PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Needs of people with rare diseases that can be supported by electronic resources: a scoping review
AUTHORS	Long, Janet; Best, Stephanie; Nic Giolla Easpaig, Bróna; Hatem, Sarah; Fehlberg, Zoe; Christodoulou, John; Braithwaite, Jeffrey

VERSION 1 – REVIEW

REVIEWER	Robinson, Peter The Jackson Laboratory for Genomic Medicine
REVIEW RETURNED	19-Feb-2022

GENERAL COMMENTS	The authors present a review of 72 papers outlining the needs of people with a rare disease, or their carers that could be addressed by an e-resource. The article is clearly presented and offers a reasonably comprehensive overview of current online resources that will be of interest to rare disease professionals. The article could be improved by describing what the added value of each type of online resource is. Also, it would be nice to have some discussion of where the field is likely to go. For instance, what is the current status of mHealth for rare diseases? Minor comments This paper is one of two results papers scoping consumer-facing electronic resources for people with a rare disease. => What is the lack in the other paper that motivates the need for the current manuscript? either hypothesised and described a particular electronic resource => How can one hypothesise an electronic resource? Do you mean propose or design? Bleeding disorders in women From the context I think this item refers to the specific experiences of women with non sex-specific Mendelian rare bleeding disorders? etc => etc should be etc.

REVIEWER	Atalaia, Antonio INSERM, Centre de Recherche en Myologie U974
REVIEW RETURNED	03-May-2022

GENERAL COMMENTS	The current paper scans the needs of people with a rare disease and how they can be addressed and improved through different electronic resources. A PRISMA for scoping reviews tool guides the scoping exercise, guaranteeing solid methodological background. The authors pre-selected 21 different rare diseases or disease groups to cover and justify the choice with the findings of a "2017 report by the global investment bank, Torreya that looked at the most common types of rare diseases that were a focus for therapeutic companies around the world". This sentence points to reference 32. It took me some time to find ref 32 as several entries from the Haemophilia journal in Bibliography are incomplete and need to be corrected. The correct reference is D'Ambrosio, C. "Open versus closed social networking groups". Haemophilia 2014 May;20 Suppl 3:1-188" (doi: 10.1111/hae.12400), which is part of a volume with "Abstracts of the WFH 2014 World Congress, May 11-15, 2014, Melbourne, Australia". The abstract does not mention the point made in the sentence, and some adequate referencing is required to justify the selection of diseases. The choice was guided by the existence of in-pipeline treatments for the conditions. However, the found Bibliography has to do with different support needs (disease management, education/information, localisation of expert centres and peer-to-peer social network support). Still, it does not relate to any drug treatment in specific, and the criterium used may need further discussion given this. However, two of the entities are self-justified for inclusion because of the high frequency of papers found (Cystic Fibrosis and Haemophilia). The assessment of needs in Table 2 is a main deliverable of the paper, serving for current and future investigation on the subject. However, identifying four domains and 23 sub-domains presumably follows a framework neither explained in the text nor based on a bibliographic reference. I would say that the papers listed fall into six divisions (instead of the four domains): 1- disease management tools/apps (31, with one finding triggering multiple reports: 3 duplications and 1 triplication) 2- expert-centres locating tools/apps 3- education or information supplied by websites/apps (21 references) 4- peer-to-peer disease-specific social media tools/apps (14 references, with one duplication) 5- assessment of needs addressable by electronic tools (2 references) 6- patient registries (2 references) Therefore, a revised version will benefit from clarifying the subdivision presented more transparently. The discussion contains valuable conclusions regarding the use of telehealth and teleconsultation. It shows how remote diagnosis can be made in chronic conditions using tools and wearables that provide exact follow-up measurements. I would have valued a more extensive discussion regarding information and education tools on one side and peer-to-peer networks as sources of knowledge and aids for case management. In the case of peer-to-peer networks, I fear that without proper curation, misinformation may spread. At the finish of the paper, the authors point toward its limitations. However, I think that the article is not systematic and exhaustive, as the authors have chosen a group of entities to explore, as previously explained. I am bothered by the criteria of selection that need a better explanation and the organisation of the findings. I

	believe that with a bit of review of these aspects, beneficial suggestions can arise from this manuscript, though.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1: P Robinson	The authors present a review of 72 papers outlining the needs of people with a rare disease, or their carers that could be addressed by an e-resource. The article is clearly presented and offers a reasonably comprehensive overview of current online resources that will be of interest to rare disease professionals.	Thank you for your review.
	The article could be improved by describing what the added value of each type of online resource is.	We have added into the Methods section a table that explains further the features and benefits of different types of e-resources. Table 2 p.9
	Also, it would be nice to have some discussion of where the field is likely to go. For instance, what is the current status of mHealth for rare diseases?	We make the point more clearly now in the Introduction that we are (to our knowledge) the first to scope the rare disease field. We have added some comments in the discussion, including on page 16: *Currently, the efficacy of e-resources for people with a rare disease is being realised one disease group at a time. While each disease has its unique features, we have shown here that the needs of all people with rare disease are basically the same. These domains of needs should be addressed by any team wishing to develop new e-resources for this cohort*.
	Minor comments	
	This paper is one of two results papers scoping consumer-facing electronic resources for people with a rare disease. => What is the lack in the other paper that motivates the need for the current manuscript?	We agree this was not explained well and have decided to remove the sentence. The other paper is a review of apps sourced from Google Play and the Apple App store. This paper provided the framework of needs it used to assess the apps but is not yet published.
	either hypothesised and described a particular electronic resource => How can one hypothesise an electronic resource? Do you mean propose or design?	We agree it is confusing language – we have amended in the text.

	Bleeding disorders in women From the context I think this item refers to the specific experiences of women with non sex-specific Mendelian rare bleeding disorders?	This was the language used by people with the disorder. We have added a footnote as suggested.
	etc => etc should be etc.	This has been corrected.
Reviewer 2: A Atalaia		
	The current paper scans the needs of people with a rare disease and how they can be addressed and improved through different electronic resources. A PRISMA for scoping reviews tool guides the scoping exercise, guaranteeing solid methodological background	Thank you for your close reading of the paper.
	The authors pre-selected 21 different rare diseases or disease groups to cover and justify the choice with the findings of a "2017 report by the global investment bank, Torreya that looked at the most common types of rare diseases that were a focus for therapeutic companies around the world". This sentence points to reference 32. It took me some time to find ref 32 as several entries from the Haemophilia journal in Bibliography are incomplete and need to be corrected. The correct reference is D'Ambrosio, C. "Open versus closed social networking groups". Haemophilia 2014 May;20 Suppl 3:1-188" (doi: 10.1111/hae.12400), which is part of a volume with "Abstracts of the WFH 2014 World Congress, May 11-15, 2014, Melbourne, Australia". The abstract does not mention the point made in the sentence, and some adequate referencing is required to justify the selection of diseases. The choice was guided by the existence of in-pipeline treatments for the conditions. However, the found Bibliography has to do with different support needs (disease management, education/information, localisation of expert centres and peer-to-peer social network support). Still, it does not relate to any drug treatment in specific, and the criterium used may need further discussion given this. However, two of the entities are self-justified for inclusion	We apologise for the confusion caused here by an incorrect reference. The correct reference is 18: Ghosh 2019. There are an estimated 7-8,000 rare diseases and many have synonyms. It was unfeasible to search for all by name, of course. As the generic search terms “rare dis*” or “orphan dis*” yielded very few papers we settled on the only published list we could find of the most common rare diseases. As these are targets of therapeutic investment, we also added in MRCD as a significant class of rare diseases which have no pharmaceutical treatments at this time. We state very clearly that it is not ideal and this is covered in the limitations.

	because of the high frequency of papers found (Cystic Fibrosis and Haemophilia).	
	The assessment of needs in Table 2 is a main deliverable of the paper, serving for current and future investigation on the subject. However, identifying four domains and 23 sub-domains presumably follows a framework neither explained in the text nor based on a bibliographic reference.	The framework is an inductive product of the data extraction from the articles and conference abstracts. As explained in the Methods on page 7: *The final step was collating and synthesising the needs of people with a rare disease discussed in the articles, looking for similarities and differences across different rare diseases, and the electronic solutions proposed for each. From this, a framework was developed describing the synthesised domains of needs and examples of electronic resources designed to meet the need.*
	I would say that the papers listed fall into six divisions (instead of the four domains): 1- disease management tools/apps (31, with one finding triggering multiple reports: 3 duplications and 1 triplication) 2- expert-centres locating tools/apps 3- education or information supplied by websites/apps (21 references) 4- peer-to-peer disease-specific social media tools/apps (14 references, with one duplication) 5- assessment of needs addressable by electronic tools (2 references) 6- patient registries (2 references) Therefore, a revised version will benefit from clarifying the subdivision presented more transparently.	Thank you for your engagement with the review and careful re-analysis. We have reviewed both sets of classifications (ours and yours) and have made a few changes. The review was very much focussed on consumer-facing resources (inclusion /exclusion criteria p6) and was inductively developed from the set of literature that we found. It therefore contrasts slightly from recommendations and policy documents (e.g., from EURORDIS). So, for example, we deliberately placed patient registries with provision of information to consumers. The domains of need now read: 1. Chronic diseases requiring self-management 2. Lack of high-quality information on all aspects of the rare disease 3. Specialist centres may be geographically dispersed and/or hard to find (your division 2 and 5) 4. Social isolation from peers and advice networks
	The discussion contains valuable conclusions regarding the use of telehealth and teleconsultation. It shows how remote diagnosis can be made in chronic conditions	This is a good point about the possibility of misinformation on peer support sites. We have added to our section in the discussion on page 16:

	using tools and wearables that provide exact follow-up measurements. I would have valued a more extensive discussion regarding information and education tools on one side and peer-to-peer networks as sources of knowledge and aids for case management. In the case of peer-to-peer networks, I fear that without proper curation, misinformation may spread.	*Resources supporting peer to peer support for people and carers of children with a rare disease were well represented in the articles. The value of social support from someone who is on the same journey is well documented. (e.g., 1)*) Although the quality of the advice and information exchanged on social support platforms is *often criticised,(2) there was no evidence of this in our sample (possibly a publication bias). Four studies critiqued the content of posts on social support platforms for people with different rare diseases and found them to be overwhelmingly positive and supportive.(3-6) Real-time, knowledgeable solutions to problems, plus emotional support were demonstrated as highly valuable to members and these benefits were noted as important goals for any proposed new e-resources.(7, 8).*
	At the finish of the paper, the authors point toward its limitations. However, I think that the article is not systematic and exhaustive, as the authors have chosen a group of entities to explore, as previously explained. I am bothered by the criteria of selection that need a better explanation and the organisation of the findings. I believe that with a bit of review of these aspects, beneficial suggestions can arise from this manuscript, though.	Thank you for your supportive comments. We have amended our wording in the Limitations on page 18 to be clearer: *The main limitation to our review was the difficulty capturing articles focussed on people with a rare disease. Our search was systematic but does not claim to be exhaustive. In particular, the search term set to capture rare diseases was problematic*…

1. Foronda CL, Kelley CN, Nadeau C, Prather SL, Lewis-Pierre L, Sarik DA, et al. Psychological and Socioeconomic Burdens Faced by Family Caregivers of Children With Asthma: An Integrative Review. Journal of Pediatric Health Care. 2020;34(4):366-76.
2. Suarez-Lledo V, Alvarez-Galvez J. Prevalence of Health Misinformation on Social Media: Systematic Review. J Med Internet Res. 2021;23(1):e17187.
3. Haik D, Kashanchi K, Tajran S, Heilbronn C, Anderson C, Francis DO, et al. The Online Support Group as a Community: A Thematic Content Analysis of an Online Support Group for Idiopathic Subglottic Stenosis. Annals of Otology, Rhinology and Laryngology. 2019;128(4):293-9.
4. Kauw D, Repping-Wuts H, Noordzij A, Stikkelbroeck N, Hermus A, Faber M. The Contribution of Online Peer-to-Peer Communication Among Patients With Adrenal Disease to Patient-Centered Care. J Med Internet Res. 2015;17(3):e54.
5. Walker KK. Cognitive and affective uses of a Thoracic Outlet Syndrome Facebook support group. Health Communication. 2014;29(8):773-81.

6. Wittmeier K, Holland C, Hobbs-Murison K, Crawford E, Beauchamp C, Milne B, et al. Analysis of a Parent-Initiated Social Media Campaign for Hirschsprung's Disease. J Med Internet Res. 2014;16(12):e288.
7. Castro RA, Chougui K, Bilodeau C, Tsimicalis A. Exploring the Views of Osteogenesis Imperfecta Caregivers on Internet-Based Technologies: Qualitative Descriptive Study. J Med Internet Res. 2019;21(12):e15924.
8. Ruther DF, Sebode M, Lohse AW, Wernicke S, Bottinger E, Casar C, et al. Mobile app requirements for patients with rare liver diseases: A single center survey for the ERN RARE-LIVER. Clinics and Research in Hepatology and Gastroenterology. 2021;45(6).

VERSION 2 – REVIEW

REVIEWER	Robinson, Peter The Jackson Laboratory for Genomic Medicine
REVIEW RETURNED	13-Jun-2022

GENERAL COMMENTS	Thank you for addressing my comments.