Research priorities for Inherited Retinal Diseases in Australia: A James Lind Alliance Priority Setting Partnership

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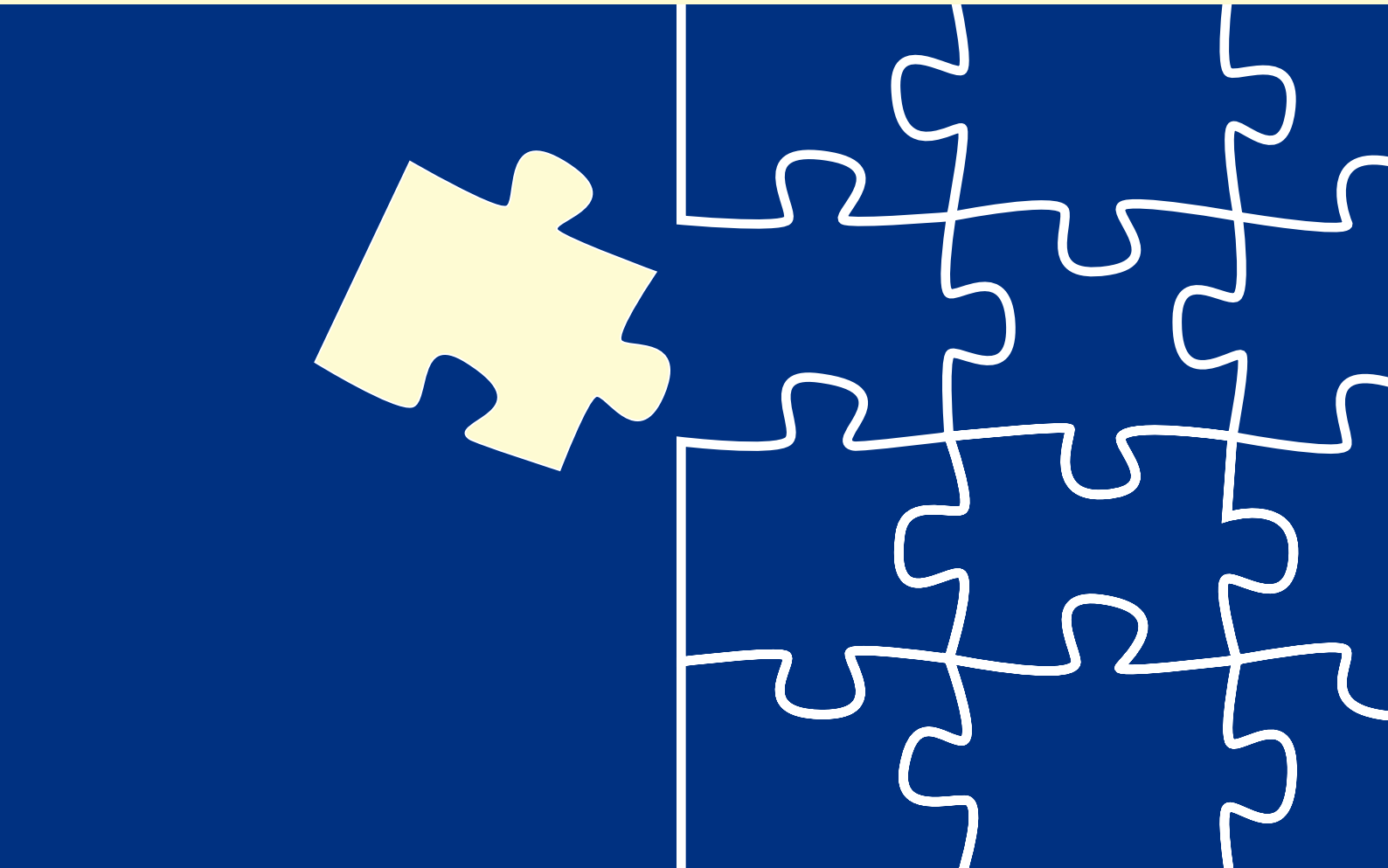
RESEARCH PRIORITIES FOR INHERITED RETINAL DISEASES IN AUSTRALIA:

A James Lind Alliance
Priority Setting Partnership



I was born with Leber Congenital Amaurosis, a degenerative inherited retinal disease. I was born visually impaired at birth and lost most of my sight when I was 12. As a result, I have experience in vision loss, navigating education and the workplace as a blind person, using a white cane and assistive technology, and participating in social activities as a blind person. I also have experience as a blind person living in a regional area, so I know how challenging and restricting it can be and what supports we need the most in such locations. I am incredibly passionate about spreading awareness about blindness and want to participate in this work as it is an amazing opportunity to create change.

Individual living with an inherited retinal disease
who participated in the final prioritisation workshops

Acknowledgements

The Inherited Retinal Disease Priority Setting Partnership team and Steering Group ***(Appendix A)*** would like to thank all the individuals who participated in the surveys and our workshops, the James Lind Alliance for their guidance throughout this process. We would also like to thank our numerous partner organisations ***(Appendix B)*** who supported recruitment and dissemination.

This report was a collaborative effort of our IRD Priority Setting Partnership team and Steering Group over the past 18-months. The following individuals contributed in writing this report: *Dr Eden Robertson, Associate Professor Anai Gonzalez-Cordero, Dr Kate Hetherington, Professor Robyn Jamieson, Professor John Grigg, Associate Professor Lauren Ayton, Dr Alan Ma, Dr Meredith Prain, Emily Shepard, Hollie Feller,* and *Professor Matthew Simunovic.*

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Forewords

The translational gap – the gap between knowledge gained through research and what goes on to benefit patients – is a key challenge that we face in our work. A commonly cited statistic emphasising this gap is that it takes an average of 17 years for knowledge gained through research to be applied in policy and practice. This challenge is no stranger in the field of inherited retinal diseases (IRDs). We must do better at reducing this gap to improve health care and ultimately the outcomes of individuals impacted by these largely untreatable conditions.

In 2021, we established a multidisciplinary collaboration – involving basic scientists, behavioural scientists and clinicians from across several Australian institutions. We agreed that meaningful consumer engagement is critical to strengthening the translation of research from bench-to-bedside. In particular, we identified the need to better engage consumers in determining what IRD research is prioritised. Discordance between the agendas of the research community and consumers, often cited in the literature, may be a contributing factor to the ongoing translational gap.

In 2022, we submitted a Medical Research Futures Fund (MRFF) Stem Cell Therapies Mission grant that included a James Lind Alliance Priority Setting Partnership (PSP) to identify consumer priorities for research into IRDs. This MRFF funding application was successful and following award in 2023, the research to undertake this ambitious consumer-focussed approach to priority setting started.

We are grateful to Dr Eden Robertson (the IRD Priority Setting Partnership Lead) for driving this work, the Steering Group for their substantial contributions, and the James Lind Alliance for their guidance.

The findings of our IRD Priority Setting Partnership will be used to drive meaningful research for many years to come. Partnering with consumers has helped shape our understanding of the challenges faced by individuals living with IRDs, and highlighted the value of incorporating consumer perspectives into every stage of the research process. Our efforts will now focus on advocating for the uptake of these priorities. By bridging the gap between researchers and consumers, we hope to accelerate the translation of research into real-world benefits for individuals impacted by IRDs and their families.

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Al & Val Rosenstrauss Fellow

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Thank you to Associate Professor Anai Gonzalez-Cordero, Dr Kate Hetherington and Professor Claire Wakefield for conceptualising this project, obtaining research funds, and trusting me to lead this work. I also would like to thank everyone who has been involved in this Priority Setting Partnership, in particular the:

- Steering Group *(Associate Professor Lauren Ayton, Leighton Boyd AM and Rosemary Boyd OAM, Hollie Feller, Associate Professor Anai Gonzalez-Cordero, Julia Hall, Dr Kate Hetherington, Professor Robyn Jamieson, Sally Karandrews, Dr Alan Ma, Dr Meredith Prain, Emily Shepard, Professor Matthew Simunovic,* and *Kanae Yamamoto);*
- research study investigators *(Associate Professor Anai Gonzalez-Cordero, Dr Kate Hetherington, Professor Claire Wakefield, Professor John Grigg, Professor Robyn Jamieson,* and *Professor Megan Munsie);*
- partner organisations;
- study participants; and
- the James Lind Alliance.

It has been a privilege to lead the first IRD Priority Setting Partnership in Australia, in partnership with our passionate and committed Steering Group. Over the past 18-months, I have had the pleasure of developing strong relationships with our Steering Group, partners, and engaging with individuals who have lived experience of an IRD and health professionals from across Australia through our surveys and online workshops. With 146+ hours of combined attendance at Steering Group meetings, 220+ survey responses, and 180+ hours of combined participation in the final workshops, we have successfully identified the top 10 research priorities for IRDs in Australia. Our rigorous approach has resulted in meaningful priorities that will be remain relevant for the next decade and beyond.

We will now use these findings to advocate for research that matters most to the IRD community to be funded and progressed. Alongside this, we are also committed to supporting health services and community organisations to address identified unmet knowledge and support needs of the IRD community. I encourage readers to support our efforts – whether this be as a researcher, health professional, funding body, community organisation, or advocate.

Beyond having identified the research priorities, this work has highlighted a more inclusive way of undertaking research. I have learnt an immense amount, and I will continue to listen and learn from those with lived experience to increase the impact of my work. I hope that seeing the value of partnering with individuals who have lived experience will inspire others to do the same.

Dr Eden Robertson (Inherited Retinal Disease Priority Setting Partnership Lead)

Research fellow, Behavioural Sciences Unit, Kids Cancer Centre, Sydney Children's Hospitals Network – Randwick; School of Clinical Medicine, UNSW Medicine & Health, UNSW Sydney

Senior research officer, Stem Cell Medicine Group, Children's Medical Research Institute

Executive summary

We undertook Australia's first James Lind Alliance Priority Setting Partnership to identify the research priorities for IRDs in Australia. Adhering to the James Lind Alliance process, our Priority Setting Partnership was guided by our multidisciplinary steering group, involving individuals who have an IRD, caregivers of a child who have an IRD, representatives from relevant community organisations, health professionals, and researchers from across Australia.

Our Steering Group defined the scope of our Priority Setting Partnership to include any questions about IRDs, in areas such as diagnosis, progression, treatment or psychosocial impact. First, we undertook an online survey to gather any unanswered questions (i.e., uncertainties) that the IRD community had. Sixty-nine eligible individuals submitted 223 in-scope uncertainties. After deduplication, we refined the uncertainties into 42 overarching, summary questions. Following a review of the literature, 41 of these summary questions were verified as evidence uncertainties – thus requiring further research. We then undertook a second survey, with 151 individuals voting for up to 10 of the 41 evidence uncertainties that they considered the most important to be answered. Sixteen of the highest ranked evidence uncertainties were taken to the final workshps for discussion. Over the two half-day, online workshops, the 24 workshop participants decided on the top 10 research priorities for IRDs in Australia. An overview of the study is presented on Page 9 (Figure 1).

The final top 10 priorities were broad in scope, representing four domains (see Table 1, Page 10):

i. treatment/cure;
ii. symptoms and disease progression;
iii. psychosocial wellbeing; and
iv. health service delivery.

This report provides a detailed summary of how we undertook our Priority Setting Partnership, with a commentary on each of the top 10 priorities. Each commentary provides context into the current state of knowledge and highlights opportunities that will drive a meaningful impact for individuals who have an IRD, their caregivers and family, and health professionals across Australia.

Figure 1. Summary of the Priority Setting Partnership stages

Table 1. Final top 10 research priorities for IRDs

Rank	Domain	Research priorities
1		What treatments can safely prevent, slow down or stop vision loss that occurs for someone with an IRD?
2		What is the psychological impact of having an IRD, and what support is most effective?
3		What treatments can safely restore vision for someone with an IRD?
4		What are the information and psychosocial needs of individuals with an IRD and their families at diagnosis?
5		What training and/or guidelines are needed for health professionals to provide optimal support for individuals with an IRD, from diagnosis and beyond?
6		What are the most effective ways to support carers and family members of an individual with an IRD?
7		How do environmental and lifestyle factors influence IRD symptoms and disease progression?
8		What are the most effective ways to manage IRD symptoms?
9		How can a program to detect IRDs as early in life as possible be implemented?
10		What is the anticipated progression of vision loss for each IRD?

11

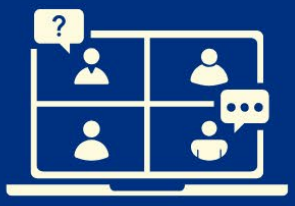
Steering Group meetings

146+ hours

of combined attendance at Steering Group meetings

421 days

from 1st Steering Group meeting to priority launch



180+ hours

of combined attendance at final workshops

220

survey responses

5/8

states/territories represented

28+

IRD diagnoses represented

84%

of survey responses from individuals with lived experience

Context to our Priority Setting Partnership

The James Lind Alliance is a non-profit making initiative that brings patients, carers, and clinicians together to undertake a Priority Setting Partnership. Priority Setting Partnerships identify and prioritise the evidence uncertainties, or 'unanswered questions', that key stakeholders agree are the most important for research in a specific topic area. The purpose of a Priority Setting Partnership is to identify the top 10 priorities that can be used to drive more meaningful and impactful research.

In 2012, a Priority Setting Partnership was undertaken in the U.K. regarding the prevention, diagnosis and treatment of sight loss and eye conditions. Their initial survey collected uncertainties from any individual who had been or may be affected by sight loss. For the interim prioritisation surveys however, data was analysed separately for the IRD community. The highest ranked priorities were then discussed in workshops specifically with individuals living with an IRD and health professionals who care for this population. Through these workshops, the top three priorities for IRDs were determined to be:

1. *"Can a treatment to slow down progression or reverse sight loss in inherited retinal diseases be developed?"*
2. *"How can sight loss be prevented in an individual with inherited retinal disease?"*
3. *"Is a genetic (molecular) diagnosis possible for all inherited retinal diseases?"*

Since 2012, there have been significant advancements in gene identification, diagnostic yield for individuals with a suspected IRD, cell biology techniques and gene-based therapies for IRDs. Our team established the IRD Priority Setting Partnership to extend and update the research priorities specifically for IRDs, and within the Australian context.

What are Inherited Retinal Diseases?

Inherited Retinal Diseases represent a broad range of diseases that are associated with abnormalities/degeneration of retinal cells, most predominantly in the light sensing photoreceptor cells and retinal pigment epithelium. In Australia, current estimates suggest that IRDs affect between 1 in 1,000 to 1 in 3,000 individuals. They are the leading cause of blindness in adults of working age and second most common cause of blindness in children.[1]

Inherited Retinal Diseases are extremely genetically heterogenous – with more than 320 causative genes and loci identified to date.[2] Phenotypically, individuals with an IRD can experience the onset of symptoms early in life, or as adults. Symptoms can also differ, depending on the genetic type of IRD and for each patient.[3] However, most individuals with an IRD will experience progressive vision loss – although uncertainty exists around the rate of vision loss given the heterogeneity of IRDs. In most cases, IRDs are limited to the retina and do not affect other organs or tissues – known as 'non-syndromic IRDs'. Some individuals experience a syndromic IRD – a condition in which the retinal disease is associated with other symptoms as part of a systemic disease.

Management of IRDs is complex. The Royal Australian and New Zealand College of Ophthalmologists (RANZCO) published guidelines for their management to assist patients and clinicians in optimising the journey from diagnosis through visual rehabilitation clinical genetic management and finally therapy.[4] These guidelines highlight the multidisciplinary approach required to manage the complex medical, psychosocial and practical challenges of living with an IRD.

In 2020, 'Luxturna', a gene therapy for *RPE65*-associated retinal dystrophy, was approved for therapeutic use in Australia. Aside from this treatment, there are no other treatments clinically available for individuals with an IRD. This is of concern given an estimated overall lifetime cost of $5.2 million per person with an IRD, of which 87% are attributed to societal costs (e.g., government support, lost income to individuals with an IRD and caregivers).[5] Research also highlights that nearly two thirds of Australians felt that going blind is worse than having a heart attack or losing a limb.[6]

METHOD

TO IDENTIFY THE RESEARCH PRIORITIES

Method

1. Establishing the Priority Setting Partnership

The IRD Priority Setting Partnership Steering Group was established to oversee the priority setting process, guide the accessibility of data collection, support recruitment, and disseminate findings. Through professional networks of the study investigators, we invited clinicians, researchers, individuals with lived experience, and representatives of relevant community organisations to join our Steering Group. Our invitation included a written overview of the Priority Setting Partnership aims, a rough timeline of milestones, and a short video explainer *(Appendix C).* Individuals selected to join the Steering Group were required to review a Terms of Reference and complete an Interests and Privacy Form (which captured accessibility needs and preferences of working). Both forms were available online via Qualtrics™ and on paper. To enable people to participate from across Australia and with accessibility in mind, Steering Group meetings were hosted via Teams. Meetings were chaired by a James Lind Alliance Advisor.

Our Steering Group included 14 members:

- 5 individuals with lived experience of an IRD
- 2 representatives from national consumer organisations
- 4 clinician-researchers
- 3 researchers

See *Appendix A* for the full list of Steering Group members and affiliations.

The first Steering Group meeting was held in August 2023. In this meeting we examined the representativeness of our Steering Group, discussed key partner organisations to approach, and decided on the scope of the Priority Setting Partnership (detailed in '2. Scope of the Priority Setting Partnership').

Partner organisations were invited based on their connection to the IRD community and relevant health professionals. They supported the project through recruitment and dissemination.

2. Scope of the Priority Setting Partnership

Together, the Steering Group agreed that the scope of this Priority Setting Partnership would include uncertainties that were related to the:

- prevention of an IRD (e.g., carrier screening tests);
- diagnosis of an IRD;
- disease progression and control;
- treatment and research into potential treatments;
- epidemiology; or
- disease management, including the physical, psychological, emotional, financial, and social aspects of living with an IRD, or caring for an individual living with an IRD.

The Steering Group decided to limit questions to those that focused on IRDs broadly (or a specific type of IRD) or on vision loss related to an IRD. Questions were considered out of scope if they were related to hearing loss that was not within the context of IRD symptoms or comorbidities, or concomitant eye diseases that are not an IRD (e.g., glaucoma).

Eligible participants

The James Lind Alliance suggest that uncertainties are captured from "patients", "carers" and "clinicians". The Steering Group defined these groups as:

- an individual who is 16 years or older and diagnosed with any type of IRD;
- a caregiver and/or family member (e.g., a parent, grandparent, sibling, or partner) who provides support to an individual with an IRD;
- a health or supportive care professional who has direct contact with the above defined individuals within their role.

All participants were required to be residing in Australia to be eligible. Individuals with age-related macular degeneration as their only condition were deemed ineligible.

3. Survey 1 – gathering uncertainties

Method

We developed Survey 1 with our Steering Group, with user-testing conducted by several members who have a vision impairment. We launched our survey on the 24th September 2023. The survey remained open for 8-weeks.

In Survey 1 *(Appendix D),* we asked individuals to respond to several optional demographic items (including their current diagnosis) and submit up to five questions that they would like answered about IRDs, within the defined scope.

The survey was available in multiple formats, including online, paper (written or in Braille), over the phone (in English or with an interpreter), and via video call in Auslan (provided pro-bono with the support of Deafblind Australia).

Participants

We received 223 in-scope submissions (out-of-scope submissions = 21) from 69 eligible participants (see Table 2). Key demographics our summarised below:

- Of the 50 participants with lived experience who specified the IRD that they were impacted by, the most common diagnoses were retinitis pigmentosa (n=20, 40%) and Usher syndrome (n=9, 18%).
- Of the 60 participants who provided their postcode, we had representation from 5/8 Australian states and territories, with most from an outer regional area (n=24, 48%).
- Of the 48 participants who indicated their primary language, most indicated English (n=45, 94%). Of the 67 who indicated their Indigenous status, only 2 (3%) indicated they were of Aboriginal and/or Torres Strait Islander background.

Table 2. Participants and submissions in Survey 1

Participant type	Eligible participants [a]		In-scope submissions	Out-of-scope submissions
Individual living with an IRD	35	69 [a]	223	21
Caregiver or family member	18			
Health professional	15			
Individual living with an IRD & health professional [a]	1			

[a] *6 participants deemed ineligible (n=1 due to diagnosis; n=5 deemed fraudulent)*

4. Summarising uncertainties and evidence checking

A sub-group of Steering Group members deduplicated and categorised the 223 in-scope submissions into overarching summary questions. These summary questions were then discussed and revised with the whole Steering Group, resulting in a final 42 summary questions.

Within the 223 submissions, we received 36 submissions related to information around availability of clinical trials, accessing clinical trials, disease heritability, and access to genetic testing. Our Steering Group deemed these questions as answerable via online search engines or through a health professional, and thus not to be taken forward to the interim prioritisation exercise. However, given the amount of these submissions, our Steering Group included three summary questions related to how to effectively communicate unmet information needs to individuals impacted by an IRD. See *Appendix E* for a list of submissions related to unmet information needs.

Given the nature of the summary questions and state of research for IRDs, the Priority Setting Partnership Lead and three Steering Group members deemed 21 of the 42 summary questions as unanswered without needing to search the literature (e.g., what is an effective treatment that is not gene-specific? What is the anticipated progression of vision loss for each IRD?). One summary question was deemed answered without needing to search the literature - "What is the likelihood of passing an Inherited Retinal Disease on to a biological child?". This question was deemed 'answered' due to established medical and scientific knowledge around genetic inheritance.

For the remaining 20 summary questions, we searched the research literature *(see Appendix F for search details)* and assigned each summary question as:

a) Answered;
b) Partially answered; or
c) Not answered

Following this evidence checking process, three summary questions were deemed 'partially answered' as they had only been answered regarding a specific type of IRD (e.g., retinitis pigmentosa). The remaining 17 were deemed unanswered. The partially answered and answered ummary questions were defined as evidence uncertainties and taken to the interim prioritisation stage.

5. Survey 2 – interim priority setting

Method

We launched our interim prioritisation survey on 23rd of March 2024. The survey remained open for 10-weeks. Survey administration (e.g., paper and online delivery) and recruitment processes aligned with Survey 1. We also directly invited 67 individuals to participate as they had consented to be notified about this survey when completing Survey 1; and invited the ~80 individuals who attended an IRD Patient and Family Engagement Day in Sydney, Australia (held March 23rd 2024) to participate. These individuals were given a paper survey which also included a QR code to enable online completion.

To aid feasibility of survey completion for our cohort, our Steering Group decided to use a two-stage prioritisation process where participants:

1. voted for as many of the 41 uncertainties that they considered important for researchers to answer; and then
2. voted for up to 10 uncertainties from this shortlist.

To minimise bias for the online surveys, the order in which evidence uncertainties were presented was randomised for each participant. Questions were in the same order for all paper surveys.

We had few individuals from a culturally and/or linguistically diverse background participate in Survey 1. As this was the generative stage for the uncertainties presented for prioritisation, we acknowledged the resultant lack of representation for our final priorities. Given this, and to reduce survey burden, we did not collect primary language or cultural background in Survey 2. Our Steering Group continued to actively drive recruitment in these harder-to-reach groups.

Participants

A total of 151 individuals responded to Survey 2. Most participants were living with an IRD (n=92), a caregiver (n=36) or both (n=7).

- Of the 135 participants with lived experience and specified a diagnosis, the most common were retinitis pigmentosa (45%) and Usher syndrome (13%).
- Of the participants who provided their postcode (n=132), there was a representation from 6/8 Australian states and territories and most resided in an outer regional area (47%).

Analysis

We analysed the interim prioritisation separately for the four groups:

- Group A. Individuals who have an IRD
- Group B. Caregivers and family members of someone with an IRD
- Group C. Lived experience (i.e., Group A and B combined)
- Group D. Health and supportive care professionals

In the scenario where an individual identified as being in more than one group (e.g., an individual who has an IRD and is a health professional), their data were included in each relevant group. For Group C (lived experience group), individual's data were only included once.

For each of the 41 evidence uncertainties, we:

1. tallied the number of votes
2. ranked the evidence uncertainties by frequency, with the uncertainty with the most votes ranked #1, and the uncertainty with the least votes ranked #41. The ranking became the score for each uncertainty (e.g., Rank #1 = score 1).

For each uncertainty, we summed the scores from Group C (lived experience group) and Group D (health and supportive care professional group) to calculate a combined score. The uncertainties with the lowest combined score represented the highest priority. This approach ensured that the rankings of individuals with lived experience were weighted equally to those of healthcare professionals, regardless of the sample size of each group.

The Steering Group reviewed the scores and rankings to determine which uncertainties to take forward to the final workshops. With a limit of 18 questions given the online format of the workshops, we decided to include the top 13 ranked questions from the combined scores of Group C and D; and an additional 5 questions so that the top 10 priorities from Group, A, B, and D were also included.

Upon further discussion of the 18 questions to take forward, the Steering Group removed 2 questions – 1 because it was deemed not possible to answer further and 1 because it fell within the scope of another question.

Appendix G includes the 41 uncertainties that were taken for interim prioritisation in Survey 2 and their respective rankings.

6. Final priority setting workshops

Method

We opened our expression of interest process for the final workshops on the 3rd June 2024, and accepted applications for four weeks. The form was available online, via Qualtrics. We received a total of 75 expressions of interest. Of these, we deemed 38 to be fraudulent based on factors such as an IP address outside of Australia, latitude and longitude, and disconnected phone number.

We screened the 37 expressions of interest deemed to be from eligible participants. We selected individuals in attempt to have a mix of individuals to ensure representation across participant groups, age, gender, caregiver role, and state. We called the selected individuals to confirm their participation and discuss any accessibility requirements.

Participants

Overall, there were 24 workshop participants of whom 13 had lived experience. Most participants identified as female and were from NSW. See Table 3, Page 21.

Image 1. Screenshot of workshop participants

Table 3. Demographics of workshop participants

Demographics		n
Participant type	Individual living with an IRD	9
	Representative from community organisation	1
	Caregiver of a child	2
	Caregiver of an adult/partner	2
	Health professional [a]	10
Age	18 – 24 years old	1
	25 – 34 years old	5
	35 – 44 years old	3
	45 – 54 years old	6
	55 – 64 years old	4
	65 years and older	4
	Missing	1
Gender	Female	19
	Male	5
State	New South Wales	13
	Victoria	6
	Queensland	3
	Western Australia	1
	South Australia	1
	Tasmania	0
	Northern Territory	0
	ACT	0
Remoteness	Major city	15
	Inner regional	3
	Outer regional	6
	Remote and very remote	0

[a] This included 2 optometrists, 2 orthoptists, 1 orientation and mobility specialist, 2 genetic counsellors, 1 clinical geneticist, and 2 social workers.

Of the nine participants who had an IRD, all indicated that they were either legally blind or had minimal vision; and two individuals also had a hearing impairment. One caregiver indicated that they required more frequent screen breaks due to a brain injury. No participants required a translator.

To cater to accessibility needs, we made the following adjustments to the pre-reading documents sent one-week prior the workshops:

- Reduced document length.
- Documents provided in minimum size 18 font, with non-stylised font, use of bullets to break up text, 1.5x line spacing, and high contrast colours (black text on white background).
- Minimal use of logos/visuals.
- Documents provided in a Word to be compatible with screen readers.

We also revised the format of workshops by:

- Allocating additional time to read out the questions.
- Reducing the length of the workshops by providing narrated videos, shared via QR codes in the workshop documents sent prior the workshops. One video from the James Lind Alliance Advisor explained the priority setting process, and one video from the Priority Setting Partnership Lead explained the background to the 16 questions to be discussed. Both videos were available online with a screen-reader accessible transcript.
- Providing workshop PowerPoint slides in maximum font sizes possible, and removing any unnecessary lines and colours.
- Providing multiple options of colour contrasts for the workshop PowerPoint slides (e.g., black text on white background, white text on black background) so that participants could choose which version to use in the small group discussions.

James Lind Alliance Facilitators were also strongly encouraged to slowly read out the research questions and their rankings, verbally communicate any non-verbal communication (e.g., head nodding) from other participants, and remain flexible during workshops to support any additional needs.

Pre-work

Along with the pre-reading documents that we sent one-week prior the workshops, we sent the 16 shortlisted questions from the interim prioritisation stage to all participants *(Appendix H).* We asked participants to reflect on the research questions, and to rank their top and bottom 3 priorities.

Workshops

The two online, half-day workshops were held on the 8th and 9th of August, 2024. Workshops were held online to allow for participation from across Australia, and was chaired by a James Lind Alliance Facilitator. See Table 4 for the workshop schedule.

Table 4. Workshop schedule

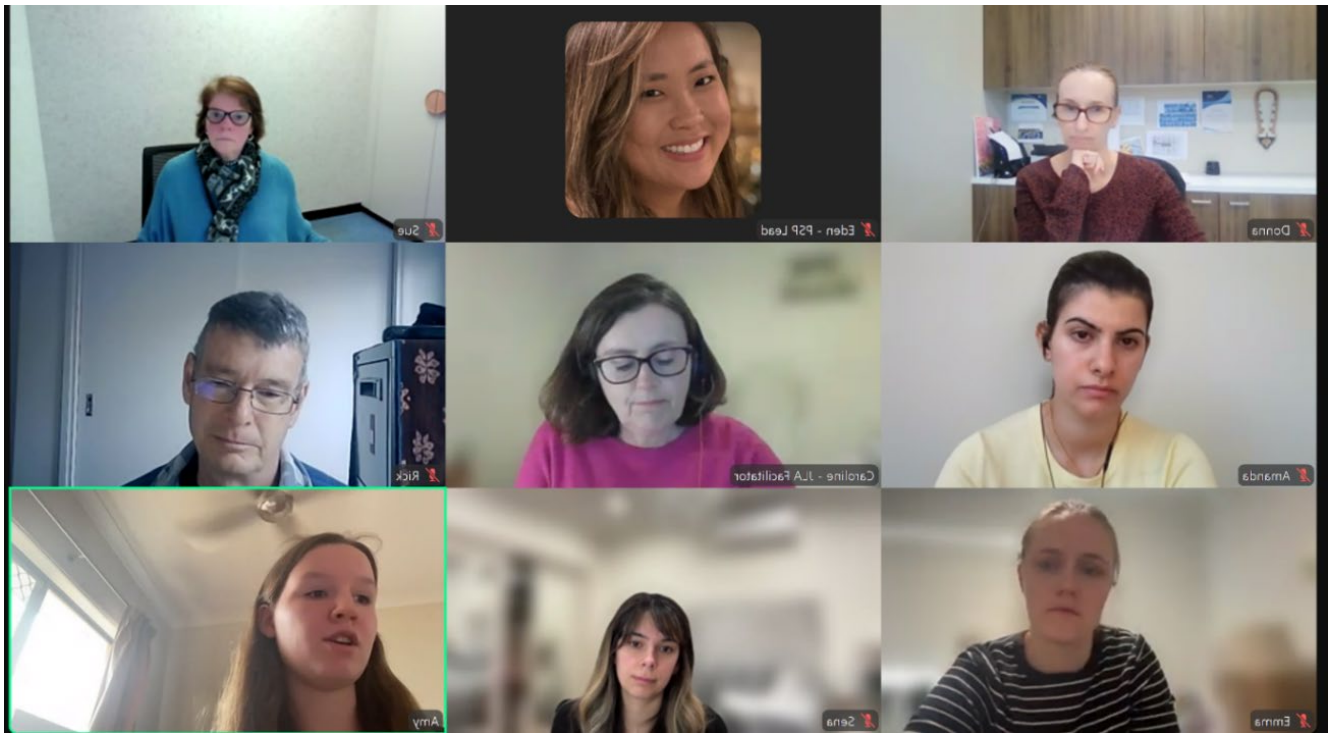
Workshop 1	
09:00	Registration and technology checks
09:15	Welcome and introduction
09:30	Session 1 – sharing priorities [a]
10:30	Break
10:50	Session 2 – first round of prioritisation [a]
11:50	Whole group - summing up and next steps
12:00	End of Day 1
Workshop 2	
13:30	Registration and technology checks
13:45	Welcome back and introduction
14:00	Session 3 – reviewing combined small group rankings [b]
15:00	Break
15:30	Presenting the final top 10 priorities
16:00	Next steps and thank you
16:15	End of Day 2

[a] *Same participants allocated to small groups for session 1 and 2*
[b] *Different participants allocated to session, with some minor overlap.*

Workshop 1

Following a brief introduction, participants were broken into four small groups (with each combining individuals who had lived experience of an IRD and health professionals) with an assigned James Lind Alliance Facilitator. Session 1 involved participants sharing their top and bottom priorities. Participants commonly expressed the challenge in identifying the lesser important areas – noting that they felt all were important.

Image 2. Screenshot of a small group sharing their top and bottom three priorities in Workshop 1



During the break, each James Lind Alliance Facilitator arranged the questions on screen based on what their group deemed important. In Session 2, participants further discussed the reasons for their priorities with the same group, which resulted in a ranked list of questions.

After Session 2, areas of research focussed on treatment were a higher priority than other areas of research across all four small groups. Considerations around achievability and feasibility drove groups to rank research to prevent vision loss as a higher priority than treatment to restore vision. The mechanism or treatment approach used for treatment - whether gene-specific or agnostic – appeared less important to participants.

> *"I'm wanting the top priority to be something we can find a solution to in the next few years, not a mountain that we can't get over the top of."*
>
> *- Workshop participant, lived experience*

The ranking/consideration of treatment-focussed priorities across groups was also balanced with consideration of the impact of having an IRD on an individual's mental health and quality of life. Participants acknowledged the importance of better understanding how individuals with an IRD can live well with their condition from point of diagnosis onwards and through critical life stages/ transitions (e.g., high school, entering the workforce). Across groups, participants agreed that access to psychosocial services and coordinated care was important, yet most still moved this to be a lower priority. Their rationale was that a lack of funding to expand services was the barrier, rather than a lack of research.

> *"When being diagnosed as a teenager, the psychological impacts are enormous... more emphasis on self worth and how to live a fulfilling life is so important."*
>
> *- Workshop participant, lived experience*

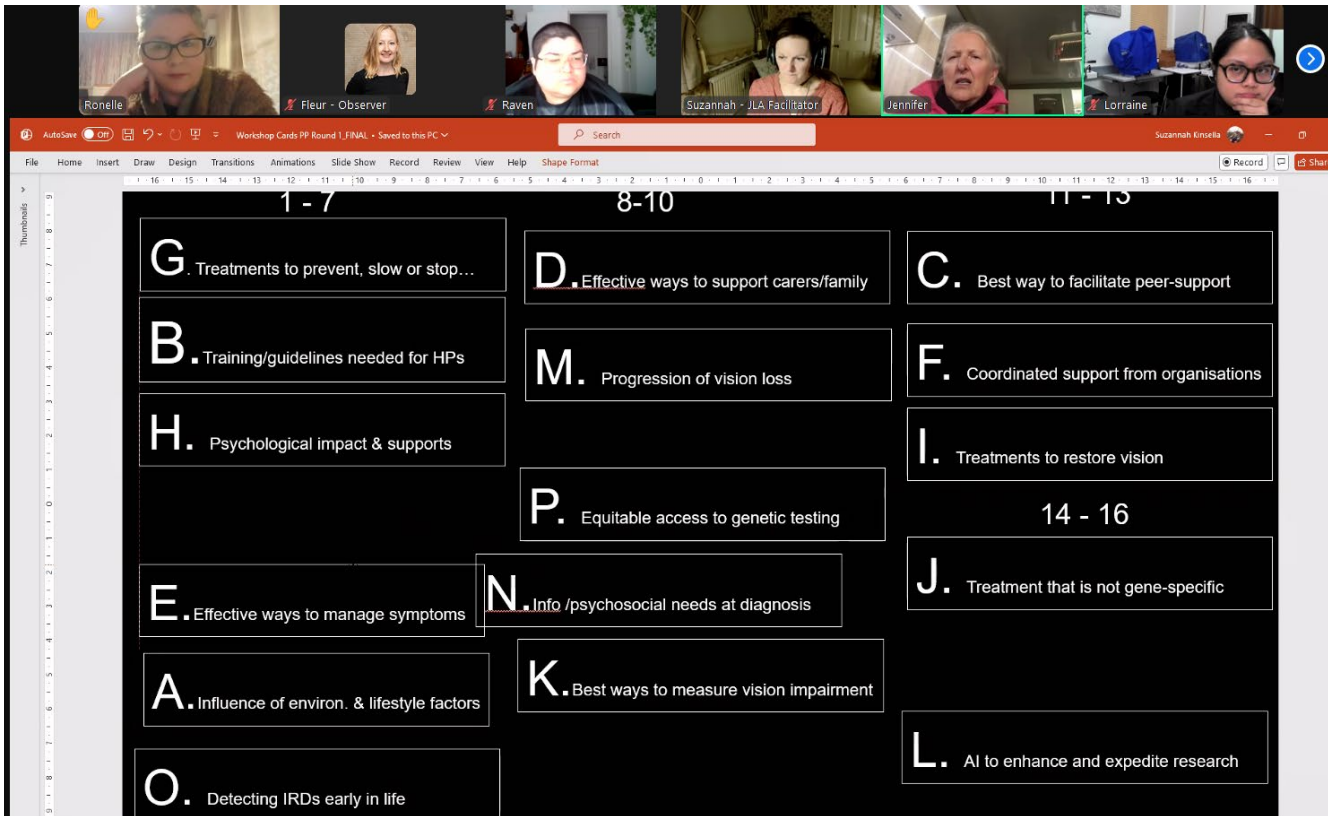
Participants with lived experience reflected on both positive and negative experiences with health professionals. They agreed on the important role that health professionals have in communicating a diagnosis, how to manage the disease, and in providing psychosocial support – while sharing examples of how this was not always done well.

> *"For me, I think what's important is how the measurement is communicated, that there is understanding and empathy. I understand that we need to be told about our vision changes, but this can be done in a supportive and caring way and to find the positives of the situation of what you can do."*
>
> *- Workshop participant, lived experience*

> *"Doctors and health professionals don't know much about inherited retinal disease, I'm pretty lost right now, I don't know how quickly I'm going to lose vision, and there's not much information out there."*
>
> *- Workshop participant, lived experience*

There were some differences of opinion between participants with lived experience and health professionals, and within these cohorts. This was particularly around the use of AI, access to genetic testing, coordination of services, and optimal tools for measuring vision. Participants who contributed alongside their partner, generally expressed the same priorities, although some had differing rationales.

Image 3. Screenshot of a small group discussing the rankings in Workshop 1



Combining small group rankings – Round 1

After Workshop 1, the James Lind Alliance Facilitators combined the rankings from each small group into an overall ranking. These were calculated by taking the average rank across the four groups. The question with the lowest score was ranked #1 (i.e., the highest priority), and the highest score was ranked #16. When two or more scores were equal, the geometric mean was used to confirm the rank order. The combined rankings were emailed to workshop participants that afternoon to review in preparation for Workshop 2 the following day.

Workshop 2

Of the 24 participants from Workshop 1, 21 also attended Workshop 2. Following a short recap of Workshop 1, participants were broken into four new small groups (again, each combining individuals who had lived experience of an IRD and health professionals) and a James Lind Alliance Facilitator. During the small group discussions, participants shared whether they agreed/disagreed with the combined rankings and their rationale why.

> *"I talked to my son about this last night, and he doesn't care about a cure. His main problem is the symptom, which is photophobia. So, for him priority about symptoms is really important."*
>
> *- Workshop participant, lived experience*

Together, each small group revised the ranking of questions. Due to differing opinions, several participants had to compromise with others in their group. In several cases, opinions around priorities shifted as new perspectives were shared.

As in Workshop 1, participants' rationale for priorities often considered the feasibility of research. Several areas of research that participants deemed *"less feasible"* were moved down the priority list to allow for areas that they considered more realistic. Some participants considered the interrelatedness and longer-term impact of research – with treatment focussed research considered the highest priority, as they felt that this would minimise the need for any research into symptoms or psychological impacts.

> *"We know how to help psychosocial aspects, we just don't have the resources/funds to train more people, employ more people. So, I think research should be allocated to finding a cause and treatments."*
>
> *- Workshop participant, health professional*

As raised in Workshop 1, participants discussed whether further research was needed to address the priority areas (e.g., equitable access to genetic testing) or whether it was that more funding is required for additional resources and staff. Several participants added that they felt they had limited knowledge about research which made it challenging for them to judge whether an area was important or not.

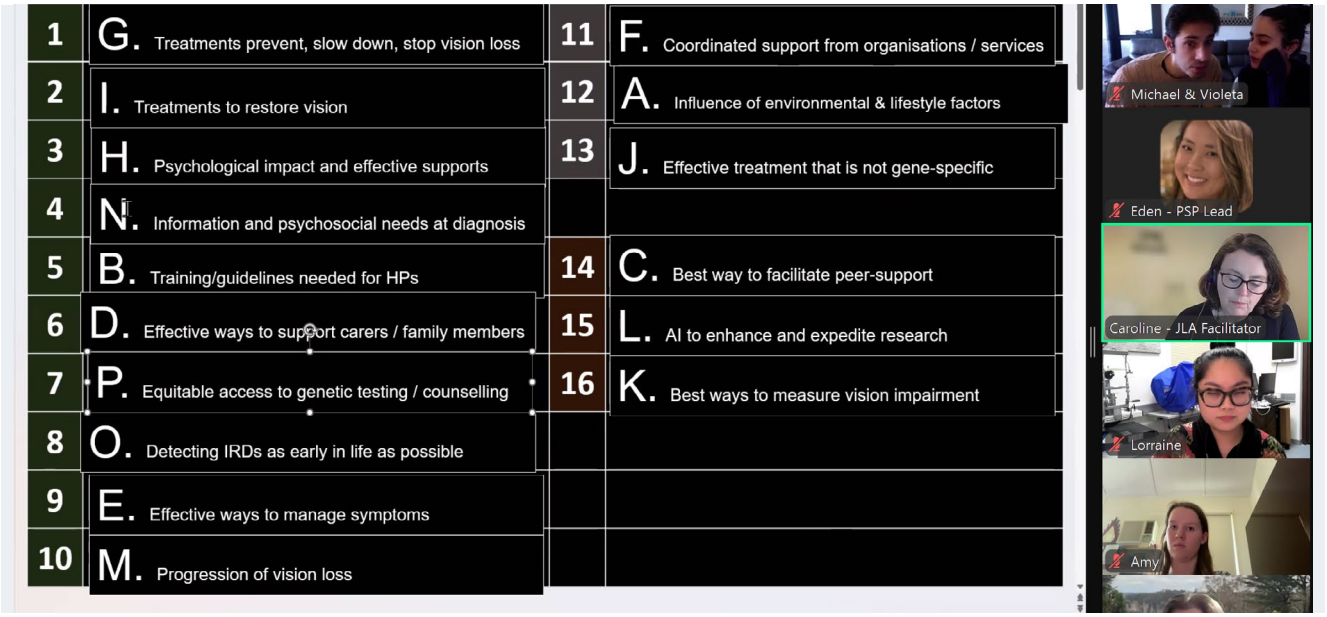
> *"I don't think further research or individual researchers have the power to change that overall outcome when it comes to coordinated support."*
>
> *- Workshop participant, lived experience*

Like Workshop 1, differences of opinion arose several times between participants with lived experience and health professionals, and within those participant groups. For Workshop 2, areas of lively discussion were around the needs for training/guidelines for health professionals, and whether the top 10 needed to include both treatment that prevents vision loss and treatments that restore vision.

Combining small group rankings – Round 2

During the break of Workshop 2, the James Lind Alliance Facilitators combined the rankings from each small group into an overall ranking, following the same approach as Round 1. This resulted in the final rankings of the 16 research questions. See *Appendix H.*

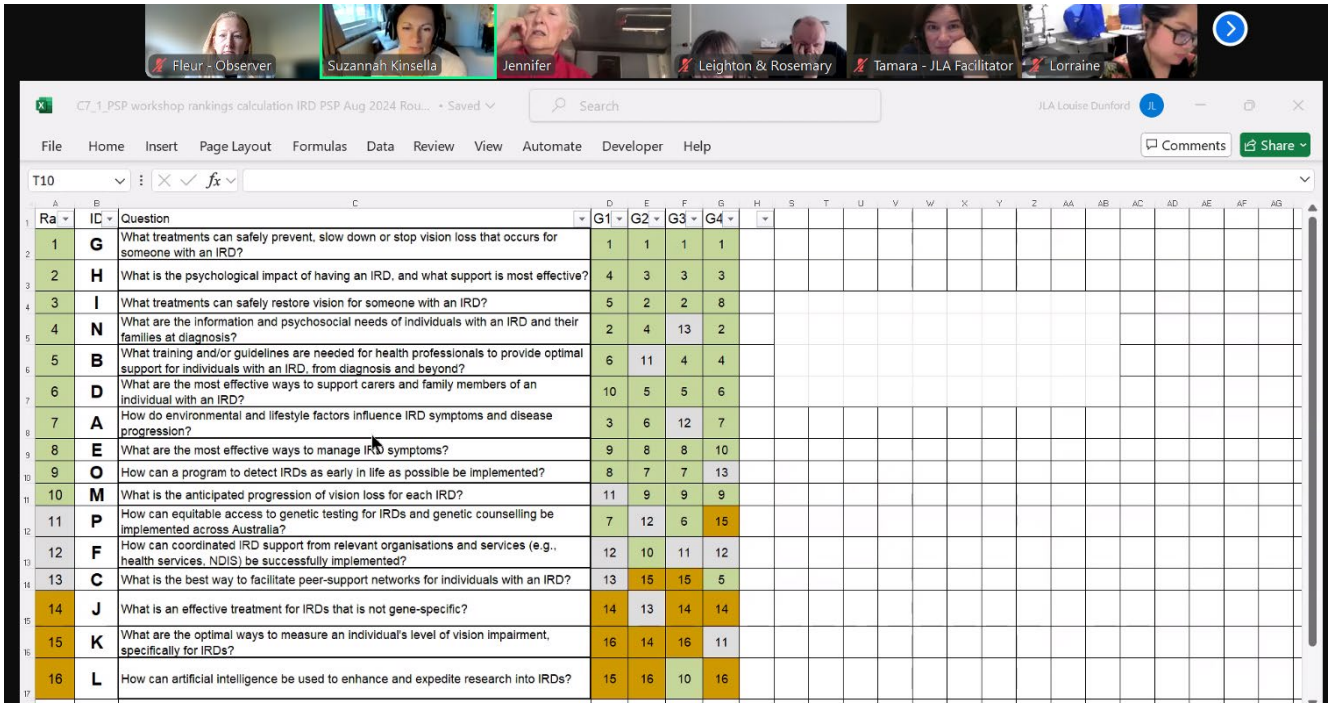
Image 4. Screenshot of a small group discussing the rankings in Workshop 2.



Presenting the final top 10 priorities

The final rankings were presented to workshop participants, with any substantial differences between the small group rankings highlighted. All small groups had at least eight of their top 10 priorities included in the combined top 10 ranking. Of note, all four small groups agreed that the #1 research priority was for treatments to safely prevent, slow down or stop vision loss.

Image 5. Screenshot of the scoring system showing the final combined rankings, and rankings across each small group.



Ra	ID	Question	G1	G2	G3	G4
1	G	What treatments can safely prevent, slow down or stop vision loss that occurs for someone with an IRD?	1	1	1	1
2	H	What is the psychological impact of having an IRD, and what support is most effective?	4	3	3	3
3	I	What treatments can safely restore vision for someone with an IRD?	5	2	2	8
4	N	What are the information and psychosocial needs of individuals with an IRD and their families at diagnosis?	2	4	13	2
5	B	What training and/or guidelines are needed for health professionals to provide optimal support for individuals with an IRD, from diagnosis and beyond?	6	11	4	4
6	D	What are the most effective ways to support carers and family members of an individual with an IRD?	10	5	5	6
7	A	How do environmental and lifestyle factors influence IRD symptoms and disease progression?	3	6	12	7
8	E	What are the most effective ways to manage IRD symptoms?	9	8	8	10
9	O	How can a program to detect IRDs as early in life as possible be implemented?	8	7	7	13
10	M	What is the anticipated progression of vision loss for each IRD?	11	9	9	9
11	P	How can equitable access to genetic testing for IRDs and genetic counselling be implemented across Australia?	7	12	6	15
12	F	How can coordinated IRD support from relevant organisations and services (e.g., health services, NDIS) be successfully implemented?	12	10	11	12
13	C	What is the best way to facilitate peer-support networks for individuals with an IRD?	13	15	15	5
14	J	What is an effective treatment for IRDs that is not gene-specific?	14	13	14	14
15	K	What are the optimal ways to measure an individual's level of vision impairment, specifically for IRDs?	16	14	16	11
16	L	How can artificial intelligence be used to enhance and expedite research into IRDs?	15	16	10	16

Participants were invited to share any comments or reflections on the final rankings. Several participants commented that they were satisfied with the top 10 priorities, and that they were pleased to see a mix of different focus areas represented. Some participants shared that they were disappointed that a particular research area they were passionate about was not included in the top 10 and acknowledged the challenge in accommodating everyone's priorities.

> *"I've realised that there's a lot I don't currently know about my condition and treatments and services available. I was frustrated with myself for my lack in ability to speak persuasively during the workshop. I'm not well informed so I felt like my opinion held little weight. I would have liked the questions about coordinated support and training for health professionals to be more prioritised, and questions about peer-support and carers to be lower, but I understand that it can be difficult to accommodate everyone's expectations."*
>
> *- Workshop participant, lived experience*

> *"We have learnt a lot from this process. All the questions are great and we feel strongly that, from the perspective [that I've] already lost quite a bit of vision, we would have liked to have seen the restoration of vision higher. But, it's up there and everything is so relevant and important so thank you."*
>
> *- Workshop participant, lived experience*

Post-workshops, several participants shared their appreciation for the workshops and the value in being able to hear others' perspectives.

> *"It was really enlightening to hear different perspectives and will help me in my interactions with different sectors going forward. I just learnt so much... thank you all so much for this opportunity to broaden my perspectives and be a part of this priority setting project!*
>
> *- Workshop participant, lived experience*

TOP 10
RESEARCH PRIORITIES FOR IRDS IN AUSTRALIA

1. What treatments can safely prevent, slow down or stop vision loss that occurs for someone with an IRD?

2. What is the psychological impact of having an IRD, and what support is most effective?

3. What treatments can safely restore vision for someone with an IRD?

4. What are the information and psychosocial needs of individuals with an IRD and their families at diagnosis?

5. What training and/or guidelines are needed for health professionals to provide optimal support for individuals with an IRD, from diagnosis and beyond?

6. What are the most effective ways to support carers and family members of an individual with an IRD?

7. How do environmental and lifestyle factors influence IRD symptoms and disease progression?

8. What are the most effective ways to manage IRD symptoms?

9. How can a program to detect IRDs as early in life as possible be implemented?

10. What is the anticipated progression of vision loss for each IRD?

Priority #1

What treatments can safely prevent, slow down or stop vision loss that occurs for someone with an IRD?

Examples of original uncertainties submitted

- *"What are the most promising lines of research into stopping the progression of degenerative conditions?"* - Individual who has an IRD
- *"Is there a current reliable and consistent treatment to slow down the progress of RP once diagnosed in a child?"* - Individual who has an IRD
- *"Is there anything to slow the progression of vision loss?"* – Caregiver

Commentary

Inherited retinal diseases are caused by a genetic variation that leads to abnormal development, dysfunction or degeneration of photoreceptor (i.e., rod and cone photoreceptor cells) and retinal pigment epithelial cells. While there are multiple mechanisms for how these cells die, these diseases typically manifest as reduced vision in low light conditions and/or reduced visual acuity.

Our understanding of the exact genetic factors and mechanisms leading to various forms of IRDs has been critical to identifying potential treatments. This basic science research underpins the development of prevention and novel therapy approaches. This includes drugs and supplements, such as antioxidants to slow down disease progression *(Priority #7),* gene replacement therapy, genetic correction (gene editing) and specific modulation therapies. These potential therapies must first be tested in preclinical studies using model systems such as patient-derived retinal organoids and animal models.[7,8] If successful, human trials to examine new treatments to prevent vision loss may be conducted.[9]

These types of basic science research and clinical trial endeavours have led to the first clinically available gene-therapy, Luxturna, specifically for biallelic *RPE65*-associated retinal dystrophy. This therapy involves delivering a healthy copy of the *RPE65* gene directly to retinal cells. This converts dysfunctional cells to working cells, with the aim of preventing vision loss and hopes that it may also restore vision *(Priority #3).* Luxturna was publicly available in Australia in 2020. Clinical trial data and experience to date has shown Luxturna improves night vision, and benefits are maintained in the years following therapy.[10]

Our understanding of the impact of Luxturna will support the development of other gene therapies to address the 300+ known causative genes and loci. Other than Luxturna, there are no other clinically available treatments available to safely prevent, slow down or stop vision loss that occurs for someone with an IRD. However, several trials for specific genes and genetic variants are underway.

Despite the implementation of genetic testing for IRDs and genetic counselling being *Priority #11* in the final workshops, and understanding the prevalence of IRDs ranked the least important of the uncertainties presented for interim prioritisation, these are two areas of work are foundational as we look to expand access to therapies.

> *"I feel frustration from having the technology available and not being able to give it to people, who will need genetic testing to then access genetic treatments."*
>
> *– Workshop participant, health professional*

The genetic and phenotypic heterogeneity of IRDs has also driven the search for single treatments that may be suitable for all or many IRDs. While this is challenging due to the complexity of IRD disease mechanisms, fundamental research has led to opportunities in this area and investigation through clinical trials.[11]

Despite substantial investment from the Australia Government to support basic discovery-based medical research, specific funding for IRDs is lacking. Funding to establish advanced therapeutics, such as cell and gene ocular therapy programs entirely developed in the country are needed from conception of novel ideas to clinical trials implementation. Investment in tertiary prevention, aimed to improve quality of life and reduce disability is equally important and usually underfunded.

Summary

- The majority of IRDs are progressive, with many individuals experiencing severe vision impairment and, in some cases, legal blindness.
- In 2020, Luxturna, a gene-therapy for *RPE65*-associated retinal dystrophy, was approved for therapeutic use in Australia.
- Other than Luxturna, there are no other treatments clinically available to safely prevent, slow down or stop vision loss for IRDs.
- Specific funding for IRD research is lacking.

Priority #2

What is the psychological impact of having an IRD, and what support is most effective?

Examples of original uncertainties submitted

- *"What are the psychological supports required to cope with the anticipatory grief of living with an IRD?"* – Caregiver
- *"Specified psychological support living with progressive vision loss?"* – Individual who has an IRD
- *"Are there people working in the mental health sector that specialise in supporting people with degenerative vision or people who have gone blind to support them with the grief?"* – Health professional

Commentary

Psychological support, from diagnosis and beyond, is critical for both individuals with an IRD and caregivers. BResearch indicates that individuals who have irreversible vision loss may experience poorer mental health compared to the general population.[12-15] With the progressive vision loss that is common to many IRDs, individuals may also experience uncertainty and anticipatory grief, and a sense of hopelessness.[16] Several studies have indicated that individuals who have an IRD have a lower quality of life compared to the general population.[17-19] Over time, declining vision may reduce quality of life; with challenges arising around education and career, independence and relationships.[16]

Current psychological support may not be appropriate to respond to the specific needs of individuals with an IRD. To date, no psychological intervention in Australia is available that responds to the unique psychological impacts of having an IRD or caring for an individual with an IRD. Further, community-based mental health professionals (e.g., psychologists) and primary health professionals (e.g., GPs) may not have the skills to provide the necessary support that is uniquely required for IRDs. Often this leaves ophthalmologists and retinal specialists responsible for providing this support. RANZCO notes in their 2020 'Guidelines for the assessment and management of patients with inherited retinal degenerations' that "*psychological support is also necessary so that individuals and families can deal with the emotional stress, and sometimes uncertainty associated with an IRD*".[4]

Yet, little guidance is available for these clinicians to provide this psychological support, nor is the Australian ophthalmology workforce set-up to address the substantial psychosocial impacts of IRDs.[20]

> *"I prefer to rely on health professionals and service providers rather than peers, friends and family… For me, services providers like the NDIS and health professionals are vital. I live alone and I don't have friends. I don't rely on family. I also have a psychosocial disability. That means I struggle to function in normal society with severe anxiety."*
>
> *– Workshop participant, lived experience*

To add further complexity, current mental health treatment plans to assist with costs of psychological support may also not suffice, given the significant impact having an IRD has on employment and income.[5] A tiered approach to addressing the ongoing psychological impacts of an IRD may be required, involving: i) coordinated interdisciplinary support through the public system for those with more complex needs; and ii) self-guided, online interventions to address common psychological challenges at diagnosis and as vision loss may progress.

Despite research into peer-support networks ranked #13 in the final workshops, research across rare diseases indicates the potential psychosocial benefits of participating in support groups. Peer-support may be particularly beneficial in early diagnosis and for those with fewer established support networks.[15] Community-organisations, such as Retina Australia, are integral for sustained facilitation of such networks. Increased awareness of available peer-support services is critical for ensuring equitable access.

Summary

- Individuals who have an IRD have a lower quality of life and mental health compared to the general population.
- Declining vision impacts individual's education and career path, income, ability to live independently, and relationships.
- No psychological services specifically for individuals impacted by an IRD that is freely available across Australia.
- Some peer-support programs available via community organisations.

Priority #3

What treatments can safely restore vision for someone who has an IRD?

Examples of original uncertainties submitted

- *"Is it possible for lost vision to be restored" - Individual who has an IRD*
- *"Are there any treatments I could consider to improve my vision?" - Individual who has an IRD*
- *"What are the most promising lines of research for restoring or improving vision in those with retinal diseases?" – Caregiver*

Commentary

In Australia, IRDs are the leading cause of blindness in working aged adults. Research in France found that among young adults diagnosed with Retinitis Pigmentosa (the most common IRD in Australia), 30% had low vision and 48% were legally blind.[16] Apart from Luxturna *(Priority #1),* there are no other treatments clinically available for IRDs.

When developing and testing new therapies for IRDs, researchers need to take into consideration the stage of the disease and how advanced the damage to the retina is. Numerous therapies are being developed and tested in clinical trials with the aim of restoring vision in individuals with an IRD. For individual at early to mid-stage disease these include gene therapy (e.g., Luxturna) and gene editing (e.g., for individuals with *CEP290*-associated retinal dystrophy[21]).

While the above approaches offer hope for many individuals, they rely on individual's having enough healthy retinal cells remaining to target. For those with advanced disease, therapies to replace lost cells into the retina are critical. Other approaches that can be used in late-stage disease include:

- gene therapy optogenetics, which involves altering certain healthy cells in the retina to ultimately take over the function of lost photoreceptor cells (e.g., for individuals with end-stage non-syndromic retinitis pigmentosa[22]);
- retinal prosthesis (electronic chip implants or bionic eyes) that works by use of an external camera and an electrode chip implanted near the surviving retinal cells to evoke a perception of light (e.g., Argus II prosthesis[23]); and
- Regenerative medicine (cell replacement therapies) by transplantation of stem cell derived retinal cells.

A benefit of the three aforementioned therapies is that they are gene-agnostic (*Priority #14* in the final workshops). Rather than targeting an underlying genetic cause, they can be applied to anyone who has lost functioning retinal cells.

Regenerative medicine in the form of stem cell therapy and cell transplantation holds great promise as a physiological method to replace the cells that are lost to disease. Progress into cell therapies is rapidly advancing. Cell therapies rely on the creation of stem cells in the laboratory, which are then differentiated to retinal cells. The ability to create stem cells in the laboratory from adult cells (i.e., reprogramming) removes the ethical challenge of stem cells historically being obtained from embryos. Preclinical testing has shown that this therapy can effectively replace photoreceptor cells in animal models. Early phase clinical trials in Japan for individuals with retinitis pigmentosa have transplanted stem cell-derived retinal cells to replace the lost cells have reported positive results.[24]

As research progresses, multidisciplinary collaborations will be necessary to facilitate the successful implementation of trials when they become available in Australia. For example, engaging with clinicians involved in natural history studies will be essential to track disease course *(Priority #10)*. Collaboration with other disciplines will expediate efforts, as already seen with advances in medical artificial intelligence (AI). Analysis of retinal images using novel AI approaches can now aid diagnosis and prognosis, with some of these deep learning techniques publicly available (ranked *Priority #16* in the final workshops). Finally, efforts to educate the IRD community about upcoming research will empower individuals and enhance their decision-making capacity once trials become available.

Summary

- Ongoing research is testing numerous new approaches aiming to restore vision for individuals with an IRD. However, there is little currently available.
- Cell therapy using stem cells to generate transplantable cells is a promising physiological approach.
- Further basic and translational research and funding are needed to establish a treatment to restore vision.

Priority #4

What are the information and psychosocial needs of individuals with an IRD and their families at diagnosis?

Examples of original uncertainties submitted

- *"What information do families need when their child is diagnosed?" – Caregiver*
- *"What social and cultural support is provided/available to people at point of diagnosis?" – health professional*

Commentary

A diagnosis of IRD is usually given by an ophthalmologist, performing clinical investigations, and sometimes specialised tests such as electrophysiology. Ideally, a genomic test can also confirm this diagnosis, although the yield of genomic testing is estimated to be between 52 and 74%.[25] A diagnosis can guide prognosis, aids informed reproductive decision-making, and can ultimately guide future treatment decisions. However, being diagnosed with an IRD can cause significant distress to individuals and their family. This may be particularly so for individuals who may not be experiencing substantial vision impairment at time of diagnosis. As highlighted in the commentary for *Priority #2*, individuals can often experience anticipatory grief and a sense of hopelessness when first diagnosed. This can be due to reasonable concerns about loss of vision, impact on lifestyle, employment, and costs of care.[5]

In addition, due to the genetic nature of IRDs, there are information needs in terms of understanding genetic inheritance and family planning options that have their own psychosocial impact on patients and their families.

Highlighted by the submissions in Survey 1 *(Appendix E),* individuals struggle to understand the inheritance of IRDs, and how to access genetic testing, and what their results mean. Similar findings of an Australian cohort indicates that at least one in three still felt uncertain about what the genetic test results meant for their or their child's/dependent's IRD.[26]

Following a diagnosis, individuals with an IRD and caregivers often seek information online.[26] However, given the rarity of each IRD, there is often minimal information available online, with even less written for the lay audience. This lack of information can cause additional distress and/or lead to misinformation.

This priority overlaps with and reflects consumers' and clinicians' concerns about both the psychosocial impact of a diagnosis *(Priority #2)* as well as the way clinicians can handle providing information, supports, and meeting needs of patients at diagnosis *(Priority #5).* While there are RANZCO 'Guidelines for the assessment and management of patients with inherited retinal degenerations' are available to support clinicians through the assessment and management of individuals with an IRD,[4] there is clearly a need for better training and implementation of these guidelines.

Further research into the unmet psychosocial and information needs will guide the necessary supports for clinicians to support their patients and families; improve more effective referral to support services; and improve overall satisfaction with the healthcare system.

> *"I have learnt so much as a clinician. The priorities vary so much from what I thought was important. I think understanding what families need at diagnosis is so important given how different what I had initially thought is to those with lived experience"*
>
> *- Workshop participant, health professional*

Summary

- A diagnosis of IRD is usually given by an ophthalmologist, and confirmed with a genetic test.
- A diagnosis can be valuable and can cause significant distress to individuals and their family.
- There are substantial information needs around genetic inheritance, likelihood of recurrence, and family planning options.
- Given the rarity of each IRD, there is often minimal and relevant information available online.
- There is a need for better training and implementation of the RANZCO guidelines, particularly around supporting clinicians in communicating with families at diagnosis.

Priority #5

What training and/or guidelines are needed for health professionals to provide optimal support for individuals with an IRD, from diagnosis and beyond?

Examples of original uncertainties submitted

- *"How do we make our health providers more cognitive of the daily challenges when we are legally blind?" – Individual who has an IRD*
- *"Can more eye doctors be educated about LCA we had a terrible experience with diagnosis." – Caregiver*
- *"How can health professionals best support individuals and families navigate changes to their vision/function over time?" – Health professional*

Commentary

Individuals with an IRD may receive support from a variety of health professionals, including:

- Ophthalmologists
- Clinical geneticists
- Genetic counsellors
- Primary health providers: such as optometrists, general practitioners
- Allied health professionals: such as occupational therapists, orthoptists

Training that is currently available is largely a function of the individual roles of these health professionals. For example, specific educational materials are available to ophthalmologists as part of their Continuing Professional Development program, with those focussing on IRDs having increased since the introduction of Luxturna *(Priority #1).* Similarly, specific sessions and material is available to other health vision health providers such as optometrists and orthoptists; lesser, if any, is available for primary health or mental health professionals.

Training for health professionals recommended by individuals with an IRD and caregivers in Survey 1 and the workshops focussed on:

- Communication skills, particularly regarding how to inform someone of their diagnosis in an empathetic way, and to communicate medical information in lay terms;
- How to support caregivers of someone with an IRD.

- What community services are available and appropriate referral pathways;
- How to remain up-to-date and informed with research in the field; and
- Early signs of an IRD to be aware of.

Despite a need to increase the skills and capacity of health professionals who support individuals impacted by an IRD, numerous barriers to implementation of training exist. These include:

- Minimal capacity and time for health professionals to complete the training.
- The rarity of IRDs means that health professionals may not encounter these conditions often, or at all.
- The rapidly advancing field, which requires a need for continuous training.
- The progressive nature of many IRDs, which requires knowledge across all stages of disease as it evolves.

While not included within the top 10 priorities, the need for coordinated support from relevant organisations and services was ranked *Priority #12* in our workshops. The RANZCO 'Guidelines for the assessment and management of patients with inherited retinal degenerations' emphasise the need for a multidisciplinary team approach to address the complex needs of patients with IRD. Training and guidelines around how to integrate this care is necessary.

> *"Let's leave in coordinating services as a priority in the top 10 as it highlights to the government that this is important and something needs to be done about it."*
>
> *– Workshop participant, lived experience*

Summary

- Individuals with an IRD may receive support from a variety of health professionals.
- Participants highlighted numerous areas for further health professional training, with a focus on communication, psychosocial support and information provision.
- Numerous barriers to training, include minimal time/capacity, rarity of conditions, and the ongoing nature of IRDs.

Priority #6

What are the most effective ways to support carers and family members of an individual with an IRD?

Examples of original uncertainties submitted

- *"There needs to be support for carers." – Individual who has an IRD*

Commentary

Despite the limited number of submissions addressing caregiver support in Survey 1, it emerged as a critical priority during the final workshops. The early onset of many IRDs often triggers a profound grieving process and significant distress for parents who have a child diagnosed with an IRD. These caregivers may experience a diminished quality of life and reduced psychosocial well-being.[27] Research across genetic conditions and other eye conditions highlights a theme of parental guilt, where caregivers report feelings of self-blame for "causing" a genetic condition[28] or for initially overlooking early signs of vision impairment.[29] This guilt can exacerbate parental stress and anxiety.[30]

Being responsible for their child's medical and health treatment, information is crucial to empowering parents to meet their definition of being a "good parent".[31] However, there is a lack of information around IRDs, how to navigate the healthcare system, and how to access funding schemes *(Priority #4).* The fragmented nature of care due to different healthcare providers and service sectors further impede parents' ability to be a "good parent".[32]

Effective support for the whole family when a child is diagnosed with an IRD is important to maintaining healthy family functioning. This is particularly relevant when a child's vision impairment is more severe.[17] Caregivers, especially parents who are providing support to their young child, are faced with substantial costs due to lost income and the unpaid caregiver role.[5]

Research on the psychological impact of having a sibling with an IRD is sparse. Some research suggests that while an IRD may have an adverse effect on the family, this may not extent to the health-related quality of life of siblings.[17] However, broader literature in siblings of children with chronic health conditions indicates that they may be at increased risk of depression.[33] Given the genetic nature of IRDs, siblings require support to understand the genetic condition, and implications for their future and affected-sibling.[34]

When a spouse is also a caregiver, shifting relationship dynamics can impact relationship quality, and introduce emotional and financial challenges. Research suggests that the level of vision impairment, level of dependence on the caregiver and presence of comorbid chronic illnesses predict the level of caregiver's psychological distress.[35,36] The lack of psychosocial support services noted for individuals with an IRD *(Priority #2)* is echoed for caregivers. Pre-existing support systems may not be sufficient for caregivers, particularly in the early stages post-diagnosis.[30] Addressing IRDs through a family-systems lens is essential in addressing the broad ripple of these conditions beyond the individual diagnosed.[37]

> *"Families are so desperate for support and we are failing. Beikng such a low incidence condition it is hard to attract money for things and we rely on parent led advocacy groups, so I think there is a big need to support this."*
>
> *– Workshop participant, community organisation representative*

> *"I am so glad to see this make it in the priorities, especially given how few submissions about caregiver wellbeing there were originally. It is interesting to see that perhaps caregivers don't put prioritise their needs, and only when prompted do they see the importance of this."*
>
> *- IRD Priority Setting Partnership Steering Group member*

Summary

- The early onset of many IRDs often causes significant distress for parents.
- Caregivers can experience guilt, poorer quality of life, and increased levels of depression and anxiety.
- Level of vision impairment predicts overall family functioning and relationship quality.
- Caregivers can experience substantial costs and a loss of income.

Priority #7

How do environmental and lifestyle factors influence IRD symptoms and disease progression?

Examples of original uncertainties submitted

- *"Do lifestyle factors (eg. Diet) affect the progression of Stargardt Disease?" - Individual who has an IRD*
- *"What lifestyle changes can preserve the sight or as long as possible?" – Caregiver*
- *"What environmental factors impact the progression of IRDs?" – Health professional*

Commentary

The importance of identifying possible environmental modifying factors that modulate disease impact has previously been highlighted in the literature.[38] Current approaches to therapies fall into two broad categories - either disease modifying or genetic therapies. Disease modifying therapies aim to preserve residual photoreceptors which include dietary modifications and supplementations. Understanding how environmental factors (e.g., air quality, UV light exposure) and lifestyle factors (e.g., diet, exercise) contribute to or exacerbate disease progression is crucial for minimising functional impairment.

The role of dietary supplementation varies across the IRD spectrum. For example, in Stargardt disease, a high intake of vitamin A is suspected to be a risk factor for progression.[39] This is in comparison to retinitis pigmentosa (the most common type of IRD in Australia), where recent findings suggest there to be no benefit or harm from vitamin A supplementation, and instead a recommendation to avoid Vitamin E.[40-42] Smoking may also cause more rapid disease progression,[43] and physical activity is hypothesised to be beneficial in preserving retinal function.[44]

Extrapolation has also been made from research in age-related macular degeneration (AMD). These studies have recognised the influence of lifestyle and dietary factors on the outcome of genetic risk.[45] The Age related Eye Disease Study (AREDS) identified the importance of nutritional supplements and diet in AMD.[46-48] Saffron has also been identified to slow progression.[49] In myopia, the higher prevalence in Asian countries compared to Western countries, has been attributed to high education pressure and less time spent outdoors given the non-significant difference in genetic risk.[50,51]

Natural history studies are critical in understanding the role of environmental and lifestyle factors specifically in IRD disease progression. They can also facilitate the exploration of genetic-phenotypic correlations, and thus identify potential therapeutic targets. Patient registries in Australia, such as West Australia Retinal Disease (WARD) study, Ocular Gene and Cell Therapies Australia, Save Sight Sydney IRD registry and Victorian Evolution Of Inherited Retinal Diseases Natural History Registry (VENTURE)[52], have been established to track disease progression, explore genetic-phenotypic correlations, and identify biomarkers. Alongside clinical testing, these registries also collect information on lifestyle factors. Given the rarity of individual genotypes, it is likely that studies on environmental and lifestyle factors will require international collaborations, such as through the Foundation Fighting Blindness Consortium.

Identifying modifiable factors to minimise symptoms may also empower individuals with an IRD to take a more active role in their health care,[53] which may support their wellbeing as vision declines.[54] More education for patients and families around genetic-phenotypic variability of IRDs, and growing knowledge around the influence of environmental and lifestyle factors is needed.

> *"While we are waiting for treatment, I am always thinking about what I can do to help prevent further vision loss or save what I have, such as diet and exercise."*
>
> *– Workshop participant, lived experience*

Summary

- Understanding how environmental and lifestyle factors contribute to disease progression is crucial for minimising functional impairment.
- The role of dietary supplementation varies across the IRD spectrum.
- Natural history studies are critical in understanding the role of environmental and lifestyle factors in disease progression.
- Education around genetic-phenotypic variability of IRDs may address any uncertainties regarding the perceived influence of external factors in disease progression.

Priority #8

What are the most effective ways to manage IRD symptoms (e.g., low vision at night)?

Examples of original uncertainties submitted

- *"What can I do to maintain my balance?" – Individual who has an IRD*
- *"How to best manage chronic symptoms eg. Migraines, eye strain, fatigue, neck/ shoulder pain" – Individual who has an IRD*
- *"Why do people with LCA eye press and how can we stop doing it?" – Caregiver*

Commentary

The age of symptom onset for individuals with an IRD varies widely. It is often assumed that the onset of IRD is in early life, however there is a spectrum in the onset of reported or observable symptoms. For example, Leber Congenital Amaurosis results in observable behavioural changes because of reduced vision in infancy. By contrast, patients with so-called Late Onset Retinal Dystrophy (LORD) present in their sixth or seventh decade. Primary symptoms across IRDs include:

- Night blindness, or difficulty seeing in low-light conditions
- Sensitivity to light and glare
- Reduced visual acuity
- Loss of central and/or peripheral vision
- Blind spots
- Difficulty differentiating colours
- Uncontrolled eye movements

Managing vision loss, as the main primary symptom of an IRD, is integral to reducing the odds of depressive symptoms and improving quality of life of individuals who have an IRD. With treatments currently lacking, a multifaceted combination of non-pharmacological strategies may be beneficial to reduce the impact of symptoms on quality of life. This may include use of low vision aids (e.g., magnifiers), wearing tinted lenses that block out specific wavelengths of light,[56] orientation and mobility training, learning braille, allowing additional time when travelling, and using a mobility aid such as a cane or guide dog.

There are many secondary symptoms that can also arise from primary symptoms. For example, sensitivity to light may lead to migraines for some people. Both primary and secondary symptoms require management to minimise impact on quality of life.

Research has also suggested that individuals with an IRD attribute a high number of symptoms to their ophthalmic disease, with higher symptoms attributed as visual acuity worsens. Whether these symptoms are psychosomatic or not remains unclear.[54] If psychosomatic, the need for specialist psychological support *(Priority #2)* is of even greater importance.

Summary

- The age of symptom onset for individuals with an IRD varies widely.
- Common symptoms across IRDs include difficulty seeing in low-light conditions, sensitivity to light and glare, loss of central and/or peripheral vision, and reduced visual acuity.
- Non-pharmacological strategies, such as low vision aids and tinted lenses, may be beneficial to reduce the impact of symptoms on quality of life.

Priority #9

How can a program to detect IRDs as early in life as possible be implemented?

Examples of original uncertainties submitted

- *"Why is there not more thorough and more consistent eye testing at birth and all healthy baby/child wellness visits so that children who may have an IRD can be detected earlier in life?" – Caregiver*

Commentary

Detecting an IRD early could potentially enable earlier intervention and management. This could theoretically occur at many stages, depending on the mode of detection. Prior to any clinical features, a genetic diagnosis can occur as early as during at preconception carrier screening for couples, during pregnancy, or at birth. Even with improved access to genetic testing, the actual diagnostic yield for individuals with an IRD undergoing genomic testing sits around 50-60%. This means not all genetic diagnosis would be identified, relying on a clinical diagnosis by an ophthalmologist. Clinically, most individuals would require symptoms before they could have the detailed diagnostic ophthalmic investigations required to diagnose an IRD.

At present, there are no screening programs for genetic or clinical diagnosis of IRDs in Australia. Access to genetic testing currently is available through genetics services, though waits may vary depending on jurisdiction, or through private genetics practices. To receive a clinical diagnosis, an individual must first receive a referral to an ophthalmologist who reviews clinical history, and undergoes examination (e.g., best corrected visual acuity) and investigations (e.g., visual field assessment) relevant to a suspected diagnosis. Alike genetic services, waits to visit an ophthalmologist can vary and can incur out-of-pocket costs.

The potential for predictive testing (i.e., before onset of symptoms) of an IRD raises complexities around whether it provides any prognostic and clinical information, and benefit for patients and families. The variability of IRDs means that even if a genetic diagnosis is made, the actual prognosis and anticipated progression of vision loss may be difficult to predict.

The lack of current treatment options or early intervention for most IRDs raises ethical concerns around predictive genetic testing in childhood.[56]

The emergence of newborn genomic screening (currently under investigation with numerous research projects in Australia and overseas) could potentially change the landscape for early diagnosis. The integration of IRDs within these national screening programs further exploration as to the impact and cost-effectiveness.

While equitable access to genetic testing and counselling was ranked as *Priority #11*, the above introduces issues around access and equity in genetic testing and counselling. Research indicates that most individuals with a suspected IRD would undergo genetic testing if it was available to them.[57] For those that choose not to engage in genetic services, low uptake may be due to out of pocket costs,[58] noted as a global challenge with ~17% of individuals in a global survey indicating that they paid for their genetic test out of pocket.[59] Individuals from rural and regional areas may also have lesser physical access to these healthcare services .

A general lack of understanding around genetic-phenotypic variability, and inheritance of IRDs, is evident by the number of submissions in Survey 1. Many focussed around "prevention" of IRDs and perception that detection prior symptom onset may be beneficial. Further efforts to educate both families and health professionals of these areas, including pathways to access testing and benefit/burden of testing, is needed.[57]

> *"How does a genetic test result influence a patient's ongoing ophthalmic management? Patients ask me this all the time - I tell them this needs to be discussed with their ophthalmologist - but the ophthalmologists often feel unsure about genetics."*
>
> *– Submission in Survey 1, health professional*

Summary

- Detecting an IRD early could potentially enable earlier intervention and management.
- Genetically, an individual could potentially be detected as early as during pregnancy or during preconception carrier screening.
- There are no screening programs for genetic or clinical diagnosis of IRDs in Australia.
- The potential for predictive testing raises ethical and logistic complexities, including whether it provides any prognostic and clinical information, and benefit for patients and families.

Priority #10

What is the anticipated progression of vision loss for each IRD?

Examples of original uncertainties submitted

- *"My vision loss has been stable for 25 years, what are the chances of it worsening?" – Individual who has an IRD*
- *"Are there signs from research to indicate the rate of progression of RP? This would result in preparation and planning." – Caregiver*
- *"How fast will my disease progress and will I end up losing my sight all together?" – Individual who has an IRD*

Commentary

One of the significant challenges with IRDs is the heterogeneity in disease presentation and prognosis. For example, some forms of IRD are rapidly progressing, and likely to end in severe vision loss, whilst others can be late onset, slow to progress, and cause milder vision loss. A diagnosis of an IRD and uncertainty around the progression of vision loss can cause immense anxiety and a feeling a lack of control. Understanding what to expect may help individuals plan for their future and for timely, preventative psychological interventions to be provided *(Priority #2)*. Further, understanding progression may be valuable information for individuals as they weigh up their options for treatment options that may aim to prevent and/or restore vision.

Currently, researchers only have a moderate level of understanding of the progression rates of some subtypes of IRDs. For rare genotypes, where there are few individuals who are affected, little is known around progression and prognoses. This is further complicated with the potential impact of environmental and lifestyle factors.

As highlighted in *Priority #7,* natural history studies are critical in understanding disease progression, and the experiences than an individual can expect. Local Australian registries are unlikely to have enough participants to be able to make clear determinations about progression for all IRD genes. Hence, international collaborations (e.g., the global Foundation Fighting Blindness Consortium) are essential to provide detailed understanding of the expected outcomes for the rarer genes.

These rigorous natural history studies of IRDs will also enable data collection for other purposes, including determination of cost-effectiveness of IRD treatments in the future.

Understanding the progression of vision loss is reliant on the validity and sensitivity of prognostic clinical measures. It is well established that standard clinical tests such as visual acuity are not sensitive enough for monitoring disease progression in IRD, nor as a biomarker of progression likelihood. Despite research into optimal ways to measure an individual's level of vision impairment specifically for IRDs only being ranked #15, an essential area for future research is the development of prognostic biomarkers (visual function and ocular structure), as well as sensitive health-related quality of life tools to monitor IRD participants over time.

> *"Without better testing, it is hard for clinicians to accurately assess children... it can be quite complex and may involve paediatric anaesthesia. This causes difficulty for families to get NDIS funding support."*
>
> *- Workshop participant, health professional*

Summary

- IRDs are highly heterogenous in disease presentation and prognosis.
- Uncertainty around the progression of vision loss can cause immense anxiety and a feeling a lack of control.
- There is only moderate knowledge around of the progression rates of some subtypes of IRDs. For rare genotypes, little is known around progression and prognoses.
- Natural history studies are critical in understanding disease progression.
- Valid and sensitive prognostic clinical measures are needed to monitoring disease progression specifically for IRDs.

Summary

This work presents the first James Lind Alliance Priority Setting Partnership for IRDs in Australia. The top 10 research priorities provide a concise and clear list of what Australian individuals living with an IRD, caregivers and family members, and health and supportive care professionals consider the most important and require further investment.

Beyond this, the process of undertaking this Priority Setting Partnership has highlighted the value of a Steering Group that involves individuals who have lived experience and/or with strong connections to partner organisations. A key challenge for our priority setting exercise was ensuring that we included the perspectives of a broad range of individuals. This required substantial consideration around accessibility needs. As this was the first time that the James Lind Alliance facilitated online workshops with individuals who have a vision impairment, we relied heavily on our Steering Group to provide guidance around necessary adaptations. We have published our learnings from our experiences conducting this work in the hopes of supporting other researchers and clinicians incorporate more accessible practices into their work.

Despite the value of this work, we acknowledge our limitations in capturing only a few submissions in Survey 1 from individuals from a culturally and linguistically diverse background. We know that around 1 in 4 Australians speak a language other than English at home (compared to the one in 1 in 69 who participated in Survey 1). Further, most participants in our workshops were female (19/24) and from NSW (13/24). Further investigation regarding the relevance of these priorities for culturally and linguistically diverse groups, males and the underrepresented states may be valuable.

The final priorities were broad in scope – with a focus on treatment/cure, symptoms and disease progression, psychosocial wellbeing, and health service delivery. The priority areas were highly interconnected, with areas that were not necessarily prioritised as foundational to progressing the areas that were prioritised. We acknowledge that some of the priority areas are highly complex, with funding, skills and capacity being critical enablers in addressing the top 10 priorities for IRDs. This highlights the need for a whole person, systems approach, to collaboratively respond to the needs of the IRD community.

To progress these priorities in practice, we are committed to:

1. **Disseminating our research** findings widely to funding bodies, researchers and research institutions, clinicians, health services, government, and community organisations.
2. **Developing calls to action** that support these priorities. This will include shorter-term goals, such as creating information resources that address key unmet information needs of families and primary health providers; and longer-term goals, such as developing psychological interventions for individuals at diagnosis and beyond.

Driving research that aligns with what matters most to individuals impacted by an IRD will ensure it is more relevant to the community end-users. This will facilitate impactful research that is more likely to be adopted and sustained.

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APPENDICES

Appendix A. Steering Group members

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[a] Priority Setting Partnership leadership team
[b] sub-group involved in the initial refining of submissions into summary questions
[c] sub-group involved in evidence checking
[d] lived experience

Appendix B. Partner organisations

The following organisations supported the IRD Priority Setting Partnership in raising study awareness, and/or supported recruitment and/or dissemination.

Appendix C. Video explainer about the project

QR code to view this video:

Appendix D. Survey 1 to gather uncertainties

About you

We would appreciate knowing a little about you to help us make sure that we hear from a wide range of people. These questions are **optional**. Your answers are confidential, and you will not be identifiable when we share our results.

1. I currently live in Australia AND

- O I am 16 years or older AND living with an Inherited Retinal Disease
- O I am a guardian or family member of an individual living with an Inherited Retinal Disease
- O I am a health or supportive care professional actively caring for patient living with an inherited retinal disease, with a focus on vision loss.

2. Optional: Please describe your relationship to the individual living with an Inherited Retinal Disease

- O I am their parent
- O I am their grandparent
- O I am their partner
- O I am their adult child
- O Other - Please specify: _____

3. Optional: What is your most current diagnosis?

- O Achromatopsia
- O Best disease/vitelliform macular dystrophy
- O Choroideremia
- O Cone-rod dystrophy
- O Leber congenital amaurosis (LCA)/early onset retinal degeneration
- O Leber Hereditary Optic Neuropathy (LHON)
- O Retinitis pigmentosa/rod-cone dystrophy
- O Stargardt disease
- O Usher syndrome (USH)
- O X-linked retinoschisis
- O Unknown
- O Other - Please specify: _____

4. **Optional: What is your role as a health or supportive care professional (e.g., Ophthalmologist, GP, teacher)? _____**

6. **Optional: How often you work with individuals with an Inherited Retinal Disease?**

   - O weekly
   - O a few times a month
   - O every few months
   - O a few times a year
   - O less than once a year

7. **Optional: How old are you today?**

   - O Less than 18 years old
   - O 18-24 years old
   - O 25 – 34 years old
   - O 35 – 44 years old
   - O 45 – 54 years old
   - O 55 – 64 years old
   - O 65 years or older

8. **Optional: What postcode do you currently live in? _____**

9. **Optional: What is the primary language you speak at home?**

   - O English
   - O Other - Please specify: _____

10. **Optional: Are you of Aboriginal and/or Torres Strait Islander background? For persons of both origins, please tick both boxes.**

    - O Aboriginal
    - O Torres Strait Islander
    - O Neither

Your unanswered questions

We want to help make sure that researchers are focusing their efforts on areas that are most important to you. What questions do you have about :

- prevention;
- diagnosis ;
- disease progression and control;
- treatment and research into potential treatments;
- epidemiology; and/or
- management, which includes management of the physical, psychological, emotional, financial, and social aspects of living with an IRD, or caring for an individual living with an IRD.

Some examples of questions submitted for other conditions include:

- **Concussion example:** After a concussion, what is the best approach for a return to physical activity, exercise, and sports to give the best outcome
- **Epilepsy example:** What underlying mechanisms cause epilepsy in children and in adults?
- **Skin cancer example:** What are the psychological support needs following skin cancer surgery for patients and families?
- **Diabetes and pregancy example:** What is the best test to diagnose diabetes in pregnant women?
- **Cystic Fibrosis example:** Which therapies are effective in delaying or preventing progression of lung disease in early life in people with Cystic Fibrosis?

Still struggling to think of questions?

We'd rather have your questions than miss out on your ideas, so just write down what you are thinking or are unsure about regarding Inherited Retinal Diseases.

You can submit up to 5 questions:

Question 1.
Question 2.
Question 3.
Question 4.
Question 5.

Appendix E. Submissions related to unmet information needs

Unmet information needs	Example submissions
How IRDs are diagnosed and how does genetic testing work?	• How is Ushers diagnosed? • How much does gene testing cost? • Where can I get gene testing? • Has research progressed enough to test for the Ushers gene?
How do IRDs occur?	• How does the defect occur? • Apart from siblings, there is no known family history of RP on either side. What caused the original mutation?
How are IRDs inherited?	• Will I pass my condition on to my children? • Should I get my children tested knowing that they have a 50/50 chance of inheriting RP? • If one parent has the gene for RP can this be passed on to their children?
What psychosocial and practical supports are currently available?	• What supports are available for people with IRDs to help them manage their condition and live a full life? • What education and support services are available for family members of someone with IRD? supports around carers roles and also future risk and health of family members who may laiter receive the same diagnosis • What financial support will I get?
What clinical trials are available and how do I access them?	• What types of research are currently taking place in Australia? • What treatments are available now or as part of research studies • Can my son participate in an overseas trial without having to travel overseas?
What research is currently in the pipeline?	• What is the timeframe for any treatments to become widely available? • How far has stem cell therapy progressed in order to help people with inherited retinal disease?

Appendix F. Literature search strategy

Sources

- Cochrane Reviews, using keywords specific to each question.
- Database searches on MEDLINE, CINAHL, PsycINFO, Embase, PubMed and Google Scholar.
- Guidelines:
    - Royal Australia and New Zealand College of Ophthalmologists (RANZCO)
    - American Academy of Ophthalmology (USA)
    - Royal College of Ophthalmology (UK)
    - German Ophthalmological Society (DOG), the Retinological Society (RG) and the Professional Association of German Ophthalmologists (BVA)
    - Optometry Australia (Australia)
    - British College of Optometrists (UK)
    - American Academy of Optometry (USA)
    - Human Genetics Society of Australia
    - American College of Medical Genetics
    - Australian and New Zealand Clinical Trials Registry (ANZCTR) and clinicaltrials.gov.

Parameters

- Evidence published from 2013 to 2024.
- Limited to publication in English in a peer-reviewed journal (or peak body, in the case of guidelines).

Category	Definition
Answered	Reliable, up-to-date systematic reviews, meta-analyses or clinical guidelines have been published.
Partially answered:	Relevant, reliable and up-to-date systematic reviews, meta-analyses and evidence-based guidelines but do not address continuing questions. Current clinical trial but not exhaustive enough to answer the question. Relevant systematic reviews but not up-to-date (i.e., published before 2013).
Not answered	No relevant systematic reviews, meta-analyses or clinical guidelines identified

Appendix G. Survey 2: Interim prioritisation and rankings

Rank	Evidence uncertainties	w/ IRD (n=99)	Caregiver (n=42)	HP (n=17)
1	What treatments can safely prevent, slow down or stop vision loss? [a]	1	1	1
2	What treatments can safely restore vision? [a]	2	2	4
3	What is the anticipated progression of vision loss for each IRD? [a]	4	3	7
4	What is the psychological impact of having an IRD, and what support is most effective? [a]	5	4	10
5	How can equitable access to genetic testing and genetic counselling be implemented across Australia? [a]	17	20	2
6	What are the most effective ways to support carers and family members of an individual with an IRD? [a]	18	5	5
7	What training and/or guidelines are needed for health professionals to provide optimal support for individuals with an IRD, from diagnosis and beyond? [a]	14	21	6
8	What is an effective treatment that is not gene-specific? [a]	6	8	15
9	How can artificial intelligence (AI) be used to enhance and expedite research into IRDs? [a]	10	7	11
10	What are the most effective ways to manage IRD symptoms (e.g., low vision at night)? [a]	11	10	16
11	How can coordinated support from relevant organisations and services (e.g., health services, NDIS) be successfully implemented? [a]	20	26	3
12	How do environmental and lifestyle factors influence symptoms and disease progression? [a]	3	6	21
13	What are the information and psychosocial needs of individuals with an IRD and their families at diagnosis? [a]	21	15	8
14	How can the latest research be effectively communicated to health professionals caring for IRD patients?	19	17	12

Rank	Evidence uncertainties	w/ IRD (n=99)	Caregiver (n=42)	HP (n=17)
15	How can IRDs be prevented? [b]	8	11	26
16	What is the best way to facilitate peer-support networks for individuals with an IRD? [a]	23	38	9
17	What is the impact of genetic testing for an IRD on patients and families, and how does this information impact disease management and patient decision-making?	27	24	13
18	In communicating about clinical trials and research updates, what methods are most effective in conveying information to patients and families?	15	13	22
19	What are the biological mechanisms that lead to vision loss for each IRD?	22	18	17
20	How does exposure to sunlight and glare impact individuals with an IRD, and what strategies can be employed to minimise this impact? [c]	7	22	32
21	How can a program to detect IRDs as early in life as possible be implemented? [a]	9	12	33
22	How do individuals with an IRD visually perceive their surroundings?	26	16	23
23	How can the pathway to diagnosis be improved so that they are accurate and efficient?	29	14	18
24	How can training and/or guidelines for health professionals caring for individuals with an IRD be successfully implemented?	30	25	14
25	What are the optimal ways to measure an individual's level of vision impairment, specifically for IRDs? [a]	12	9	34
26	How does early detection and planning impact disease outcomes?	16	40	27
27	In communicating about genetics of IRDs, genetic testing and risk of disease inheritance, what methods are most effective in conveying information to patients and families?	31	27	19
28	What are the risks of surgery for other eye conditions that may co-occur with an IRD?	13	35	35

Rank	Evidence uncertainties	w/ IRD (n=99)	Caregiver (n=42)	HP (n=17)
29	What is the benefit and burden of follow-up care after a diagnosis of an IRD?	25	36	28
30	How do clinical, genetic and demographic factors influence the effectiveness and risks of different treatment options?	32	23	29
31	What the most effective ways to manage and/or prevent related health conditions that may co-occur with an IRD?	28	30	30
32	What factors influence patient and caregiver decisions about IRD treatment options?	37	29	24
33	In communicating general health information and support resources, what methods are most effective in conveying information to patients and families?	38	33	20
34	What is the impact of having an IRD with additional health conditions on quality of life?	40	30	25
35	How can public awareness regarding IRDs and related health conditions be increased?	24	28	40
36	What is the impact of caring for a child with an IRD on quality of life?	39	19	31
37	What additional health conditions are associated with each IRD?	36	34	36
38	What is the physiological and psychological impact of restoring sight?	33	39	37
39	What is the physical impact of being a carrier of an IRD?	35	32	38
40	What other eye-related health conditions (e.g., cataracts) are associated with each IRD?	34	41	39
41	How common are IRDs and the various subtypes?	41	37	41

Note. HP = health professional

[a] *Indicates uncertainty was taken to the workshops for discussion*

[b] *Despite meeting the criteria to be taken through to workshops, this question was removed at this stage due to the only possible prevention strategy already being available.*

[c] *Despite meeting the criteria to be taken through to workshops, this question was removed at this stage due to be considered within scope of 'What are the most effective ways to manage IRD symptoms (e.g., low vision at night)*

Appendix H. Overall rankings from the final workshops

Rank	Research priorities	Small group rankings			
		1	2	3	4
1	What treatments can safely prevent, slow down or stop vision loss that occurs for someone with an IRD?	1	1	1	1
2	What is the psychological impact of having an IRD, and what support is most effective?	4	3	3	3
3	What treatments can safely restore vision for someone with an IRD?	5	2	2	8
4	What are the information and psychosocial needs of individuals with an IRD and their families at diagnosis?	2	4	13	2
5	What training and/or guidelines are needed for health professionals to provide optimal support for individuals with an IRD, from diagnosis and beyond?	6	11	4	4
6	What are the most effective ways to support carers and family members of an individual with an IRD?	10	5	5	6
7	How do environmental and lifestyle factors influence IRD symptoms and disease progression?	3	6	12	7
8	What are the most effective ways to manage IRD symptoms?	9	8	8	10
9	How can a program to detect IRDs as early in life as possible be implemented?	8	7	7	13
10	What is the anticipated progression of vision loss for each IRD?	11	9	9	9
11	How can equitable access to genetic testing for IRDs and genetic counselling be implemented across Australia?	7	12	6	15
12	How can coordinated IRD support from relevant organisations and services (e.g., health services, NDIS) be successfully implemented?	12	10	11	12
13	What is the best way to facilitate peer-support networks for individuals with an IRD?	13	15	15	5
14	What is an effective treatment for IRDs that is not gene-specific?	14	13	14	14
15	What are the optimal ways to measure an individual's level of vision impairment, specifically for IRDs?	16	14	16	11
16	How can artificial intelligence be used to enhance and expedite research into IRDs?	15	16	10	16

Note. Small groups consisted of at least 5 participants with representation from individuals who have an IRD, caregivers and health professionals.

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We acknowledge the Traditional Custodians of Country throughout Australia, and pay our respects to Elders past and present.

“My one hope is that this Priority Setting Partnership carries significant merit in the research community and that future research projects are influenced by the outcomes of this exercise.”

– IRD Priority Setting Partnership
Workshop participant, lived experience