Impacts of X-linked retinitis pigmentosa and patient pathways in European countries: results from the cross-sectional EXPLORE XLRP-1 physician survey

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Abstract

Retina specialists (n = 20) and geneticists (n = 5) in France, Germany, Italy, Spain, and the United Kingdom were interviewed to provide insights on real-world patients (n = 80) with X-linked retinitis pigmentosa (XLRP). Survey respondents reported that their patients with XLRP often required assistance as their independence decreased over time, from 37% being “completely autonomous” at diagnosis (2% were “completely dependent” on family/friends), to 23% at their most recent consultation (10% were “completely dependent”). At their last visit, 45% of patients were active in the workforce. Workforce participation was related to independence/autonomy; 67% of “completely autonomous” patients were active, compared with 13% of “completely dependent” patients. The pathways by which patients with XLRP in these five countries visit retina specialists and geneticists are complex, lengthy, and vary considerably by country. Physicians reported high usage of genetic testing to confirm XLRP diagnosis (77.5%); however, long waiting times for test results account for incomplete uptake, especially among older patients. Teleconsultations and remote management have emerged as potential solutions for monitoring patients during the COVID-19 pandemic. Physicians report that unmet needs in XLRP management include more standardized assessment of quality of life; easier and earlier access to specialists, genetic testing, patient support programs, and effective treatment options.

Introduction

Retinitis pigmentosa (RP) is a group of vision-threatening rare eye diseases with heterogeneous genotypic etiologies. RP diseases are associated with the progressive loss of photoreceptors, leading to nyctalopia, visual field constriction, and eventually blindness. RP diseases are among the most common forms of hereditary retinal dystrophies, with a worldwide prevalence of approximately 1 in 4000. They are usually inherited as autosomal recessive (50–60% of RP patients), autosomal dominant (30–40% of RP patients), or X-linked (5–15% of RP patients) monogenic diseases, but digenic and mitochondrial patterns are also described[1, 2]. X-linked retinitis pigmentosa (XLRP) is among the most aggressive forms of RP, and patients are often legally blind by the fourth decade of life[3–6]. As an X-linked recessive disorder, XLRP primarily affects men[2, 3, 5–7]. Women who are heterozygous for an XLRP mutation are often considered unaffected carriers and may be asymptomatic, but some female carriers can experience significant visual impairment, a phenomenon related to variable X-chromosome inactivation patterns[2, 3, 5–11]. Approximately 70–80% of XLRP cases are caused by mutations in the retinitis pigmentosa GTPase regulator (RPGR) gene[3–7, 9, 11]. For inherited eye diseases like XLRP, genetic testing is strongly recommended to provide a definitive diagnosis[5, 12], which enables the potential for prenatal genetic diagnosis[7, 13, 14] and the possibility of gene therapy approaches[6].

No definitive treatment is currently available for XLRP; recommended management includes the use of low-vision aids, treatment of complications and comorbidities (e.g. cataract, cystoid macular edema), and blindness rehabilitative strategies[14–20]. Published data describing details of the XLRP patient profile and patient pathways are limited; there is a need for a better real-world understanding of current standards of clinical practice and possible obstacles to diagnosis and genetic testing.

As potential targeted therapies for XLRP emerge, a more thorough understanding of the disease’s impact on patients’ quality of life (QoL), work status, and level of independence is needed. Early diagnosis and access to genetic testing for both patients and family members will likely be topics of key importance, as will efforts to streamline the patient journey. Retina specialists and geneticists in five countries in Europe (France, Germany, Italy, Spain, and the United Kingdom [UK]) were interviewed for the EXPLORE XLRP-1 survey to provide insights on their experience with recent patients with XLRP (n = 80). The survey also sought to understand the burden impact of XLRP on patients’ lives and the pathways by which patients with XLRP are referred to retina specialists and geneticists, as well as the impact of COVID-19 on patient management.

Results

Survey participants

A total of 20 retina specialists and 5 geneticists from France, Germany, Italy, Spain, and the UK participated in the survey (four retina specialists and one geneticist from each country). Retina specialists and geneticists in these countries who had at least 5 years’ experience of managing or seeing patients with XLRP, and who were responsible for the recent management of patients with XLRP (retina specialists) or who were responsible for the genetic testing of patients with XLRP (geneticists) were identified. Retina specialists provided anonymized information (patient record forms) for the four patients most recently seen in their practice diagnosed with XLRP,

including information on the diagnostic and referral process and decisions to pursue genetic testing. Patient information was collected for 80 patients (16 from each country).

Sociodemographic characteristics of patients with XLRP

The demographic and clinical characteristics of the 80 patients are summarized in **Table 1**, and the XLRP symptoms experienced by the patients are summarized in **Table 2.**

The interviewed physicians reported that at the first consultation, 65 of 80 (81%) patients were at an early-to-mild stage of the disease. The retina specialists reported that their patients with XLRP were mostly male (91%) and that 56% were aged 18–40 years. At the time of the survey, the length of time the patients had been managed by these retina specialists ranged from <1 year to >10 years, with an average of 4.6 years. Most of the patients (79%) described by the retina specialists lived with their families. For 65% of patients, visits to retina specialists required traveling to a different city.

Patient independence and workforce participation

Retina specialists indicated that patient independence decreased over time (**Fig. 1**). A total of 37% of patients were classified as "completely autonomous" at diagnosis versus 23% at the last consultation; most patients (79%) were classified as "completely or somewhat autonomous" at diagnosis, but this number had declined to 56% by the time of the last consultation. The proportion of patients classified as "completely dependent" on family/friends rose from 2% at diagnosis to 10% at the last consultation.

Retina specialists reported that at the time of the last visit, 36 of 80 (45%) patients were active in the workforce, of whom 16 of 36 (44%) worked full time, 8 of 36 (22%) worked part time, and 5 of 36 (14%) participated in disability work. Among the 36 patients active in the workforce, 47% were aged between 18 and 30 years. Workforce participation was related to the extent of independence/autonomy; 12 of 18 (67%) "completely autonomous" patients had active working status, compared with 1 of 8 (13%) "completely dependent" patients (**Fig. 2**). Seven female patients with XLRP were described by the retina specialists and those patients were similar to the overall studied population regarding independence/autonomy and their ability to work; 4 of these 7 female patients (57%) were active in the workforce, with 2 participating in full-time regular work, 1 participating in part-time regular work, and 1 participating in disability work.

Patient referral pathways

The responses to the physician survey indicated that the pathways by which patients with XLRP are referred to retina specialists and geneticists in the five European countries included can vary considerably. In Germany and the UK, patients were reported to have seen retina specialists/geneticists through multiple steps and routes, including referrals by general practitioners, optometrists, and ophthalmologists. In France, Italy, and Spain, patient pathways were reported to be more linear; most patients had seen retina specialists/geneticists as a result of referral by ophthalmologists. Retina specialists reported seeing patients with XLRP typically once or twice a year for consultation.

Diagnosis and genetic testing

The average time between the onset of symptoms and diagnosis also varied between countries. Retina specialists indicated that more than half (58%) of their patients with XLRP were initially referred to the retina specialist without a specific suspicion of XLRP. Physicians estimated that their patients experienced an average time of 4 years between the onset of XLRP symptoms and diagnosis of XLRP, and that some patients experienced even longer delays (more than 10 years for 10% of patients) (**Fig. 3**). Once diagnosed, patients were provided with information about the disease, how it progresses, and their prognosis. Patients were encouraged to speak to a genetic counselor to understand the hereditary nature of the disease. The importance of monitoring is highlighted, especially given the complications that can arise. Before genetic testing was undertaken, key tools used to support XLRP diagnosis included optical coherence tomography, electroretinography, fundus autofluorescence, visual acuity testing, and static perimetry.

Genetic testing was used as part of XLRP diagnosis in 77.5% of patients, whereas 22.5% of patients did not have their disease confirmed by genetic testing. Among the five countries, the lowest rate of genetic testing (50%) was reported in France (**Fig. 4**). Retina specialists reported that the majority (56%) of patients who had not undergone genetic testing were older than 40 years (**Fig. 5**).

Retina specialists estimated that it usually took longer than 6 weeks to receive the results of XLRP genetic testing, and some patients waited up to 6 months to receive test results. The costs of genetic testing were fully reimbursed for most patients in all countries included in the survey, except Spain, where more than half of the genetic tests were reported to be paid for in full by patients. In the UK, testing costs were co-paid by 14% of patients.

Despite barriers to genetic testing (e.g. costs, long waiting times for results), physicians agreed that genotypic diagnosis is helpful for predicting disease progression and to allow patients the option of participating in clinical trials. Additional perceived barriers to genetic testing included the distances some patients needed to travel, the fact that no treatment is available for the disease, and the concerns of some physicians regarding reliable identification of mutations by the genetic tests. The clinical experts often recommend that the family members of patients with suspected or confirmed XLRP also be genetically tested, even without symptoms. Seven of 16 retina specialists reported discussing this with patients and their families at the time of diagnosis.

Social/emotional/psychological support and QoL

Physicians in the UK and Germany estimated that social/emotional/psychological support was offered to the majority (>69%) of patients with XLRP, while physicians in France, Italy, and Spain indicated that it was offered to patients only rarely (up to <20% of patients).

Retina specialists indicated the importance of the impact of XLRP on patients' QoL, but many responded that they evaluate QoL only informally; QoL is monitored with validated instruments in only 23% of patients. QoL instruments utilized by some retina specialists include the visual function (VF) QoL, the VF index (VF-14), and the 25-item visual function (VFQ-25) questionnaires.

Unmet needs, current challenges, and impact of COVID-19

Selected verbatim insights from the interviewed retina specialists and geneticists are provided in **Table 3**. The clinical experts generally agreed that the patients most in need of new XLRP treatment options are younger patients in the early stages of the disease; this is because delay of disease progression in these patients would have the greatest effect on preserving vision and QoL. Given that there are no effective treatments available for XLRP, physicians generally only monitor the disease progression and provide specific management of visual symptoms and impairment as disease severity progresses, focusing on the treatment of ocular complications and comorbidities together with several personalized rehabilitative strategies. In addition, the low level of social and psychological support for patients in the majority of the countries surveyed is likely to negatively impact the well-being of and clinical outcomes for these patients. Rehabilitation efforts are key healthcare goals for older patients with XLRP who have already experienced significant disease progression, vision loss, and impairment of QoL.

The COVID-19 pandemic led to a reduction of in-person clinic visits, which was thought to be a consequence of patients fearing infection. Healthcare providers are interested in solutions for remote management of patients (such as remote visual acuity or color perception tests, or having some tests performed in local facilities), with some physicians having seen patients via virtual (video) consultations.

Discussion And Clinical Implications

Even in light of this exploratory survey's limitations, several real-world key findings emerged that provide novel insight into people affected by XLRP, warranting further discussion and evaluation to better address effective, patient-centered care. Consistent with the findings of previous literature reviews[3, 21], patients with XLRP in our survey were found to rely on assistance from family/friends and became increasingly dependent on this assistance over time. Many individuals with XLRP were reported to be completely dependent on family and/or friends. Patients with XLRP and their caregivers would benefit from psychological/social/emotional support efforts, the provision of which was lacking for most patients (with the exception of those in the UK).

Patients with RP diseases are known to experience difficulties with finding and maintaining employment, including reduced opportunities for work, challenges navigating unfamiliar or busy environments, and trouble reading computer screens[3]. Indeed, fewer than 45% of patients in our survey were found to be active in the workforce, though the visual impairment itself does not explain such a low employment rate. Policies and financial incentives, access to enabling technologies, and more openness and support from employers (which may include part-time and/or facilitated work) are called for to enable workplace participation for patients with XLRP and other rare, vision-threatening eye diseases.

Work status and QoL are impacted by disease progression and reduced patient autonomy, and as patients with XLRP advance in age, these challenges are likely to worsen. Although published studies describing the humanistic burden of XLRP are lacking, the current survey's findings are consistent with those describing the larger RP population, which report that patients with RP do indeed experience difficulties with everyday tasks, barriers to work and career, and a considerable psychosocial burden[3, 18, 21].

The pathways by which patients with XLRP arrive to retina specialists and geneticists in the five European countries included in the survey have not previously been described using real-world survey data. These pathways are often complex and lengthy, and vary considerably by country, emphasizing an iniquity of access to rare disease services and other appropriate resources.

Early diagnosis is important for patients to best understand the impact of their disease on their life and family, and also to allow them the option of participating in clinical trials. Accurate population-based estimates of genetic testing rates among the XLRP patient population are not available. In our survey, 78% of patients were found to have used genetic testing to confirm their XLRP diagnosis. However, suboptimal access and long waiting times for test results accounted for incomplete uptake, especially among older patients. Additional perceived barriers to genetic testing included: the costs of the test; the distances testing required patients to travel; the lack of treatment options for the disease; and the reliability of the tests to identify mutations.

More detailed information about the possibility of gene-based prevention for patients with inherited retinal dystrophy including XLRP[13] and the likely emergence of gene therapy approaches in the near future[6] could increase the patient need for easier access to retina specialists and to faster diagnosis.

In our survey, patients with XLRP were reported to be seen by retina specialists once or twice a year, with the COVID-19 pandemic reducing the frequency of visits. Teleconsultations and remote management have emerged as possible solutions for monitoring patients during the COVID-19 pandemic (and potentially beyond), as well as to reduce the travel burden for patients and their caregivers/supporters.

Physicians perceive maintaining QoL to be very important for patients with XLRP, but most evaluate QoL informally (i.e. without a specific questionnaire), rather than by periodically administering validated QoL instruments. As potential targeted XLRP therapies emerge, reliable measurement of patient QoL will become increasingly important; QoL outcomes, including symptom burden, level of autonomy, and impact on work and activities, will be important for assessing the benefit of potential new treatments.

Self-monitoring tools to support patients with XLRP and their caregivers should include skills for planning and communication to facilitate assistance patients will eventually need from family/friends as vision loss progresses[21]. Evaluating the psychological burden of XLRP using validated questionnaires is important, especially when discussing access to psychological support resources for individual patients and their families.

More efforts are required to increase awareness of XLRP and underline the importance of genetic testing to healthcare providers and regulatory authorities, which may have limited knowledge of this rare disorder. The collaboration of ophthalmologists and general practitioners with other experts, including genetic counselors and retina specialists, is encouraged for optimal decision-making and accurate diagnoses of XLRP and other inherited eye diseases[12, 22]. Patients with inherited retinal disorders also vary regarding their understanding of genetic testing, but the majority respond that they would be likely to undergo genetic testing if it was offered[23].

Solutions must be found to improve the long waiting times of patients for genetic test results and the distances patients (and their close relatives and caregivers) have to travel in order to undergo testing. Cost-related barriers to genetic testing—which potentially limit access to some patients and thereby decrease overall uptake—should also be addressed.

Approaches to help streamline the patient referral and diagnosis pathways include providing better information to both healthcare providers/physicians and patients to educate them about the disease, as well as more efficient routes for performing genetic testing.

Innovative digital tools are needed to help plan appointments, which could include access to local, or even mobile, examination rooms and remote telemedicine options for monitoring of visual acuity and/or other vision-related morpho-functional indicators.

Limitations of this exploratory survey include the small sample size of physician respondents and their patients, which may limit the generalizability of the findings to larger populations. The small sample size was driven by the fact that XLRP is a rare disease with a limited number of retina centers and retina specialists in each country. In fact, this survey was designed to provide a descriptive investigation only, without statistical or comparative analyses. Additionally, all patient-related findings were provided via the perspectives of retina specialists and geneticists through market research methodology; these insights represent the valuable clinical experiences of the physicians interviewed and not patient-reported insights and experiences. Additional studies are warranted to address the valuable process of patient empowerment, including those that more thoroughly evaluate the impact of XLRP on self-reported QoL, independence/autonomy, and workplace participation.

Although this cross-sectional physician survey was exploratory in nature, it demonstrated that XLRP has a major impact on patients' lives and provides valuable real-world insights from retina specialists and geneticists that may not otherwise be available through clinical studies or health economic research. There is a scarcity of information available describing the real-world experiences of patients with XLRP; this interview-based survey approach is an attempt to address that scarcity.

Unmet needs in XLRP management include more standardized QoL assessment, improved and earlier access to patient support/rehabilitation programs, and effective treatment options. Additional patient and caregiver needs include policies that provide better access to employment, streamlined patient pathways that enable earlier diagnosis and management, and broader access to genetic testing with faster delivery of testing results.

Methods

Study design

EXPLORE XLRP-1 was an exploratory cross-sectional physician survey conducted in France, Germany, Italy, Spain, and the UK. The research did not involve direct collection of data from patients. Potential retina specialists and geneticists for interviews were identified from clinical trial research publications and by leveraging IQVIA prime and partner sites and IQVIA specialist centers. The specialists were given a screener to complete in order to be eligible for the study. Retina specialists and geneticists in these countries were identified who had at least 5 years' experience of seeing and managing patients with XLRP, and who were responsible for the recent clinical management of patients with XLRP (retina specialists) or for the genetic testing of patients with XLRP (geneticists). Each retina specialist provided anonymized patient record forms supplying information for the four patients most recently seen in their practice diagnosed with XLRP (with or without genetic testing), including details of the diagnostic and referral process and decisions to pursue genetic testing. The sample size of 20 retina specialists and five geneticists for this descriptive and exploratory survey was determined by the rarity of the disease and the ability to enroll a sufficient number of eligible participants to draw meaningful conclusions.

The anonymized patient information was collected through an online survey completed by the retina specialists and stored in a secure database. The anonymized data from the patient record forms were prepared in an aggregated tabular format and a descriptive analysis of these data was performed.

Individual 60-minute telephone interviews were then conducted with the retina specialists and geneticists in order to capture their perspectives on management approaches for patients with XLRP. Discussion guides were used to conduct the interviews; these were used to prompt physicians to describe and comment on items including diagnostic and genetic testing tools, reliability of diagnostic data, frequency of patient follow-up, and physicians' personal experiences with XLRP management and/or genetic testing (copies of the interview discussion guides are provided as supplemental material). Interviews with the physicians were audio-recorded and capture sheets containing physician responses were provided to the study analysts, who conducted a thematic analysis of the interviews. To complement the findings of the thematic analysis, verbatim quotes were also collected.

Declarations

Data availability

The datasets generated and analyzed during the current survey are available from the corresponding author upon reasonable request.

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Author contributions

Authors KP and KA contributed to the survey design, developed the interview discussion guides, and conducted the physician interviews. All authors contributed to interpretation of the survey findings and preparation/approval of this manuscript.

Ethics declarations

This survey and manuscript were supported by Janssen Pharmaceuticals, Inc. This survey was not overseen by an independent review board or similar oversight body. The research did not involve direct collection of patient-level data, and therefore no ethics committee approval was sought. The survey was compliant with applicable market research regulations, including guidance and best practices offered by European Society for Opinion and Marketing Research, European Pharmaceutical Market Research Association, and the British Healthcare Business Intelligence Association. Written consent was obtained from the retina specialists and geneticists interviewed, and no personal or identifiable patient information was collected.

Competing interests statement

Authors KP, JL, TD, YK, and RN are employees of Janssen Pharmaceuticals, Inc. KA is an employee of IQVIA and has a consulting agreement with Janssen Pharmaceuticals, Inc. Authors MP and FP have no competing interest to report.

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Tables

Table 1. Patient demographic and clinical characteristics

		Total (N=80)		Germany (n=16)		France (n=16)		Italy (n=16)		Spain (n=16)		UK (n=16)	
Variable	**Outputs**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**
Sex	Male	91.25	73	93.75	15	93.75	15	93.75	15	93.75	15	81.25	13
	Female	8.75	7	6.25	1	6.25	1	6.25	1	6.25	1	18.75	3
Age group, y	<18	18.75	15	25.00	4	12.50	2	12.50	2	18.75	3	25.00	4
	18–30	37.50	30	37.50	6	37.50	6	37.50	6	37.50	6	37.50	6
	31–40	18.75	15	6.25	1	31.25	5	25.00	4	6.25	1	25.00	4
	≥41	25.00	20	31.25	5	18.75	3	25.00	4	37.50	6	12.50	2
Family status	Living in own household with family	78.75	63	62.50	10	87.50	14	75.00	12	100.00	16	68.75	11
	Living alone	16.25	13	25.00	4	12.50	2	12.50	2	0.00	0	31.25	5
	Living in care home	1.25	1	6.25	1	0.00	0	0.00	0	0.00	0	0.00	0
	Other	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0
	Don’t know	3.75	3	6.25	1	0.00	0	12.50	2	0.00	0	0.00	0
Employment status	Active	45.00	36	37.50	6	37.50	6	50.00	8	37.50	6	62.50	10
	Non-active	45.00	36	62.50	10	62.50	10	25.00	4	37.50	6	37.50	6
	Don’t know	10.00	8					25.00	4	25.00	4		
Patient’s working status	Full-time: regular work	44.44	16	66.67	4	33.33	2	50.00	4	33.33	2	40.00	4
	Full-time: disability work	5.56	2	0.00	0	0.00	0	0.00	0	0.00	0	20.00	2
	Part-time: regular work	22.22	8	33.33	2	33.33	2	12.50	1	0.00	0	30.00	3
	Part-time: disability work	8.33	3	0.00	0	16.67	1	12.50	1	0.00	0	10.00	1
	Self-employed	2.78	1	0.00	0	0.00	0	0.00	0	16.67	1	0.00	0
Relevant comorbidities	Cataracts	8.75	7	18.75	3	0.00	0	0.00	0	12.50	2	12.50	2
	Asthma	1.25	1	0.00	0	6.25	1	0.00	0	0.00	0	0.00	0
	Hypertension	7.50	6	6.25	1	6.25	1	0.00	0	6.25	1	18.75	3
	Myopia	2.50	2	12.50	2	0.00	0	0.00	0	0.00	0	0.00	0
	Astigmatism	2.50	2	12.50	2	0.00	0	0.00	0	0.00	0	0.00	0
	Rheumatoid arthritis	1.25	1	6.25	1	0.00	0	0.00	0	0.00	0	0.00	0
	Hypercholesterolemia	1.25	1	0.00	0	0.00	0	0.00	0	0.00	0	6.25	1
	Cardiovascular disease	1.25	1	6.25	1	0.00	0	0.00	0	0.00	0	0.00	0
	Cystoid macular edema	2.50	2	6.25	1	0.00	0	0.00	0	0.00	0	6.25	1
	Smoking	1.25	1	0.00	0	0.00	0	0.00	0	0.00	0	6.25	1
	Diabetes mellitus	2.50	2	6.25	1	0.00	0	0.00	0	6.25	1	0.00	0

	None of the above	75.00	60	50.00	8	87.50	14	100.00	16	81.25	13	56.25	9
Diagnosis of XLRP that included genetic testing	Yes	77.50	62	81.25	13	50.00	8	93.75	15	75.00	12	87.50	14
	No	22.50	18	18.75	3	50.00	8	6.25	1	25.00	4	12.50	2

XLRP, X-linked retinitis pigmentosa.

Table 2. Symptoms experienced by patients with XLRP

		Total (N=80)		Germany (n=16)		France (n=16)		Italy (n=16)		Spain (n=16)		UK (n=16)	
Variable	**Outputs**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**
Symptoms that made you suspect/ recognize XLRP	Light blindness	5.84	15	7.58	5	5.66	3	1.92	1	8.11	3	6.12	3
	Progressive constriction of field of vision	21.01	54	18.18	12	22.64	12	26.92	14	13.51	5	22.45	11
	Loss of central vision	10.51	27	10.61	7	5.66	3	17.31	9	8.11	3	10.20	5
	Pigmentary changes in the retina	23.35	60	18.18	12	20.75	11	26.92	14	27.03	10	26.53	13
	Dyschromatopsia	10.51	27	10.61	7	11.32	6	7.69	4	10.81	4	12.24	6
	Photophobia	12.06	31	16.67	11	20.75	11	7.69	4	5.41	2	6.12	3
	Cataracts in the posterior subcapsular area	5.84	15	9.09	6	3.77	2	5.77	3	5.41	2	4.08	2
	Cystoid macular edema	1.56	4	3.03	2	0.00	0	0.00	0	2.70	1	2.04	1
	Others	9.34	24	6.06	4	9.43	5	5.77	3	18.92	7	10.20	5
Symptoms the patient presents today	Light blindness	5.57	17	8.33	6	7.46	5	1.61	1	7.84	4	1.89	1
	Progressive constriction of field of vision	19.34	59	19.44	14	17.91	12	24.19	15	15.69	8	18.87	10
	Loss of central vision	10.82	33	9.72	7	4.48	3	16.13	10	15.69	8	9.43	5
	Pigmentary changes in the retina	21.64	66	18.06	13	20.90	14	24.19	15	21.57	11	24.53	13
	Dyschromatopsia	11.48	35	9.72	7	13.43	9	11.29	7	11.76	6	11.32	6
	Photophobia	10.82	33	15.28	11	16.42	11	8.06	5	3.92	2	7.55	4
	Cataracts in the posterior subcapsular area	7.54	23	8.33	6	7.46	5	6.45	4	3.92	2	11.32	6
	Cystoid macular edema	3.93	12	5.56	4	5.97	4	1.61	1	1.96	1	3.77	2
	Others	8.85	27	5.56	4	5.97	4	6.45	4	17.65	9	11.32	6

XLRP, X-linked retinitis pigmentosa.

Table 3. Selected XLRP insights from the retina specialists and geneticists interviewed

Patient independence/autonomy in XLRP
“In most cases, the first time they are always accompanied because either it is the first time or they have some serious visual impairment. In the other cases it depends on their degree of autonomy: autonomous patients also come alone.” *—Retina specialist, UK*
“Many of them come alone with a dog and white stick. I would say around 50% of them do have someone along with them.” *—Retina specialist, UK*
“We have lots of patients facing research studies, so I guess the research study funds their travel. So they come with a driver paid for by the sponsor of the clinical study.” *—Retina specialist, UK*
XLRP diagnosis and genetic testing
“The goal is to treat a patient as early as possible. Where it makes no sense at all is in a patient where the visual field is already very, very limited. When you can no longer prevent progression. The final stage has already been reached.” *—Retina specialist, Germany*
“This being a rare disease, it certainly takes a longer time… In some cases, certainly 1 or 2 years until it is really recognized.” *—Retina specialist, Germany*
“So, the most important thing is, of course, that molecular genetics is performed to ensure that a patient really has XLRP. Of course, this is becoming more and more common.” *—Retina specialist, Germany*
“Almost all of those who are affected agree to genetic testing. Very few are unwilling to undergo genetic testing.” *—Geneticist, Germany*
“Some of them don’t want genetic testing. Some of them don’t want to know. It has implications for them… They’re like, ‘Oh, well, if there’s no treatment then there’s no point. I don’t really want to know.’” *—Geneticist, UK*
“For the genetic diagnosis instead, it takes time for the test. That, in Italy, still takes around 6 months before getting a report. I think it is because they wait for more samples of the same diagnostic suspect to run together on the same NGS. I think this is simply the reason.” *—Retina specialist, Italy*
“To get the results of the genetic testing back, also between 1 and 3 months.” *—Geneticist, Germany*
“Patients send the bloods off and then that can be about 6–8 weeks to get the results. Sometimes earlier; 4–6 weeks sometimes if we get the multipanel.” *—Geneticist, UK*
Impact of XLRP on patients and QoL
“Especially the mothers, because they themselves are carriers and develop feelings of guilt, as the child inherited something from them.” *—Retina specialist, Germany*
“Their family life can get frustrating, because they have become people with the possibility of having genetic family problems.” *—Retina specialist, Spain*
“Many of them need to change their profession, or not to continue with their ongoing studies as they will not be able to benefit from them.” *—Retina specialist, Spain*
“However, when you sit people down and ask quality of life questionnaires, it does force them to think about the things that they can’t do anymore, which is often quite emotional for them.” *—Retina specialist, UK*

"Waking up and knowing that when you're 40 you're going to be blind. It's very hard. Many of them accept it normally. A human being's ability to adapt surprises me. And the more patients I see, the more I realize it."

—Retina specialist, Spain

NGS, next-generation sequencing; XLRP, X-linked retinitis pigmentosa.

Figures

Fig 1

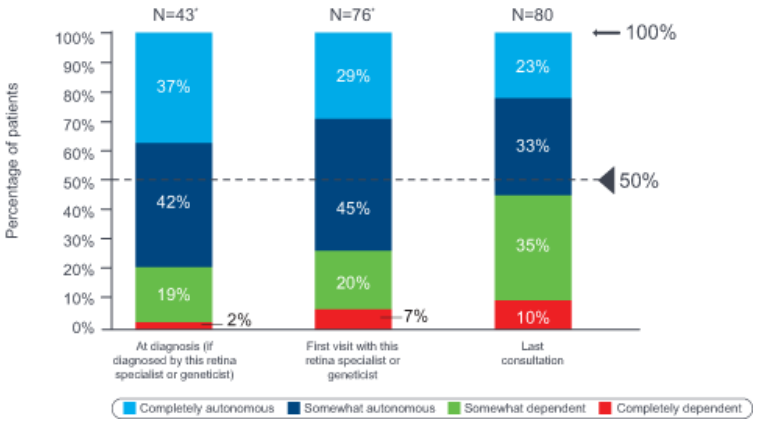

Figure 1

Patient independence over time. Number of patients does not add up to 80 due to some respondents answering "don't know." The number for this response was 37 at diagnosis and 4 at first visit.

Fig 2

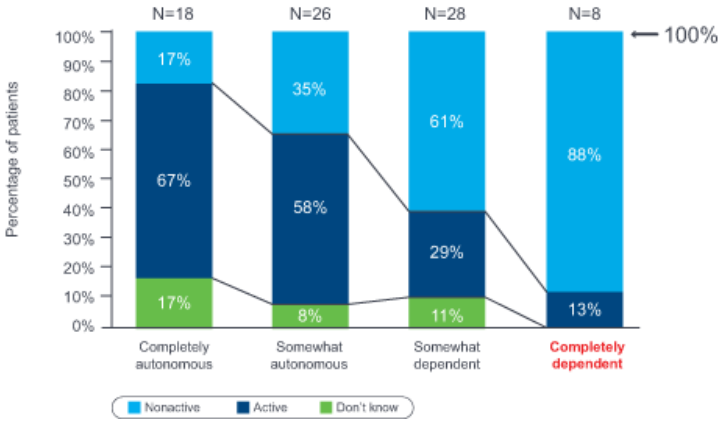

Figure 2

Patient dependence and employment status

Fig 3

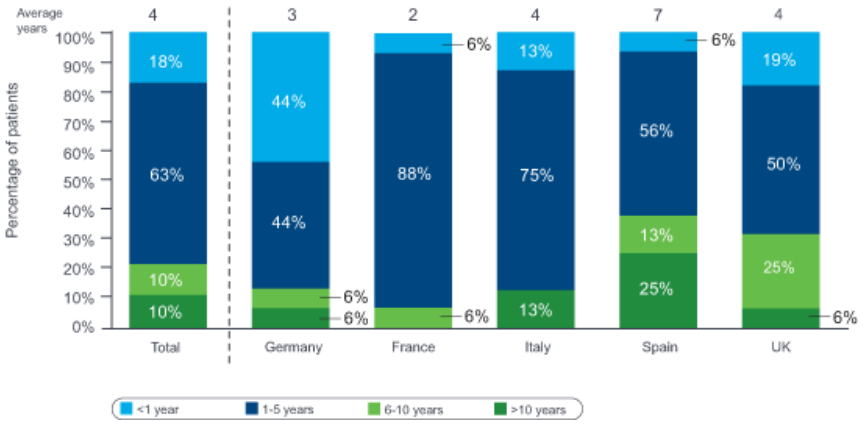

Figure 3

Time to diagnosis: average duration in years between the onset of symptoms and diagnosis. Total, N=80; country, N=16.

Fig 4

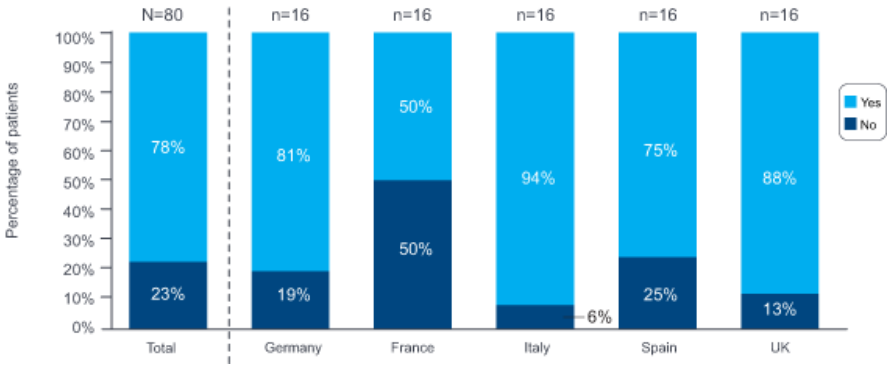

Figure 4

Proportion of XLRP diagnoses confirmed with genetic testing.

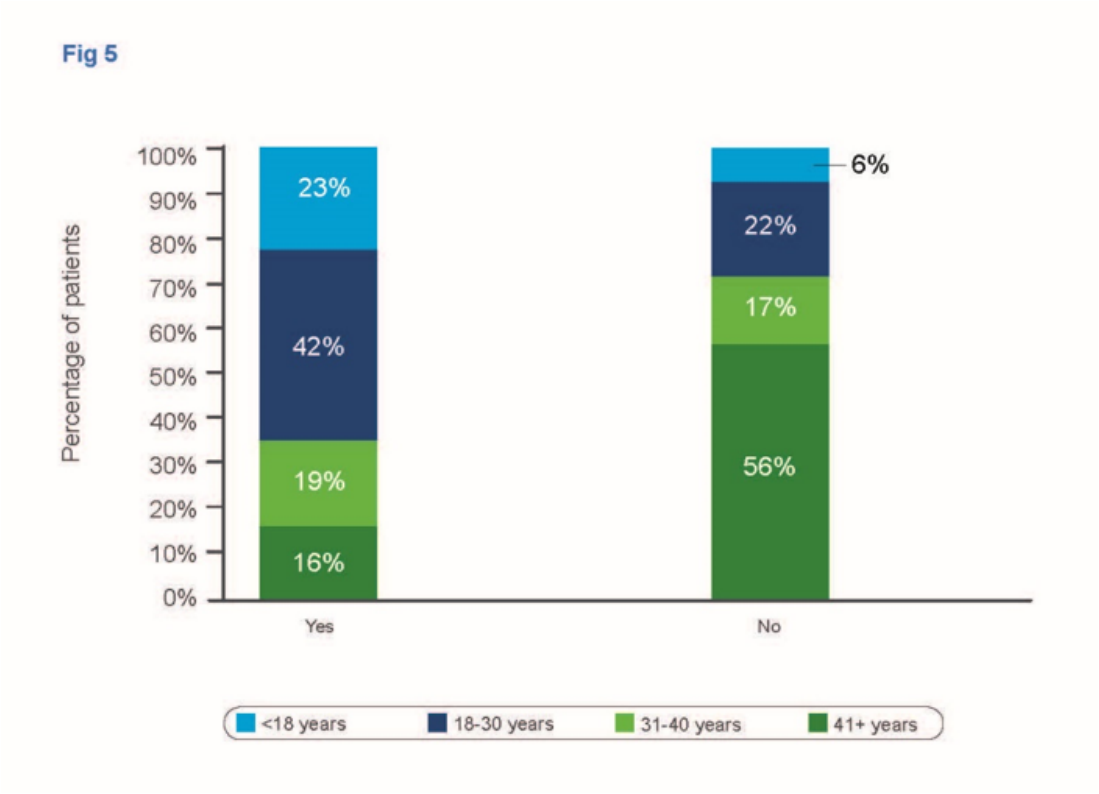

Figure 5

Age distribution of patients who did and did not receive genetic testing for XLRP. N=80.