

Improving visual outcomes in patients with rare paediatric eye diseases

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ABSTRACT

Introduction: Rare paediatric eye diseases (RPEDs) threaten both vision and life. Recently, rare diseases were recognised as a global public health agenda, with children specified as a priority in the World Health Organization's VISION 2020 against avoidable visual loss.

Method: We conducted a review through a query of online databases (PubMed, Embase and Cochrane Library). Articles related to RPEDs were selected based on relevance by 2 authors, with any disagreements adjudicated by the third author.

Results: We synthesise the current state of knowledge regarding RPEDs, barriers to their care, and recommendations for the future. RPEDs often result in significant visual loss, profoundly impacting the way children comprehend and participate in the world. These diseases may also reduce life expectancy and even be life-threatening. Barriers to the care of RPEDs include an unclear definition of "rare diseases", missed or delayed diagnosis, inadequate knowledge and expertise in management, and challenging research environments.

Conclusion: Our findings provide an update on the diagnosis and management of RPEDs, which is of relevance to ophthalmologists, paediatricians, healthcare policymakers and social workers. We propose supportive policies and adequate resource allocation to these diseases, comprehensive and patient-centred care, alongside improved education and training, enhanced research capabilities and continued collaboration across institutions.

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Keywords: disease burden, eye disease, paediatric disability, preventable visual loss, rare disease

CLINICAL IMPACT

What is New

- We present, to our knowledge, the first review synthesising literature on rare paediatric eye diseases (RPEDs) and their burden, and a tabular list of these diseases and their characteristics.
- Barriers to care for RPEDs include lack of a consensus definition; insufficient knowledge, experience and expertise; and inadequate policy provision and resource allocation.

Clinical Implication

- Further understanding and awareness of RPEDs can encourage earlier recognition of these diseases and patient-centric care.

people in Japan.² Rare diseases are an important healthcare issue and a challenge to public health.³ Although the individual incidence is low, rare diseases collectively affect 5–8% of the worldwide population or 1 in 15 persons,⁴ reflecting individual, societal and global significance. The majority of rare diseases affect children, with 69.9% of these being exclusively paediatric in onset.¹

Rare paediatric eye diseases (RPEDs) are serious and usually lifetime conditions resulting in visual impairment and blindness. In some instances, they can also be life-threatening. Recently, rare diseases were recognised as a global public health agenda,⁶ and children were specified as a priority in the World Health Organization's VISION 2020 against avoidable visual loss.⁵ There has also been increasing attention towards these diseases from international consortia and registries, disease-specific clinics, and divisions of academic children's hospitals.⁶

RPEDs significantly affect the quality of life and result in substantial loss of income and economic

INTRODUCTION

Rare diseases are generally understood as those that affect less than 1 in 2000–2500 people in the general population.¹ They are defined to affect fewer than 200,000 people in the US, lesser than 1 in 2000 people in Europe and lesser than 1 in 2500

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productivity,⁷ especially in the context of a globally ageing population. Furthermore, paediatric patients are a vulnerable demographic as they are unable to care for themselves. Their well-being is susceptible to external factors and can be compromised by poor access to healthcare, socioeconomic deprivation and parental neglect.⁸

Given the emerging importance of RPEDs, we conducted a review of literature synthesising the current understanding of these diseases, their morbidity and mortality, along with barriers and gaps relating to their care. We cite examples of RPEDs, such as retinoblastoma (RB) and retinitis pigmentosa, contrasting them to more common childhood ocular conditions, such as myopia and amblyopia. We also included a list of the most common RPEDs, detailing their age of onset, course of the disease, area of primary involvement in the eye, treatment options, and whether they have any genetic basis (Table 1). Our findings that map the current landscape of RPEDs and recommendations for the treatment of these diseases will be of relevance to paediatric ophthalmologists, researchers and health policymakers.

METHOD

We conducted a search of 3 online databases (PubMed, Embase and Cochrane library) with the keywords “paediatric”, “pediatric”, “children”, “child”, “rare disease”, “orphan disease”, “neglected disease”, “eye disease”, “orbitopathy”, “visual loss”, “vision loss” and “blindness.” Articles were included based on their relevance to the subject of RPEDs by 2 authors (FYCN and GS), with any conflicts resolved by the third author (PLT). The nature of the review article did not require an Institutional Review Board or ethical approval. The study adhered to the tenets of the Declaration of Helsinki.

RESULTS

Definition and prevalence

There is no universally accepted definition of “rare disease.” A systematic review identified 296 definitions from 1109 organisations across 32 international jurisdictions,² and another review found a global average prevalence of 1 in 2500 people.⁹ “Rare disease” may also be known as “orphan disease”, a term emphasising the underappreciated and overlooked nature of these diseases by the medical community and drug companies.¹⁰

Similarly, there is no consensus on what constitutes a “rare paediatric eye disease”, although these diseases are broadly understood to occur infrequently in the eyes of patients below the age of 18.¹¹ They comprise a heterogeneous group of

conditions encompassing over 900 eye disorders ranging from relatively prevalent conditions, such as retinitis pigmentosa, to extremely rare entities such as developmental eye anomalies.¹² Functionally, RPEDs can be divided into 2 categories: those that occur predominantly in children (e.g. inherited retinal disorders, RB, chloridaemia, coloboma), and those that more commonly occur in adults, but may occasionally present in children (e.g. uveitis, keratoconjunctivitis, optic nerve hypoplasia, optic nerve sheath meningioma). There are also other systemic rare diseases that involve the eye (e.g. Joubert syndrome, Revesz syndrome, Muckle-Well syndrome), but they are beyond the premise of this review.

Impact, morbidity and mortality

Although the total prevalence of rare diseases is low, their overall burden is socially and economically significant. Overall, there are up to 6000–8000 rare diseases affecting 400 million people worldwide;²² 72% of these diseases are genetic and 70% of them originate in childhood.¹² RPEDs have severe consequences, posing a threat to both vision and life in children and young adults all around the world. Moreover, 35% of these result in deaths in the first year of life and reduced life expectancy in 36.8% of these diseases, with 25.7% of children born with rare diseases dying before 5 years old.²²

Rare diseases are often complex and chronic. Their manifestation during childhood is associated with significant disability, impaired quality of life and premature death. The global burden of disease is conventionally measured using disability-adjusted life years (DALYs). However, the lack of national epidemiological studies on visual impairment and data on children requires the burden of childhood blindness to be inferred from the years lived with disability (YLD) component of DALYs instead.²³ YLD is substantially higher in children than in adults since disability occurs much earlier in the life course, by an average of 7 decades.⁵ The impact of visual impairment and blindness on paediatric patients is lifelong and life-changing, given their young age and potential for development. In addition, most types of RPEDs are bilateral and progressive in nature, causing more severe vision loss and impediment to daily functioning as patients grow and mature. Visual loss can profoundly and irreversibly impact the way children interact with others, acquire information and interpret the world.²⁴ RPEDs such as retinitis pigmentosa and coloboma often result in permanent visual disability with the former being progressive, while more lethal conditions such as RB and Batten’s disease might lead to early demise before children even have a chance to

Table 1. List of common rare paediatric eye diseases by age of onset, course of disease, area of primary involvement, treatment option and genetic basis.

Disease	Age of onset	Course of disease	Area of primary involvement	Treatment option	Genetic basis
Retinitis pigmentosa	Adolescence to adulthood	Bilateral progressive, eventual vision loss	Retina and RPE	No established therapeutic options	Present (AD)
Stargardt's disease (juvenile macular degeneration)	Adolescence to adulthood	Bilateral progressive, eventual vision loss	Macula	No established therapeutic options	Present (AR)
Anophthalmia/microphthalmia	At birth	Unilateral or bilateral stationary	Entire globe	No established therapeutic options	Present (combined genetic and environmental factors)
Coloboma	At birth	Unilateral or bilateral stationary	Eye/lens/macular/optic nerve/uveal/chorioretinal ¹³	No established therapeutic options	Present (AD and AR)
Leber's hereditary optic neuropathy	Adolescence	Unilateral progressive with sequential involvement of other eye, painless loss of central vision	Optic nerve	No established therapeutic options	Present (inherited mitochondrial disorder)
Usher syndrome	10 years to early adolescence	Bilateral progressive, eventual vision loss	Retina and RPE (due to retinitis pigmentosa)	No established therapeutic options	Present (AR)
Congenital ectopia lentis	<10 years	Bilateral stationary	Lens	Refractive correction and co-management of systemic disease, possible lensectomy ¹⁴	Present (AD and AR)
Retinoblastoma	<5 years	Unilateral progressive, vision loss and life-threatening if untreated	Entire globe	Intravenous chemotherapy, intra-arterial chemotherapy, intravitreal chemotherapy, intracameral chemotherapy, consolidation therapies (cryotherapy and transpupillary thermotherapy), radiation-based therapies (external beam radiotherapy and plaque radiotherapy), and enucleation ¹⁵	Present (AD)
Best disease (vitelliform macular dystrophy)	Early childhood to second decade of life	Bilateral progressive, gradual vision loss	Retina and RPE	No established therapeutic options	Present (AD)
Batten disease (juvenile neuronal ceroid lipofuscinosis)	6–10 years old	Bilateral progressive, eventual vision loss	Retina and RPE	No established therapeutic options	Present (AR)
Leber congenital amaurosis	At birth to infancy	Bilateral progressive, eventual vision loss	Retina and RPE	No established therapeutic options	Present (AR)

Table 1. List of common rare paediatric eye diseases by age of onset, course of disease, area of primary involvement, treatment option and genetic basis. (Cont'd)

Disease	Age of onset	Course of disease	Area of primary involvement	Treatment option	Genetic basis
Autosomal dominant optic atrophy	Childhood to adolescence	Bilateral progressive, eventual vision loss	Retina	No established therapeutic options	Present (AD)
Optic nerve hypoplasia	At birth to infancy	Unilateral or bilateral stationary	Optic nerve	No established therapeutic options	Present (AR)
Bietti's crystalline dystrophy	Adolescence to third decade of life	Bilateral progressive, eventual vision loss	Cornea, retina and RPE	No established therapeutic options	Present (AR)
Primary congenital glaucoma	<3 years	Bilateral progressive, eventual vision loss	Trabecular meshwork and anterior chamber angle	Angle surgery to lower IOP	Present (AR)
Cystinosis	Infancy to childhood	Bilateral progressive, eventual vision loss	Cornea, retina and RPE	Oral and topical cysteamine ¹⁶	Present (AR)
Axenveld-Rieger syndrome	Infancy to childhood	Bilateral progressive, eventual vision loss	Anterior chamber	No established therapeutic options, prevention of 2° glaucoma ¹⁷	Present (AD)
Choroideraemia	Childhood to adolescence	Bilateral progressive, eventual peripheral vision loss	Choroid, retina and RPE	No established therapeutic options	Present (X-linked)
Paediatric Graves' disease	<16 years, peaks from 11 to 15 years ¹⁸	Bilateral progressive, pain, blurring of vision, and photophobia	Extraocular muscles, fatty and connective tissue	Anti-thyroid medication, surgical subtotal thyroidectomy, radioactive iodine ¹⁹	Present (combined genetic, environmental and immune factors) ²⁰
Paediatric Behcet's disease	Childhood to adolescence	Bilateral progressive, pain, blurring of vision and photophobia	Uveal tract, retina and optic nerve ²¹	Systemic corticosteroids and immunomodulatory therapy	Absent

AD: autosomal dominant; AR: autosomal recessive; IOP: intraocular pressure; RPE: retinal pigment epithelium
Superscript numbers: refer to REFERENCES

reach adulthood. Furthermore, most types of RPEDs do not have any known or established therapeutic options.

Psychologically, socially and economically, the impact of rare diseases is often unseen but deeply felt by families grappling with these diseases. Families supporting children with such rare diseases reported substantial stress and frustration from delays in diagnosis, misdiagnosis, need for constant medical care, inadequate services and treatment options, and high costs, among others. Despite their increased need for support, few families can receive the psychological help they need. This contrasts with the abundant resources and support parents have for more common childhood eye diseases such as myopia and amblyopia, where there is abundant information online for parents to educate themselves, and readily available access to expert care and treatment options both in the developing and developed world. Many of these common childhood eye diseases also have straightforward treatment options (corrective lenses and surgeries) and relatively benign courses, hence not requiring as many visits to the clinic.

Children living with RPEDs are at increased risk of social isolation and psychological distress. Their illnesses have a major impact on their schooling and other social experiences, resulting in reduced health-related quality of life and emotional difficulties.²⁵ For example, children with RPEDs such as microphthalmia or severe colobomas, especially when bilateral, often miss out on school events and physical education (sports) as they have to attend medical appointments or are unable to participate for health reasons. Many RPEDs are associated with other physical deficiencies, such as hearing loss in Usher syndrome and neurological disturbances in Best disease. They are also at a greater risk of bullying and physical aggression due to their frequent absenteeism and physical deficiencies, with their peers finding it difficult to accept their differences or understand their struggles and experiences.²⁶ RPEDs such as anophthalmia/microphthalmia and RB present with obvious cosmetic and visual defects on inspection, and children may grow self-conscious or ashamed of their appearances, especially when poorly rehabilitated. Academically, with poor vision, these children are unable to capture information as easily and learn alongside their peers in the classroom. This contrasts with more common childhood diseases such as myopia and amblyopia, which are easily correctable, do not result in visual or cosmetic defects and are shared by many children in a similar age group—thus without social stigma or handicap. In addition, as paediatric patients with rare diseases progress through adolescence,

transitional care to adult services becomes critical but is often lacking.²⁷ As a result, many teenagers with rare diseases feel abandoned by the healthcare systems and have trouble navigating the changes in service providers when they need the most support. This is common across all paediatric disorders, but especially acute in rare diseases, as access to qualified care providers with both knowledge of the diseases and aptitude to deal with the complex emotional and mental turmoil of adolescents with rare diseases is exceedingly rare.

Economically, rare diseases take a toll on healthcare resources, families and societies at large.²⁸ The complexity of rare disorders requires multidisciplinary care and an interplay of services from various healthcare providers and specialists from different disciplines.²⁹ Hospital admissions and the use of emergency services are common in rare diseases, driving up healthcare costs. For example, between 2003 and 2014, total health expenditures for the treatment of rare diseases in Taiwan increased from US\$18.65 million to US\$137.44 million, with a 20.43-fold difference in average health expenditures and a 69.46-fold difference in average drug expenditures between patients with rare diseases and the overall population.³⁰ In the US, the total economic burden of rare diseases in 2019 was \$997 billion, including a direct medical cost of \$449 billion (45%), \$437 billion (44%) in indirect costs and \$73 billion in non-medical costs (7%).³¹ The top drivers for excess medical costs associated with rare diseases are hospital inpatient care and prescription medication; the top indirect cost categories are labour market productivity losses due to absenteeism, presenteeism and early retirement. Nevertheless, more research is required to ascertain the true economic impact of rare diseases, as a recent scoping review found a paucity of cost-of-illness studies in rare diseases.³²

Barriers

Lack of consensus on the definition of RPEDs

The absence of a definition for RPEDs results in difficulty qualifying and quantifying their burden, hampering efforts to diagnose and treat these diseases. This is further exacerbated by the lack of an internationally or nationally unified systemic approach for diagnosis and surveillance, as well as the lack of a classified medical nomenclature for documentation in health information systems. The International Classification of Diseases 11th version (ICD-11), which most countries use to identify diseases, does not include individual codes for RPEDs,³³ and the Systematised Nomenclature of Medicine only lists around 40% of rare diseases.³⁴

Disease-specific patient registries are an alternate means to identify patients with RPEDs.³ However, the quality, scope and capacity of many registries are limited. They may not be updated to reflect the most current records of patients and may not have a classification system in place for RPEDs. This contrasts with the robust patient records for more prevalent childhood eye diseases like myopia and amblyopia, allowing high-quality and large-scale epidemiological studies to be carried out.³⁵

Insufficient knowledge, experience and expertise

There is often a paucity of experience and expertise in the diagnosis and treatment of RPEDs. Due to the limited number of patients affected, especially in smaller, even in medically advanced countries like Singapore, there are only a handful of eye specialists who have direct experience with any given RPEDs, with most physicians having little to no exposure to these diseases. For example, in 2022, an 11-year-old girl was the first patient with orbital rhabdomyosarcoma in Singapore and Southeast Asia to receive interstitial brachytherapy treatment.³⁶ Many RPEDs also exhibit great genetic and phenotypic heterogeneity in their presentation, confounding the diagnostic conundrum. For example, in diffuse anterior retinoblastoma, a rare variant of RB, the retinal fundus examination may have atypical findings suggesting inflammation, leading to misdiagnosis and even mismanagement.³⁷ In addition, despite the impetus for a more in-depth understanding of RPEDs, there is a paucity of knowledge describing the field. The lack of widespread information and precedents of case studies to infer from hampers advancements in the care of RPEDs.

Furthermore, delayed diagnosis, misdiagnosis, or even failure of diagnosis are common in RPEDs. Studies show that half of those suspected to have a rare disease are undiagnosed, whereas those who receive a diagnosis have an average lag time of 5–6 years, with diagnostic delays as long as several decades.³⁸ For example, retinitis pigmentosa is a condition with a vast array of differential diagnoses, and the combination of multiple causative genes and the broad spectrum of clinical severity make both diagnosis and prognosis challenging, with genotypic multiplicity and phenotypic variability confounding the picture.³⁹ In a systematic review, time to diagnosis was prolonged by 3–5 months in RB with dire consequences, such as extraocular disease and higher mortality rates.⁴⁰ In another review, 42% of patients initially diagnosed with RB were found to be suffering from “pseudo-RB causes” such as Coats disease, persistent fetal vasculature—previously termed persistent

hyperplastic primary vitreous and familial exudative vitreo-retinopathy⁴¹.

In comparison, the diagnosis of common childhood eye diseases like myopia is often made early and with great accuracy, owing to early childhood eye screening in nationwide health programmes and developed eye screening protocols. Singapore, for example, formed the National Myopia Prevention Programme to address the high incidence of childhood myopia through public education and vision screening, for which the prevalence of myopia among students decreased from 37.7% to 31.6% between 2004 and 2015.⁴² Similarly, prevalent childhood eye conditions like amblyopia or strabismus are often picked up during routine developmental health screenings for children, even when they are unable to complain of poor vision or other ocular symptoms.³⁹

Even upon diagnosis, patients with RPEDs are commonly faced with inappropriate or inadequate treatment due to a lack of access to novel drugs, therapeutic modalities or professional expertise. Formalised diagnostic standards and clinical guidelines are not available for many rare diseases, leading to extreme variability and efficacy of treatment.⁴³ Due to the complexity of RPEDs, treatment options are involved, controversial and multidisciplinary. RB, for example, requires advanced treatment technology, techniques and expertise, for which there are discrepancies in protocols and a wide range of clinical outcomes.⁴⁴ Similarly, inherited retinal diseases require advanced treatment techniques, such as RNA editing and bionic vision.⁴⁵ This is opposed to the treatment of well-understood childhood eye diseases like myopia, which are uncomplicated and easily correctable with a pair of prescription glasses at a low cost even by allied health specialists such as optometrists.

Lack of consolidated and conclusive research

Randomised controlled trials (RCTs), the gold standard for clinical research, are difficult to carry out in RPEDs. The initial investment in capital is extensive, with unmet needs for staff and expertise limiting the number of centres able to conduct these trials.⁴⁶ In addition, it is challenging to enter sufficient patients into trials due to a small patient base. Problems in diagnosis, lack of standardised reporting and loss of patients to follow-up further compound the difficulty of identifying relevant patients. The majority of research on RPEDs is retrospective, non-randomised and underpowered by low participant numbers, consisting of mostly case reports or series. Research conclusions

derived are thus inadequate and subject to further validation, preventing the innovation of disease-specific therapies.⁴⁷

Furthermore, the developmental trajectory of children with rare diseases is altered and unpredictable, making it difficult to establish common outcome measures at various developmental stages and prognosticate outcomes.⁴⁸ Studies are also complicated by the measurement and selection biases at play in rare paediatric diseases due to their complex disease states and the lack of understanding of these diseases.⁴⁸ Finally, the challenge of assessing clinical outcomes in very young children may prevent their inclusion in research and contribute to representation bias.⁴⁹

Inadequate policy provision and resource allocation

From a public health point of view, rare diseases generally receive little policy support and resource allocation. They are not considered a national health priority, unlike prevalent childhood eye diseases like myopia that have nationwide health screening programmes.⁵⁰ Instead, RPEDs are diverse and heterogeneous in nature, with any specific disease affecting only a few individuals at a time. Any advancements in their management only benefit a small segment of the population, skewing the cost-benefit analysis to disfavour the uptake of RPEDs by the public healthcare system.

From an industry point of view, the large amount of initial investment required for the development of novel therapies in RPEDs presents a substantial barrier to entry.⁵¹ Research on these diseases will seldom produce tangible financial benefits, such as returns on investment or patents for intellectual property rights due to the small consumer base. Consequently, these diseases receive less attention and research grants from both government and pharmaceutical companies, requiring patient advocacy groups and private organisations to step in to bridge the gap.⁵²

Recommendations

Supportive policies and adequate resource allocation

To enable children with RPEDs to receive timely treatment, a concerted effort is needed across key stakeholders, including paediatric ophthalmologists, healthcare policymakers, academic healthcare organisations, administrators and industry leaders.

Funding for research on RPEDs, together with financial support to enable patients to acquire these treatment therapies, is central to the management of these diseases, as few patients can afford the

otherwise costly treatment. Society as a whole may stand to benefit from this, through reduced rates of preventable blindness, mortality, disability, years of life lost, rate of admission or readmission to hospital settings and cost of illness. In particular, more attention could be dedicated to the research of gene therapy options, as most RPEDs have an underlying genetic basis,⁵³ as shown in Table 1.

With the right screening programmes and systemic infrastructure, diagnosis and treatment for RPEDs can be made effective from an economic standpoint, even in developing countries. In India, a rapid screening strategy prioritising the order of exons to be analysed was developed for RB and identified mutations in 76% of patients in half the time and one-third the cost, facilitating better risk prediction in affected families and genetic counselling.⁵⁴ Another study on RB found a 3.5-fold cost saving for genetic screening as compared to conventional screening by clinical examination, demonstrating the potential of medical technology in the management of RPEDs. Moving forward, new models of risk and incentive sharing can be explored between the public and private sectors, spurring the development of novel technologies and therapies for RPEDs.

Enhanced research capabilities and continued collaboration

There is a need for wide-ranging and organised collaboration between tertiary care centres and research laboratories involved in the treatment of RPEDs on an international level. Multicentric, multinational collaboration is essential to the research and advancement of treatment options, and effective recruitment of patients can be achieved through partnership with patient organisations, rare disease registries and centres of expertise. Given how RPEDs are a group of heterogeneous disorders with significant variability between diseases, individual research laboratories targeting specific diseases would need to run in parallel with each other, while sharing strategies and best practices that can be applied across rare diseases.

Researchers can collaborate with local healthcare professionals to administer these trials in local healthcare settings to overcome the barrier of patients having to travel to be a part of clinical trials. Technology can be leveraged to monitor responses to interventions remotely and facilitate the collection of real-time data, allowing synchronous delivery of these trials across different geographical settings. This will create greater convenience and feasibility of enrolment in trials, encouraging greater participation.

To overcome the challenge of a relatively small number of patients with RPEDs available to participate in research studies and difficulties in recruiting paediatric patients for clinical trials, various strategies can be employed. For example, statistical methods for small samples can be utilised, including continual reassessment methods for phase 1 trials,⁵⁵ along with dose-response modelling and adaptive designs for phase 2 and 3 trials.⁵⁶ Furthermore, international natural history studies can take into account the genetic heterogeneity of RPEDs in paediatric patients to predict the ages when rapid changes in disease progression occur, identifying key periods for therapeutic intervention and proof of efficacy.⁴⁶ Patient registries and databases, such as the Genetic and Rare Diseases (GARD) Information Centre, as well as eyeGENE, the US National Eye Institute's National Ophthalmic Disease Genotyping and Phenotyping Network, have also been established to recruit more patients and advance research in the genetic causes and mechanisms of RPEDs.⁵⁷

Comprehensive and patient-centred care

Communication between physicians and patients is crucial in the management of RPEDs. Patients and their families often feel alone and isolated due to the rarity of their conditions and the lack of available information to understand them.⁵⁸ Physicians need to give adequate guidance to patients, providing regular progress updates and explaining possible treatment plans, involving them in the decision-making process and taking into account their fears, desires and unique circumstances. Physicians should also be forthcoming in admitting the gaps in their knowledge and expertise when unsure, explaining the rarity of these diseases and the lack of available information, and adopting a consultative and collaborative approach with patients.

Educational materials on RPEDs can be curated by healthcare professionals in collaboration with patient advocacy groups, to address the lack of authoritative and reliable information sources on these conditions. These can be given as pamphlets to patients and be used by doctors to explain information during consultations. By empowering patients and their families with knowledge, they are better equipped to understand and manage their conditions. Organisations such as EURODIS and Orphanet are already working towards this aim, by building an online database for rare diseases.⁵⁹

Finally, as more clinical trials on RPEDs allow patients access to highly experimental interventions, it is important to discuss and define realistic

expectations. Adequate information and advice should be provided about involvement in trials, as well as the personal use of nonregulated, experimental therapies. Paediatric patients are a special demographic who do not yet possess full personal autonomy due to their young age, relying instead on their parents to make medical decisions on their behalf in their best interests.⁶⁰ Nevertheless, the wishes, values and priorities of paediatric patients should still be considered when making decisions relating to their health and well-being. This can be facilitated through open dialogue and active discussion involving healthcare providers, patients and their families.⁶¹ In the event where efficacy of treatment has yet to be proven or evidence is lacking for novel, experimental treatment options, a careful risk-to-benefit analysis should be undertaken with patients and their families.

Improved education and training, cross-sector collaboration

All healthcare professionals involved in the care of paediatric patients should be educated on RPEDs. Medical education can endeavour to spur the interests of young doctors and scientists in RPEDs, encouraging them to contribute further to the field. To this end, undergraduate, postgraduate and continuing educational curricula can include a segment covering the basics of RPEDs. Of note, general practitioners, who are usually the first point of contact for patients in the community, should be trained to pick up anomalies on routine eye examination suggesting a more severe disease, and be informed of the workflow of subsequent referrals.

Furthermore, cross-sector collaboration is required between healthcare professionals and industry researchers. More physicians should be involved in the design and administration of clinical trials for RPEDs, lending their clinical experience and expertise to the development of therapeutic options. Physicians serve as advocates for their patients when interacting with drug developers and regulatory bodies, ensuring research targets fulfil patients' needs and are aligned with patients' best interests. More emphasis can also be placed on providing better care for patients using a multidisciplinary approach, involving paediatricians, ophthalmologists, and other allied healthcare workers such as psychologists and medical social workers.

More can also be done to facilitate open and free access to information between institutions and across borders for learning and development. Experts in the field of RPEDs can collaborate on projects and coordinate research efforts, promoting

scientific exchange and sharing of discoveries, outcomes and best practices. This can be facilitated by conferences and symposiums on RPEDs where physicians convene to learn from each other. Potential areas of interest in RPEDs include gene therapeutics, intrauterine screening, and early postnatal diagnosis of these diseases.

CONCLUSION

The future for RPEDs is promising. Although RPEDs remain an underserved need and a substantial burden to public health, it is receiving more attention from governments and public healthcare institutions. Rapid advancements in the discovery and application of novel technologies and therapeutics for these diseases have also been encouraging, providing patients with more treatment possibilities. Nevertheless, efforts towards better understanding of RPEDs, and to increase awareness among the public, general and family practitioners, and general and subspecialty ophthalmologists must continue to help patients preserve their vision and lead active, fulfilled lives.

Disclosure

The authors declare no conflicts of interest with any commercial organisation with a direct financial interest in the subject or materials discussed in the manuscript.

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