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Using crowdsourcing to understand patients attitudes toward a clinical trial for retinitis pigmentosa requiring 4 years of participation

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Abstract

Background: Clinical trials for retinitis pigmentosa (RP) likely require long follow-ups because of the slow progression of RP. Understanding patients' attitudes toward participation in a long trial and their acceptability of strategies aimed at promoting retention/compliance is important for assessing feasibility and resource needs and optimizing trial design.

Methods: A crowdsourcing survey to adult RP patients was administered on social media in 2020 July-November. Patient enthusiasm level of study participation, acceptability of attending clinic visits every 4–5 months for 45-months, tele-visits with doctors, and of receiving text messages for medication reminders and for reporting missed dosages were surveyed.

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Declaration of interest:

There is no conflict of interest to disclose for XK, CD, ST, FN and CAL. The disclosure for PAC is as below: Personal financial interest with Aerpio Pharmaceuticals, Allegro, Applied Genetic Technologies Corporation, Asclepix Therapeutics, Ashvattha Therapeutics, Bausch and Lomb, Clearside, CUREVAC, Exonate Ltd., Genentech/Roche Inc, Graybug Vision, Merck & Co., Novartis Pharmaceuticals, Perfuse, Wave Life Sciences; Financial support with Asclepix Therapeutics, Genentech/Roche Inc, Mallinckrodt Pharmaceuticals, Oxford Biomedica, Regeneron Pharmaceuticals, Inc., RegenixBio Sanofi/Genzyme.

Results: Among the 1473 respondents, over 95% use email or a mobile phone and receive text messages; 1157 (79%) respondents were very/somewhat enthusiastic about participation, among them, 80.6% were “very willing” to attend clinic visits every 4–5 months for 45 months; 90.3% were “very willing” to have tele-visits; 64.7% and 77.1% were willing to receive text reminders to take medication and messages surveying missed doses, respectively. The youngest age group (18–30) (22.1%) and oldest age group (70+) (26.1%) compared to the 41–50 years age group (14%) and women (23.5%) compared to men (14.2%) were statistically significantly more likely not to report high willingness to participate in clinical visits for 45 months.

Conclusions: A trial requiring 4-years of commitment is feasible although retention can be challenging. Strategies including supplementing in-clinic visits with tele-visits and frequent communications may facilitate retention. This study also demonstrates a methodology useful for planning clinical trials for chronic diseases.

Keywords

inherited retinal degeneration; patients’ willingness for clinical trial participation; multi-center clinical trial planning; patient compliance

Introduction

Retinitis Pigmentosa (RP) is one of the most common causes of visual disability and blindness in people aged 20 to 60 years[1] and is the most prevalent inherited retinal disease. The inheritance mode for RP includes autosomal dominant, autosomal recessive, and X-linked recessive. Over 20% of RP patients also have other sensory or systemic deficits[1,2]. Mutations in many genes have been linked to RP, yet in about 40% of RP patients, a pathogenic mutation(s) has not been identified[3]. The mutations first cause visual difficulty at night and then patients start to notice constricted visual fields followed by gradual loss of visual acuity over years until legal blindness. Thereafter total blindness often occurs. Currently there is no treatment to prevent vision loss in RP [4].

Potential therapeutic options are emerging and will be tested in clinical trials. The success of a trial starts with patients’ willingness to participate and requires their compliance and retention throughout the trial. Clinical trials for RP will likely need relatively long follow-up because of the disease’ slow progression. Thus, understanding RP patients’ attitudes toward participation in a long trial and the acceptability of different strategies aimed at promoting retention and compliance will facilitate assessment of study feasibility and resource needs, and help optimize trial design.

We conducted a crowdsourcing survey of the RP patient community to assess RP patients’ interest levels in participating in a planned clinical trial requiring twice a day oral administration of study drug or placebo with follow up for about 4 years. The goal of the trial is to evaluate the efficacy and safety of an oral medication in delaying vision loss in patients with RP. The survey also inquired about patients’ attitudes toward potential strategies for promoting compliance and retention that were identified previously through our qualitative personal interviews with several patients. Herein this study reports the survey results.

Materials and Methods

Crowdsourcing utilizes social media to quickly connect with a group of people to solicit ideas. Guided by behavior change theories[5], a brief questionnaire was first developed by the study team and pilot tested with the USHER 2020 Foundation. Google Form was then used by the USHER 2020 Foundation as the crowd-source platform to collect responses to the questionnaire among RP patient communities. The survey was open on Google Form from July 20 to November 1 of 2020. The survey link was posted on the USHER 2020 Foundation website and sent to email lists of retinal patient advocacy groups and to RP patients through Foundation Fighting Blindness' "My Retina Tracker". It was also posted on social media (Twitter, Instagram, Facebook, LinkedIn) and was adopted by listserves of RP patient groups. Respondents were requested to be over 18 years old and have RP (or to fill out the survey for a person with RP). Respondents were not requested to provide any information considered protected health information such as their names or date of birth (the survey questionnaire in Google Forms is available in Supplemental Material). The study was determined as not constituting human subjects research by the Johns Hopkins Medicine Institutional Review Boards.

Attitude toward enrollment in the trial was assessed by the question "*…a study being planned for an oral medication to slow or stop vision loss caused by RP. The study would be over a 4 year period and require taking medication two times per day over the length of the study. In addition, participants would be asked to record their usage and any missed dosing, as well as periodic visits with a participating physician*." "*Assuming you met eligibility requirements, how enthusiastic would you be about participating in such a study*?", and patients who responded "Very enthusiastic" or "Somewhat enthusiastic" were considered as likely being enrolled. Their retention potential was further assessed by the question "*… how willing would you be to participate in the following: A clinical visit with a doctor every 4 to 5 months for 45 months*." The response of "Somewhat willing" and "Not willing" was combined as low retention potential, as compared to the response category of "Very willing".

Chi-square tests were used to assess whether patient characteristics were associated with low potential for retention. Risk ratios were estimated for factors significantly associated with low potential for retention at $p<0.05$. SAS 9.4 (SAS Inc. Cary, NC) was used for all analysis.

Results

There were 1473 responses, 642 (43.6%) from men and 825 (56.0%) from women. Table 1 shows the age distribution and response summaries for each question. About 37.3% of patients required assistance from others to get around while 44.5% did not need assistance during the day. Most, but not all, respondents use email (94.8%) or a mobile phone (96.3%). Among those who use a mobile phone, 96.2% receive text messages. There were 16 respondents (1.1%) who neither use email nor use a mobile phone. A total of 1157 (78.8%) respondents were very or somewhat enthusiastic about study participation; among them, 80.6% were "very willing" to have in-person study visits every 4–5 months for 45 months; 90.3% were "very willing" to have telemedicine contact with a doctor between clinical visits; 64.7% were willing to receive text message reminders to take medication twice a day;

and 77.2% were willing to receive a text message surveying missed medication doses daily or weekly.

Table 2 shows the retention potential by patient characteristic. Compared to the age 41–50 years group that had the lowest risk of low retention potential(14.0%) (Figure 1), the youngest age group (18–30) and oldest age group (70 and over) had significantly higher risks of low retention (RR=1.58 95%CI 1.01–2.50, and RR=1.87, 95%CI 1.23–2.82, respectively). Women had a significantly higher risk of low retention compared with men (RR=1.65, 95%CI: 1.28–2.13). Other patient characteristics were not statistically significantly associated with low retention potential. Not using email and not using a mobile phone had higher risk of low retention (29% vs. 19.2% and 24.3% vs. 19.3%, respectively). The associations were not statistically significant because of the small sample sizes of patients not using email or a mobile phone.

Discussion

The survey received a high number of responses in 3 months and respondents included patients at various stages of vision loss. The results show that patients with RP are highly enthusiastic regarding participation in a 4-year long trial. This suggests that the trial being planned is feasible and enrollment in a relatively short period of time may be possible. A likely explanation is that RP is a blinding disease with no effective treatments and patients are highly motivated to try new treatments that may slow their vision loss. However, despite high enthusiasm for trial participation, about 20% of RP patients were hesitant to commit to attending study visits every 4–5 months for 4 years. This suggests the need for frequent, intensive efforts to communicate, educate, and engage participants throughout the trial.

Several strategies to maximize retention should be considered. For example, our survey suggests that tele-visits would be highly acceptable in the post-COVID-19 pandemic period. Thus, the frequency of in-clinic visits may be reduced by replacing some in-clinic visits with tele-visits. RP is a slowly progressing disease allowing infrequent assessments of visual outcome measurements; however, it is important to have more frequent interactions with patients to assess safety and encourage compliance and this is the purpose of tele-visits. There will be no outcome measurements during tele-visits. The reduction of in-clinic visits will reduce participant burden and should encourage enrollment and retention.

The majority of RP patients expressed willingness to receive daily text messages reminding them to take study medication and weekly surveys to assess missed doses. These may provide useful tools to encourage and assess compliance. On the other hand, a subset of participants may opt out of receiving text messages, indicating that other communication options such as email, post mail, and other approaches for monitoring compliance such as pill counting by study coordinators are necessary. In-between two visits with the physician, a phone call between the study coordinator and participant may also facilitate the participant's interaction and engagement with the study.

Younger (18–30 years) and older age groups (70+) may have higher risks of early termination (Figure 1). This age-related pattern is consistent with other studies with

relatively long follow-up[6–8]. Women expressed greater hesitancy than men regarding the commitment to attending study visits for 4 years. The need to avoid pregnancy throughout the trial may contribute to the hesitancy but further investigation is warranted to elucidate and address other sources of hesitancy.

Other sociodemographic characteristics such as patient's education level, family income level and race were not asked in the questionnaire. Future similar survey studies should include relevant questions to collect this information. The socidemographic data will allow better characterization of subgroups of patients that may have lower interest in participating a research study or higher risk of loss to follow-up. The information may also inform the development of targeted strategies to promote clinical trial participation and retention among subgroups of patients.

Our survey assessed RP patients' attitudes and acceptability of the planned clinical trial. It is known as the KAP (Knowledge-Attitude-Practice) gap that knowledge and positive attitudes toward a health related behavior does not always translate to the actual uptake of the behavior[9]. Therefore, other strategies may be considered to facilitate enrollment and study compliance. For example, our brief crowdsourcing questionnaire did not provide detailed information about the oral medication that will be evaluated in the trial. In practice, interactive conversations between patients and study personnel can improve patients' knowledge about the trial. Based on the health belief model, better knowledge may lead to better informed decisions about study participation[5]. A guide for study personnel regarding the key points of study information that should be delivered during such conversations may be developed during the study planning phase. In addition, our survey suggested some RP patients required assistance from a family member or friend to move around. The social ecological theory suggests family, friends or peers may exert influences on patients' decisions regarding study participation and compliance. [5,10]. Thus, engaging members of participants' support network may help facilitate study compliance.

Using crowdsourcing it was not possible to know how many RP patients were aware of the survey link but chose not to respond. It was possible that such patients were less interested in the trial. However, for clinical trial planning, it was more important to assess whether there would be a reasonable level of enthusiasm toward the trial. A crowdsourcing based survey of the patient community represents a low-cost methodology for the assessment. Our survey received a high number of responses in a relatively short period, suggesting a sufficient number of RP patients were interested in clinical trials for the disease. Should there be low response from a survey for a clinical trial for another disease, more intensive efforts would be needed to educate the disease'-related patient community about the potential benefits of a clinical trial.

In summary, the survey results suggest positive attitudes from RP patients toward participating in the planned clinical trial and inform the design of study protocol and strategies that may promote study compliance and retention. Strategies identified through the survey include supplementing in-clinic visits with tele-visits and phone calls. Multiple ways to assess and maintain study drug compliance may be useful along with frequent communication to promote participant engagement. In addition to informing design for the

planned trial for RP, our study findings may inform planning for future clinical trials for chronic diseases. This study also demonstrates a general and low-cost methodology derived from behavioral science theories and that can be used to facilitate the design and planning of clinical trials requiring long-term commitment from participants.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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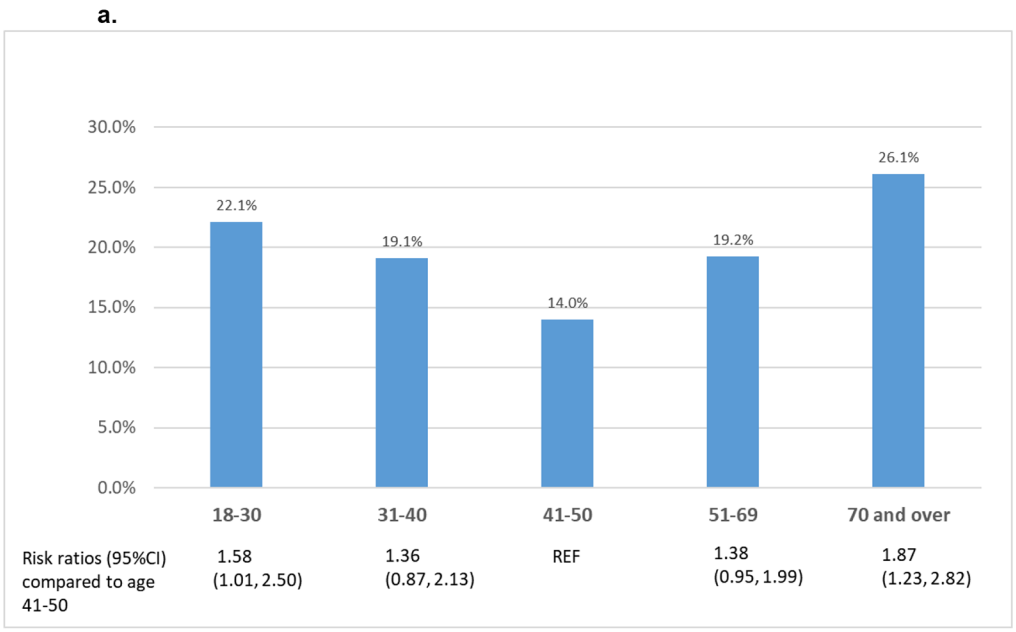
References

1. Parmeggiani F Clinics, epidemiology and genetics of retinitis pigmentosa. Current genomics. 2011;12(4):236–237. [PubMed: 22131868]
2. Campochiaro PA, Mir TA. The mechanism of cone cell death in Retinitis Pigmentosa. Progress in retinal and eye research. 2018;62:24–37. [PubMed: 28962928]
3. Fahim A Retinitis pigmentosa: recent advances and future directions in diagnosis and management. Current opinion in pediatrics. 2018;30(6):725–733. [PubMed: 30234647]
4. AAO. American Academy of Ophthalmology. Eye Health A-Z Retinitis Pigmentosa Diagnosis and Treatment. https://www.aao.org/eye-health/diseases/retinitis-pigmentosa-treatment. Published 2019. Accessed.
5. Hagger M, Cameron L, Hamilton K, Handonen N, Liutunen T. The handbook of behavior change. Cambridge, IK: Cambridge University Press; 2020.
6. Becker SJ, Guitton TG, Ring D. Predictors of missed research appointments in a randomized placebo-controlled trial. Arch Bone Jt Surg. 2014;2(3):192–198. [PubMed: 25386581]
7. Orr PR, Blackhurst DW, Hawkins BS. Patient and clinic factors predictive of missed visits and inactive status in a multicenter clinical trial. The Macular Photocoagulation Study Group. Controlled clinical trials. 1992;13(1):40–49. [PubMed: 1315662]
8. Goldman AI, Holcomb R, Perry HM Jr., Schnaper HW, Fitz AE, Frohlich ED. Can dropout and other noncompliance be minimized in a clinical trial? Report from the Veterans Administrative National Heart, Lung and Blood Institute cooperative study on antihypertensive therapy: mild hypertension. Controlled clinical trials. 1982;3(2):75–89. [PubMed: 6749426]
9. Rogers EM. Diffusion of Innovations. 5th ed. New York, NY: Free Press, A Division of Simon & Schuster, Inc.; 2003.
10. Latkin C, Dayton LA, Yi G, et al. COVID-19 vaccine intentions in the United States, a social-ecological framework. Vaccine. 2021;39(16):2288–2294. [PubMed: 33771392]



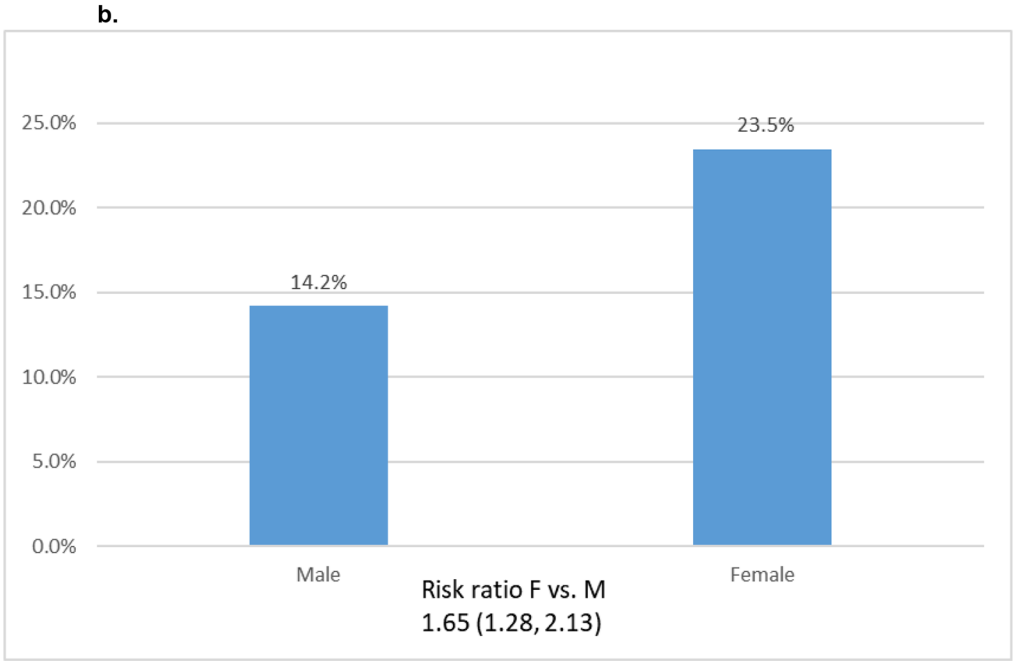


Figure 1.

a. Percentage of Low Potential of Retention by Age Group

b. Percentage of Low Potential of Retention by Gender

Table 1.

Demographics and Survey Response Summaries. A total of 1473 respondents participated the survey.

What is your age?	**N (%)**
18–30	162 (11)
31–40	197 (13.4)
41–50	284 (19.3)
51–69	602 (40.9)
70 and over	228 (15.5)
With which gender do you identify?	
Male	642 (43.6)
Female	825 (56)
Other	2 (0.1)
Prefer not to say	4 (0.3)
Approximately how long have you known that you have Retinitis Pigmentosa (RP)?	
Less than 10 years	381 (25.9)
10–20 years	301 (20.4)
21–30 years	288 (19.6)
More than 30 years	503 (34.2)
Have you done genetic testing and do you know which gene causes your RP?	
No, I have not had testing.	301 (20.4)
Yes, I have had genetic testing and the genetic cause was found.	773 (52.5)
Yes, I have had genetic testing but the genetic cause was not found.	287 (19.5)
Yes, I have had genetic testing, but I did not receive the results.	112 (7.6)
What is your level of visual acuity?	
Between 20/20 and 20/40	431 (29.3)
Between 20/50 and 20/80	267 (18.1)
Worse than 20/80	435 (29.5)
Don’t know	340 (23.1)
To get around, I use:	
Assistance of flashlight, guide dog, app, glasses	59 (4)
I don’t need any additional assistance during the day	656 (44.5)
A cane only	209 (14.2)
Requiring assistance of others	549 (37.3)
Do you use email? [a]	
No	53 (3.6)
Yes	1396 (94.8)
Do you use a mobile phone?	
No	54 (3.7)
Yes	1419 (96.3)

What is your age?	N (%)
(If Yes above) Do you receive text messages with your mobile phone?	
No	54 (3.8)
Yes	1364 (96.2)
Please answer the following questions that would be specific to a study being planned for an oral medication to slow or stop vision loss caused by RP. The study would be over a 4-year period and require taking medication two times per day over the length of the study. In addition, participants would be asked to record their usage and any missed dosing, as well as periodic visits with participating a physician.	
Assuming you met eligibility requirements, how enthusiastic would you be about participating in such a study?	
Very enthusiastic	895 (60.8)
Somewhat enthusiastic	262 (18)
Potentially interested	265 (17.8)
Not interested	51 (3.5)
If you entered in the study mentioned in the previous section, how willing would you be to participate in the following:	
A clinical visit with a doctor every 4 to 5 months for 45 months. [b]	
Very willing	932 (80.6)
Somewhat willing	218 (18.8)
Not willing	7 (0.6)
Telemedicine contact with a doctor between clinical visits. [b]	
Very willing	1045 (90.3)
Somewhat willing	95 (8.2)
Not willing	17 (1.5)
Would you like to receive text message reminders twice per day that alert you when it is time to take the medication required by the aforementioned study? [b]	
Yes	748 (64.7)
No	254 (22)
I don’t know	124 (10.7)
I don’t receive text messages	31 (2.7)
If there was a system that would allow you to report missing dosages or problems related to medication prompted by a text message, how often would you be willing to receive these text message prompts? [b]	
Daily	549 (47.5)
Weekly	343 (29.6)
Every 2 weeks	32 (2.8)
Monthly	40 (3.5)
I would not want to receive text messages	70 (6.1)
I don’t know how I would feel about that	84 (7.3)
I don’t receive text messages	39 (3.4)

a: This question was added to the survey after 24 respondents have participated in the survey and thus response is not available for the first 24 respondents.

b: N=1157 for patients who responded “Very enthusiastic” or “Somewhat enthusiastic” about trial participation and thus considered as likely being enrolled.

Table 2.

Risk of Low Retention Potential by Patient Characteristic

	Low Retention Potential	
	N (%)	p-value
Age group		
18 to 30	29 (22.14)	
31 to 40	32 (19)	
41 to 50	32 (14)	0.049
51 to 69	90 (19.2)	
70 and over	42 (26.1)	
Gender [a]		
Male	72 (14.2)	<.001
Female	152 (23.5)	
Approximately how long have you known that you have Retinitis Pigmentosa (RP)?		
Less than 10 years	50 (16.2)	
10 to 20 years	48 (20.6)	0.29
21 to 30 years	52 (22.7)	
More than 30 years	75 (19.4)	
Have you had genetic testing?		
No, I have not had testing.	45 (20.4)	
Yes, I have had genetic testing and the genetic cause was found.	110 (17.6)	0.32
Yes, I have had genetic testing but the genetic cause was not found.	51 (22.9)	
Yes, I have had genetic testing, but I did not receive the results.	19 (21.8)	
What is your visual acuity level?		
Between 20/20 and 20/40	63 (17.6)	
Between 20/50 and 20/80	45 (20.8)	0.21
Don’t know	59 (23.5)	
Worse than 20/80	58 (17.5)	
Do you use email?		
No	9 (29)	0.17
Yes	212 (19.2)	
Do you use a mobile phone?		
No	9 (24.3)	0.45
Yes	216 (19.3)	

[a]: Responses other than male/female were excluded from the analysis due to low numbers.