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IRDs: - Investing in ATMPs to address a High Unmet Need

A Patient & Community Perspective

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Avril Daly – CEO, Retina International

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Editorial

Therapies for Inherited Retinal Dystrophies: What is Enough?

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- This presentation is based on a multistakeholder paper following the ERN-EYE workshop on clinical trials (Ghent, Belgium, December 2022) DOI: 10.1016/j.drudis.2024.104095

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The Promise

Advanced therapies in ophthalmology have the potential;

- To treat rare, inherited, complex and age-related retinal disease.
- To change lives and address high unmet need.
- To reduce burden of disease on patients, those who care for them, and society at large.
- To improve the delivery of care and treatment, by reducing burden on health and social care systems.
- To address societal inequalities.

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A small and complex population

- Made up of specific genetic subtypes
- Underrepresented in part due to the lack of uniform access to genetic testing
- Challenges in patient identification

Establishment of coordinated registries & cohorts, would allow patient identification & collection of robust data for natural history models, essential for understanding disease progression and treatment impacts.

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Impact of IRDs

- The prevalence and impact of IRDs at a national and global level has remained largely underestimated and misunderstood.
- The socioeconomic burden of IRDs, in addition to their impact on wellbeing and mental health, has been felt by patients, health advocacy organisations, HCPs, and scientists globally.
- Studies undertaken by RI to understand the Social and Economic Impact of IRDs on the individuals affected and society at large demonstrated a significant burden, on wellbeing, mental health, access to education and employment as well as in productivity.
- Yet in the context of **VALUE** IRDs are measured in their cost to the healthcare system, which highlights the challenges this community faces in accessing treatment and support.

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IRDs Count The Cost

RI's 2019 IRD Counts study on the burden and economic impact of IRDs in the ROI and UK from a societal perspective found that:

- 33.8% (16m Euro) IRE
- 38.4% (138 mSTG) UK

attributed to **Wellbeing**

- 9.4m Euro
- 114,1m Pounds Stg

Were attributed to **Productivity Costs**

50,7% of people living with an IRD in ROI and
40,2% in UK were **not in paid employment**
In both regions IRDs result in 9.6% loss of **productivity while at work.**

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What is enough

- **Preservation**
- **Slowing degeneration**
- **Stabilization**

- **‘If someone told me right now they could keep my sight at 5 degrees visual field….it would be MAGIC’ Paul, Dublin Ireland.**

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A Question of Value

Experience of the IRD Community:

- **Inherited Retinal Dystrophies are unlike other rare conditions, those living with vision impairment are not patients. They are not sick – but live with a degenerative disease that can cause disability and affects wellbeing.**
- **Health systems costs are the lowest when conducting a socio-economic analysis of the impact of vision loss of inherited retinal conditions.**

Cost is in Social Care – Social Services – Access to Education, Employment and impacts mental health.

- High rates of depression, anxiety and financial stress.
- Impact on education, employment and productivity losses.
- Impact on caregiver.
- Intangible costs.

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The Question we should be asking?

- Where a confirmatory Genetic Test is available it is possible to diagnose and understand how an IRD is likely to progress?
- Early intervention has the potential to halt or slow down the degeneration of the retinal leading to longer life with visual function and functional vison resulting in changes that impact the course of a life.
- Preventing the development and progression of disease is a key pillar of national health care systems – *why is it so undervalued in Retinal Health?*

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New approaches offer new hope

Range of therapeutic approaches

- Optogenetics
- Antisense oligonucleotides
- Gene editing
- **Enthusiasm fading – Clinical trials abruptly halted as a result of missed primary endpoints/investor withdrawal**

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Choosing the measurements

Challenge in The selection of appropriate outcome measures that at the same time are meaningful to the patient and of interest to the regulatory agencies.

- A lack of understanding about the pathophysiology of IRD and what is important to the patient
- Leading to the selection of **wrong** outcome measures in consideration of the stage of disease
- Decreasing the chance of success
- Regulatory agencies dealing with clinical trials for IRDs are still too heavily reliant on commonly used metrics, derived from trials in common ophthalmic diseases. (BCVA/Visual Field)

Many p atients IRD believe easures are often irrelevant in IRD patient populations.

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Measuring for success

Many different types of measures of visual function and measures relevant to the disease and the patient, which should be considered.

- VN was approved after a Multi-Luminance Mobility Test was developed and tailored to specifically reflect activities of patients daily living and was accepted as a novel primary endpoint that enabled VN to be approved by FDA.
- IRD patients will consider marginal visual improvements, but also halting or even slowing down the disease course, as very meaningful.
- For someone on a progressive course towards blindness, simple maintenance of the current state of vision can be life changing.

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Designing the trials for patient need

- Design of clinical trials for rare diseases such as IRDs should be adapted to known challenges.
- Optimizing small populations and incorporating adaptive designs.
- A framework for continuous assessment & learning from the first patients can help with size and cost of study issues.
- Identifying reasonable controls such as the fellow eye, or stratifying control groups to correctly match trial populations could increase data quality and volume.

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Including the patient perspective

Thpatient voice has not been heard enoughe,

- Until recently there was no reliable patient reported outcome measure tailored to IRD
- Of all trials conducted none have reported on the results of the tools used.

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Delivering on the promise of ATMPs

- Successfully bringing IRD therapies to market will require a combination of initiatives.
- Regulatory agencies need to work together towards global harmonisation of procedures for a more universal and rapid approval process,
- Further expand options for conditional approvals.
- Conditional approvals of safe and promising products, followed by close monitoring of real-life results, would expedite access, and enable re-evaluations.
- increasing investors' awareness about the unique challenges of the longer trial duration required to prove treatment efficacy would secure long-term financial trial support, provided a simplified, solid pathway to approval is attained.

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Conclusion

- IRDs are emblematic of rare diseases that are becoming ‘actionable’ as we enter a new era of innovative medicine and tailored therapies.
- We can now in some cases prevent blindness.
- Clinical trials have to be specifically designed for the IRD under study with selection of outcome measures that are meaningful to the patient, reflecting the disease process and acceptable to regulatory agencies.
- Trial results will require evaluation through global regulatory pathways, to streamline efforts to alleviate otherwise inescapable blindness.

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Related Publications

CLINICAL OPHTHALMOLOGY
2021, AHEAD-OF-PRINT, 2855-2866

Taylor & Francis
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Open access

The Impact of Inherited Retinal Diseases in the United States of America (US) and Canada from a Cost-of-Illness Perspective

Jennifer Gong[1], Simone Cheung[2], Alivia Fasso-Opie[3], Orla Galvin[4], Larissa S Moniz[5], Doug Earle[5], Todd Durham[6], Jason Menzo[6], Nan Li[7], Stephanie Duffy[7], Jill Dolgin[8], Mark S Shearman[8], Chiara Fiorani[9], Judit Banhazi[9], and Avril Daly[4]

- https://doi.org/10.2147/OPTH.S241928

CLINICAL OPHTHALMOLOGY
2020, AHEAD-OF-PRINT, 707-719

Taylor & Francis
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Open access

The Impact of Inherited Retinal Diseases in the Republic of Ireland (ROI) and the United Kingdom (UK) from a Cost-of-Illness Perspective

Orla Galvin[1], Gloria Chi[2], Laura Brady[3], Claire Hippert[4], Marta Del Valle Rubido[4], Avril Daly[1], and Michel Michaelides[5,6]

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- https://doi.org/10.2147/OPTH.S313719

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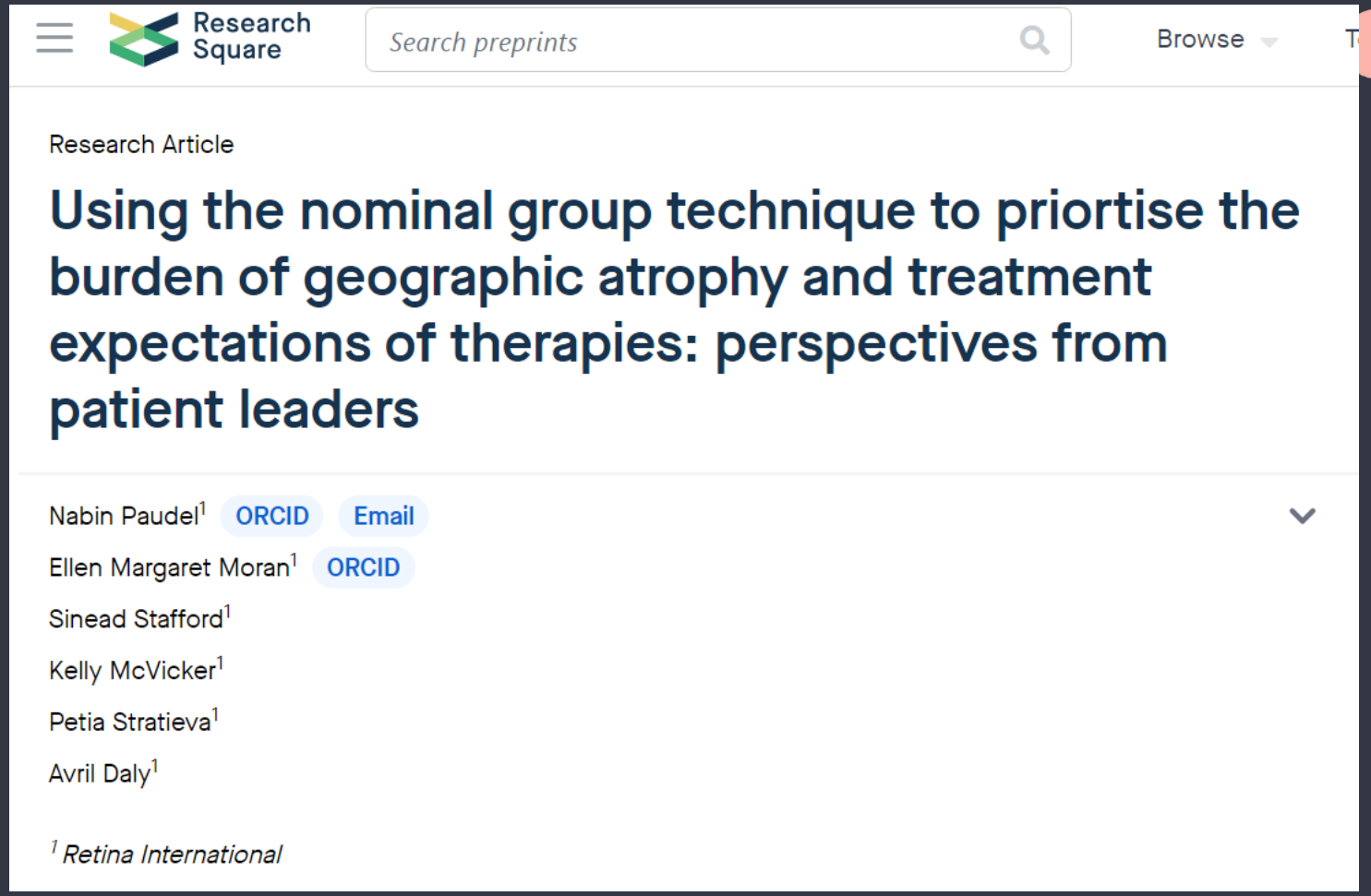
Related Publications

Nabin Paudel, Ellen Margaret Moran, Sinead Stafford et al. Using the nominal group technique to prioritise the burden of geographic atrophy and treatment expectations of therapies: perspectives from patient leaders, 29 August 2024, PREPRINT (Version 1) available at Research Square [https://doi.org/10.21203/rs.3.rs-4957856/v1]



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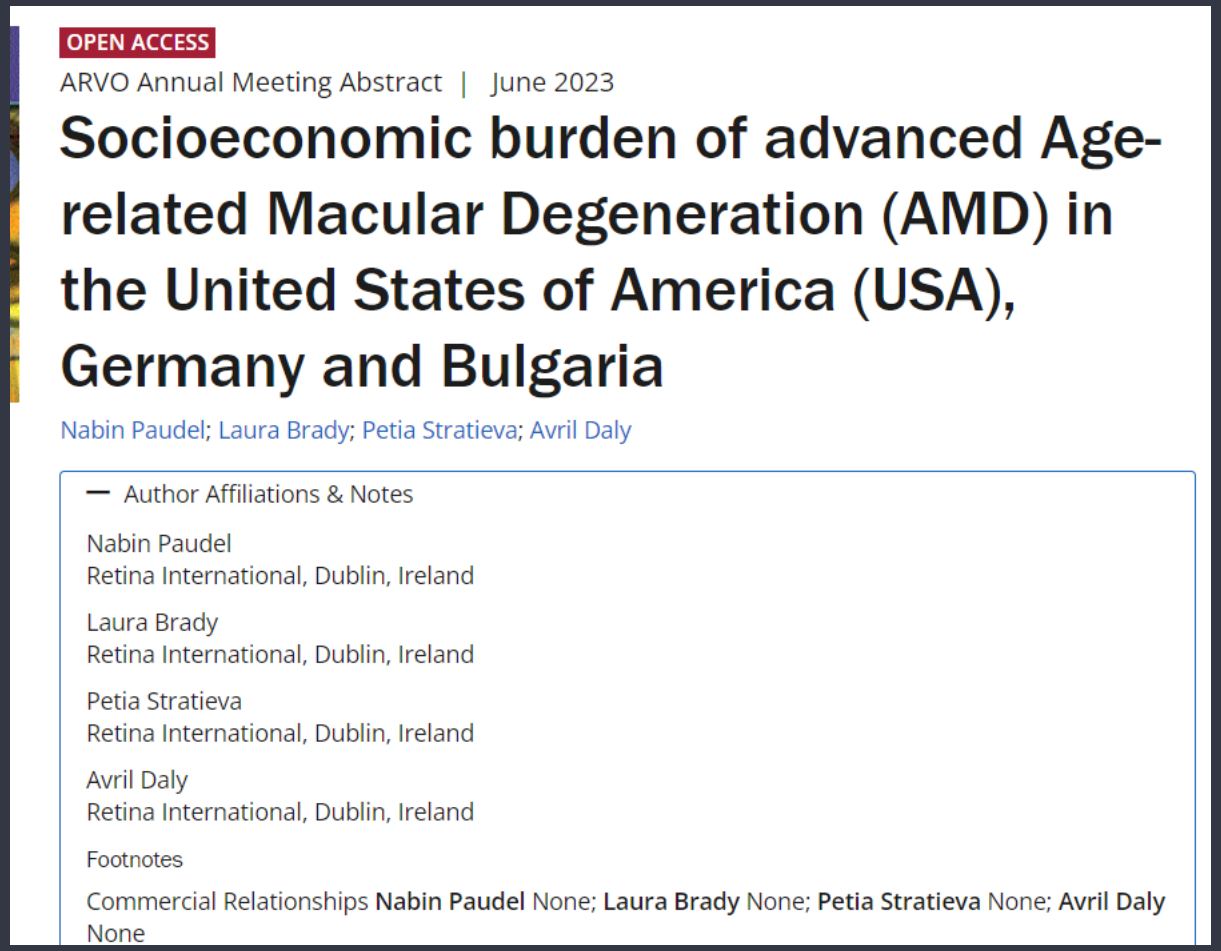
Related Publications

Nabin Paudel, Laura Brady, Petia Stratieva, Avril Daly.

Economic burden of late-stage Age-related Macular Degeneration in Bulgaria, Germany and the USA

JAMA Opthalmology (Accepted)



OPEN ACCESS

ARVO Annual Meeting Abstract | June 2023

Socioeconomic burden of advanced Age-related Macular Degeneration (AMD) in the United States of America (USA), Germany and Bulgaria

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Footnotes

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Thank You

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