucoma in 2017. A Spanish cohort population study of 16,797 participants over 8.5 years demonstrated a direct association between current smokers and glaucoma incidence, and the risk increased with number of pack-years. ${ }^{38}$

Additionally, a retrospective study looking at risk factors for rapid glaucoma progression showed rapid progressors were older, had significantly lower baseline IOP and central corneal thickness, and significantly higher rates of cardiovascular disease and hypotension. ${ }^{39}$

A Taiwanese study evaluated the influence of differen socioeconomic factors on vision-related quality of life in glaucoma. A lower education - but not income - affected QoL detrimentally, suggesting the importance of additional counselling for patients with a lower educational level to help them cope with the disease. 40
"there seems to be an increasing role for dietary and nutritional supplementation in preventing glaucoma and/or halting progression"

## Other Medical Therapies

Drug development for new glaucoma therapies has been slow but continues.

Rhopressa (Netarsudil 0.02 per cent) is a once daily topical agent with two mechanisms of action and two targets. Rhopressa targets rho-kinase (ROCK) and a norepinephrine transporter (NET). Trial results (ROCKET1 4) yet to be published seem promising. The most common side effect was mild redness of the eyes.

A combination product, Roclatan, is a once daily, combination of netarsudil 0.02 per cent + latanopros 0.005 per cent made by the same company (Aerie Pharmaceuticals). Initial results from two trials (Mercury 1 and 2) also seem promising.

A new pathway for treatment was discovered this yea that may also show promise. The angiopoietin-Tie system is crucial in the development and maintenance of Schlemm's canal and hence IOP control. Antibody mediated activation of Tie2 resulted in an increase in drainage apparatus in Schlemm's canal when injected in mice. Further development of this pathway may lead to a new IOP lowering agent in the future. ${ }^{37}$

## Conclusion

As clinical and laboratory science marches forward, we must stay nimble in our approach to clinical practice, and translate the new knowledge into better, more efficient and more inclusive glaucoma care delivery to all patients.

This article first appeared in mivision issue 132 March 2018. It has been reprinted with the permission of mivision (Toma Publishing)
References supplied

## Welcome Sapna Nand

Glaucoma Australia is delighted welcome orthoptist Sapna Nand to our growing education eam. Along with Jan Howlett, Sapna will provide over the phone support and education o people with glaucoma, their amilies, carers and friends to help them to understand glaucoma and the treatment options available to them.


Sapna joins Glaucoma Australia with 10 years' experience as an orthoptist with a strong background in clinical trials and preparing patients for SLT and/or surgery.
Sapna is passionate about early detection and reatment adherence to prevent vision loss and helping patients minimise the impact of glaucoma on their lifestyle and independence.

Sapna provides information, education and support to people regarding treatment options and procedures, what to expect during ophthalmic appointments and the strong hereditary nature of glaucoma.

Sapna also works at Marsden Eye Specialists with highly experienced Glaucoma surgeons, which has given her the opportunity to view a range of minimally invasive glaucoma surgeries (MIGS) being conducted by Dr Ashish Agar.

Glaucoma Australia is proud to be able to continue to offer a service that enables a one-on-one conversation to take place to educate and support people living with glaucoma

## GIVING HOPE

By leaving a charitable bequest to Glaucoma Australia you are giving hope to future generations.

We know that most forms of glaucoma are hereditary. Your generosity will help improve glaucoma awareness, detection, treatment and support for families at risk as well as helping to fund valuable research.

If you would like to become a GIVER OF HOPE please call Annie Gibbins on 0294117722 or email ceo@glaucoma.org.au

## Many Thanks

Many thanks to the companies, clubs and organisations who provided financial and other support to Glaucoma Australia

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## Bequests 2018

- The estate of the Late Dorothea Watt
- The estate of the Late Eileen Doris Gabriel
- The estate of the Late Isabel Mary Tangie
- The estate of the Late Eileen Merle Masters
- The estate of the Late Katherine Mander

We recently filmed a series of videos with orthoptist and Glaucoma Australia educator Jan Howlett to answer some of your more frequently asked questions. You can watch these videos on YouTube www.youtube.com/GlaucomaAustralia or read the questions and answers below.

## Does surgery improve my vision?

Glaucoma surgery, like all other glaucoma treatment options, aims to reduce the risk of any further vision loss but is unable to give back vision already lost from glaucoma. Vision loss through glaucoma is permanent.

## How does the eye specialist determine

 my follow-up time?Eye health follow-ups fall into two categories:

1. for patients with glaucoma; and
2. for patients who are at risk of developing glaucoma.

The time between appointments for both categories is determined by a complex combination of factors, which include, but are not limited to:

- whether you have a family member with glaucoma,
- your health status
- your age, and
- the medications you take.

For those with glaucoma additional factors are considered:

- the degree of your optic nerve damage and the visual field loss.
- how recently your diagnosis was made
- how recently you started or changed treatment

So at your initial and all subsequent appointments, your eye specialist will determine when your eyes need to be checked again based on this data.

## Why should I keep taking my eye drops?

Glaucoma can't be cured. The aim of all glaucoma treatment is to prevent any further vision loss from the disease.

Eye drops are prescribed to reduce your eye pressure. When your eye pressure is too high, it damages the optic nerve which in turn causes irreparable damage to your vision. So if you have been prescribed eye drops it is very
important to keep using them exactly in the manner your eye care professional has prescribed.

If you stop using the prescribed eye drops, the pressure in your eye will go up again and the damage to the optic nerve and your vision will restart.

Always tell your eye care professional if you are having trouble using your eye drops and your treatment will be adjusted accordingly to address your problems

## Why do I need a visual field test?

A glaucoma diagnosis is based on evidence of optic nerve damage and/or visual field loss. However, visual field damage will not be obvious to you during your daily activities because firstly this initial glaucoma damage affects the very extremities of eyesight and second because we turn our head to view objects to our far right or left, up or down, such vision field loss is rarely noticed.

The automated visual field test accurately maps out your field of vision one eye at a time. This shows the level of function of the millions of vision fibres that give you sight. Any damage to either eye's vision fibres will show up in this test. At your initial consultation, this test, when abnormal, indicates a likely glaucoma diagnosis. The optic nerve and any damage is reviewed in conjunction with this visual field test result. Together they are the evidence your eye care professional relies on to determine whether you have glaucoma or not. Subsequent visual field tests monitor treatment efficacy.

Once glaucoma is confirmed, treatment is started immediately to prevent any further vision loss. This visual field test needs to be performed regularly to check that treatment is adequate. If this automated field test shows further vision loss is occurring, your treatment is adjusted accordingly until such time that there are no longer any signs of ongoing damage and vision loss.

If you have a question for one of our educators please
call 1800500880 or email glaucoma@glaucoma.org.au.

