

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Narrative Medicine to investigate the quality-of-life and emotional impact of inherited retinal disorders through the perspectives of patients, caregivers, and clinicians: an Italian multicentre project.
<b>AUTHORS</b>	Simonelli, Francesca; Sodi, Andrea; Falsini, Benedetto; Bacci, Giacomo; Iarossi, Giancarlo; Di Iorio, Valentina; Giorgio, Dario; Placidi, Giorgio; Andrao, Assia; WG, BIRDS; Reale, Luigi; Fiorencis, Alessandra; Aoun, Manar

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Roborel de Climens, Aude IQVIA France, Patient-Centered Solutions
<b>REVIEW RETURNED</b>	14-Mar-2022

<b>GENERAL COMMENTS</b>	<p>L110 – ISTUD to be developed</p> <p>L121 - Did caregivers of pediatrics also receive guidelines to support pediatrics in writing? Were they recommended to ask specific questions? or only to write down pediatrics' thoughts?</p> <p>L139 to 141 – why providing this paragraph if patients and caregivers were NOT involved in a, b and c?</p> <p>L160 to 161- as for Bury's classification, the authors should clarify definitions of the disease-, illness- and sickness-related aspects, what is considered within each, and the differences between them.</p> <p>L193 – surprising to see that none of the patients' narratives included contingent narratives; i.e. condition's immediate effects on their daily life, to be discussed</p> <p>L268-271 - What about overall writing experience for patients? Information collected from the patients is missing here.</p> <p>L290- typo: 'they' should be replaced by 'their'</p> <p>L332-334 – the difference in patient overall perception of QoL compared to caregivers' perception (Figure 5) should be further discussed here. Patients' coping strategies could be one explanation, another one could be that caregivers with no visual impairment could have a different perception of how the disease impact patients' life/ patients may consider their sight as more acceptable than caregivers without knowing better</p> <p>L375 – the authors should discuss more the PROs &amp; CONS of NM, comparing it to semi-structured in-depth interviews that are frequently used in qualitative research to investigate disease symptoms and daily life impacts from the patient or caregiver perspective, as highlighted in reference 35 (Bredart et al.). They should also explain the reasons for doing NM with some populations here but in-depth interviews with MDT professionals and PA members.</p>
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<b>REVIEWER</b>	Garip, Gulcan University of Derby
<b>REVIEW RETURNED</b>	14-Apr-2022

<b>GENERAL COMMENTS</b>	Thank you for the opportunity to review the paper titled "Narrative Medicine to investigate the quality-of-life and emotional impact of
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RPE65-related inherited retinal disorders through the perspectives of patients, caregivers, and clinicians: an Italian multicentre project".

At the start of the paper, it could be useful to some readers to spell out 'BIRDS' working group at the first instance. This does come later on in the paper "The Beat of IRD stories".

#### Abstract

The objectives state that the study is about the impact of vision-related quality of life but then in key words, quality of life, is stated. Please adopt a consistent approach in terms of which is being explored. It would be useful to provide some detail about whether interviews took place online, over the phone or face to face?

#### Strengths and limitations

Of the three bullet points included as Strengths and limitations of the study, the first point is definitely a strength but the latter two points could be explained a bit further as to how they are a strength (2nd point) or limitation (3rd point).

#### Introduction

Line 68 - 'for' functional vision

Line 81 - reference 17 is a review of studies, rather than an example of a study

Line 102 - consider adding 'in Italy' at the end of the sentence.

#### Methods

Please further clarify whether the Patient Association member was part of the research team or a participant of the study? Line 134 states these individuals were interviewed but unclear whether they had experience of the condition themselves (so a patient?).

Please clarify whether there was a minimum duration of time that a patient needed to be diagnosed with IRD to be eligible to take part in the study.

Narrative Medicine is a method and does not automatically tell us what philosophical stance was adopted in the analysis of the data.

Could a sentence to define illness plot be provided?

Please could you explain at around line 159 why paediatric narratives were not included?

The statement under Patient and public involvement seems a bit odd. If there's any explanation for why this was the case, this would be useful to some readers.

Under analysis, the authors mention open interpretive coding but no references are cited. If the classifications were applied deductively then it is unclear how this is open interpretive coding to establish topics. What was the justification for asking participants to use metaphors to describe their experiences? A reference would be useful.

#### Results

In Table 1, under which category is the PA member info included in? It would be helpful for line 178 to be further clarified for readers to understand which data informed the findings for each of the 4 main lines. For example, (b) what data fed into this section? As there are narratives and interviews, and other forms of data collected - it is

	<p>difficult for the reader to know what data the authors are drawing on when presenting findings.</p> <p>Discussion Insightful considerations and implications for clinical practice have been presented.</p> <p>Overall, it is commendable that the authors have brought together the perspectives of many different groups to investigate the experiences of people with RPE65-related IRDs. Each sub-sample could have formed its own study so as to allow more in-depth focus in capturing the views of a particular group, particularly where there are differences in the responses from different groups as based on the descriptive data.</p> <p>Thank you for submitting SRQR - this is very helpful and good practice.</p> <p>Supplementary file 2, 2.1 - do you have considerations about how well the instructions in 2.1 worked for paediatric patients? Supplementary file 3 does not contain any examples from younger patients and so I wonder whether this is something to think about for future research, i.e., different approach to gaining narratives from younger patients?</p>
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## VERSION 1 – AUTHOR RESPONSE

### Reviewer 1

**Comment 1** – ISTUD to be developed.

Response – Thank you for inviting us to be clearer. We revised accordingly.

Changes – We revised the sentence as follows (changes are marked in red):

[Methods] In July 2020, the Steering Committee – composed of five retinologists working in these centres and a Patient Association (PA) member – participated in an online meeting conducted by researchers from Istituto Studi Direzionali (ISTUD), Healthcare Area to be trained in NM and to discuss the project’s goals and design; the Steering Committee, together with other IRD specialists from these centres, were then invited to engage patients and caregivers in participating in the research by accessing the project’s webpage <http://www.medicinanarrativa.eu/birds>.

**Comment 2** – Did caregivers of pediatrics also receive guidelines to support pediatrics in writing?

Were they recommended to ask specific questions? or only to write down pediatrics’ thoughts?

Response – Thank you for inviting us to be more precise. Caregivers did not receive guidelines to support paediatric patients in writing, except oral recommendations by involved clinicians. The investigation tool addressed to paediatric patients corresponded to that addressed to adult patients. We revised accordingly.

Changes – We revised this part as follows:

[Methods] Patients were invited to share their narratives either by writing or recording an audio file; also, caregivers were allowed to support paediatric patients in writing their narratives following the project's data collection tools.

**Comment 3** – Why providing this paragraph if patients and caregivers were NOT involved in a, b and c?.

Response – Thank you for this comment. However, the BMJ Open requires this paragraph even if patients are not involved: [https://bmjopen.bmj.com/pages/authors/#reporting\\_patient\\_and\\_public\\_involvement\\_in\\_research](https://bmjopen.bmj.com/pages/authors/#reporting_patient_and_public_involvement_in_research).

Changes – No changes to the manuscript.

**Comment 4** – as for Bury’s classification, the authors should clarify definitions of the disease-, illness- and sickness-related aspects, what is considered within each, and the differences between them.

Response – Thank you for inviting us to be clearer. We revised accordingly.

Changes – We revised the sentence as follows (changes are marked in red):

[Methods] Moreover, adult patients’ and caregivers’ narratives and parallel charts were classified following: (a) Kleinman’s classification [23], which identifies *disease-*, *illness-*, and *sick-ness*-related aspects in narratives, respectively concerning the biomedical description of a condition, its personal and emotional experience, and its social and cultural perception; (b) Bury’s classification [39], which distinguishes among *contingent narratives* (concerning a condition’s immediate effects on daily life), *core narratives* (connecting the illness experience to deeper and cultural levels of meaning) and *moral narratives* (highlighting an evaluative and social dimension).

**Comment 5** – surprising to see that none of the patients’ narratives included contingent narratives; i.e. condition’s immediate effects on their daily life, to be discussed.

Response – Thank you for inviting us to further discuss this point. The voluntary basis of the participation in the project may partially explain the lack of contingent narratives among patients: it is possible that patients that did not want to share their narrative avoided to participate in the project. We highlighted this point together with the other limitations.

Changes – We revised as follows (changes are marked in red):

[Discussion] Since narratives were anonymous, we are not able to precisely state the misalignment between patients and caregivers regarding the performance of daily activities and the perception of VRQoL; moreover, the voluntary participation in the project may have constituted a selection bias and included mostly patients more comfortable in writing.

**Comment 6** – What about overall writing experience for patients? Information collected from the patients is missing here.

Response – Thank you for inviting us to highlight this finding. We revised accordingly.

Changes – We revised the sentence as follows:

[Results] Overall, participants described writing as a positive experience: 80% of patients re-ported that narrative was a positive experience, and 20% stated to have felt a sense of free-dom in sharing the illness experience. Twenty-seven percent of the caregivers' narratives and 21% of the parallel charts reported to consider it useful to raise awareness about these conditions; however, they also highlighted negative feelings, such as fatigue or sadness, in 14% and 8% of cases, respectively.

**Comment 7** – typo: 'they' should be replaced by 'their'.

Response – Thank you for this typo correction. We revised accordingly.

Changes – We revised the sentence as follows:

[Results] While the latter may face a couple crisis due to the progression of the impairment, the former often deal with the failure of the “perfect child” dream, the hope that their chil-dren will heal and a strong sense of guilt for the inheritability of the condition.

**Comment 8** – the difference in patient overall perception of QoL compared to caregivers' perception (Figure 5) should be further discussed here. Patients' coping strategies could be one explanation, another one could be that caregivers with no visual impairment could have a different perception of how the disease impact patients' life/ patients may consider their sight as more acceptable than caregivers without knowing better.

Response – Thank you for this important insight. We highlighted the different perception between patients and caregivers in the Discussion, and we believe that this issue is close to the concept of “normal sight” emerging from early onset patients' narratives. We already highlighted the misalign-ment between patients and caregivers, but we have no further elements to precisely address it – as stated in the limitations. However, we believe that your point is critical, we therefore integrated it in our Discussion.

Changes – We revised as follows:

[Discussion] Two considerations may be emphasised. On the one side, the narratives and survey data show misalignment between the patient's and the caregiver's perception of the former's limitation in activities and in VRQoL, where patients report a higher perceived VRQoL, and conversely a lower performance while carrying out daily tasks: we remark that patients' coping strategies may represent a possible explanation and – at the same time – not visually impaired caregivers may have a different perception of IRD impact on patients' life; however, this issue needs further investigations.

**Comment 9** – the authors should discussed more the PROs & CONs of NM, comparing it to semi-structured in-depth interviews that are frequently used in qualitative research to investigate disease symptoms and daily life impacts from the patient or caregiver perspective, as highlighted in

reference 35 (Bredart et al.). They should also explain the reasons for doing NM with some populations here but in-depth interviews with MDT professionals and PA members.

Response – Thank you for inviting us to discuss this issue further. The illness plot allows a more introspective and reflecting exercise, that we – also basing on previous NM projects – decided to address to patients, caregivers, and treating clinicians; the illness plot also allows confrontation within the same group. We decided to address in-depth interviews to MDT professionals and PA member since we were not looking for an introspective experience for them, but for insights into clinical practice and suggestions regarding the broader care pathway.

Changes – We revised as follows (changes are marked in red):

[Methods] Furthermore, in-depth interviews [35] were conducted with MDT professionals involved in IRD care pathway and a PA member, caregiver of a person with an RPE65-related IRD, to facilitate the emergence of patient- and care pathway- related issues further and to delve into organisational aspects without proposing to these professionals the introspective experience of writing; the interviewees approved the transcripts before the analysis.

[Discussion] RPE65-related IRDs critically impact several quality-of-life domains, while the emotional aspects of RPE65-related IRDs emerge as crucial while making sense of the condition and during the clinical encounter: the tension between the individual and the social dimensions of these conditions emerged as informative of the care pathway challenges and real-life experiences, and may be better addressed through new investigation tools, as claimed by the in-depth interviews. The NM approach has proved suitable for this purpose since sharing the illness experience by writing allows for more introspective and reflective knowledge, that may integrate the one-to-one level of in-depth interviews used in researching the living with a certain condition.

## **Reviewer 2**

**Comment 1** – At the start of the paper, it could be useful to some readers to spell out 'BIRDS' work-ing group at the first instance. This does come later on in the paper "The Beat of IRD stories".

Response – Thank you for inviting us to be clearer. We revised accordingly.

Changes – We spelled out “BIRDS” at the first instance.

**Comment 2** – The objectives state that the study is about the impact of vision-related quality of life but then in key words, quality of life, is stated. Please adopt a consistent approach in terms of which is being explored. It would be useful to provide some detail about whether interviews took place online, over the phone or face to face?



Response – Thank you for inviting us to be clearer and more consistent. We revised accordingly.

Changes – We changed the keywords “quality of life” in “vision-related quality of life”. In the abstract, we specified that the in-depth interview were remote.

**Comment 3** – Of the three bullet points included as Strengths and limitations of the study, the first point is definitely a strength but the latter two points could be explained a bit further as to how they are a strength (2nd point) or limitation (3rd point).

Response – Thank you for inviting us to be clearer. We revised accordingly.

Changes – We implemented this section as follows (changes are marked in red):

- Inclusion of paediatric patients’ perspectives.
- Integration of patients’ and caregivers’ perspectives to that of retinologists and hospital-based multidisciplinary professionals.
- Participants did not equally represent the geographical areas of Italy.
- Restrictions due to Sars-CoV-2 pandemic impacted the number of patients visiting the clinics, so involved healthcare professionals had to engage them virtually.
- Patients and caregivers participated in the project on a voluntary basis, and Sars-CoV-2 pandemic could have created a bias on the on the motivation to join the research.

**Comment 4** – 'for' functional vision.

Response – Thank you for suggesting this change. We revised accordingly.

Changes – We revised as follows (changes are marked in red):

A progressive loss of photoreceptor cells and an impairment for visual function characterise the IRDs related to mutations involving the RPE65 gene and gradually lead to an irreversible visual decline [3], and potentially to blindness [4]; Leber congenital amaurosis (LCA) and retinitis pigmentosa (RP) represent the most common forms [5,6]

**Comment 5** – reference 17 is a review of studies, rather than an example of a study.

Response – Thank you for inviting us to be clearer. We revised accordingly.

Changes – We revised as follows (changes are marked in red):

[Introduction] Against this backdrop, other studies and reviews [16,17] suggest that a holistic and multidisciplinary approach – also addressing IRDs emotional and social aspects – is crucial to support patients and their caregivers.

**Comment 6** – consider adding 'in Italy' at the end of the sentence.

Response – Thank you for inviting us to be clearer. We revised accordingly.

Changes – We revised as follows (changes are marked in red):

[Introduction] Although other studies integrated the perspectives of both patients and care-givers [28, 29], to the best of our knowledge, this is the first project that also engages the retinologists and hospital-based multidisciplinary professionals (MDTs) in investigating the RPE65-related IRDs illness experience in Italy.

**Comment 7** – Please further clarify whether the Patient Association member was part of the re-search team or a participant of the study? Line 134 states these individuals were interviewed but unclear whether they had experience of the condition themselves (so a patient?).

Response – Thank you for inviting us to be more precise. The PA member was interviewed as a caregiver of a person with an RPE65-related IRD. We revised accordingly.

Changes – We revised as follows (changes are marked in red):

[Methods] Furthermore, in-depth interviews [35] were conducted with MDT professionals involved in IRD care pathway and a PA member, caregiver of a person with an RPE65-related IRD, to facilitate the emergence of patient-related issues further; the interviewees approved the transcripts before the analysis.

**Comment 8** – Please clarify whether there was a minimum duration of time that a patient needed to be diagnosed with IRD to be eligible to take part in the study.

Response – Thank you for inviting us to be more precise. There was no minimum length of follow up time post-diagnosis to participate in the research. We revised accordingly.

Changes – We revised as follows (changes are marked in red):

[Methods] A clinical RPE65-related IRD diagnosis without a minimum length of follow-up time post-diagnosis or the caregiving of a person with an RPE65-related IRD constituted the eligibility criteria for patients and caregivers, as well as the willingness to share their illness experience; however, the ability to write or communicate in Italian was critical for the inclusion.

**Comment 9** – Narrative Medicine is a method and does not automatically tell us what philosophical stance was adopted in the analysis of the data.

Response – Thank you for inviting us to be clearer. We revised accordingly.

Changes – We revised as follows (changes are marked in red):

[Methods] Researchers analysed the sociodemographic data through descriptive statistics; answering survey questions or filling in fields in the illness plots and parallel charts was not mandatory, so sample size may vary. Narratives were entered into Nvivo software [38] for coding and content analysis [39]. Three narratives for each group and one in-depth interview

were collectively coded to assess the consistency across team members; then, each narrative and in-depth interview were separately coded and reviewed during weekly peer debriefings to limit any interpretation bias.

Open interpretive coding was employed to identify and analyse the emerging contents in all narratives and in-depth interviews.

**Comment 10** – Please could you explain at around line 159 why paediatric narratives were not included?

Response – Thank you for inviting us to be more precise. We revised accordingly.

Changes – We included the following sentence:

[Methods] Researchers did not apply retrospective classifications of narratives to paediatric patients' narratives since their caregivers' in-writing support could have affected the narrative style and the word choice.

**Comment 11** – The statement under Patient and public involvement seems a bit odd. If there's any explanation for why this was the case, this would be useful to some readers.

Response – Thank you for this useful comment. However, this paragraph is required the journal

even if patients are not involved:

[https://bmjopen.bmj.com/pages/authors/#reporting\\_patient\\_and\\_public\\_involvement\\_in\\_research](https://bmjopen.bmj.com/pages/authors/#reporting_patient_and_public_involvement_in_research).

Changes – No changes in the manuscript.

**Comment 12** – Under analysis, the authors mention open interpretive coding but no references are cited. If the classifications were applied deductively then it is unclear how this is open interpretive coding to establish topics. What was the justification for asking participants to use metaphors to describe their experiences? A reference would be useful.

Response – Thank you for inviting us to be clearer. We revised accordingly.

Changes – We added a reference for interpretive coding and content analysis; we highlight that retrospective classifications constitute a different moment in the analysis process, as reported in Methods. We added a reference to support the investigation of metaphors to trace spontaneous associations through daily language on the illness experience.

**Comment 13** – In Table 1, under which category is the PA member info included in?

Response – Thank you for inviting us to be clearer. We revised accordingly.

Changes – We named the last category in Table 1 as “Participants to in-depth interviews”, to include both the five professionals from multidisciplinary teams and the PA member.

**Comment 14** – It would be helpful for line 178 to be further clarified for readers to understand which data informed the findings for each of the 4 main lines. For example, (b) what data fed into this section? As there are narratives and interviews, and other forms of data collected – it is difficult for the reader to know what data the authors are drawing on when presenting findings.

Response – Thank you for inviting us to be clearer. We revised accordingly.

Changes – We included the following sentence:

[Results] Narratives informed (a) and (b), while (c) was investigated through both narratives and quantitative data from the survey; in-depth interviews alone informed (d).

**Comment 15** – Supplementary file 2, 2.1 - do you have considerations about how well the instructions in 2.1 worked for paediatric patients? Supplementary file 3 does not contain any examples from younger patients and so I wonder whether this is something to think about for future research, i.e., different approach to gaining narratives from younger patients?

Response – Thank you for inviting us to give more details on this critical topic. However, we did not have any further consideration on the illness plot addressed to paediatric patients related to our findings, but we believe it represents an issue to be discussed in further research. Supplementary File 3 contains an underage patient's narrative.

Changes – No changes in the manuscript and in Supplementary file 3.

#### VERSION 2 – REVIEW

<b>REVIEWER</b>	Garip, Gulcan University of Derby
<b>REVIEW RETURNED</b>	04-Jul-2022
<b>GENERAL COMMENTS</b>	Thank you for the revisions. Congratulations.