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Needs of people with rare diseases that can be supported by electronic resources: a scoping review

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Abstract

Objectives:

Rare diseases are characterised by low incidence, often with little evidence for effective treatments. Isolated patients and specialist centres for rare diseases are increasingly connected thanks to the internet. This scoping review aimed to identify issues facing people with a rare disease that authors report may be addressed by electronic resources (mobile applications, websites, social media platforms, telehealth and online portals).

Methods:

Guided by the PRISMA-ScR guidelines, peer-reviewed literature was searched using terms for rare disease (incidence <1:2,000), electronic modalities (e.g., mobile phone) and patient support terms. Medline, Embase and PsycInfo were searched, supplemented by hand searches of selected journals, in July 2021. Conference abstracts were included.

Results:

The search found 383 papers. After screening there were 72 papers. Fifty-six electronic resources were described in 64 papers, while 12 papers were exploratory studies. Cystic fibrosis (n=28) was most frequently addressed, followed by haemophilia (n=16).

Four domains and 23 subdomains of needs were extracted from the papers. The domains of needs were: support for self-management, access to high-quality information, access to appropriate specialist services, and social support. Subdomains sometimes related to needs of individual rare diseases (e.g., social isolation due to infection risk in people with cystic fibrosis). Fifteen electronic resources were identified that supported parents of children with rare disorders.

Conclusions:

While it can be argued that rare diseases per se may be no less distressing or onerous to care for than a high prevalence disease, rare diseases have unique features: the lengthy odyssey to find a

diagnosis, then appropriate specialists, the lack of evidence around effective treatments, guidelines, or access to knowledgeable general health service providers. Designers of electronic resources are urged to consult key stakeholders to enhance the effectiveness and usability of resources for people with a rare disease.

Article summary

Strengths and limitations of this study

- As global pooling of data from patients with a rare disease is made possible through the internet it is timely to scope how electronic resources are changing the support available for this cohort.
- Needs were mapped out across 21 different rare diseases or disease groups.
- Electronic resources found were categorised into mobile applications, social support platforms, telehealth tools and online portals, and active (containing interactive content e.g., quizzes) and passive websites (information only).
- Individual named rare diseases/groups of diseases were included in the search terms to overcome deficiencies of searching only using “rare diseases,” but could not cover all rare diseases.

Key words

Rare disease, patient resources, patient empowerment, e-health, mobile apps

Introduction

There are an estimated 6-7,000 different types of rare disease, many of them genetic.(1) We define a rare disease as a condition that has an incidence of less than 1 per 2,000 live births in the population.(1) Examples of rare diseases are Fragile X syndrome, haemophilia A, osteogenesis imperfecta, cystic fibrosis, spinal muscular atrophy type 1, and neurofibromatosis type 2. The low incidence of rare diseases mean that specifics of individual diseases are not covered in medical education programs which must prioritise more common conditions, and also that many health professionals will have never seen a case before.(2) Rare diseases are often difficult to diagnose, leading to the often described "diagnostic odyssey."(3) The case has been made that even after this odyssey is concluded with a definitive diagnosis, the journey continues as people with a rare disease seek to access the best management care.(4)

Less than 5% of the estimated 7,000 rare diseases currently have an effective treatment.(1) The low numbers of cases of each rare disease means that evidence is often lacking to guide best practice. For example, CLN12 disease with an incidence of only 1 per million has too few people with the disease to set up a clinical trial to test the effectiveness of potential treatments or even map the "typical" progression of the disease.(5) Guidance on best practice must be determined through consensus recommendations of specialists in the condition(6, 7), which are often enhanced by the input of consumers who are living with the condition.(8)

A number of studies have explored the specific needs of people with a rare condition.(e.g., 9, 10, 11) Access to appropriate specialist services, finding a generalist health provider who is willing to learn about the condition, living with uncertainty of what is best practice and the trial and error nature of discovering it have all been reported.(e.g., 4)

Electronic resources, by which we mean mobile applications, websites, virtual monitoring devices, social media platforms, telehealth capability and online portals, hold promise of greater connectivity and collaboration in the field of rare diseases. Electronic resources are already being used to

improve understandings of rare diseases as national and international online registries, (e.g., 12, 13) and virtual research consortiums (14, 15) pool their data and consolidate findings.

Electronic resources have a key role for people living with a rare disease. It is recognised that a useful lever to accessing the best management care for people with a rare disease is empowerment, in which people become knowledgeable about their illness and feel able to advocate for their care.(16) Tools to foster empowerment are particularly relevant in this group and electronic resources hold great promise to make information and resources more easily accessible.

This paper aims to systematically scope the peer-reviewed literature to: (i) identify issues facing people with a rare disease that authors report may be addressed by electronic resources, and (ii) collate evidence around features of effective and user-friendly e-resources. This paper is one of two results papers scoping consumer-facing electronic resources for people with a rare disease.

Methods

We systematically searched for peer-reviewed literature on consumer-facing electronic resources for people with a rare disease, guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (17) (see supplementary file 1 for the completed PRISMA-ScR checklist). The search was supplemented with a hand search of relevant peer-reviewed journals. Patients and public were not directly involved in the design, reporting or dissemination plan of this paper.

Three databases, Medline, Embase and PsycInfo were searched in July 2021. No date limits were set but we only included articles in the English language. We targeted empirical peer-reviewed full articles but initial exploratory searches showed that a large proportion of the retrieved items were conference presentations on resources not reported elsewhere. These were therefore also included in the review. Search terms were developed through exploration of Medical Subject Heading terms, and key words from equivalent papers from other fields. Search strings combined terms for rare

disease, (including specific named rare disease conditions to maximise results), with patient and carer facing resources (e.g., health resources, patient participation), and terms associated with electronic resources (e.g., mobile applications, cell phone, e-health). In addition, a hand search was performed in *Orphanet Journal of Rare Diseases* (searching for patient focused electronic resources) and *Journal of Medical Internet Research* (searching for applications for rare diseases).

The definition of a rare disease as having an incidence of less than 1:2,000 was used as a guide only as the grouping together of related rare diseases muddied the waters on exact rates, as did the range of definitions employed when reporting on rare diseases. The search therefore drew on named rare conditions/groups of conditions listed in 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.[32] Imperfect as that list is, it retrieved many more useful articles than the generic rare disease terms. “Mitochondrial respiratory chain disorders” was also added as a large group of rare diseases that are not amenable to pharmaceutical treatment. The condition groups searched for by name therefore were narcolepsy, primary biliary cholangitis, Fabry disease, cystic fibrosis, haemophilia, spinal muscular atrophy, retinal dystrophy, X-linked hypophosphatemia, urea cycle disorders, pulmonary arterial hypotension, cerebral adrenoleukodystrophy, hereditary angioedema, AA amyloidosis, Cushing's syndrome, and mitochondrial respiratory chain disorders.

The following inclusion criteria needed to be met for a paper to be included: (a) the paper was framed around the needs of people diagnosed with a rare disease or group of rare diseases (defined as incidence <1:2,000 (1)); (b) the focus was on how an electronic resource could meet that need in some way (c) either hypothesised and described a particular electronic resource, or reported on the development, testing or evaluation of an actual electronic resource. Exclusion criteria were: (i) not about a rare disease or group of rare diseases; (ii) electronic resources were not consumer-facing (e.g., virtual monitoring where the consumer has a passive role and no access to the data,

applications that consumers used altruistically to collect data for researchers; electronic tools for health care professionals only).

Search results were downloaded into reference management software EndNote X9 and two researchers (JL and SB) independently screened 50% of titles and abstracts using the eligibility criteria. Disagreements were discussed until consensus was met. Remaining articles were screened by JL. Included articles were read in full and eligibility criteria again applied (by JL and validated by SB). Data was extracted from the final set: rare disease/group of diseases, name of the e-resource, need identified in the patient cohort, features of the e-resource, any other findings or observations of interest.

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.

Results

The search resulted in 383 papers. Title and abstract screening removed 223 papers and full text screening, another 33. This left 72 papers for data extraction and analysis. Figure 1 shows the PRISMA flow chart for the search.

Studies were set in 16 different countries including seven papers that included all of Europe. United States of America (n=14), the United Kingdom (n=11), and Canada (n=10) were the best represented countries. Figure 2 shows frequencies of all countries. Twenty-one different rare diseases were represented mostly in single papers, while 8 papers focused on rare diseases generally (n=8). The most common rare disease reported was cystic fibrosis (n=28) followed by haemophilia (n=19). Table 1 gives details.

<<Figure 1: PRISMA flowchart for the search. (*JMIR* = *Journal of Medical Internet Research*; *OJRD* = *Orphanet Journal of Rare Diseases*)>>

<<Figure 2: Countries in which included studies were undertaken (frequency of papers).>>

Table 1: Overview of included papers

Rare disease / group of diseases	**Number of papers**
Acute Intermittent Porphyria (AIP)	1
Addison's disease	3
Autoimmune liver diseases	1
Bleeding disorders in women	1
Complex regional pain syndrome	1
Congenital hypogonadotropic hypogonadism, Kallmann syndrome	1
Cystic fibrosis	28
Genetic eye disorders	1
Haemophilia	19
Hirschsprung's Disease	1
Idiopathic subglottic stenosis	1
Inborn errors of metabolism	1
Lymphangioleiomyomatosis	1
Narcolepsy	2
Osteogenesis Imperfecta	1
Phenylketonuria, maple syrup urine disease or tyrosinemia	1
Rare and Congenital Anaemias	1
Rare diseases	6
Rare Multisystemic Vascular Diseases	1
Thoracic Outlet Syndrome	1

Most papers reported on e-resources that were being trialled or were under development (n=56 e-resources from 64 papers), while 12 were framed as scoping exercises or explored usability of existing websites. For example, Nicholl and colleagues (18) explored the needs of people with rare diseases that could be met by a consumer facing website, Ruther and colleagues (19) researched

what people with rare liver disorders need in an app, and Aizawa and colleagues (20) critiqued information available on the internet for people with narcolepsy.

E-resources fell into five broad categories: (i) mobile applications (apps) for cell phones or tablets (n=22), (ii) social networking platforms (n=14), (iii) telehealth and virtual care platforms (n=13), (iv) websites (interactive content e.g., education modules with quizzes) (n=15), and (v) websites (passive content e.g., information) (n=7). Some e-resources fit into more than one category (e.g., WhatsApp platform for parents of newly diagnosed infants with haemophilia provided social support from other parents as well as virtual consults with specialists.(21) In these cases, the main function decided the category.

Articles described four domains and 23 sub-domains of needs of people with a rare disease or parents of children with a rare disease. A range of unique needs arising from features of individual diseases were identified (e.g., risk of life-threatening acute episodes in Addison's Disease in a context of few emergency health professionals being knowledgeable or confident to deal with adrenal crisis (22)), as well as more global needs that were common across all presentations (e.g., the scarcity of high quality, relevant information about individual rare diseases). (18-49)

Needs are summarised in Table 2 giving examples of disease specific needs in each sub-domain, and examples of the e-resources that had been developed or proposed to address those needs. Data extracted from the final set of items is given in full in supplementary file 2.

Domain	Sub-domains with disease-specific examples	e-resource examples
Chronic diseases requiring self-management	Complicated self-management (e.g., monitoring for bleeds and factor usage for haemophilia (33, 50))	Online tool (Metabolic DietAppSuite) for smartphones/desktops for 15 different Inborn Errors of Metabolism. Creates a personalised dashboard including specific nutrient goals. Food diary, nutrient counts (51)
	Some treatment regimes require detailed record keeping to optimise outcomes (e.g., treatment of infections in CF (31, 49, 52, 53))	MyCBDR (linked to Canadian Bleeding Disorder Registry (CBDR) is an app that allows people with a bleeding disorder to track infusions and add symptoms. Data can be share with all l Haemophilia Treatment Centres in Canada (33)
	Transition to self-care as adolescents become adults (e.g., teens with severe haemophilia (27, 54-56))	Smartphone app (Faccio Centro) aimed at adolescents with CF that lists daily therapy, with instructions on order, progress tracking, alerts for when to start and when checks are needed. Also can email questions to healthcare team (57)
	Exercise programs need to be tailored to the rare disease (e.g., reduced lung function and exercise tolerance in people with CF (58-60))	LAM App on smartphone with interfacing wearable devices for women with Lymphangioleiomyomatosis (LAM). Tailored exercise program physio check in (61)
	Monitoring changes in symptoms and treatments (e.g., recognising bleeds in mild haemophilia (62, 63))	MyCyFAPP calculates Pancreatic enzyme replacement therapy-doses for fat digestion, a symptoms diary, educational material, and linked to a web tool allowing health professionals to view data and give feedback (26, 28, 64)
	Burden of hospital attendance (e.g., living far away from only specialist centre for narcolepsy (65); rare diseases with high disease burden (e.g., CF (66))	An ultrasound diagnostic solution for children with haemophilia, the EMO.TI.ON. System used at home by parents or caregivers to diagnose suspected bleeds. System can transfer live images to specialist physician (67)
	Depression, anxiety, distress affect adherence to treatment regimes, which in turn affect health and quality of life (e.g., distress of parents of newly diagnosed children with haemophilia (21))	Internet delivered cognitive behavioural therapy sessions, eHealth CF-CBT guided by a qualified therapist for people with cystic fibrosis experiencing depression or anxiety (68)
Lack of high-quality information on the rare disease	Information that is readable, accessible and from a credible source (e.g., lack of specific information on rare and congenital anaemias (39))	Newborn Screening Connect (NBS Connect) provides high quality information for parents of children diagnosed with a disorder included in the newborn screening panel performed routinely in USA (41)
	Information available in your language, appropriate for your culture (e.g., Canadian haemophila resources in English and French (54, 62))	Online education package for congenital hypogonadotropic hypogonadism and the olfacto-genital syndrome is available in 20 European languages. Readability score meets recommended level (25)
	Appropriate to age group, or special needs (e.g., information for teens with CF (69))	Gene.vision website on genetic eye disorders optimised for people with impaired vision (38)
	Access to relevant clinical trials, or new research findings may be difficult to find (43)	NIH Rare Diseases Clinical Research Network (RDCRN) notifies registrants with a range of rare disorders of relevant studies (43)
	Disease specific information on niche topics like family planning (e.g., for genetic disorders such as CF (30))	Facebook group (MyGirlsBlood) for women with bleeding disorders where women can ask questions or share experiences especially around menstruation (32)

	Urgent need for disease specific information during COVID-19 pandemic (44)	Weekly webcasts on COVID for people with CF with questions through Google forms. Email notifications of webcasts sent to known patients in USA (44)
Specialist centres may be geographically dispersed and hard to find	Identifying appropriate care for rare disease (e.g., nearest specialist; appropriately trained allied health professionals (e.g., physios who know risks of exercise with haemophilia (70))	Mobile app developed by VASCERN (European Reference Network on Rare Multisystemic Vascular diseases) contains an easily searchable Directory to find closest expert and to find appropriate patient advocacy group within Europe (42)
	Burden of hospital attendance (e.g., living far away from only specialist centre; rare diseases with high disease burden (e.g., severe haemophilia (71))	Virtual Reality Visual Feedback Module for people with complex regional pain syndrome (who have few treatment options and for whom travel is onerous). After initial in-person training and assessment, can be continued at home (72)
	Knowledgeable emergency care for acute events may be hard to find (e.g., for infants with newly diagnosed haemophilia (21))	Quick response (QR coded) bracelet has a scannable QR code that links to emergency management information for people in adrenal crisis (22)
	Information on daily management may be lacking for both the person with the rare disease and the health professionals supporting them (e.g., for parents of infants with Hirschsprung's Disease (48))	Thoracic Outlet Syndrome (TOS) Awareness Facebook group for both people with TOS and health professionals. Most posts encouraging and giving sound advice (47)
Social isolation	Unable to connect with people with the same disorder (e.g., being the only parent you know with a child with a rare disorder (24))	Online forum for people with Addison's Disease or Cushing's syndrome, moderated by the Dutch Adrenal Society (35)
	Disorders that require isolation for infection control, or safety are isolated from unaffected peers as well (e.g., fracture risk for children with OI in new surroundings (29))	Online conferences (BreatheCon) for people with cystic fibrosis who must isolate for infection control (30)
	Emotional support needed for distressed parents (e.g., for parents of children with OI (29))	Skype support groups for women with acute intermittent porphyria mediated by a porphyria experts (73)
	Support for daily management issues (e.g., online for people with idiopathic subglottic stenosis (34))	Social media campaign around living with Hirschsprung's Disease: Shit happens on Facebook, Twitter, Blog posts (48)
	Information and peer knowledge sharing for adolescents transitioning to full self-management (e.g., for teens with CF (69))	hiFIve - small online group for 11-19 year-olds living with severe haemophilia. Closed to parents. Trying to harness peer to peer transmission of self-management skills (55)
	Social support associated with better mental health / health outcomes (e.g., parents of newly diagnosed infants with Phenylketonuria (41))	Online peer support program (CFOne) for adolescents and young adults with CF (74)

Table 2: Domains and sub-domains of needs of people with a rare disease that can be solved or supported by a consumer-facing electronic resource. (CF = cystic fibrosis, OI = osteogenesis imperfecta)

Chronic diseases requiring complicated self-management

Many rare diseases were described as having a high disease burden relying on complicated self-management regimes. The association of adherence to specific treatments with better health outcomes is strongly supported by evidence for cystic fibrosis (75), metabolic diseases requiring medical diets (76), and haemophilia (77), providing a clear rationale for supporting self-management. Optimal self-management in many cases required careful record-keeping of symptoms and tracking of treatments. Mobile apps were often designed to assist with this need. Symptom trackers were a common feature with or without medication alerts or treatment information (pancreatic enzyme replacement therapy for people with cystic fibrosis (26, 64)). Some had a function that allowed sharing of patient entered data with their health care team (e.g., 52, 60). Others tracked dietary intake for those on a medical diet (e.g., 51).

Lack of high-quality information

A common problem across all the rare diseases represented in this review was access to high-quality, culturally and demographically appropriate information from a credible source that was easy to find and understand. Information sought could be around the nature of the disease, medical treatments, prognoses, etc for the person with the disease and sometimes also for the health professionals supporting them (e.g., 22, 25, 47). Links to registries and research consortiums helped people stay up to date with treatment options (e.g., 43). Information about day-to-day management issues was often sought from social networks of people with experience of the same disease rather than specialist health professionals (e.g., 32, 35, 36). One paper critiqued existing online information on the rare disorder narcolepsy, following a study that showed access to high quality web-based information could reduce time to diagnosis through better understanding of signs and symptoms (20). Some informational needs related to “niche” topics, e.g., an app for the subset of people with mild haemophilia to help them assess for cryptic bleeds after injury (62).

Specialist centres for rare diseases may be geographically dispersed

Another common problem was the small number of rare disease specialist centres that could be widely dispersed geographically. Some e-resources provided directories for the nearest specialist centre (38, 46), or nearest, appropriately skilled allied health provider or patient advocacy agency (39). Others proved virtual consultations (e.g., 71) or tailored exercise (e.g., 58) or mental health services (68) via telehealth.

Social isolation

The social isolation that comes from having a rare disease is often discussed as a need unique to people with a rare disease. Khair and colleagues (78) note that for many adolescent boys with haemophilia, the only person other than their doctor who knows about their disease is their parent. Limited access to specialist services means people or parents of a child with a rare condition have to face non-urgent day-to-day issues themselves unless they find appropriate social support. Social support could be with people with the same disease (e.g., Facebook / Twitter group for Hirschsprung's disease (48)) or include health professionals (e.g., online support group for thoracic outlet syndrome (47)).

Discussion

This review found 72 papers outlining the needs of people with a rare disease, or their carers that could be addressed by an e-resource. Four domains and 23 subdomains of needs were identified and e-resources to address or support those needs were broadly categorised into five groups: mobile apps, social support platforms, telehealth and virtual health tools, and active and passive websites.

A range of unique needs arising from features of individual diseases were identified. Examples included the burden of physical isolation to prevent infection for people with cystic fibrosis (30), the acute distress of parents of infants with osteogenesis imperfecta at suspicions of child abuse that

often preceded diagnosis (29), and the difficulty of recognising signs of an impending adrenal crisis for people with Addison's Disease that can be life threatening.(22, 35) While the burden of disease for rare disorders may be similar to higher incidence conditions such as stroke or breast cancer, the added burden of the lack of a solid evidence base of effective treatments, best practice guidelines and competent and knowledgeable health service providers is not. The well documented diagnostic odyssey for people with rare diseases (3) and laments that health professionals had never heard of their disease (4) is a burden unique to this group.

This burden of uniqueness spills over to other needs. Exercise is crucial for physical and mental wellbeing but for many people with a rare disease, any exercise program must be tailored and supervised by a suitably knowledgeable health professional. Reduced exercise tolerance for people with cystic fibrosis and LAM, and risk of bleeds into their joints for people with haemophilia were addressed by telehealth or online modules.(58, 60, 61, 79-81) Social support of group exercise classes is known to be motivating but is not possible for people with cystic fibrosis who are at risk of cross infection. Online solutions went some way to solving this need (e.g., 80).

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.(34, 35, 47, 48) 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 hypothesised new e-resources.(19, 29)

It has been argued that an often overlooked need for people with a rare disease is support for their parents or carers, on whom the burden of management often falls.(82) This review identified 15 e-resources that supported carers (mostly parents). The distress that parents feel on diagnosis of a child with a rare disease was frequently discussed and provided the rationale for social support platforms and messaging apps, management support apps, and telehealth tools. One German study

provided parents of children with cystic fibrosis online writing-based therapy to alleviate psychological distress and anxiety.(83)

Readability of information found on the internet has been widely critiqued and criticised. A typical example is a review of online education resources from government and health care organisations on multiple sclerosis and rheumatoid arthritis (neither considered rare diseases) were found to be written at 11th or 12th grade standard, whereas the average American reads at a 5th grade standard.(84) The authors state material that is too complex limits its usefulness and increases inequities. E-resources in this review were often noted to be co-designed by health professionals, patient advocacy agencies, parents, and people with a rare disease as well as education experts to mitigate this risk. (e.g., 25, 51) Usability and acceptability studies were reported for some but not all the resources found in this review. Ensuring resources are easy to understand, appeal to the target group's demographics (e.g., adolescents versus older adults), and suited to the skills of the users is an obvious goal but one that this scoping review did not always find was done well. Patient advocacy agencies are noted in the broader literature to be particularly proactive in ensuring acceptable and easy to understand resources. A survey of patient advocacy groups for people with rare diseases, found 100% of respondents would be interested in collaborating with relevant healthcare or research groups to develop complementary resources suited to their members, and avoid wasted effort involved in duplication.(82)

Strengths and limitations

The nature of the topic (e-resources) lent itself more to conference presentations rather than full peer-reviewed articles. A strength of our search was that we included these items although a weakness is that limited information was able to be extracted from some abstracts. As with all searches that aim to be systematic and exhaustive, our search terms could have missed some papers. In particular, the search terms to capture rare diseases was problematic. Since there are over 7,000 rare diseases, it was not feasible to search for each by name. Our strategy was therefore

to search for a limited number of named rare disease groups. The list of needs identified are characteristic of any rare disease, and while some needs are unique to some specific disease manifestation, the majority were applicable to all. This generalisability will be useful for anyone designing e-resources to support people with a rare disease.

Conclusion

This review scoped the peer-reviewed literature to identify needs unique to people, or carers of people with a rare disease. It identified four broad domains of need: (i) support for complicated self-management regimes, (ii) access to high-quality, easy to understand information, (iii) access to appropriate specialist services, and (iv) social support. Most studies involved needs of people or carers of children with haemophilia or cystic fibrosis but also addressed another 20 named rare diseases or rare disease groups (e.g., inborn errors of metabolism). While the physical burden of a rare disease may be comparable to higher prevalence conditions such as stroke or cancer, rare diseases have unique overlying issues: the lengthy odyssey to find a diagnosis, the quest to find appropriate specialists to manage your care, the lack of a solid evidence base of effective treatments or best practice guidelines, or access to competent and knowledgeable general health service providers are unique to those with a rare disease. E-resources are well placed to address many of these problems but must be carefully co-designed with key stakeholders lest their complexity, narrow scope or cultural inappropriateness further disempower this already marginalised group.

Abbreviations

AIP	Acute intermittent porphyria
CF	cystic fibrosis
e-resource	electronic resource

JMIR	*Journal of Medical Internet Research*
LAM	Lymphangioleiomyomatosis
OI	osteogenesis imperfecta
OJRD	*Orphanet Journal of Rare Diseases*

Declarations

Conflict of interest

The authors have no conflicts of interest to declare.

Ethics

No ethical approval was required as all data was publicly available.

Patient consent for publication

Not applicable

Data availability statement

All data is provided in the paper, supplementary files or in the public domain.

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Author contributions

JL, SB, SH and BNGE designed the study. JL and SB collected data and undertook the analysis. SH, ZF, BNGE, JC and JB critically reviewed and commented on the results. JL wrote the first draft of the paper which was reviewed by SB, SH, ZF, BNGE, JC and JB. All authors approved the final version.

Supplementary file 1: PRISMA-ScR Checklist

Supplementary file 2: Full data extraction sheet for included papers

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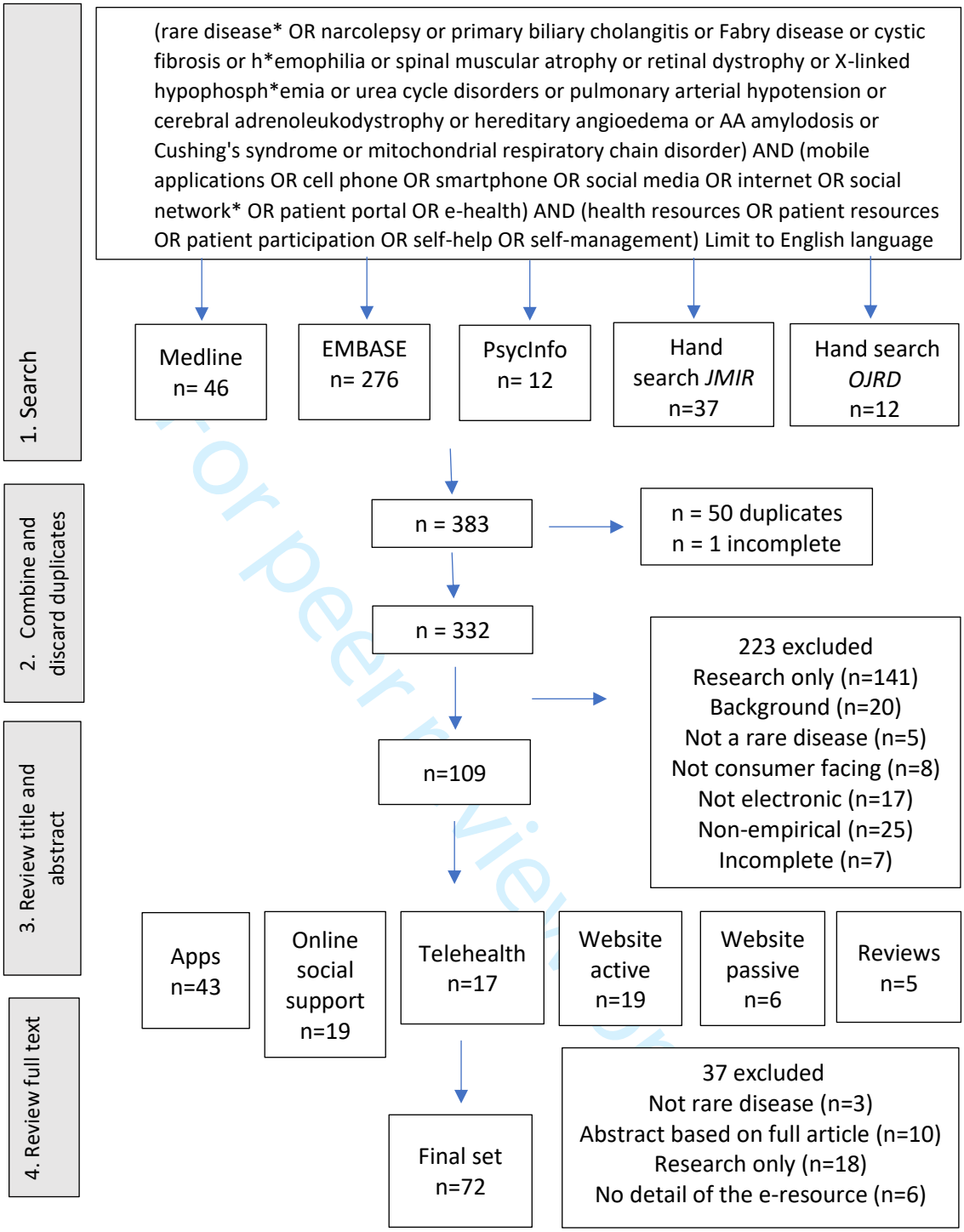
Figure legends

Figure 1: PRISMA flowchart for the search. (*JMIR* = *Journal of Medical Internet Research*; *OJRD* = *Orphanet Journal of Rare Diseases*)

Figure 2: Countries in which included studies were undertaken (frequency of papers).



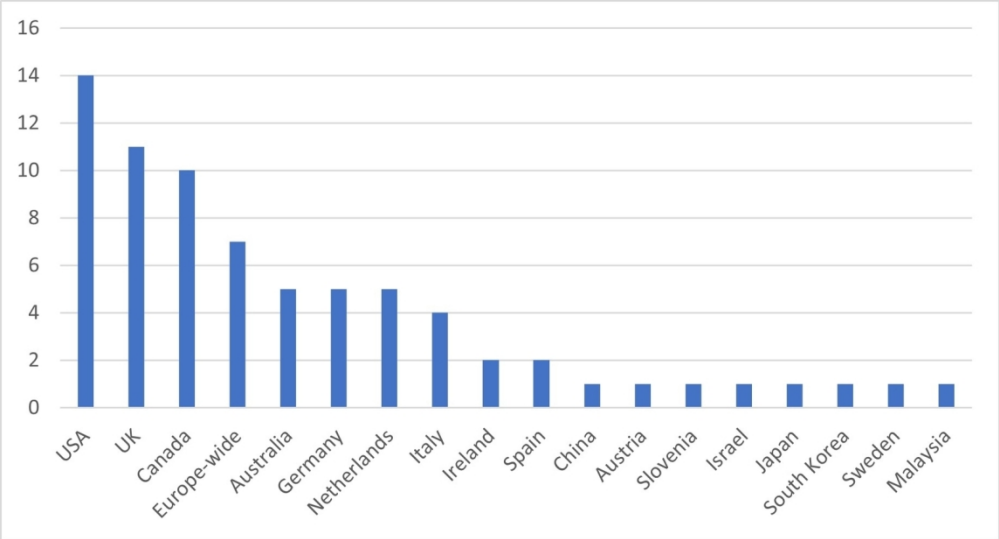


Figure 2: Countries in which included studies were undertaken (frequency of papers).

141x76mm (300 x 300 DPI)

PRISMA-ScR Checklist

Section	Subsection	Item	Page of Mss
Title		1	1
Abstract	Structured summary	2	1
Introduction	Rationale	3	3
	Objectives	4	4
Methods	Protocol and registration	5	4
	Eligibility criteria	6	4
	Information sources	7	4
	Search	8	4
	Selection of sources of evidence	9	4
	Data charting process	10	5
	Data items	11	5
	Critical appraisal of individual sources of evidence	12	NA for this scoping review
	Summary measures	13	NA for scoping reviews
	Synthesis of results		5
	Risk of bias across studies	15	NA for scoping reviews
	Additional analysis	16	NA for scoping reviews
Results	Selection of sources of evidence	17	5 ff
	Characteristics of sources of evidence	18	7 ff
	Critical appraisal within sources of evidence	19	NA for this scoping review
	Synthesis of results	20	8, 12
	Risk of bias across studies	22	NA for scoping reviews
	Additional analysis	23	NA for scoping reviews
Discussion	Summary of evidence	24	13
	Limitations	25	14
	Conclusions	26	14
Funding		27	15

From: Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. Ann Intern Med. 2018;169(7):467-73.

	A	B	C	D	E	F	G	H	I	J	K	L	M
1	**Reference**	**Year**	**Country**	**Rare disease**	**Name of intervention/resource if applicable**	**Research or available**		**Needs/barriers to care**	**Details**	**e-resource**	**Language/s**	**e-resource details**	**Findings (If research only)**
2	Ackbarali TA, et al. Assessing Patient and Provider Perspectives, Clinical Practice, Behaviors, and Knowledge on Hemophilia A Care. Blood; 05 Nov2020. p. 24-5.	2020	USA	Haemophilia	a web-based joint educational initiative for patients/caregivers and HCPs	Research	Conference abstract	Management of severe haemophilia is rapidly evolving - patients, carers and HCPs alike unsure of new treaments but keen to learn		website active	Not given	1-hour online video-based CME activity for HCPs and 1-hour healthcare education activity for patients were created in June, 2020 to address identified practice and knowledge needs among HCPs, and knowledge, communication and self-efficacy behaviors among patients. Each activity consisted of slides, polling and live questions, and remains on-demand	
3	Aizawa R, et al. Status of narcolepsy-related information available on the Internet in Japan and its effective use. Sleep and Biological Rhythms. 2008;6(4):201-7.	2008	Japan	Narcolepsy	Existing internet resources	publicly available	Journal article	High quality web-based information can reduce time to diagnosis for people with narcolepsy	Useful, harmful information is low on search engine rankings.	website passive	Not given	Existing web-based resources	Patients were asking for info on the hereditary nature of the disease and ways to deal with their disease.
4	Al-Saleh H, et al. Beta testing of the "MY CF" smartphone/tablet app: In patients with cystic fibrosis. Conference Abstract presented at American Journal of Respiratory and Critical Care Medicine. Conference: American Thoracic Society International Conference, ATS; 2014.	2014	USA	Cystic fibrosis	MY CF	Research	Conference abstract	Complicated self-management	Difficulties keeping track of medications, test results and symptoms for adolescents or parents of younger children with CF.	App		Android OS for phone or tablet. The three most favored functionalities of the app were: Medication list, Symptom Diary, and Weight/Height/Body Mass Index monitoring. 32 invited to participate; of 23 who did, majority wanted to continue using it and would recommend it	
5	Armayones M, et al. APTIC: A social network to improve the quality of life of members of patients' associations. Conference Abstract presented at Orphanet Journal of Rare Diseases. Conference: 5th European Conference on Rare Diseases, ECRD; 2010.	2010	Spain	Rare diseases	APTIC	publicly available	Conference abstract	Fragmentation of information regarding rare diseases	Need for people to learn from one another, share expereiences	social platform	Not given	Social networking platform that aims at enabling the individual members of patients' associations (mostly parents of children with chronic and rare diseases) to share experiences, information, advice	
6	Aznar J, et al. Telemedicine in Hemophilia: Virtual consultation for the hematologist at patient's home. Haemophilia; July2012. p. 72.	2012	Spain	Haemophilia	domiciliary virtual consultation and virtual monitoring tools	Research	Conference abstract	Frequent hospital visits impact QoL	Domiciliary replacement therapy (DRT) ensures rapid infusion of lacking factors when any bleeding episode occurs and reduces hospital dependency of patients with hemophilia. However, these patients still have to visit the hospital frequently because the hematologist can prescribe general guidelines for home-replacement therapy but cannot adapt them to the bleeding evolution	telehealth	Not reported	Three interventions: (1) patient entered bleeding episode and self managed treatment; (2) virtual monitoring by ultrasound of haemarthroses, (3) Virtual consult	Successful in 45 patients which in turn may decrease depency on hosptial visits and by association QoL

	A	B	C	D	E	F	G	H	I	J	K	L	M
7	Badiu C, et al. Developing and evaluating rare disease educational materials co-created by expert clinicians and patients: the paradigm of congenital hypogonadotropic hypogonadism. Orphanet Journal of Rare Diseases. 2017;12(1)	2017	Europe	congenital hypogonadotropic hypogonadism (CHH) and the olfacto-genital (Kallmann) syndrome	Educational package	Research	Journal article	Need for high quality information/education on rare diseases	Important it is easy to read and engaging	website passive	20 languages	patient education materials	Appropriate reading level and accessibility
8	Balestri E, et al. 'F (accio) C (entro)': Project for a smartphone application to increase adherence to aerosol treatment in adolescents with cystic fibrosis. Conference Abstract presented at Italian Journal of Pediatrics. Conference: 25th Italian Congress of Cystic Fibrosis and the 15th National Congress of Cystic Fibrosis Italian Society. Milan Italy; 2020.	2020	Italy	Cystic fibrosis	Faccio Centro	Research	Conference abstract	Complicated self-management with decreasing adherence from adolescents	Patients with Cystic fibrosis have onerous therapy - respiratory physiotherapy, therapy by aerosol, oral, intravenous and physical activity. During adolescence the therapy adherence, that is undergoing treatments at the right time of the day, in the right sequence and dosage, considerably decreases with negative consequences in terms of: health status, quality of life and hospitalization	App		Mobile phone app - lists daily therapy, with instructions on order, progress tracking, alerts for when to start and when checks are needed. Also can email questions to HCP team.	
9	Barazani Brutman T, et al. New communication technologies improve hemophilia care. Haemophilia. 2017;23(Supplement 2):134-5.	2017	Israel	Haemophilia	WhatsApp social support group messaging	Research	Conference abstract	Parents with newly diagnosed children require immediate response when things happen		social platform	Not given	Social support groups of parents, patients and medical staff WhatsApp. Parents, patients and medical staff used the WhatsApp application installed on smartphone to provide immediate response to various issues: queries regarding bleeds (with relevant photos), queries regarding dosage/ frequency of therapy, queries about quality of life (QOL) and specific situations noted at school/ kindergarden, personal communication and general consult and support.	Extension of physical groups at the treatment centre.
10	Blackwell LS, et al. CFfone: A social networking site for adolescents and young adults with cf. Pediatric Pulmonology. 2012;35):430.	2012	USA	Cystic fibrosis	CFOne	Research	Conference abstract	Transition from child to adult requires increased independence and self efficacy	Social support associated with better psychological wellbeing and better outcomes.	social platform	Not given	online peer support program for adolescents and young adults with CF	Social networking sites for adolescents and young adults with CF may be useful for increasing knowledge of disease management, increasing perceptions of social support and improving mental health and quality of life.
11	Boon M, et al. Use of a mobile application for self-management of pancreatic enzyme replacement therapy is associated with improved gastro-intestinal related quality of life in children with Cystic Fibrosis. Journal of Cystic Fibrosis. 2020;19(4):562-568	2020	Europe	Cystic fibrosis	MyCyFAPP	Research	Journal article	Complicated self (parental)-management for gastrointestinal distress in children	Most patients with cystic fibrosis (CF) suffer from pancreatic insufficiency, leading to fat malabsorption, malnutrition, abdominal discomfort and impaired growth. Pancreatic enzyme replacement therapy (PERT) effective but evidence-base on dosing still being built. This uses a new algorithm.	App	Dutch, English, Flemish, Italian, Portugese, Spanish	App calculates individual PERT-doses for optimal fat digestion and includes a symptoms diary, educational material, and it is linked to a web tool allowing HCPs to view data and give feedback.	Increased GI QoL measures.
12	Breakey VR, et al. A feasibility study of "managing hemophilia online": An Internet-based self-management and transitional care program for teens. Haemophilia. 2012;3):207-8.	2012	Canada	Haemophilia	online self-management intervention	Research	Conference abstract	Adolescents have heightened educational needs as they learn to manage their disease and become self-sufficient in preparation for transition to adult health care.		website passive	English and French	Online course - not clear if it is interactive. Pilot - still working it out	

	A	B	C	D	E	F	G	H	I	J	K	L	M
13	Breakey VR, et al. A pilot randomized control trial to evaluate the feasibility of an Internet-based self-management and transitional care program for youth with haemophilia. Haemophilia. 2014;20(6):784-93.	2014	Canada	Haemophilia	Teens Taking Charge: Managing Hemophilia Online'	Research	Journal article	Adolescents have heightened educational needs as they learn to manage their disease and become self-sufficient in preparation for transition to adult health care.		website active	English and French	8 week educational program on line with weekly telephone support from a trained Research Assistant.	Teens on the intervention arm showed significant improvement in disease-specific knowledge (P = 0.004), self-efficacy (P = 0.007) and transition preparedness (P = 0.046). There was a statistically significant improvement in knowledge in the intervention group when compared to the control group (P = 0.01). Overall, the teens found the website to be informative, comprehensive and easy to use and were satisfied with the program.
14	Breakey VR, et al. Feasibility study of a randomized control trial to evaluate an internet-based self-management program for adolescents with hemophilia: Preliminary results and observations. Journal of Thrombosis and Haemostasis; July2013. p. 1058.	2013	Canada	Haemophilia	Teens Taking Charge: Managing Hemophilia Online'	Research	Conference abstract	Adolescents have heightened educational needs as they learn to manage their disease and become self-sufficient in preparation for transition to adult health care.		website active	English and French	8 week educational program on line with weekly telephone support from a trained Research Assistant.	Overall, these teens found the website to be informative, comprehensive and easy to use and were satisfied with the program.
15	Breakey VR, et al. The value of usability testing for Internet-based adolescent self-management interventions: "Managing Hemophilia Online". BMC medical informatics and decision making. 2013;13:113.	2013	Canada	Haemophilia	Teens Taking Charge: Managing Hemophilia Online'	Research	Conference abstract	Adolescents have heightened educational needs as they learn to manage their disease and become self-sufficient in preparation for transition to adult health care.		website active	English and French	8 week educational program on line. Course contained multimedia components (videos, animations, quizzes)	
16	Calvo-Lerma J, et al. Clinical evaluation of an evidence-based method based on food characteristics to adjust pancreatic enzyme supplements dose in cystic fibrosis. Journal of Cystic Fibrosis. 2020.	2020	Europe	Cystic fibrosis	MyCyFAPP	Research	Journal article	Complicated self (parental)-management for gastrointestinal distress in children	Most patients with cystic fibrosis (CF) suffer from pancreatic insufficiency, leading to fat malabsorption, malnutrition, abdominal discomfort and impaired growth. Pancreatic enzyme replacement therapy (PERT) effective but evidence-base on dosing still being built. This uses a new algorithm.	App	Dutch, English, Flemish, Italian, Portugese, Spanish	App calculates individual PERT-doses for optimal fat digestion and includes a symptoms diary, educational material, and it is linked to a web tool allowing HCPs to view data and give feedback.	Improved fat absorption for those with poor baseline measures.
17	Calvo-Lerma J,et al. Change in nutrient and dietary intake in european children with cystic fibrosis after a 6-month intervention with a self-management mhealth tool. Nutrients. 2021;13(6)	2021	Europe	Cystic fibrosis	MyCyFAPP	Research	Journal article	People with CF have increased energy needs and a diet with a specific nutrient distribution. Nutritional status is an indicator of disease prognosis and survival. Self(parental)-management is complicated	App provided educational resources about nutrition and dietary advice for parents	App	Dutch, English, Flemish, Italian, Portugese, Spanish	Food diary, nutrition follow-up (goals), symptoms diary (health diary), nutrition educational material (living with CF) and messages among other functions	Users had modest improvements towards the nutritional guidelines
18	Carr SB, et al. Children and adults Tai Chi study (CF-CATS2): A randomised controlled feasibility study comparing internet-delivered with face-to-face Tai Chi lessons in cystic fibrosis. ERJ Open Research. 2018;4(4)	2018	UK	Cystic fibrosis	NA	Research	Journal article	Maintaining exercise difficult for people with CF due to isolation.	8 lessons over 3 months, delivered face to face (n=22) or via internet (n=18) for 40 adults and children with CF.	telehealth	English	Lessons delivered over Skype; also had a DVD, booklet, stickers and tshirts aimed at different ages to increase adherence.	Feasibility and safety were demonstrated. All participants showed significant improvements in self-reported sleep, cough (both daytime and night-time), stomach ache and breathing. No differences in lung function, health status, quality of life, sleep or mindfulness was shown before or after completing the lessons.
19	Carr SB,et al. Children and adults Tai Chi study (CF-CATS2): A randomised controlled feasibility study comparing internet-delivered with face-to-face Tai Chi lessons in cystic fibrosis. ERJ Open Research. 2018;4(4).	2018	UK	Cystic fibrosis	Internet delivered Tai-Chi class	Research	Journal article	Isolation yet needing tailored exercise	Maintaining an exercise regime can be difficult in cystic fibrosis: group classes risk potential infection, yet motivation is hard to maintain when alone.	telehealth	English	Comparison of F2F and internet classes	Improvements in sleep, cough, GI symptoms and breathing but no diff in lung function, ehalth status and QoL. Findings same in both groups.

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20	Castro RA, et al. Exploring the Views of Osteogenesis Imperfecta Caregivers on Internet-Based Technologies: Qualitative Descriptive Study. J Med Internet Res. 2019;21(12):e15924.	2019	Canada	Osteogenesis Imperfecta (OI)	Exploring use of what's available online and what is needed	publicly available	Journal article	Multiple needs	(1) Distraction for children after surgery to promote rest and immobilization, or to distract from painful or frightening procedures etc; (2) Isolation from family or friends at a distance or in unsafe places for the child to visit; (3) Carers' self care; (4) Parents and carers feeling distressed by the disease and child's suffering; (5) Managing logistics of caregiving/ HCPs (6) Communication with HCP; (7) Facilitating care; (8) Information seeking; (9) social isolation (10) Updates on research and new treatments (11) Concern about quality, security (12) wishlist (13) caregivers desired child-friendly and age-appropriate (14) In their own language	other			(1) Games, videos, audio books have a calming affect to distract from broedom, pain or fear; (2) Social media platforms like FaceTime useful for staying in touch; (3) Can be a lot of waiting for appointments and then keeping the child quiet at home after surgeries etc. Yoga apps, games and ; (4) Watching inspirational videos of other children with OI doing well gave hope; (5) Booking online much easier and e-calendars useful to store all appointments; (6) Some allowed email or messaging (e.g., to SW or PT); (7) Some tools allowed carers to find local community and care resources - e.g., wheelchair accessibility of local shopping centre etc. Appropriately adapted sports programs; (8) Found via Google so not optimal (9) Social media specifically for OI - share day-to-day care information rather than using it for specific information on prognoses or treatments. Some caregivers were more interested in answering others' questions than in having their own questions answered. OI parents were the ones who know practical day-to-day care strategies, such as where to find adaptive clothing and winter boots that would fit her child's physique. Claimed to get faster information from a social media platform group ratehr than an HCP. (10) Access to information; (11) Concerned about web-based predators or cyberbullies or judgement from other parents. Often were confronted with worst-case scenarios that were not applicable to their own children. (12)Web-based home fracture-splinting videos with diverse techniques for every fracture possible • Web-based videos portraying OI patients before and after various
21	Cipriani D, Dulcan E. See and be seen: The CF community. Pediatric Pulmonology. 2017;52(Supplement 47):147-148.	2017	USA	Cystic fibrosis	BreatheCon	limited availability	Conference abstract	CF considered an invisible disease; social support limited by infection risk; niche information hard to find; mental health often impacted.	Lack of understanding of peers and family when the disease is "invisible." Desire to connect with people with the same disease (who "get it") but face-to-face not possible. telling your boss about CF as well as colleagues, classmates, friends, in-laws and other new family. The alienation of invisibility is compounded by uncomfortable, lonely, boring treatments. When life expectancy improves for a cohort of patients, little information about reproduction, family planning, safe pregnancies, genetic	social platform	Not given	Online conferences for people with CF subdivided into adults, parents/children and young people.	
22	Colman AW, et al. Use of Quick Response (QR) coded bracelets and cards for the improvement of cortisol deficiency/Addison's disease management: An audit of quality of care of the management of steroid deficiency in acute illness. BMJ Innovations. 2018;4(3):115-22.	2018	UK (England)	Addison's disease	Quick response coded bracelet	Research	Journal article	Adrenal crisis is life-threatening and requires swift intervention but is very rare	Study of HCPs - clinically needed / useful?	website passive	Not given	Bracelet has a scannable QR code that links to emergency management information	Clinical need identified
23	Cox NS, et al. A web-based intervention to promote physical activity in adolescents and young adults with cystic fibrosis: protocol for a randomized controlled trial. BMC polm. 2019;19(1):253.	2019	Australia	Cystic fibrosis	ActivOnline	Research	Journal article	Tailored exercise program without risk of infection		website active	Not given	internet-based physical activity program for 12 weeks for adolescents and young adults	Protocol

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24	Cox NS, et al. Feasibility and acceptability of an Internet-Based program to promote physical activity in adults with cystic fibrosis. Respiratory Care. 2015;60(3):422-9.	2015	Australia	Cystic fibrosis	ActivOnline	Research	Journal article	Tailored exercise program without risk of infection		website active	Not given	internet-based physical activity program for 8 weeks for adults. Also fortnightly phone consult	Feasible and acceptible
25	Cummings E, et al. Enhancing self-efficacy for self-management in people with cystic fibrosis. Studies in Health Technology and Informatics. 2011;169:33-37.	2011	Australia	Cystic fibrosis				Complicated self-management	Health mentoring project with 3 groups: (1) Self-efficacy web-based program + mentor via phone, (2) mentor via phone + self-efficacy program +App, (3) usual care.	App	English	App consisted on Symptom diary plus optional feedback on progress	Results show the intervention was generally considered to be useful and allowed CF individuals to focus on changes in symptoms. Self-efficacy increased in subjects in both intervention groups, but it is unclear from the results if the application provided additional benefits beyond supporting the mentoring intervention.
26	D'Ambrosio C. Open versus closed social networking groups. Haemophilia. 2014;3):183.	2014	USA	Bleeding disorders in women	MyGirlsBlood	publicly available	Conference abstract	Little information for this group of women; social isolation	Debate over whether open or closed group better. Closed for safety discussing personal details but reinforces it as a "secret" and shuts out others who may help / get it on the research agenda.	social platform	Not given	Open group (not closed) on Facebook where people can ask questions or share experiences.	Having closed social networks are needed for groups that need privacy and security in their communications. WWBD need privacy to learn from one another and to solve intimate problems. However, when there are only closed groups, awareness ceases to exist across the larger multi-disciplinary and diverse worldwide community. Many would like to help, but would not be permitted in a closed group for WWBD.
27	Decker K, Meilleur C. CBDR and MyCBDR advancing hemophilia nursing practice in Canada. Conference Abstract presented at Haemophilia; May, 2018	2018	Canada	Haemophilia	MyCBDR (linked to Canadian Bleeding Disorder Registry (CBDR)	limited availability	Conference abstract	Complicated self-management	Better outcomes from new treatement regimes but requires detailed record keeping to accurately monitor bleeding episodes, factor usage and adherence to treatment regimens.	App	Not reported	Links to CBDR - app allows people with a bleeding disorder to add track infusions and symptoms.Data available to all Haemophilia Treatment Centres in canada meaning greater integration fo specialist services.	Useful tool that allows access to detailed information to the care tems and by implication, better treatment outcomes
28	Fidika A, et al. A web-based psychological support program for caregivers of children with cystic fibrosis: A pilot study. Health and Quality of Life Outcomes. 2015;13(1)	2015	Germany	Cystic fibrosis	WEP-CARE	Research	Journal article	Parents caring for a child with Cystic Fibrosis (CF) are at high risk for psychological distress and have limited access to psychological care.	Severe distress not unusual. Lack of appropriate and knowledgable support.	website active	Not given	Web-based writing therapy - 9 sessions, tailored for the specific needs of caregivers. Written assignments that were given feedback within 48 hours. The intervention program was provided by two trained and supervised psychotherapists with expertise in psychosocial care for patients with CF and their families.	On average, the caregivers' symptoms of anxiety decreased statistically significant and clinical relevant about five points from an elevated (M=11.4; SD =2.6) to a normal level (M=6.7; SD =2.6; p < .001) between pre and post treatment. Fear of disease progression (p < .001) and symptoms of depression (p = .02) significantly decreased as well. Quality of life significantly improved (p = .01). The effects were maintained at the 3-months follow-up assessment.
29	Floch J, et al. Users' Experiences of a Mobile Health Self-Management Approach for the Treatment of Cystic Fibrosis: Mixed Methods Study. JMIR mHealth and uHealth. 2020;8(7):e15896.	2020	Europe	Cystic fibrosis	MyCyFAPP	Research	Journal article	Complicated self-management	Overall positive experience but food recording was seen as too complicated. Once people met their goals, lost motivation to continue using the app. HCPs also reported that information communicated by patients is more reliable and accurate. Normally, patients do not record data systematically. They forget details or get information mixed up. Empowering patients to record events at the time they occur, HCPs felt that the data they receive are more precise and better reflect the reality of patients' status	App	Dutch, English, Flemish, Italian, Portugese, Spanish	Food diary, nutrition follow-up (goals), symptoms diary (health diary), nutrition educational material (living with CF) and messages among other functions	Patients and parents had different skills, requiring follow-up by HCPs in an introductory phase. HCPs valued obtaining precise information about the patients, allowing for more personalized advice. However, the tight follow-up of several patients led to an increased workload. Over time, as patient self-efficacy increased, patient motivation for using the app decreased and the quality of the reported data was reduced. They suggest focusing on patients with poor control using the app; all patients using it for the week before a consult.Introduing all the dfeatures of the app at once can be overwheming - staged approach better. Personalising it with help from the HCP alos useful.

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30	Gow J, et al. Participation in patient support forums may put rare disease patient data at risk of re-identification. Orphanet Journal of Rare Diseases. 2020;15(1)	2020	UK	Rare diseases	Social support groups generally for people with RD	publicly available	Journal article	Vulnerable to re-identification on social support platforms	Online social support groups may not have sufficient security to prevent malicious matching of health and personal data to re-identify anonymised data	social platform			
31	Grande SW, et al. Improving care for pediatric cystic fibrosis in Sweden using a successful mHealth patient support system. Conference Abstract presented at Pediatric Pulmonology; September, 2017.	2017	Sweden	Cystic fibrosis	Genia	limited availability	Conference abstract	Complicated self-management/tracking symptoms and treatments	Parents don't always recall symptoms and treatments for their child making it hard for HCPs to accurate assess the patient.	App	Not reported	Patients/parents record daily health observations and complete reports about symptoms, medications, and goals immediately prior to a clinic appointment. Data available to HCPs at the consult.	High uptake at the study hospital; HCP took QI approach to its implementation. Considered to have improved coordination and patient-provider consensus ye without greater HCP burden.
32	Guilliams JM, et al. Feasibility and usefulness of a mobile health exercise intervention in women with lymphangioleiomyomatosis. Conference Abstract presented at Cardiopulmonary Physical Therapy Journal; July, 2021.	2021	Not given	Lymphangioleiomyomatosis (LAM)	Home based exercise program for women with LAM	Research	Conference abstract	Require tailored expercise program	Patients have reduced lung function and exercise tolerance; and a recent report indicates lower physical activity levels in LAM compared to patients with COPD and healthy populations.	App	Not reported	App on smartphone with interfacing wearable and home monitoring devices. Check in with Physio weekly.	12 wk trial. Initial findings indicate feasibility and usefulness of an mHealth home exercise program for LAM, including good patient adherence and satisfaction with the program.
33	Haik D, 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):293-299.	2019	USA	Idiopathic subglottic stenosis (iSGS)	Living With Idiopathic Subglottic Stenosis (LwiSGS),	publicly available	Conference abstract	Access to information, sharing of experiences		social platform	Not given	Online community specifically for people with iSGS	Analysis demonstrated that communications primarily encompassed three major thematic elements: (1) information sharing; (2) emotional support, expression, and experience sharing; and (3) community building. Positively toned posts grossly overshadowed negatively toned posts by almost a factor of 3. A significant portion of group members requested information from their peers, suggesting a high level of trust toward the resources provided in this group, even those involving a surgical procedure or medication.
34	Ho G, et al. Metabolic Diet App Suite for inborn errors of amino acid metabolism. Molecular Genetics and Metabolism. 2016;117(3):322-327.	2016	Canada	Inborn errors of metabolism (IEM)	Metabolic DietAppSuite	publicly available	Journal article	Burden of daily adherence to complex and time-consuming medical diet to attain metabolic control and prevent organ damage	Diet is only one of a number of competing priorities for people with IEM, but one of the most onerous. Poor nutritional labelling on many foods - restricts diet further.	App	Not reported	Online tool for mobile phones and desktops for 15 different IEMs. Creates a personalised dasshboard including specific nutrient goals. Food diary, nutrient counts and able to add your homemade recipes.	
35	Howard S, The All Wales Adult Cystic Fibrosis Centre (AWACFC) Virtual Instruction of Exercise with Technology to Enhance Care-VIEWTEC Programme. Journal of Cystic Fibrosis. 2014;2):S20	2014	UK (Wales)	Cystic fibrosis	VIEWTEC Programme	Research	Conference abstract	Patients live 2 and 3 hours away from treatment centre but benefit from tailored exercise programs	Group exercise is more motivating	telehealth	Not given	virtual exercise sessions with a CF Gym Instructor. Email invitations and delivered via Cisco Webex	Feasibe and patients liked it.

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36	Huang X, et al. Developing and evaluating HE-APP: Acceptability and usability of a smartphone APP system to improve self-management in Chinese patients with hemophilia. Conference Abstract presented at Haemophilia; June, 2020	2020	China	Haemophilia	HE-APP		Conference abstract	Complicated self-management linked to outcomes	Outcomes linked to self management and accurate symptom-tracking.	App	Mandarin?	(1) recording of bleeding symptoms; (2) monitoring of treatment adherence; (3) education, training and support system; (4) accounting and analysing the use of the medicine; and (5) recording the economic cost.	Acceptability and susability levels high among patients and their parents. Small trial with 10 patients.
37	Ingravallo F, et al. Telemedicine with mobile internet devices for innovative multidisciplinary patientcentred care of patients with narcolepsy. Protocol of the randomized controlled trial TENAR (TElemedicine for NARcolepsy). European Journal of Neurology. 2020;27(Supplement 1):516.	2020	Italy	Narcolepsy	TENAR trial (Protocol)	Research	Conference abstract	disease burden is increased by the need for traveling for medical consultations, with high costs for patients and families.		telehealth			
38	Kauw D,et al. 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.	2015	The Netherlands	Addison's disease and Cushing's syndrome	online forum moderated by the Dutch Adrenal Society	publicly available	Journal article	Peer-to-peer information sharing		social platform	Not given	Public area and password protceted area. Rules for posting e.g., posting medical information - must provide references. Moderated by vounteers.	Analysis of content: 81% asking for more info about the disease; 10% asking for emotional support; Answers mostly practical tips and sharing own experiences. Seen as an important information source. Social support in the form of experiential info and emotional support - not able to be obtained from HCPs.
39	Khair K, et al. Social networking for adolescents with haemophilia. Haemophilia. 2011;17(2):369.	2011	UK	Haemophilia	VivaSix	Research	Conference abstract	Adherence to treatment difficult for adolescent boys with severe haemophilia	Parents are oftensole source of information outside of HCPs. Few know of other boys with heamophilia	social platform	Not given	Restricted social network for boys 11-18 years with severe haemophilia. Will include games and other features to promote sharing of self management skills.	
40	Khair K, et al. The role of social networking in haemophilia management. Haemophilia. 2010;4):129-130.	2010	UK	Haemophilia	hiFive	Research	Conference abstract	Adherence to treatment difficult for adolescent boys with severe haemophilia	Parental influence lessens. Potential for peer to peer transmission of self management skills	social platform	Not given	hiFIve - small group for 11-19 year olds living with severe haemophilia. Closed to parents.	
41	Kirk S, Milnes L. An exploration of how young people and parents use online support in the context of living with cystic fibrosis. Health expectations. 2016;19(2):309-321.	2016	UK	Cystic fibrosis	Online forum for people with CF	Research	Journal article	Can be hard to find information and support for people with a rare diease or caring for a child with a rare disease		social platform	Not given	Participants exchanged experientially derived advice and views on how to manage treatments, emotions, relationships, identity and support from services. While parents sought information and support on managing specific therapies/services and ways of maintaining their child's health, the information and support young people desired appeared to be more directed at how to 'fit' CF into their everyday lives	Online support groups appear to supplement professional support in relation to self-management. They enable young people and parents to share experiences, feelings and strategies for living with long-term conditions with peers and develop the expertise to empower them in interactions with health-care professionals.
42	Kühnle L,et al. Development of a Social Network for People Without a Diagnosis (RarePairs): Evaluation Study. J Med Internet Res. 2020;22(9):e21849	2020	Germany	Undiagnosed rare diseases	RarePairs	Research	Journal article	Diagnostic delay is a regular feature of rare diseases	Diagnosis can be difficult with limited infromation and experience of rare diseases. This uses information from a database of 973 diagnosed people	social platform	German, English, Chinese, Portuguese, and Finnish	Social network platform with built in algorithm to match individuals with similar disease burden in the lead up to diagnosis.	

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43	Lassandro G,et al. EMO.TI.ON.: Technologies for the safety of children with hemophilia. Blood Transfusion; November2017. p. s539.	2017	Italy	Haemophilia	EMO.TI.ON. system	Research	Conference abstract	Home care decreasing reliance on hospital	Diagnosing suspected bleeds into joints requiring hospital visit for diagnosis	telehealth	Not given	an ultrasound diagnostic solution using at home by parents or caregivers. Moreover, the system can transfer, live, images by world wide web to specialist physician creating a network. The solution will be achieved by attending the design related to familiarization processes. Other function of the system are: teleconsulting tools, semantic scientific search, recording data (i.e. clinical chart, infusional diary...).	Ongoing trial but results of parent use comparable to HCP use.
44	Lee Yeong J, et al. A Newly Developed Web-Based Resource on Genetic Eye Disorders for Users With Visual Impairment (Gene.Vision): Usability Study. J Med Internet Res. 2021;23(1):e19151.	2021	UK (England)	Genetic eye disorders	Gene.Vision	Research	Journal article	Educational web-based materials need to be accessible by people with low vision		website passive	Not given	Gene.vision web site on genetic eye disorders optimised for people with vision problems	
45	Lewis T. Improving quality of life in patients with cystic firbosis with exercise: CF foundation impact grant update. Conference Abstract presented at Pediatric Pulmonology; October, 2019.	2019	USA	Cystic fibrosis	Exercise program via App	Research	Conference abstract	Require tailored expercise program in isolation	Deliver an at home exerise program to people with CF - indirect supervision by exercise physiologist.	App	English	Guided exercise program (3 levels to choose from) and assessment tasks. Supported by live recorded discussions and Q and A sessions.	Suggests it is feasible and could lead to improvements in QoL
46	Lomotey RK, et al. Mobile self-management guide for young men with mild hemophilia in cases of minor injuries. Network Modeling Analysis in Health Informatics and Bioinformatics. 2014;3(1).	2014	Canada	Haemophilia	Hemophilia Injury Recognition Tool (''HIRT?'')	limited availability	Journal article	Patients may be slow to recognise injuries if their disease is mild	People with mild haemophilia may only experience bleeds after a significant injury and so not recognise sequelae of milder events - not seek appropriate treatment.	App	English, French	Structured assessment of suspected bleeds plus approriate first-aid if needed. If more help required, ohone number sof all Haemophilia Treatment Centres in Canada are given to enquire about further management.	High usability for all users whether tech savvy or not.
47	Manu-Pereira MM, et al. ENERCA: Towards a European Reference Network (ERN) in rare haematological diseases. British Journal of Haematology. 2016;173(Supplement 1):39-40.	2016	Europe	Rare and Congenital Anaemias	e-ENERCA (European Network for Rare and Congenital Anaemias (ENERCA))	Research	Conference abstract	Distance from specialist centres, lack of relelvant information and need to share data with expert HCP.	European reference Networks - hub and spoke model fo rare disease care	website active	Not given	3 separate platforms linked to the e-ENERCA website 1) e-Registry, a Pan European registry of RAs for epidemiological surveillance 2) e-Learning for the dissemination of knowledge, continuous medical education, and best practices awareness, and 3) Telemedicine, a platform to provide expertise, at distance, for complex cases.	
48	Moon H, Moon J. Comparative readability analysis of information on exercise for hemophilia patients. Haemophilia. 2021;27(SUPPL 2):57.	2021	South Korea	Haemophilia	Existing online exercise programs for Haemophilia	publicly available	Conference abstract	Tailored online exercise programs need to be understandable.	Readability and other access features not always present	website passive	Not given	Existing web-based resources	Sites had higher than recommended readability scores and came low down in search algorithm rankings making them hard to find.
49	Naik H, et al. Experience with a pilot skype internet support group for symptomatic patients with acute intermittent porphyria. Clinical Chemistry and Laboratory Medicine. 2013;51(5):eA10.	2013	USA	Acute Intermittent Porphyria (AIP)	Skype support group mediated by HCPs	Research	Conference abstract	Psychosocial and emotional isolation leading to poor mental health in this group	Life-threatening acute episodes - painful with sequelae - chronic symptoms. Poorly understood psychosocial needs.	social platform	Not given	Skype support group mediated by a porphyria expert physician, and the genetic counselor/coordinator of the porphyria clinic and an available psychologist with 4 women with AIP.	Participants reported that this was a very comforting experience, reducing the feeling of isolation and increasing their understanding of the disease.

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50	Nicholl H, et al. Internet Use by Parents of Children With Rare Conditions: Findings From a Study on Parents? Web Information Needs. J Med Internet Res. 2017;19(2):e51.	2017	Ireland	Rare diseases	Hypothetical	publicly available	Journal article	Recommendatinos for a consumer facing website	• The content needs to be relevant, accurate, trustworthy, and up to date. • The topics most frequently searched for (Table 5) need to be addressed. • It should contain a Web-based forum or a social network component. • The website should be integrated with social media and be mobile friendly.	other			
51	Nilson J, et al. Are you HIRT? (Hemophilia Injury Recognition Tool): Perceptions of the mobile app on injury self-management from young men with mild hemophilia in Canada. Conference Abstract presented at Haemophilia; July, 2016.	2016	Canada	Haemophilia	Hemophilia Injury Recognition Tool (''HIRT?'')	limited availability	Conference abstract	Patients may be slow to recognise injuries if their disease is mild	People with mild haemophilia may only experience bleeds after a significant injury and so not recognise sequelae of milder events - not seek appropriate treatment.	App	English, French	Structured assessment of suspected bleeds plus approriate first-aid if needed. If more help required, ohone number sof all Haemophilia Treatment Centres in Canada are given to enquire about further management.	Increased confidence dealing with injuries but no change in self management
52	Osara Y, et al. Development of newborn screening connect (NBS connect): a self-reported patient registry and its role in improvement of care for patients with inherited metabolic disorders. Orphanet Journal Of Rare Diseases. 2017;12(1):132.	2017	USA	Phenylketonuria (PKU), maple syrup urine disease (MSUD) or tyrosinemia (TYR)	Newborn Screening Connect (NBS Connect)	Research	Journal article	Patients/carers isolated by rareness of disease.	Linking patients/carers with information. Registries are generating useful data and contributing to the research agenda.	website active	Not given	Registry - patient initiated and enters data. Resources such as education materials, information on the latest research and clinical trials, recipes, interactive health tracking systems, and professional support tools	
53	Paglialonga A, et al. eHealth for patients with rare diseases: the eHealth Working Group of the European Reference Network on Rare Multisystemic Vascular Diseases (VASCERN). Orphanet Journal of Rare Diseases. 2021;16(1):164.	2021	Europe	Rare Multisystemic Vascular Diseases	Mobile app developed by VASCERN (European Reference Network on Rare Multisystemic Vascular diseases); Pills of Knowledge YouTube channel	limited availability	Journal article	(1) Finding a suitable expert; (2) finding a patient support agency; (3) need for timely info about the patient in an emergency situation; (4) information needs of the patient	(1) In Europe can mean travelling across borders, languages - incurring time and money. Difficult to find appropriate RD expert. This RD is multisystem so may need several specialists; (2) Not always named after your disease / group of diseases (3) Paper records carried by the patient are common but may be lost and can only contain a limited amount of information; (4) High quality and easy to understand - combining patient and carer needs, HCP expertise and patient advocacy agency perspectives	App	Multiple European languages	However, further research is needed as digital patient passports may also pose new challenges, for example in terms of data management, patient privacy, informed consent, and control of shared data. In addition, digital passports may not necessarily fit the needs of every patient with the disease as, for example, people with limited digital skills and people not willing to use a smartphone to handle clinical issues might still prefer to use conventional paper documents. Issues about confidentiality and ethical rules in various EU countries, remain to be solved.	
54	Parrott H, et al. A digital solution for virtual consultation and sharing health data in adults with cystic fibrosis. Journal of Cystic Fibrosis. 2019;18(Supplement 1):S51	2019	UK	Cystic fibrosis	Virtual consults and remote monitoring	Research	Conference abstract	Frequent clinic visits are having a huge impact on the quality of life.	Also growing cohort of patients as they are living longer - concerns about Health system capacity	telehealth	Not given	Virtual clinics and spirometry done by patients at home	Considerable savings of time for both patients and clinicians. So far no issues. Patients like it.
55	Polineni D, et al. A stakeholder-informed feasibility study of tele-coaching to improve treatment adherence in patients with cystic fibrosis. Pediatric Pulmonology. 2017;52(Supplement 47):479.	2017	USA	Cystic fibrosis	Tele-coaching	Research	Conference abstract	Adherence to treatment not optimal	Proposed intervention= tele-coaching	telehealth			

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56	Richesson RL, et al. An automated communication system in a contact registry for persons with rare diseases: Scalable tools for identifying and recruiting clinical research participants. Contemporary Clinical Trials. 2009;30(1):55-62.	2009	USA	Rare diseases	Notifications of relevant new research projects	Research	Journal article	Patients have a lack of access to new trials; Researchers - hard to recruit patients	All related to rarity of the conditions	website passive	Not given	web-based automated system generates periodic and customized communications to notify registrants of relevant studies in the NIH Rare Diseases Clinical Research Network (RDCRN).	
57	Rits S,et al. Weekly patient webcasts: An adult CF center's response to the COVID-19 pandemic. Conference Abstract presented at Pediatric Pulmonology; October, 2020.	2020	USA	Cystic fibrosis	Webcasts on COVID	publicly available	Conference abstract	Urgent need for disease specific information during COVID pandemic	Plenty of information for the general public but not for people with a rare disease. Concerns from people with CF adequate infection control, access to care, medications and supplies, clinical outcomes as they relate to CF, employment status and disability, and overall mental health	other	Not given	Weekly webcasts on COVID made available Could ask questions through Google form. Email notification out to patients and carers.	
58	Rodman J, et al. Patient perspectives on electronic access to registry health records: An Irish-Slovene online survey. Journal of Cystic Fibrosis. 2016;15(Supplement 1):S36.	2016	Ireland and Slovenia	Cystic fibrosis	European CF Registry	Research	Conference abstract	Lack of patient access to their own medical records	Thought to be useful for self management	website active	Not given	Hypothetical access to the Register	Patients in favour of it but concerned about security
59	Rudolf I, et al. Assessment of a Mobile App by Adolescents and Young Adults With Cystic Fibrosis: Pilot Evaluation. JMIR mHealth and uHealth. 2019;7(11):e12442.	2019	Germany	Cystic fibrosis	Kinderhilfe Organtransplantation (KiOAPP)	publicly available	Journal article	Lung function decline in transition from 12 and 24 years.	Improving self management and independence from parents important for ongoing outcomes. Poor self management only slowly manifests itself.	App	?German	App contains a diary function for recording vital signs and personal observations, communication platform for sending information to the HCP, a medication plan, and medication reminder function. Age appropriate format	Perceived as useful and supportive overall. Most useful feature was the medication plan and reminders. Diary use became less frequent quickly at odds with its high usefulness rating.
60	Ruther DF, 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).	2021	Europe	autoimmune liver diseases (AILD)	Hypothetical	Research	Journal article	Research into what consumers want in a Rare Liver disorder app		App	Not reported	Hypothetical	A substantial majority of patients expected to benefit from the app due to constant access to health data (81%), better overview of the course of the disease (80%), better understanding of the disease (70%) and faster detection of drug side effects (64%). only the minority of patients believed that an app could help to improve quality of life (21%), reduce fears associated with the disease (24%), reduce mistakes in taking medication (32%) or improve medication adherence (37%) (Fig. 3). Significantly desired features were information on new developments (93%), access to one's own medical records (89%), notifications to practitioner in case of concerns (84%), automatic ordering of follow-up prescriptions (81%), information on clinical trials (79%), disease information (79%) and recording of health concerns with symptom trackers (73%). In contrast, significantly undesired features were gamification or reward system (5%), networking (27%) and comparisons (35%) with other persons affected (Fig. 3). Did not all match with HCP responses.
61	Sottilotta G, et al. The HEMONLINE project: Preliminary results. Haemophilia. 2012;3):77.	2012	Italy	Haemophilia	HEMONLINE	Research	Conference abstract	Distance to treatment centre burdensome and results in expenses including loss of wages.		telehealth	Not given	Web-cam and internet connection provided to patients to allow them to contact HCPs in addition to in person home visits by the MDT	In progress but suggests better use of health services and patient satisfaction

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62	Stevenson Won A, et al. Assessing the Feasibility of an Open-Source Virtual Reality Mirror Visual Feedback Module for Complex Regional Pain Syndrome: Pilot Usability Study. J Med Internet Res. 2021;23(5):e16536.	2021	USA	Complex regional pain syndrome (CRPS)	Virtual Reality Visual Feedback Module	Research	Journal article	Few treatment options for CRPS.	Mirror visual feedback therapies promising. Can be delivered using VR but costly and not so far popular. Now cheaper and HCPs developing skills to deliver it	Website active	Not reported	HCP led VR sessions in a clinic with a view to extending it to home use. Provides therapy platform and information.	Did not improve pain but usability, feasibility and all good.
63	Storf H,et al. Vision and challenges of a cartographic representation of expert medical centres for rare diseases. Studies in health technology and informatics. 2014;205:677-81.	2014	Germany	Rare diseases	se-atlas	Research	Journal article	Difficult for people with rare diseases to find appropriate specialist centre in Germany		website active	Not given	Interactive map and list	
64	Timmer AM, et al. A Blended Physiotherapy Intervention for Persons With Hemophilic Arthropathy: Development Study. J Med Internet Res. 2020;22(6):e16631.	2020	Netherlands	Haemophilia	e-Exercise HA	Research	Journal article	Few PTs understand haemophilic arthropathy and so accesss to one is difficult for this common complication; Cost of specialist physio	most critical barriers to adhering to physiotherapy were the limited reimbursement by the health insurance, execution of boring exercises, and stubbornness of the patients to accept advice. The patients mentioned that a good relationship with their physiotherapist facilitated their adherence to the physiotherapy treatment.	website active	Not given	A 12-week blended intervention was developed, integrating face-to-face physiotherapy sessions with a web-based app.The intervention consists of information modules for persons with HA and information modules for physiotherapists, a graded activity program using a self-chosen activity, and personalized video-supported exercises. The information modules	
65	Verkleij M, et al. Development and evaluation of an internet-based cognitive behavioral therapy intervention for anxiety and depression in adults with cystic fibrosis (eHealth CF-CBT): An international collaboration. Internet Interventions. 2021;24.	2021	Netherlands	Cystic fibrosis	eHealth CF-CBT	Research	Journal article	Anxiety and depression in people with CF common and can affect adherence, health and QoL	Access to evidence-based mental health care can be limited adding to the cost and burden of care for people with CF.	website active	English and Dutch	Internet delivered CBT sessions guided bya therapist. Trialled with 16 people with CF	high levels of acceptability and usability
66	Verkleij M, et al. Development of a therapist-guided internet-delivered cognitive behavioral therapy intervention for anxiety and depression in adults with cystic fibrosis (e-Health CF-CBT): An international collaboration. Pediatric Pulmonology. 2019;54(Supplement 2):406-7.	2019	Netherlands	Cystic fibrosis	eHealth CF-CBT	Research	Conference abstract	Anxiety and depression in people with CF common and can affect adherence, health and QoL	Access to evidence-based mental health care can be limited adding to the cost and burden of care for people with CF.	website active	English and Dutch	Pilot Internet delivered CBT sessions guided by a therapist	
67	Verkleij M,et al. Development and evaluation of an internet-based cognitive behavioral therapy intervention for anxiety and depression in adults with cystic fibrosis: An international collaboration. Pediatric Pulmonology. 2020;55(SUPPL 2):267.	2020	Netherlands	Cystic fibrosis	eHealth CF-CBT	Research	Conference abstract	Anxiety and depression in people with CF common and can affect adherence, health and QoL	Access to evidence-based mental health care can be limited adding to the cost and burden of care for people with CF.	website active	English and Dutch	Internet delivered CBT sessions guided bya therapist. Trialled with 16 people with CF	High levels of acceptability and usability
68	Wagner B,et al. Establishing an online physical exercise program for people with hemophilia. Wiener Klinische Wochenschrift. 2019;131(21-22):558-66.	2019	Germany and Austria	Haemophilia	online exercise program	limited availability	Journal article	Distance to attend exercise program at the specialist centre not feasible		website passive	Not given	Online exercise lessons for adults and young people conducted by physician. Also have consultation hours (? Online) when you can speak to someone at the clinic about the program)	

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69	Walker KK. Cognitive and affective uses of a Thoracic Outlet Syndrome Facebook support group. 2014	2014	USA	Thoracic Outlet Syndrome (TOS)	Thoracic Outlet Syndrome (TOS) Awareness Facebook group	publicly available	Journal article	Finding reliable information difficult for people with a rare disease	HCPs may not be knowledgable. Support from peers difficult due to rarity.	social platform	Not given	Facebook group for people with TOS	Analysis of cognitive needs indicated TOS patients used the site more to share information about their own TOS symptoms and journey with diagnosis than to seek information. Analysis of affective needs found patients were more likely to use the site to give support and encouragement to others than to express concerns and complaints. The complaints they did express were primarily related to their frustration with the general medical community's perceived inability to diagnose and understand their disease or to question a specific doctor's diagnosis/recommendation
70	Wittmeier K, et al. Analysis of a Parent-Initiated Social Media Campaign for Hirschsprung's Disease. J Med Internet Res. 2014;16(12):e288.	2014	Canada	Hirschsprung's Disease	Social media campaign "Shit happens"	publicly available	Journal article	Families of children with rare diseases can feel isolated and unsupported		social platform	English	Social media campaign to raise awareness and provide support for families dealing with Hirschsprung's disease. Facebook, Twitter, Blog posts and question and answer style postings. Very engaging for the community	Analytics showed 5400 views of the blog from 37 countries. Across platforms - within 2 hours of posting a question could get 143 views, 20 responses increasing to 30 responses within 5 hours.
71	Wood J, et al. A smartphone application for reporting symptoms in adults with cystic fibrosis improves the detection of exacerbations: Results of a randomised controlled trial. Journal of Cystic Fibrosis. 2020;19(2):271-276.	2020	Australia	Cystic fibrosis	Not given	Research	Journal article	Delayed reporting of symptoms can result in more severe exacerbations and worse outcomes.		App	Not reported	12 questions re symptoms associated with exacerbation that alert a nurse if respondents answer yes.	No change in IV antibiotic use. Number of courses of oral antibiotics increased and the median (IQR) time to detection of exacerbation requiring oral or IV antibiotics was shorter in the intervention group compared with the control group. No detectable change in lung function.
72	Wood J, et al. High usability of a smartphone application for reporting symptoms in adults with cystic fibrosis. J Telemed Telecare. 2018;24(8):547-552.	2018	Australia	Cystic fibrosis	Not given	Research	Journal article	Delayed reporting of symptoms can result in more severe exacerbations and worse outcomes.		App	Not reported	12 questions re symptoms associated with exacerbation that alert a nurse if respondents answer yes.	Study looked at HCP response to the app questions using 45 clinical scenarios. Excellent usability and near-perfect agreement interpreting the app responses.

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Needs of people with rare diseases that can be supported by electronic resources: a scoping review

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Abstract

Objectives:

Rare diseases are characterised by low incidence, often with little evidence for effective treatments. Isolated patients and specialist centres for rare diseases are increasingly connected thanks to the internet. This scoping review aimed to identify issues facing people with a rare disease that authors report may be addressed by electronic resources (mobile applications, websites, social media platforms, telehealth and online portals).

Design:

Scoping review guided by the PRISMA-ScR guidelines.

Data sources:

Medline, Embase and PsycInfo were searched, supplemented by hand searches of selected journals, in July 2021.

Eligibility Criteria:

Peer-reviewed literature in English was searched using terms for rare disease (incidence <1:2,000), electronic modalities (e.g., mobile phone) and patient support terms. No date limit was set. Conference abstracts were included.

Data extraction and synthesis:

Data extracted: rare disease/group of diseases, name of the e-resource, need identified in the patient cohort, features of the e-resource, any other findings or observations of interest. From this, a framework was developed synthesising features across diseases and resources.

Results:

Seventy-two papers were found (from 383). Fifty-six electronic resources were described in 64 papers, while 12 papers were exploratory studies. Cystic fibrosis (n=28) was most frequently addressed, followed by haemophilia (n=16).

Four domains and 23 subdomains of needs were extracted from the papers. The domains of needs were: support for self-management, access to high-quality information, access to appropriate specialist services, and social support. Subdomains sometimes related to needs of individual rare diseases (e.g., social isolation due to infection risk in people with cystic fibrosis). Fifteen electronic resources were identified that supported parents of children with rare disorders.

Conclusions:

While it can be argued that rare diseases per se may be no less distressing or onerous to care for than a high prevalence disease, rare diseases have unique features: the lengthy odyssey to find a diagnosis, then appropriate specialists, the lack of evidence around effective treatments, guidelines, or access to knowledgeable general health service providers. Designers of electronic resources are urged to consult key stakeholders to enhance the effectiveness and usability of resources for people with a rare disease.

Article summary

Strengths and limitations of this study

- Individual named rare diseases/groups of diseases were included in the search terms to overcome deficiencies of searching only using “rare diseases,” but could not cover all rare diseases.
- There are estimated to be 7-8,000 rare diseases so searching by name (plus their synonyms) was not feasible.
- Data extraction considered the type of electronic resource proposed, by disease and by need the resource addressed.

- Electronic resources were categorised into mobile applications, social support platforms, telehealth tools and online portals, and active (containing interactive content e.g., quizzes) and passive websites (information only).

Key words

Rare disease, patient resources, patient empowerment, e-health, mobile apps

Introduction

There are an estimated 6-7,000 different types of rare disease, many of them genetic.(1) We define a rare disease as a condition that has an incidence of less than 1 per 2,000 live births in the population.(1) Examples of rare diseases are Fragile X syndrome, haemophilia A, osteogenesis imperfecta, cystic fibrosis, spinal muscular atrophy type 1, and neurofibromatosis type 2. The low incidence of rare diseases mean that specifics of individual diseases are not covered in medical education programs which must prioritise more common conditions, and also that many health professionals will have never seen a case before.(2) Rare diseases are often difficult to diagnose, leading to the often described "diagnostic odyssey."(3) The case has been made that even after this odyssey is concluded with a definitive diagnosis, the journey continues as people with a rare disease seek to access the best management care.(4)

Less than 5% of the estimated 7,000 rare diseases currently have an effective treatment.(1) The low numbers of cases of each rare disease means that evidence is often lacking to guide best practice. For example, CLN12 disease with an incidence of only 1 per million has too few people with the disease to set up a clinical trial to test the effectiveness of potential treatments or even map the "typical" progression of the disease.(5) Guidance on best practice must be determined through consensus recommendations of specialists in the condition(6, 7), which are often enhanced by the input of consumers who are living with the condition.(8)

A number of studies have explored the specific needs of people with a rare condition.(e.g., 9, 10, 11) Access to appropriate specialist services, finding a generalist health provider who is willing to learn about the condition, living with uncertainty of what is best practice and the trial and error nature of discovering it have all been reported.(e.g., 4)

Electronic resources, by which we mean mobile applications, websites, virtual monitoring devices, social media platforms, telehealth capability and online portals, hold promise of greater connectivity and collaboration in the field of rare diseases. Electronic resources are already being used to

improve understandings of rare diseases as national and international online registries, (e.g., 12, 13) and virtual research consortiums (14, 15) pool their data and consolidate findings.

Electronic resources have a key role for people living with a rare disease. It is recognised that a useful lever to accessing the best management care for people with a rare disease is empowerment, in which people become knowledgeable about their illness and feel able to advocate for their care.(16) Tools to foster empowerment are particularly relevant in this group and electronic resources hold great promise to make information and resources more easily accessible. To our knowledge no one has surveyed this fragmented field to determine the role of electronic resources for people with a rare disease.

This paper aims to systematically scope the peer-reviewed literature to: (i) identify issues facing people with a rare disease that authors report may be addressed by electronic resources, and (ii) collate evidence around features of effective and user-friendly e-resources.

Methods

We systematically searched for peer-reviewed literature on consumer-facing electronic resources for people with a rare disease, guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (17) (see supplementary file 1 for the completed PRISMA-ScR checklist). The search was supplemented with a hand search of relevant peer-reviewed journals. Patients and public were not directly involved in the design, reporting or dissemination plan of this paper.

Three databases, Medline, Embase and PsycInfo were searched in July 2021. No date limits were set but we only included articles in the English language. We targeted empirical peer-reviewed full articles but initial exploratory searches showed that a large proportion of the retrieved items were conference presentations on resources not reported elsewhere. These were therefore also included in the review. Search terms were developed through exploration of Medical Subject Heading terms, and key words from equivalent papers from other fields. Search strings combined terms for rare

disease, (including specific named rare disease conditions to maximise results), with patient and carer facing resources (e.g., health resources, patient participation), and terms associated with electronic resources (e.g., mobile applications, cell phone, e-health). In addition, a hand search was performed in *Orphanet Journal of Rare Diseases* (searching for patient focused electronic resources) and *Journal of Medical Internet Research* (searching for applications for rare diseases). Search strings are shown in supplementary file 2.

The definition of a rare disease as having an incidence of less than 1:2,000 was used as a guide only as the grouping together of related rare diseases muddied the waters on exact rates, as did the range of definitions employed when reporting on rare diseases. The search therefore drew on named rare conditions/groups of conditions the most common types of rare diseases (based on research effort for therapeutic companies around the world.(18) Imperfect as that list is, it retrieved many more useful articles than the generic rare disease terms. “Mitochondrial respiratory chain disorders” was also added as a large group of rare diseases that are not amenable to pharmaceutical treatment. The condition groups searched for by name therefore were narcolepsy, primary biliary cholangitis, Fabry disease, cystic fibrosis, haemophilia, spinal muscular atrophy, retinal dystrophy, X-linked hypophosphatemia, urea cycle disorders, pulmonary arterial hypotension, cerebral adrenoleukodystrophy, hereditary angioedema, AA amyloidosis, Cushing's syndrome, and mitochondrial respiratory chain disorders.

The following inclusion criteria needed to be met for a paper to be included: (a) the paper was framed around the needs of people diagnosed with a rare disease or group of rare diseases (defined as incidence <1:2,000 (1)); (b) the focus was on how an electronic resource could meet that need in some way (c) either proposed and described a particular electronic resource, or reported on the development, testing or evaluation of an actual electronic resource. Exclusion criteria were: (i) not about a rare disease or group of rare diseases; (ii) electronic resources were not consumer-facing (e.g., virtual monitoring where the consumer has a passive role and no access to the data,

applications that consumers used altruistically to collect data for researchers; electronic tools for health care professionals only).

Search results were downloaded into reference management software EndNote X9 and two researchers (JL and SB) independently screened 50% of titles and abstracts using the eligibility criteria. Disagreements were discussed until consensus was met. Remaining articles were screened by JL. Included articles were read in full and eligibility criteria again applied (by JL and validated by SB). Data was extracted from the final set: rare disease/group of diseases, name of the e-resource, need identified in the patient cohort, features of the e-resource, any other findings or observations of interest.

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.

Results

The search resulted in 383 papers. Title and abstract screening removed 223 papers and full text screening, another 33. This left 72 papers for data extraction and analysis. Figure 1 shows the PRISMA flow chart for the search.

Studies were set in 16 different countries including seven papers that included all of Europe. United States of America (n=14), the United Kingdom (n=11), and Canada (n=10) were the best represented countries. Figure 2 shows frequencies of all countries. Twenty-one different rare diseases were represented mostly in single papers, while 8 papers focused on rare diseases generally (n=8). The most common rare disease reported was cystic fibrosis (n=28) followed by haemophilia (n=19). Table 1 gives details.

<<Figure 1: PRISMA flowchart for the search. (*JMIR* = *Journal of Medical Internet Research*; *OJRD* = *Orphanet Journal of Rare Diseases*)>>

<<Figure 2: Countries in which included studies were undertaken (frequency of papers).>>

Table 1: Overview of included papers. (* refers to papers focussed on women with non sex-specific Mendelian rare bleeding disorders)

Rare disease / group of diseases	**Number of papers**
Acute Intermittent Porphyria (AIP)	1
Addison's disease	3
Autoimmune liver diseases	1
Bleeding disorders in women*	1
Complex regional pain syndrome	1
Congenital hypogonadotropic hypogonadism, Kallmann syndrome	1
Cystic fibrosis	28
Genetic eye disorders	1
Haemophilia	19
Hirschsprung's Disease	1
Idiopathic subglottic stenosis	1
Inborn errors of metabolism	1
Lymphangioleiomyomatosis	1
Narcolepsy	2
Osteogenesis Imperfecta	1
Phenylketonuria, maple syrup urine disease or tyrosinemia	1
Rare and Congenital Anaemias	1
Rare diseases	6
Rare Multisystemic Vascular Diseases	1
Thoracic Outlet Syndrome	1

Most papers reported on e-resources that were being trialled or were under development (n=56 e-resources from 64 papers), while 12 were framed as scoping exercises or explored usability of existing websites. For example, Nicholl and colleagues (19) explored the needs of people with rare

diseases that could be met by a consumer facing website, Ruther and colleagues (20) researched what people with rare liver disorders need in an app, and Aizawa and colleagues (21) critiqued information available on the internet for people with narcolepsy.

E-resources fell into five broad categories: (i) mobile applications (apps) for cell phones or tablets (n=22), (ii) social networking platforms (n=14), (iii) telehealth and virtual care platforms (n=13), (iv) websites (interactive content e.g., education modules with quizzes) (n=15), and (v) websites (passive content e.g., information) (n=7). Some e-resources fit into more than one category (e.g., WhatsApp platform for parents of newly diagnosed infants with haemophilia provided social support from other parents as well as virtual consults with specialists.(22) In these cases, the main function decided the category. Table 2 lists the types of resources, their features and their benefits.

Type of e-resource	Features and benefits
Mobile applications (apps)	Apps for phones and tablets can provide portable, always available and easily accessed information, data entry (e.g., symptom trackers, guidelines, calculators), and links to other resources.
Social networking platforms	Facilitating contact /emotional support between isolated people with the same rare disease; access to advice for day to day management queries
Telehealth and virtual care platforms	Rare disease specialists are also rare, often involving long journeys to see them face to face. Telehealth consults allow easier access. Virtual care, where patient uploaded data can be shared with a health professional also overcomes the burden of travel and facilitates access to care from an appropriate specialist.
Websites (interactive)	Websites with interactive components allow the patient to enter their data and tailor content. Patient education through quizzes and games especially useful for younger people.
Websites (passive)	High quality information can be made easily accessible on a website

Synthesised themes from the data extraction led to the identification of four domains and 23 sub-domains of needs of people with a rare disease or parents of children with a rare disease. A range of unique needs arising from features of individual diseases were identified (e.g., risk of life-threatening acute episodes in Addison's Disease in a context of few emergency health professionals being knowledgeable or confident to deal with adrenal crisis (23)), as well as more global needs that were common across all presentations (e.g., the scarcity of high quality, relevant information about individual rare diseases). (19-21, 23-51)

Needs are summarised in Table 3 giving examples of disease specific needs in each sub-domain, and examples of the e-resources that had been developed or proposed to address those needs. Data extracted from the final set of items is given in full in supplementary file 3.

Domain	Sub-domains with disease-specific examples	e-resource examples
Chronic diseases requiring self-management	Complicated self-management (e.g., monitoring for bleeds and factor usage for haemophilia **(35, 52)**)	Online tool (Metabolic DietAppSuite) for smartphones/desktops for 15 different Inborn Errors of Metabolism. Creates a personalised dashboard including specific nutrient goals. Food diary, nutrient counts **(53)**
	Some treatment regimes require detailed record keeping to optimise outcomes (e.g., treatment of infections in CF **(33, 51, 54, 55)**)	MyCBDR (linked to Canadian Bleeding Disorder Registry (CBDR) is an app that allows people with a bleeding disorder to track infusions and add symptoms. Data can be shared with all Haemophilia Treatment Centres in Canada **(35)**
	Transition to self-care as adolescents become adults (e.g., teens with severe haemophilia **(29, 56-58)**)	Smartphone app (Faccio Centro) aimed at adolescents with CF that lists daily therapy, with instructions on order, progress tracking, alerts for when to start and when checks are needed. Also can email questions to healthcare team **(59)**
	Exercise programs need to be tailored to the rare disease (e.g., reduced lung function and exercise tolerance in people with CF **(60-62)**)	LAM App on smartphone with interfacing wearable devices for women with Lymphangioleiomyomatosis (LAM). Tailored exercise program and physio check in **(63)**
	Monitoring changes in symptoms and treatments (e.g., recognising bleeds in mild haemophilia **(64, 65)**)	MyCyFAPP calculates Pancreatic enzyme replacement therapy-doses for fat digestion, a symptoms diary, educational material, and linked to a web tool allowing health professionals to view data and give feedback **(28, 30, 66)**
	Burden of hospital attendance (e.g., living far away from only specialist centre for narcolepsy **(67)**; rare diseases with high disease burden (e.g., CF **(68)**)	An ultrasound diagnostic solution for children with haemophilia, the EMO.TI.ON. System used at home by parents or caregivers to diagnose suspected bleeds. System can transfer live images to specialist physician **(69)**
	Depression, anxiety, distress affect adherence to treatment regimes, which in turn affect health and quality of life (e.g., distress of parents of newly diagnosed children with haemophilia **(27)**)	Internet delivered cognitive behavioural therapy sessions, eHealth CF-CBT guided by a qualified therapist for people with cystic fibrosis experiencing depression or anxiety **(70)**
Lack of high-quality information on all aspects of the rare disease	Information that is readable, accessible and from a credible source (e.g., lack of specific information on rare and congenital anaemias **(71)**)	Newborn Screening Connect (NBS Connect) provides high quality information for parents of children diagnosed with a disorder included in the newborn screening panel performed routinely in USA **(43)**
	Information available in your language, appropriate for your culture (e.g., Canadian haemophilia resources in English and French **(56, 64)**)	Online education package for congenital hypogonadotropic hypogonadism and the olfacto-genital syndrome is available in 20 European languages. Readability score meets recommended level **(26)**
	Appropriate to age group, or special needs (e.g., information for teens with CF **(72)**)	Gene.vision website on genetic eye disorders optimised for people with impaired vision **(40)**
	Access to relevant clinical trials, or new research findings may be difficult to find **(45)**	NIH Rare Diseases Clinical Research Network (RDCRN) notifies registrants with a range of rare disorders of relevant studies **(45)**

	Disease specific information on niche topics like family planning (e.g., for genetic disorders such as CF **(32)**)	Facebook group (MyGirlsBlood) for women with bleeding disorders where women can ask questions or share experiences especially around menstruation **(34)**
	Urgent need for disease specific information during COVID-19 pandemic **(46)**	Weekly webcasts on COVID for people with CF with questions through Google forms. Email notifications of webcasts sent to known patients in USA **(46)**
Specialist centres may be geographically dispersed and hard to find	Identifying appropriate care for rare disease (e.g., nearest specialist; appropriately trained allied health professionals (e.g., physios who know risks of exercise with haemophilia **(73)**)	Mobile app developed by VASCERN (European Reference Network on Rare Multisystemic Vascular diseases) contains an easily searchable Directory to find closest expert and to find appropriate patient advocacy group within Europe **(44)**
	Burden of hospital attendance (e.g., living far away from only specialist centre; rare diseases with high disease burden (e.g., severe haemophilia **(74)**)	Virtual Reality Visual Feedback Module for people with complex regional pain syndrome (who have few treatment options and for whom travel is onerous). After initial in-person training and assessment, can be continued at home **(75)**
	Knowledgeable emergency care for acute events may be hard to find (e.g., for infants with newly diagnosed haemophilia **(27)**)	Quick response (QR coded) bracelet has a scannable QR code that links to emergency management information for people in adrenal crisis **(23)**
	Information on daily management may be lacking for both the person with the rare disease and the health professionals supporting them (e.g., for parents of infants with Hirschsprung's Disease **(50)**)	Thoracic Outlet Syndrome (TOS) Awareness Facebook group for both people with TOS and health professionals. Most posts encouraging and giving sound advice **(49)**
Social isolation from peers and advice networks	Unable to connect with people with the same disorder (e.g., being the only parent you know with a child with a rare disorder **(25)**)	Online forum for people with Addison's Disease or Cushing's syndrome, moderated by the Dutch Adrenal Society **(37)**
	Disorders that require isolation for infection control, or safety are isolated from unaffected peers as well (e.g., fracture risk for children with OI in new surroundings **(31)**)	Online conferences (BreatheCon) for people with cystic fibrosis who must isolate for infection control **(32)**
	Emotional support needed for distressed parents (e.g., for parents of children with OI **(31)**)	Skype support groups for women with acute intermittent porphyria mediated by a porphyria experts **(76)**
	Support for daily management issues (e.g., online for people with idiopathic subglottic stenosis **(36)**)	Social media campaign around living with Hirschsprung's Disease: Shit happens on Facebook, Twitter, Blog posts **(50)**
	Information and peer knowledge sharing for adolescents transitioning to full self-management (e.g., for teens with CF **(72)**)	hiFIve - small online group for 11-19 year-olds living with severe haemophilia. Closed to parents. Trying to harness peer to peer transmission of self-management skills **(57)**
	Social support associated with better mental health / health outcomes (e.g., parents of newly diagnosed infants with Phenylketonuria **(43)**)	Online peer support program (CFOne) for adolescents and young adults with CF **(77)**

Table 3: Domains and sub-domains of needs of people with a rare disease that can be solved or supported by a consumer-facing electronic resource. (CF = cystic fibrosis, OI = osteogenesis imperfecta)

Chronic diseases requiring complicated self-management

Many rare diseases were described as having a high disease burden relying on complicated self-management regimes. The association of adherence to specific treatments with better health outcomes is strongly supported by evidence for cystic fibrosis (78), metabolic diseases requiring medical diets (79), and haemophilia (80), providing a clear rationale for supporting self-management. Optimal self-management in many cases required careful record-keeping of symptoms and tracking of treatments. Mobile apps were often designed to assist with this need. Symptom trackers were a common feature with or without medication alerts or treatment information (pancreatic enzyme replacement therapy for people with cystic fibrosis (28, 66)). Some had a function that allowed sharing of patient entered data with their health care team (e.g., 54, 81). Others tracked dietary intake for those on a medical diet (e.g., 53).

Lack of high-quality information

A common problem across all the rare diseases represented in this review was access to high-quality, culturally and demographically appropriate information from a credible source that was easy to find and understand. Information sought could be around the nature of the disease, medical treatments, prognoses, etc. for the person with the disease and sometimes also for the health professionals supporting them (e.g., 23, 26, 49). Links to registries and research consortiums helped people stay up to date with treatment options (e.g., 45). Information about day-to-day management issues was often sought from social networks of people with experience of the same disease rather than specialist health professionals (e.g., 34, 37, 38). One paper critiqued existing online information on the rare disorder narcolepsy, following a study that showed access to high quality web-based information could reduce time to diagnosis through better understanding of signs and symptoms (21). Some informational needs related to “niche” topics, e.g., an app for the subset of people with mild haemophilia to help them assess for cryptic bleeds after injury (64).

Specialist centres for rare diseases may be geographically dispersed

Another common problem was the small number of rare disease specialist centres that could be widely dispersed geographically. Some e-resources provided directories for the nearest specialist centre (40, 48), or nearest, appropriately skilled allied health provider or patient advocacy agency (71). Others proved virtual consultations (e.g., 82) or tailored exercise (e.g., 60) or mental health services (70) via telehealth.

Social isolation from peers and advice networks

The social isolation that comes from having a rare disease is often discussed as a need unique to people with a rare disease. Khair and colleagues (83) note that for many adolescent boys with haemophilia, the only person other than their doctor who knows about their disease is their parent. Limited access to specialist services means people or parents of a child with a rare condition have to face non-urgent day-to-day issues by themselves unless they find appropriate social support. Social support could be with people with the same disease (e.g., Facebook / Twitter group for Hirschsprung's disease (50)) or include health professionals (e.g., online support group for thoracic outlet syndrome (49)).

Discussion

This review found 72 papers outlining the needs of people with a rare disease, or their carers that could be addressed by an e-resource. Four domains and 23 subdomains of needs were identified and e-resources to address or support those needs were broadly categorised into five groups: mobile apps, social support platforms, telehealth and virtual health tools, and active and passive websites.

A range of unique needs arising from features of individual diseases were identified. Examples included the burden of constant physical isolation to prevent infection for people with cystic fibrosis (32), the acute distress of parents of infants with osteogenesis imperfecta at suspicions of child

abuse that often preceded diagnosis (31), and the difficulty of recognising signs of an impending adrenal crisis for people with Addison's Disease that can be life threatening.(23, 37) While the burden of disease for rare disorders may be similar to higher incidence conditions such as stroke or breast cancer, the added burden of the lack of a solid evidence base of effective treatments, best practice guidelines and competent and knowledgeable health service providers is not. The well documented diagnostic odyssey for people with rare diseases (3) and laments that health professionals had never heard of their disease (4) is a burden unique to this group.

This burden of uniqueness spills over to other needs. Exercise is crucial for physical and mental wellbeing but for many people with a rare disease, any exercise program must be tailored and supervised by a suitably knowledgeable health professional. Reduced exercise tolerance for people with cystic fibrosis and LAM, and risk of bleeds into their joints for people with haemophilia were addressed by telehealth or online modules.(60, 63, 81, 84-86) Social support of group exercise classes is known to be motivating but is not possible for people with cystic fibrosis who are at risk of cross infection. Online solutions went some way to solving this need (e.g., 85).

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., 87)) Although the quality of the advice and information exchanged on social support platforms is often criticised,(88) there was no evidence of this in our sample, with some sites convened or facilitated by a trained health professional. 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.(36, 37, 49, 50) 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.(20, 31)

It has been argued that an often overlooked need for people with a rare disease is support for their parents or carers, on whom the burden of management often falls.(89) This review identified 15 e-

resources that supported carers (mostly parents). The distress that parents feel on diagnosis of a child with a rare disease was frequently discussed and provided the rationale for social support platforms and messaging apps, management support apps, and telehealth tools. One German study provided parents of children with cystic fibrosis online writing-based therapy to alleviate psychological distress and anxiety.(90)

Readability of information found on the internet has been widely critiqued and criticised. A typical example is a review of online education resources from government and health care organisations on multiple sclerosis and rheumatoid arthritis (neither considered rare diseases) were found to be written at 11th or 12th grade standard, whereas the average American reads at a 5th grade standard.(91) The authors state material that is too complex limits its usefulness and increases inequities. E-resources in this review were often noted to be co-designed by health professionals, patient advocacy agencies, parents, and people with a rare disease as well as education experts to mitigate this risk. (e.g., 26, 53) Usability and acceptability studies were reported for some but not all the resources found in this review. Ensuring resources are easy to understand, appeal to the target group's demographics (e.g., adolescents versus older adults), and suited to the skills of the users is an obvious goal but one that this scoping review did not always find was done well. Patient advocacy agencies are noted in the broader literature to be particularly proactive in ensuring acceptable and easy to understand resources. A survey of patient advocacy groups for people with rare diseases, found 100% of respondents would be interested in collaborating with relevant healthcare or research groups to develop complementary resources suited to their members, and avoid wasted effort involved in duplication.(89)

The very low incidence of rare diseases mean that patients and appropriate services are geographically widely distributed. Electronic resources such as telehealth, social networking platforms and specialised apps are therefore ideal solutions to provide appropriate care. Progress in understanding diseases that are rare has been accelerated in recent years as clinicians and scientists

around the world pool the data they have on local. A similar benefit comes for patients as they find or are linked to others with knowledge and experience of their unique situation. 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.

Strengths and limitations

The nature of the topic (e-resources) lent itself more to conference presentations rather than full peer-reviewed articles. A strength of our search was that we included these items although a weakness is that limited information was able to be extracted from some abstracts. Further there was likely an element of publication bias where only successfully developed e-resources were reported. 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 terms to capture rare diseases was problematic. Since there are over 7,000 rare diseases, it was not feasible to search for each by name. Our strategy was therefore to search for a limited number of named rare disease groups. The list of needs identified are characteristic of any rare disease, and while some needs are unique to some specific disease manifestation, the majority were applicable to all. This generalisability will be useful for anyone designing e-resources to support people with a rare disease.

Conclusion

This review scoped the peer-reviewed literature to identify needs unique to people, or carers of people with a rare disease. It identified four broad domains of need: (i) support for complicated self-management regimes, (ii) access to high-quality, easy to understand information, (iii) access to appropriate specialist services, and (iv) social support. Most studies involved needs of people or

carers of children with haemophilia or cystic fibrosis but also addressed another 20 named rare diseases or rare disease groups (e.g., inborn errors of metabolism). While the physical burden of a rare disease may be comparable to higher prevalence conditions such as stroke or cancer, rare diseases have unique overlying issues: the lengthy odyssey to find a diagnosis, the quest to find appropriate specialists to manage your care, the lack of a solid evidence base of effective treatments or best practice guidelines, or access to competent and knowledgeable general health service providers are unique to those with a rare disease. E-resources are well placed to address many of these problems but must be carefully co-designed with key stakeholders lest their complexity, narrow scope or cultural inappropriateness further disempower this already marginalised group.

Abbreviations

AIP	Acute intermittent porphyria
CF	cystic fibrosis
e-resource	electronic resource
JMIR	*Journal of Medical Internet Research*
LAM	Lymphangioleiomyomatosis
OI	osteogenesis imperfecta
OJRD	*Orphanet Journal of Rare Diseases*

Declarations

Conflict of interest

The authors have no conflicts of interest to declare.

Ethics

No ethical approval was required as all data was publicly available.

Patient consent for publication

Not applicable

Patient and Public Involvement

No involvement

Data availability statement

All data is provided in the paper, supplementary files or in the public domain.

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Author contributions

JL, SB, SH and BNGE designed the study. JL and SB collected data and undertook the analysis. SH, ZF, BNGE, JC and JB critically reviewed and commented on the results. JL wrote the first draft of the paper which was reviewed by SB, SH, ZF, BNGE, JC and JB. All authors approved the final version.

Supplementary file 1: PRISMA-ScR Checklist

Supplementary file 2: Search strings

Supplementary file 3: Full data extraction sheet for included papers

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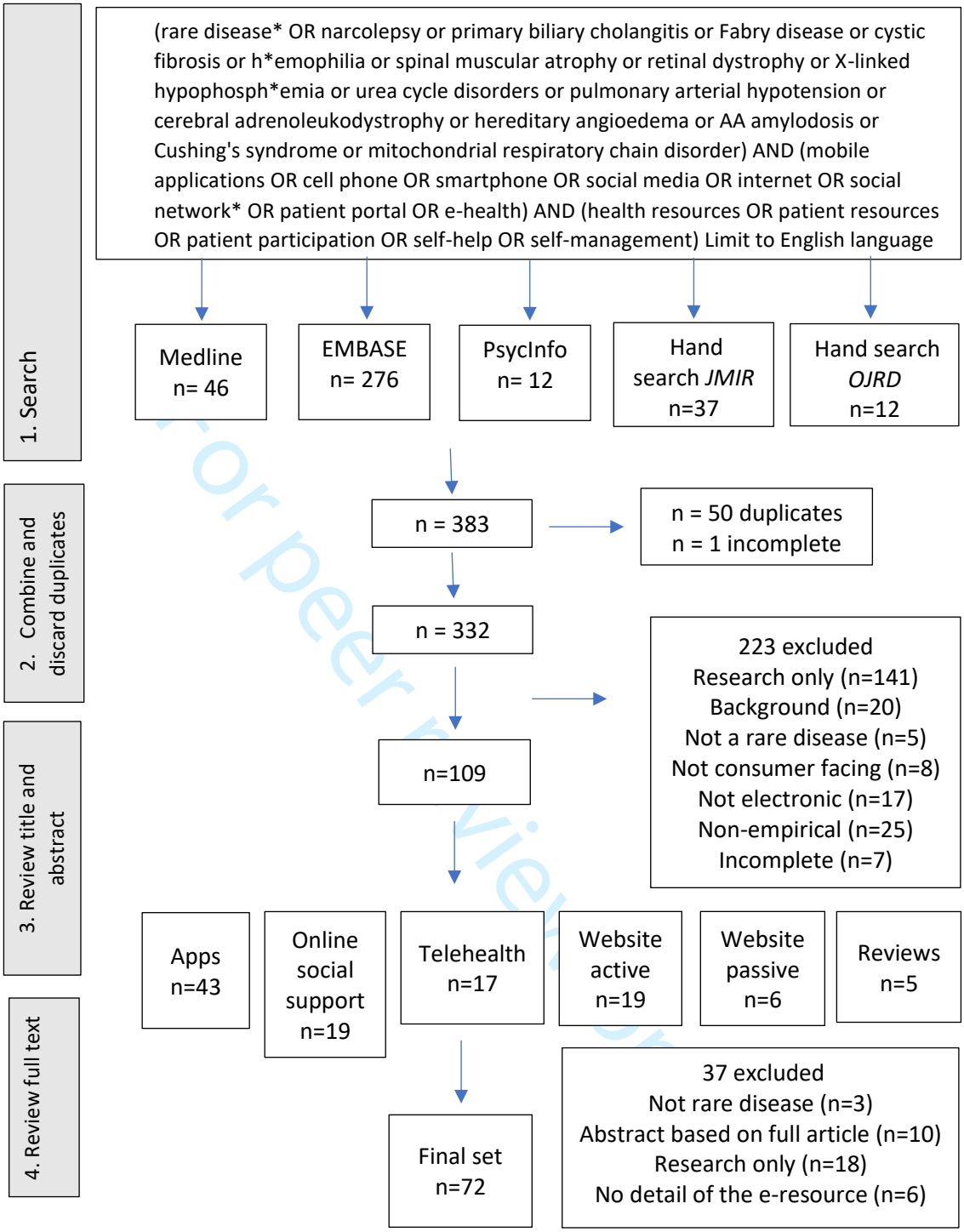
Figure legends

Figure 1: PRISMA flowchart for the search. (*JMIR* = *Journal of Medical Internet Research*; *OJRD* = *Orphanet Journal of Rare Diseases*)

Figure 2: Countries in which included studies were undertaken (frequency of papers).



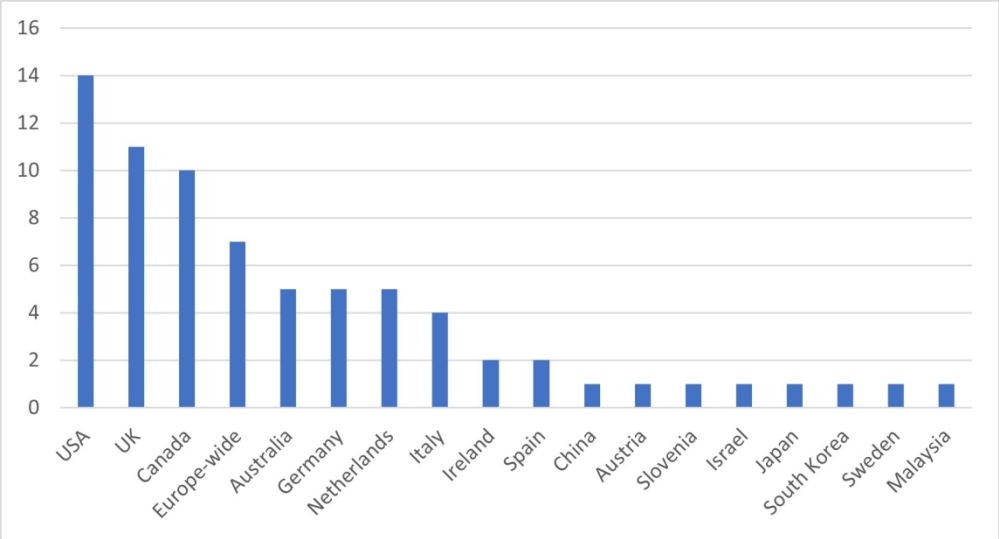


Figure 2: Countries in which included studies were undertaken (frequency of papers).

141x76mm (330 x 330 DPI)

PRISMA-ScR Checklist

Section	Subsection	Item	Page of Mss
Title		1	1
Abstract	Structured summary	2	1
Introduction	Rationale	3	3
	Objectives	4	4
Methods	Protocol and registration	5	4
	Eligibility criteria	6	4
	Information sources	7	4
	Search	8	4
	Selection of sources of evidence	9	4
	Data charting process	10	5
	Data items	11	5
	Critical appraisal of individual sources of evidence	12	NA for this scoping review
	Summary measures	13	NA for scoping reviews
	Synthesis of results		5
	Risk of bias across studies	15	NA for scoping reviews
	Additional analysis	16	NA for scoping reviews
Results	Selection of sources of evidence	17	5 ff
	Characteristics of sources of evidence	18	7 ff
	Critical appraisal within sources of evidence	19	NA for this scoping review
	Synthesis of results	20	8, 12
	Risk of bias across studies	22	NA for scoping reviews
	Additional analysis	23	NA for scoping reviews
Discussion	Summary of evidence	24	13
	Limitations	25	14
	Conclusions	26	14
Funding		27	15

From: Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. Ann Intern Med. 2018;169(7):467-73.

Search string Ovid: Medline, Embase, Psycinfo

rare disease.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fx, dq, nm, kf, ox, px, rx, an, ui, sy, tc, id, tm, mh]

OR

(narcolepsy or primary biliary cholangitis or Fabry disease or cystic fibrosis or h*emophilia or spinal muscular atrophy or retinal dystrophy or X-linked hypophosph*emia or urea cycle disorders or pulmonary arterial hypotension or cerebral adrenoleukodystrophy or hereditary angioedema or AA amylodosis or Cushing's syndrome or mitochondrial respiratory chain disorders).mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fx, dq, nm, kf, ox, px, rx, an, ui, sy, tc, id, tm, mh]

AND

"Quality of Life"/ or "Delivery of Health Care"/ or Patient Advocacy/ or Patient Participation/ or patient education.mp / or Self-Help Groups/ or Health Resources.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fx, dq, nm, kf, ox, px, rx, an, ui, sy, tc, id, tm, mh]

AND

Mobile Applications/ or Cell Phone/ or Smartphone/ or Social Media/ or Internet/ or Social Networking/ or Patient Portal.mp/ e-health [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fx, dq, nm, kf, ox, px, rx, an, ui, sy, tc, id, tm, mh]

Limit to English language

Hand search of Orphanet Journal of Rare Diseases

Electronic resources/ or e-health/ or m-health/ or apps/ or mobile/ or telehealth/ or virtual

Hand search of Journal of Medical Internet Research

Rare dis*/ narcolepsy/ or primary biliary cholangitis/ or Fabry disease/ or cystic fibrosis/ or h*emophilia/ or spinal muscular atrophy/ or retinal dystrophy/ or X-linked hypophosph*emia/ or urea cycle disorders/ or pulmonary arterial hypotension/ or cerebral adrenoleukodystrophy/ or hereditary angioedema/ or AA amyloidosis/ or Cushing's syndrome/ or mitochondrial respiratory chain disorders.

	A	B	C	D	E	F	G	H	I	J	K	L	M
1	**Reference**	**Year**	**Country**	**Rare disease**	**Name of intervention/resource if applicable**	**Research or available**		**Needs/barriers to care**	**Details**	**e-resource**	**Language/s**	**e-resource details**	**Findings (If research only)**
2	Ackbarali TA, et al. Assessing Patient and Provider Perspectives, Clinical Practice, Behaviors, and Knowledge on Hemophilia A Care. Blood; 05 Nov2020. p. 24-5.	2020	USA	Haemophilia	a web-based joint educational initiative for patients/caregivers and HCPs	Research	Conference abstract	Management of severe haemophilia is rapidly evolving - patients, carers and HCPs alike unsure of new treaments but keen to learn		website active	Not given	1-hour online video-based CME activity for HCPs and 1-hour healthcare education activity for patients were created in June, 2020 to address identified practice and knowledge needs among HCPs, and knowledge, communication and self-efficacy behaviors among patients. Each activity consisted of slides, polling and live questions, and remains on-demand	
3	Aizawa R, et al. Status of narcolepsy-related information available on the Internet in Japan and its effective use. Sleep and Biological Rhythms. 2008;6(4):201-7.	2008	Japan	Narcolepsy	Existing internet resources	publicly available	Journal article	High quality web-based information can reduce time to diagnosis for people with narcolepsy	Useful, harmful information is low on search engine rankings.	website passive	Not given	Existing web-based resources	Patients were asking for info on the hereditary nature of the disease and ways to deal with their disease.
4	Al-Saleh H, et al. Beta testing of the "MY CF" smartphone/tablet app: In patients with cystic fibrosis. Conference Abstract presented at American Journal of Respiratory and Critical Care Medicine. Conference: American Thoracic Society International Conference, ATS; 2014.	2014	USA	Cystic fibrosis	MY CF	Research	Conference abstract	Complicated self-management	Difficulties keeping track of medications, test results and symptoms for adolescents or parents of younger children with CF.	App		Android OS for phone or tablet. The three most favored functionalities of the app were: Medication list, Symptom Diary, and Weight/Height/Body Mass Index monitoring. 32 invited to participate; of 23 who did, majority wanted to continue using it and would recommend it	
5	Armayones M, et al. APTIC: A social network to improve the quality of life of members of patients' associations. Conference Abstract presented at Orphanet Journal of Rare Diseases. Conference: 5th European Conference on Rare Diseases, ECRD; 2010.	2010	Spain	Rare diseases	APTIC	publicly available	Conference abstract	Fragmentation of information regarding rare diseases	Need for people to learn from one another, share expereiences	social platform	Not given	Social networking platform that aims at enabling the individual members of patients' associations (mostly parents of children with chronic and rare diseases) to share experiences, information, advice	
6	Aznar J, et al. Telemedicine in Hemophilia: Virtual consultation for the hematologist at patient's home. Haemophilia; July2012. p. 72.	2012	Spain	Haemophilia	domiciliary virtual consultation and virtual monitoring tools	Research	Conference abstract	Frequent hospital visits impact QoL	Domiciliary replacement therapy (DRT) ensures rapid infusion of lacking factors when any bleeding episode occurs and reduces hospital dependency of patients with hemophilia. However, these patients still have to visit the hospital frequently because the hematologist can prescribe general guidelines for home-replacement therapy but cannot adapt them to the bleeding evolution	telehealth	Not reported	Three interventions: (1) patient entered bleeding episode and self managed treatment; (2) virtual monitoring by ultrasound of haemarthroses, (3) Virtual consult	Successful in 45 patients which in turn may decrease depency on hosptial visits and by association QoL

	A	B	C	D	E	F	G	H	I	J	K	L	M
7	Badiu C, et al. Developing and evaluating rare disease educational materials co-created by expert clinicians and patients: the paradigm of congenital hypogonadotropic hypogonadism. Orphanet Journal of Rare Diseases. 2017;12(1)	2017	Europe	congenital hypogonadotropic hypogonadism (CHH) and the olfacto-genital (Kallmann) syndrome	Educational package	Research	Journal article	Need for high quality information/education on rare diseases	Important it is easy to read and engaging	website passive	20 languages	patient education materials	Appropriate reading level and accessibility
8	Balestri E, et al. 'F (accio) C (entro)': Project for a smartphone application to increase adherence to aerosol treatment in adolescents with cystic fibrosis. Conference Abstract presented at Italian Journal of Pediatrics. Conference: 25th Italian Congress of Cystic Fibrosis and the 15th National Congress of Cystic Fibrosis Italian Society. Milan Italy; 2020.	2020	Italy	Cystic fibrosis	Faccio Centro	Research	Conference abstract	Complicated self-management with decreasing adherence from adolescents	Patients with Cystic fibrosis have onerous therapy - respiratory physiotherapy, therapy by aerosol, oral, intravenous and physical activity. During adolescence the therapy adherence, that is undergoing treatments at the right time of the day, in the right sequence and dosage, considerably decreases with negative consequences in terms of: health status, quality of life and hospitalization	App		Mobile phone app - lists daily therapy, with instructions on order, progress tracking, alerts for when to start and when checks are needed. Also can email questions to HCP team.	
9	Barazani Brutman T, et al. New communication technologies improve hemophilia care. Haemophilia. 2017;23(Supplement 2):134-5.	2017	Israel	Haemophilia	WhatsApp social support group messaging	Research	Conference abstract	Parents with newly diagnosed children require immediate response when things happen		social platform	Not given	Social support groups of parents, patients and medical staff WhatsApp. Parents, patients and medical staff used the WhatsApp application installed on smartphone to provide immediate response to various issues: queries regarding bleeds (with relevant photos), queries regarding dosage/ frequency of therapy, queries about quality of life (QOL) and specific situations noted at school/ kindergarden, personal communication and general consult and support.	Extension of physical groups at the treatment centre.
10	Blackwell LS, et al. CFfone: A social networking site for adolescents and young adults with cf. Pediatric Pulmonology. 2012;35):430.	2012	USA	Cystic fibrosis	CFOne	Research	Conference abstract	Transition from child to adult requires increased independence and self efficacy	Social support associated with better psychological wellbeing and better outcomes.	social platform	Not given	online peer support program for adolescents and young adults with CF	Social networking sites for adolescents and young adults with CF may be useful for increasing knowledge of disease management, increasing perceptions of social support and improving mental health and quality of life.
11	Boon M, et al. Use of a mobile application for self-management of pancreatic enzyme replacement therapy is associated with improved gastro-intestinal related quality of life in children with Cystic Fibrosis. Journal of Cystic Fibrosis. 2020;19(4):562-568	2020	Europe	Cystic fibrosis	MyCyFAPP	Research	Journal article	Complicated self (parental)-management for gastrointestinal distress in children	Most patients with cystic fibrosis (CF) suffer from pancreatic insufficiency, leading to fat malabsorption, malnutrition, abdominal discomfort and impaired growth. Pancreatic enzyme replacement therapy (PERT) effective but evidence-base on dosing still being built. This uses a new algorithm.	App	Dutch, English, Flemish, Italian, Portugese, Spanish	App calculates individual PERT-doses for optimal fat digestion and includes a symptoms diary, educational material, and it is linked to a web tool allowing HCPs to view data and give feedback.	Increased GI QoL measures.
12	Breakey VR, et al. A feasibility study of "managing hemophilia online": An Internet-based self-management and transitional care program for teens. Haemophilia. 2012;3):207-8.	2012	Canada	Haemophilia	online self-management intervention	Research	Conference abstract	Adolescents have heightened educational needs as they learn to manage their disease and become self-sufficient in preparation for transition to adult health care.		website passive	English and French	Online course - not clear if it is interactive. Pilot - still working it out	

	A	B	C	D	E	F	G	H	I	J	K	L	M
13	Breakey VR, et al. A pilot randomized control trial to evaluate the feasibility of an Internet-based self-management and transitional care program for youth with haemophilia. Haemophilia. 2014;20(6):784-93.	2014	Canada	Haemophilia	Teens Taking Charge: Managing Hemophilia Online'	Research	Journal article	Adolescents have heightened educational needs as they learn to manage their disease and become self-sufficient in preparation for transition to adult health care.		website active	English and French	8 week educational program on line with weekly telephone support from a trained Research Assistant.	Teens on the intervention arm showed significant improvement in disease-specific knowledge (P = 0.004), self-efficacy (P = 0.007) and transition preparedness (P = 0.046). There was a statistically significant improvement in knowledge in the intervention group when compared to the control group (P = 0.01). Overall, the teens found the website to be informative, comprehensive and easy to use and were satisfied with the program.
14	Breakey VR, et al. Feasibility study of a randomized control trial to evaluate an internet-based self-management program for adolescents with hemophilia: Preliminary results and observations. Journal of Thrombosis and Haemostasis; July2013. p. 1058.	2013	Canada	Haemophilia	Teens Taking Charge: Managing Hemophilia Online'	Research	Conference abstract	Adolescents have heightened educational needs as they learn to manage their disease and become self-sufficient in preparation for transition to adult health care.		website active	English and French	8 week educational program on line with weekly telephone support from a trained Research Assistant.	Overall, these teens found the website to be informative, comprehensive and easy to use and were satisfied with the program.
15	Breakey VR, et al. The value of usability testing for Internet-based adolescent self-management interventions: "Managing Hemophilia Online". BMC medical informatics and decision making. 2013;13:113.	2013	Canada	Haemophilia	Teens Taking Charge: Managing Hemophilia Online'	Research	Conference abstract	Adolescents have heightened educational needs as they learn to manage their disease and become self-sufficient in preparation for transition to adult health care.		website active	English and French	8 week educational program on line. Course contained multimedia components (videos, animations, quizzes)	
16	Calvo-Lerma J, et al. Clinical evaluation of an evidence-based method based on food characteristics to adjust pancreatic enzyme supplements dose in cystic fibrosis. Journal of Cystic Fibrosis. 2020.	2020	Europe	Cystic fibrosis	MyCyFAPP	Research	Journal article	Complicated self (parental)-management for gastrointestinal distress in children	Most patients with cystic fibrosis (CF) suffer from pancreatic insufficiency, leading to fat malabsorption, malnutrition, abdominal discomfort and impaired growth. Pancreatic enzyme replacement therapy (PERT) effective but evidence-base on dosing still being built. This uses a new algorithm.	App	Dutch, English, Flemish, Italian, Portugese, Spanish	App calculates individual PERT-doses for optimal fat digestion and includes a symptoms diary, educational material, and it is linked to a web tool allowing HCPs to view data and give feedback.	Improved fat absorption for those with poor baseline measures.
17	Calvo-Lerma J,et al. Change in nutrient and dietary intake in european children with cystic fibrosis after a 6-month intervention with a self-management mhealth tool. Nutrients. 2021;13(6)	2021	Europe	Cystic fibrosis	MyCyFAPP	Research	Journal article	People with CF have increased energy needs and a diet with a specific nutrient distribution. Nutritional status is an indicator of disease prognosis and survival. Self(parental)-management is complicated	App provided educational resources about nutrition and dietary advice for parents	App	Dutch, English, Flemish, Italian, Portugese, Spanish	Food diary, nutrition follow-up (goals), symptoms diary (health diary), nutrition educational material (living with CF) and messages among other functions	Users had modest improvements towards the nutritional guidelines
18	Carr SB, et al. Children and adults Tai Chi study (CF-CATS2): A randomised controlled feasibility study comparing internet-delivered with face-to-face Tai Chi lessons in cystic fibrosis. ERJ Open Research. 2018;4(4)	2018	UK	Cystic fibrosis	NA	Research	Journal article	Maintaining exercise difficult for people with CF due to isolation.	8 lessons over 3 months, delivered face to face (n=22) or via internet (n=18) for 40 adults and children with CF.	telehealth	English	Lessons delivered over Skype; also had a DVD, booklet, stickers and tshirts aimed at different ages to increase adherence.	Feasibility and safety were demonstrated. All participants showed significant improvements in self-reported sleep, cough (both daytime and night-time), stomach ache and breathing. No differences in lung function, health status, quality of life, sleep or mindfulness was shown before or after completing the lessons.
19	Carr SB,et al. Children and adults Tai Chi study (CF-CATS2): A randomised controlled feasibility study comparing internet-delivered with face-to-face Tai Chi lessons in cystic fibrosis. ERJ Open Research. 2018;4(4).	2018	UK	Cystic fibrosis	Internet delivered Tai-Chi class	Research	Journal article	Isolation yet needing tailored exercise	Maintaining an exercise regime can be difficult in cystic fibrosis: group classes risk potential infection, yet motivation is hard to maintain when alone.	telehealth	English	Comparison of F2F and internet classes	Improvements in sleep, cough, GI symptoms and breathing but no diff in lung function, ehalth status and QoL. Findings same in both groups.

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20	Castro RA, et al. Exploring the Views of Osteogenesis Imperfecta Caregivers on Internet-Based Technologies: Qualitative Descriptive Study. J Med Internet Res. 2019;21(12):e15924.	2019	Canada	Osteogenesis Imperfecta (OI)	Exploring use of what's available online and what is needed	publicly available	Journal article	Multiple needs	(1) Distraction for children after surgery to promote rest and immobilization, or to distract from painful or frightening procedures etc; (2) Isolation from family or friends at a distance or in unsafe places for the child to visit; (3) Carers' self care; (4) Parents and carers feeling distressed by the disease and child's suffering; (5) Managing logistics of caregiving/ HCPs (6) Communication with HCP; (7) Facilitating care; (8) Information seeking; (9) social isolation (10) Updates on research and new treatments (11) Concern about quality, security (12) wishlist (13) caregivers desired child-friendly and age-appropriate (14) In their own language	other			(1) Games, videos, audio books have a calming affect to distract from broedom, pain or fear; (2) Social media platforms like FaceTime useful for staying in touch; (3) Can be a lot of waiting for appointments and then keeping the child quiet at home after surgeries etc. Yoga apps, games and ; (4) Watching inspirational videos of other children with OI doing well gave hope; (5) Booking online much easier and e-calendars useful to store all appointments; (6) Some allowed email or messaging (e.g., to SW or PT); (7) Some tools allowed carers to find local community and care resources - e.g., wheelchair accessibility of local shopping centre etc. Appropriately adapted sports programs; (8) Found via Google so not optimal (9) Social media specifically for OI - share day-to-day care information rather than using it for specific information on prognoses or treatments. Some caregivers were more interested in answering others' questions than in having their own questions answered. OI parents were the ones who know practical day-to-day care strategies, such as where to find adaptive clothing and winter boots that would fit her child's physique. Claimed to get faster information from a social media platform group ratehr than an HCP. (10) Access to information; (11) Concerned about web-based predators or cyberbullies or judgement from other parents. Often were confronted with worst-case scenarios that were not applicable to their own children. (12)Web-based home fracture-splinting videos with diverse techniques for every fracture possible • Web-based videos portraying OI patients before and after various
21	Cipriani D, Dulcan E. See and be seen: The CF community. Pediatric Pulmonology. 2017;52(Supplement 47):147-148.	2017	USA	Cystic fibrosis	BreatheCon	limited availability	Conference abstract	CF considered an invisible disease; social support limited by infection risk; niche information hard to find; mental health often impacted.	Lack of understanding of peers and family when the disease is "invisible." Desire to connect with people with the same disease (who "get it") but face-to-face not possible. telling your boss about CF as well as colleagues, classmates, friends, in-laws and other new family. The alienation of invisibility is compounded by uncomfortable, lonely, boring treatments. When life expectancy improves for a cohort of patients, little information about reproduction, family planning, safe pregnancies, genetic	social platform	Not given	Online conferences for people with CF subdivided into adults, parents/children and young people.	
22	Colman AW, et al. Use of Quick Response (QR) coded bracelets and cards for the improvement of cortisol deficiency/Addison's disease management: An audit of quality of care of the management of steroid deficiency in acute illness. BMJ Innovations. 2018;4(3):115-22.	2018	UK (England)	Addison's disease	Quick response coded bracelet	Research	Journal article	Adrenal crisis is life-threatening and requires swift intervention but is very rare	Study of HCPs - clinically needed / useful?	website passive	Not given	Bracelet has a scannable QR code that links to emergency management information	Clinical need identified
23	Cox NS, et al. A web-based intervention to promote physical activity in adolescents and young adults with cystic fibrosis: protocol for a randomized controlled trial. BMC polm. 2019;19(1):253.	2019	Australia	Cystic fibrosis	ActivOnline	Research	Journal article	Tailored exercise program without risk of infection		website active	Not given	internet-based physical activity program for 12 weeks for adolescents and young adults	Protocol

	A	B	C	D	E	F	G	H	I	J	K	L	M
24	Cox NS, et al. Feasibility and acceptability of an Internet-Based program to promote physical activity in adults with cystic fibrosis. Respiratory Care. 2015;60(3):422-9.	2015	Australia	Cystic fibrosis	ActivOnline	Research	Journal article	Tailored exercise program without risk of infection		website active	Not given	internet-based physical activity program for 8 weeks for adults. Also fortnightly phone consult	Feasible and acceptible
25	Cummings E, et al. Enhancing self-efficacy for self-management in people with cystic fibrosis. Studies in Health Technology and Informatics. 2011;169:33-37.	2011	Australia	Cystic fibrosis				Complicated self-management	Health mentoring project with 3 groups: (1) Self-efficacy web-based program + mentor via phone, (2) mentor via phone + self-efficacy program +App, (3) usual care.	App	English	App consisted on Symptom diary plus optional feedback on progress	Results show the intervention was generally considered to be useful and allowed CF individuals to focus on changes in symptoms. Self-efficacy increased in subjects in both intervention groups, but it is unclear from the results if the application provided additional benefits beyond supporting the mentoring intervention.
26	D'Ambrosio C. Open versus closed social networking groups. Haemophilia. 2014;3):183.	2014	USA	Bleeding disorders in women	MyGirlsBlood	publicly available	Conference abstract	Little information for this group of women; social isolation	Debate over whether open or closed group better. Closed for safety discussing personal details but reinforces it as a "secret" and shuts out others who may help / get it on the research agenda.	social platform	Not given	Open group (not closed) on Facebook where people can ask questions or share experiences.	Having closed social networks are needed for groups that need privacy and security in their communications. WWBD need privacy to learn from one another and to solve intimate problems. However, when there are only closed groups, awareness ceases to exist across the larger multi-disciplinary and diverse worldwide community. Many would like to help, but would not be permitted in a closed group for WWBD.
27	Decker K, Meilleur C. CBDR and MyCBDR advancing hemophilia nursing practice in Canada. Conference Abstract presented at Haemophilia; May, 2018	2018	Canada	Haemophilia	MyCBDR (linked to Canadian Bleeding Disorder Registry (CBDR)	limited availability	Conference abstract	Complicated self-management	Better outcomes from new treatement regimes but requires detailed record keeping to accurately monitor bleeding episodes, factor usage and adherence to treatment regimens.	App	Not reported	Links to CBDR - app allows people with a bleeding disorder to add track infusions and symptoms.Data available to all Haemophilia Treatment Centres in canada meaning greater integration fo specialist services.	Useful tool that allows access to detailed information to the care tems and by implication, better treatment outcomes
28	Fidika A, et al. A web-based psychological support program for caregivers of children with cystic fibrosis: A pilot study. Health and Quality of Life Outcomes. 2015;13(1)	2015	Germany	Cystic fibrosis	WEP-CARE	Research	Journal article	Parents caring for a child with Cystic Fibrosis (CF) are at high risk for psychological distress and have limited access to psychological care.	Severe distress not unusual. Lack of appropriate and knowledgable support.	website active	Not given	Web-based writing therapy - 9 sessions, tailored for the specific needs of caregivers. Written assignments that were given feedback within 48 hours. The intervention program was provided by two trained and supervised psychotherapists with expertise in psychosocial care for patients with CF and their families.	On average, the caregivers' symptoms of anxiety decreased statistically significant and clinical relevant about five points from an elevated (M=11.4; SD =2.6) to a normal level (M=6.7; SD =2.6; p < .001) between pre and post treatment. Fear of disease progression (p < .001) and symptoms of depression (p = .02) significantly decreased as well. Quality of life significantly improved (p = .01). The effects were maintained at the 3-months follow-up assessment.
29	Floch J, et al. Users' Experiences of a Mobile Health Self-Management Approach for the Treatment of Cystic Fibrosis: Mixed Methods Study. JMIR mHealth and uHealth. 2020;8(7):e15896.	2020	Europe	Cystic fibrosis	MyCyFAPP	Research	Journal article	Complicated self-management	Overall positive experience but food recording was seen as too complicated. Once people met their goals, lost motivation to continue using the app. HCPs also reported that information communicated by patients is more reliable and accurate. Normally, patients do not record data systematically. They forget details or get information mixed up. Empowering patients to record events at the time they occur, HCPs felt that the data they receive are more precise and better reflect the reality of patients' status	App	Dutch, English, Flemish, Italian, Portugese, Spanish	Food diary, nutrition follow-up (goals), symptoms diary (health diary), nutrition educational material (living with CF) and messages among other functions	Patients and parents had different skills, requiring follow-up by HCPs in an introductory phase. HCPs valued obtaining precise information about the patients, allowing for more personalized advice. However, the tight follow-up of several patients led to an increased workload. Over time, as patient self-efficacy increased, patient motivation for using the app decreased and the quality of the reported data was reduced. They suggest focusing on patients with poor control using the app; all patients using it for the week before a consult.Introduing all the dfeatures of the app at once can be overwheming - staged approach better. Personalising it with help from the HCP alos useful.

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30	Gow J, et al. Participation in patient support forums may put rare disease patient data at risk of re-identification. Orphanet Journal of Rare Diseases. 2020;15(1)	2020	UK	Rare diseases	Social support groups generally for people with RD	publicly available	Journal article	Vulnerable to re-identification on social support platforms	Online social support groups may not have sufficient security to prevent malicious matching of health and personal data to re-identify anonymised data	social platform			
31	Grande SW, et al. Improving care for pediatric cystic fibrosis in Sweden using a successful mHealth patient support system. Conference Abstract presented at Pediatric Pulmonology; September, 2017.	2017	Sweden	Cystic fibrosis	Genia	limited availability	Conference abstract	Complicated self-management/tracking symptoms and treatments	Parents don't always recall symptoms and treatments for their child making it hard for HCPs to accurate assess the patient.	App	Not reported	Patients/parents record daily health observations and complete reports about symptoms, medications, and goals immediately prior to a clinic appointment. Data available to HCPs at the consult.	High uptake at the study hospital; HCP took QI approach to its implementation. Considered to have improved coordination and patient-provider consensus ye without greater HCP burden.
32	Guilliams JM, et al. Feasibility and usefulness of a mobile health exercise intervention in women with lymphangioleiomyomatosis. Conference Abstract presented at Cardiopulmonary Physical Therapy Journal; July, 2021.	2021	Not given	Lymphangioleiomyomatosis (LAM)	Home based exercise program for women with LAM	Research	Conference abstract	Require tailored expercise program	Patients have reduced lung function and exercise tolerance; and a recent report indicates lower physical activity levels in LAM compared to patients with COPD and healthy populations.	App	Not reported	App on smartphone with interfacing wearable and home monitoring devices. Check in with Physio weekly.	12 wk trial. Initial findings indicate feasibility and usefulness of an mHealth home exercise program for LAM, including good patient adherence and satisfaction with the program.
33	Haik D, 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):293-299.	2019	USA	Idiopathic subglottic stenosis (iSGS)	Living With Idiopathic Subglottic Stenosis (LwiSGS),	publicly available	Conference abstract	Access to information, sharing of experiences		social platform	Not given	Online community specifically for people with iSGS	Analysis demonstrated that communications primarily encompassed three major thematic elements: (1) information sharing; (2) emotional support, expression, and experience sharing; and (3) community building. Positively toned posts grossly overshadowed negatively toned posts by almost a factor of 3. A significant portion of group members requested information from their peers, suggesting a high level of trust toward the resources provided in this group, even those involving a surgical procedure or medication.
34	Ho G, et al. Metabolic Diet App Suite for inborn errors of amino acid metabolism. Molecular Genetics and Metabolism. 2016;117(3):322-327.	2016	Canada	Inborn errors of metabolism (IEM)	Metabolic DietAppSuite	publicly available	Journal article	Burden of daily adherence to complex and time-consuming medical diet to attain metabolic control and prevent organ damage	Diet is only one of a number of competing priorities for people with IEM, but one of the most onerous. Poor nutritional labelling on many foods - restricts diet further.	App	Not reported	Online tool for mobile phones and desktops for 15 different IEMs. Creates a personalised dasshboard including specific nutrient goals. Food diary, nutrient counts and able to add your homemade recipes.	
35	Howard S, The All Wales Adult Cystic Fibrosis Centre (AWACFC) Virtual Instruction of Exercise with Technology to Enhance Care-VIEWTEC Programme. Journal of Cystic Fibrosis. 2014;2):S20	2014	UK (Wales)	Cystic fibrosis	VIEWTEC Programme	Research	Conference abstract	Patients live 2 and 3 hours away from treatment centre but benefit from tailored exercise programs	Group exercise is more motivating	telehealth	Not given	virtual exercise sessions with a CF Gym Instructor. Email invitations and delivered via Cisco Webex	Feasibe and patients liked it.

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36	Huang X, et al. Developing and evaluating HE-APP: Acceptability and usability of a smartphone APP system to improve self-management in Chinese patients with hemophilia. Conference Abstract presented at Haemophilia; June, 2020	2020	China	Haemophilia	HE-APP		Conference abstract	Complicated self-management linked to outcomes	Outcomes linked to self management and accurate symptom-tracking.	App	Mandarin?	(1) recording of bleeding symptoms; (2) monitoring of treatment adherence; (3) education, training and support system; (4) accounting and analysing the use of the medicine; and (5) recording the economic cost.	Acceptability and susability levels high among patients and their parents. Small trial with 10 patients.
37	Ingravallo F, et al. Telemedicine with mobile internet devices for innovative multidisciplinary patientcentred care of patients with narcolepsy. Protocol of the randomized controlled trial TENAR (TElemedicine for NARcolepsy). European Journal of Neurology. 2020;27(Supplement 1):516.	2020	Italy	Narcolepsy	TENAR trial (Protocol)	Research	Conference abstract	disease burden is increased by the need for traveling for medical consultations, with high costs for patients and families.		telehealth			
38	Kauw D,et al. 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.	2015	The Netherlands	Addison's disease and Cushing's syndrome	online forum moderated by the Dutch Adrenal Society	publicly available	Journal article	Peer-to-peer information sharing		social platform	Not given	Public area and password protceted area. Rules for posting e.g., posting medical information - must provide references. Moderated by vounteers.	Analysis of content: 81% asking for more info about the disease; 10% asking for emotional support; Answers mostly practical tips and sharing own experiences. Seen as an important information source. Social support in the form of experiential info and emotional support - not able to be obtained from HCPs.
39	Khair K, et al. Social networking for adolescents with haemophilia. Haemophilia. 2011;17(2):369.	2011	UK	Haemophilia	VivaSix	Research	Conference abstract	Adherence to treatment difficult for adolescent boys with severe haemophilia	Parents are oftensole source of information outside of HCPs. Few know of other boys with heamophilia	social platform	Not given	Restricted social network for boys 11-18 years with severe haemophilia. Will include games and other features to promote sharing of self management skills.	
40	Khair K, et al. The role of social networking in haemophilia management. Haemophilia. 2010;4):129-130.	2010	UK	Haemophilia	hiFive	Research	Conference abstract	Adherence to treatment difficult for adolescent boys with severe haemophilia	Parental influence lessens. Potential for peer to peer transmission of self management skills	social platform	Not given	hiFIve - small group for 11-19 year olds living with severe haemophilia. Closed to parents.	
41	Kirk S, Milnes L. An exploration of how young people and parents use online support in the context of living with cystic fibrosis. Health expectations. 2016;19(2):309-321.	2016	UK	Cystic fibrosis	Online forum for people with CF	Research	Journal article	Can be hard to find information and support for people with a rare diease or caring for a child with a rare disease		social platform	Not given	Participants exchanged experientially derived advice and views on how to manage treatments, emotions, relationships, identity and support from services. While parents sought information and support on managing specific therapies/services and ways of maintaining their child's health, the information and support young people desired appeared to be more directed at how to 'fit' CF into their everyday lives	Online support groups appear to supplement professional support in relation to self-management. They enable young people and parents to share experiences, feelings and strategies for living with long-term conditions with peers and develop the expertise to empower them in interactions with health-care professionals.
42	Kühnle L,et al. Development of a Social Network for People Without a Diagnosis (RarePairs): Evaluation Study. J Med Internet Res. 2020;22(9):e21849	2020	Germany	Undiagnosed rare diseases	RarePairs	Research	Journal article	Diagnostic delay is a regular feature of rare diseases	Diagnosis can be difficult with limited infromation and experience of rare diseases. This uses information from a database of 973 diagnosed people	social platform	German, English, Chinese, Portuguese, and Finnish	Social network platform with built in algorithm to match individuals with similar disease burden in the lead up to diagnosis.	

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43	Lassandro G,et al. EMO.TI.ON.: Technologies for the safety of children with hemophilia. Blood Transfusion; November2017. p. s539.	2017	Italy	Haemophilia	EMO.TI.ON. system	Research	Conference abstract	Home care decreasing reliance on hospital	Diagnosing suspected bleeds into joints requiring hospital visit for diagnosis	telehealth	Not given	an ultrasound diagnostic solution using at home by parents or caregivers. Moreover, the system can transfer, live, images by world wide web to specialist physician creating a network. The solution will be achieved by attending the design related to familiarization processes. Other function of the system are: teleconsulting tools, semantic scientific search, recording data (i.e. clinical chart, infusional diary...).	Ongoing trial but results of parent use comparable to HCP use.
44	Lee Yeong J, et al. A Newly Developed Web-Based Resource on Genetic Eye Disorders for Users With Visual Impairment (Gene.Vision): Usability Study. J Med Internet Res. 2021;23(1):e19151.	2021	UK (England)	Genetic eye disorders	Gene.Vision	Research	Journal article	Educational web-based materials need to be accessible by people with low vision		website passive	Not given	Gene.vision web site on genetic eye disorders optimised for people with vision problems	
45	Lewis T. Improving quality of life in patients with cystic firbosis with exercise: CF foundation impact grant update. Conference Abstract presented at Pediatric Pulmonology; October, 2019.	2019	USA	Cystic fibrosis	Exercise program via App	Research	Conference abstract	Require tailored expercise program in isolation	Deliver an at home exerise program to people with CF - indirect supervision by exercise physiologist.	App	English	Guided exercise program (3 levels to choose from) and assessment tasks. Supported by live recorded discussions and Q and A sessions.	Suggests it is feasible and could lead to improvements in QoL
46	Lomotey RK, et al. Mobile self-management guide for young men with mild hemophilia in cases of minor injuries. Network Modeling Analysis in Health Informatics and Bioinformatics. 2014;3(1).	2014	Canada	Haemophilia	Hemophilia Injury Recognition Tool (''HIRT?'')	limited availability	Journal article	Patients may be slow to recognise injuries if their disease is mild	People with mild haemophilia may only experience bleeds after a significant injury and so not recognise sequelae of milder events - not seek appropriate treatment.	App	English, French	Structured assessment of suspected bleeds plus approriate first-aid if needed. If more help required, ohone number sof all Haemophilia Treatment Centres in Canada are given to enquire about further management.	High usability for all users whether tech savvy or not.
47	Manu-Pereira MM, et al. ENERCA: Towards a European Reference Network (ERN) in rare haematological diseases. British Journal of Haematology. 2016;173(Supplement 1):39-40.	2016	Europe	Rare and Congenital Anaemias	e-ENERCA (European Network for Rare and Congenital Anaemias (ENERCA))	Research	Conference abstract	Distance from specialist centres, lack of relelvant information and need to share data with expert HCP.	European reference Networks - hub and spoke model fo rare disease care	website active	Not given	3 separate platforms linked to the e-ENERCA website 1) e-Registry, a Pan European registry of RAs for epidemiological surveillance 2) e-Learning for the dissemination of knowledge, continuous medical education, and best practices awareness, and 3) Telemedicine, a platform to provide expertise, at distance, for complex cases.	
48	Moon H, Moon J. Comparative readability analysis of information on exercise for hemophilia patients. Haemophilia. 2021;27(SUPPL 2):57.	2021	South Korea	Haemophilia	Existing online exercise programs for Haemophilia	publicly available	Conference abstract	Tailored online exercise programs need to be understandable.	Readability and other access features not always present	website passive	Not given	Existing web-based resources	Sites had higher than recommended readability scores and came low down in search algorithm rankings making them hard to find.
49	Naik H, et al. Experience with a pilot skype internet support group for symptomatic patients with acute intermittent porphyria. Clinical Chemistry and Laboratory Medicine. 2013;51(5):eA10.	2013	USA	Acute Intermittent Porphyria (AIP)	Skype support group mediated by HCPs	Research	Conference abstract	Psychosocial and emotional isolation leading to poor mental health in this group	Life-threatening acute episodes - painful with sequelae - chronic symptoms. Poorly understood psychosocial needs.	social platform	Not given	Skype support group mediated by a porphyria expert physician, and the genetic counselor/coordinator of the porphyria clinic and an available psychologist with 4 women with AIP.	Participants reported that this was a very comforting experience, reducing the feeling of isolation and increasing their understanding of the disease.

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50	Nicholl H, et al. Internet Use by Parents of Children With Rare Conditions: Findings From a Study on Parents? Web Information Needs. J Med Internet Res. 2017;19(2):e51.	2017	Ireland	Rare diseases	Hypothetical	publicly available	Journal article	Recommendatinos for a consumer facing website	• The content needs to be relevant, accurate, trustworthy, and up to date. • The topics most frequently searched for (Table 5) need to be addressed. • It should contain a Web-based forum or a social network component. • The website should be integrated with social media and be mobile friendly.	other			
51	Nilson J, et al. Are you HIRT? (Hemophilia Injury Recognition Tool): Perceptions of the mobile app on injury self-management from young men with mild hemophilia in Canada. Conference Abstract presented at Haemophilia; July, 2016.	2016	Canada	Haemophilia	Hemophilia Injury Recognition Tool (''HIRT?'')	limited availability	Conference abstract	Patients may be slow to recognise injuries if their disease is mild	People with mild haemophilia may only experience bleeds after a significant injury and so not recognise sequelae of milder events - not seek appropriate treatment.	App	English, French	Structured assessment of suspected bleeds plus approriate first-aid if needed. If more help required, ohone number sof all Haemophilia Treatment Centres in Canada are given to enquire about further management.	Increased confidence dealing with injuries but no change in self management
52	Osara Y, et al. Development of newborn screening connect (NBS connect): a self-reported patient registry and its role in improvement of care for patients with inherited metabolic disorders. Orphanet Journal Of Rare Diseases. 2017;12(1):132.	2017	USA	Phenylketonuria (PKU), maple syrup urine disease (MSUD) or tyrosinemia (TYR)	Newborn Screening Connect (NBS Connect)	Research	Journal article	Patients/carers isolated by rareness of disease.	Linking patients/carers with information. Registries are generating useful data and contributing to the research agenda.	website active	Not given	Registry - patient initiated and enters data. Resources such as education materials, information on the latest research and clinical trials, recipes, interactive health tracking systems, and professional support tools	
53	Paglialonga A, et al. eHealth for patients with rare diseases: the eHealth Working Group of the European Reference Network on Rare Multisystemic Vascular Diseases (VASCERN). Orphanet Journal of Rare Diseases. 2021;16(1):164.	2021	Europe	Rare Multisystemic Vascular Diseases	Mobile app developed by VASCERN (European Reference Network on Rare Multisystemic Vascular diseases); Pills of Knowledge YouTube channel	limited availability	Journal article	(1) Finding a suitable expert; (2) finding a patient support agency; (3) need for timely info about the patient in an emergency situation; (4) information needs of the patient	(1) In Europe can mean travelling across borders, languages - incurring time and money. Difficult to find appropriate RD expert. This RD is multisystem so may need several specialists; (2) Not always named after your disease / group of diseases (3) Paper records carried by the patient are common but may be lost and can only contain a limited amount of information; (4) High quality and easy to understand - combining patient and carer needs, HCP expertise and patient advocacy agency perspectives	App	Multiple European languages	However, further research is needed as digital patient passports may also pose new challenges, for example in terms of data management, patient privacy, informed consent, and control of shared data. In addition, digital passports may not necessarily fit the needs of every patient with the disease as, for example, people with limited digital skills and people not willing to use a smartphone to handle clinical issues might still prefer to use conventional paper documents. Issues about confidentiality and ethical rules in various EU countries, remain to be solved.	
54	Parrott H, et al. A digital solution for virtual consultation and sharing health data in adults with cystic fibrosis. Journal of Cystic Fibrosis. 2019;18(Supplement 1):S51	2019	UK	Cystic fibrosis	Virtual consults and remote monitoring	Research	Conference abstract	Frequent clinic visits are having a huge impact on the quality of life.	Also growing cohort of patients as they are living longer - concerns about Health system capacity	telehealth	Not given	Virtual clinics and spirometry done by patients at home	Considerable savings of time for both patients and clinicians. So far no issues. Patients like it.
55	Polineni D, et al. A stakeholder-informed feasibility study of tele-coaching to improve treatment adherence in patients with cystic fibrosis. Pediatric Pulmonology. 2017;52(Supplement 47):479.	2017	USA	Cystic fibrosis	Tele-coaching	Research	Conference abstract	Adherence to treatment not optimal	Proposed intervention= tele-coaching	telehealth			

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56	Richesson RL, et al. An automated communication system in a contact registry for persons with rare diseases: Scalable tools for identifying and recruiting clinical research participants. Contemporary Clinical Trials. 2009;30(1):55-62.	2009	USA	Rare diseases	Notifications of relevant new research projects	Research	Journal article	Patients have a lack of access to new trials; Researchers - hard to recruit patients	All related to rarity of the conditions	website passive	Not given	web-based automated system generates periodic and customized communications to notify registrants of relevant studies in the NIH Rare Diseases Clinical Research Network (RDCRN).	
57	Rits S,et al. Weekly patient webcasts: An adult CF center's response to the COVID-19 pandemic. Conference Abstract presented at Pediatric Pulmonology; October, 2020.	2020	USA	Cystic fibrosis	Webcasts on COVID	publicly available	Conference abstract	Urgent need for disease specific information during COVID pandemic	Plenty of information for the general public but not for people with a rare disease. Concerns from people with CF adequate infection control, access to care, medications and supplies, clinical outcomes as they relate to CF, employment status and disability, and overall mental health	other	Not given	Weekly webcasts on COVID made available Could ask questions through Google form. Email notification out to patients and carers.	
58	Rodman J, et al. Patient perspectives on electronic access to registry health records: An Irish-Slovene online survey. Journal of Cystic Fibrosis. 2016;15(Supplement 1):S36.	2016	Ireland and Slovenia	Cystic fibrosis	European CF Registry	Research	Conference abstract	Lack of patient access to their own medical records	Thought to be useful for self management	website active	Not given	Hypothetical access to the Register	Patients in favour of it but concerned about security
59	Rudolf I, et al. Assessment of a Mobile App by Adolescents and Young Adults With Cystic Fibrosis: Pilot Evaluation. JMIR mHealth and uHealth. 2019;7(11):e12442.	2019	Germany	Cystic fibrosis	Kinderhilfe Organtransplantation (KiOAPP)	publicly available	Journal article	Lung function decline in transition from 12 and 24 years.	Improving self management and independence from parents important for ongoing outcomes. Poor self management only slowly manifests itself.	App	?German	App contains a diary function for recording vital signs and personal observations, communication platform for sending information to the HCP, a medication plan, and medication reminder function. Age appropriate format	Perceived as useful and supportive overall. Most useful feature was the medication plan and reminders. Diary use became less frequent quickly at odds with its high usefulness rating.
60	Ruther DF, 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).	2021	Europe	autoimmune liver diseases (AILD)	Hypothetical	Research	Journal article	Research into what consumers want in a Rare Liver disorder app		App	Not reported	Hypothetical	A substantial majority of patients expected to benefit from the app due to constant access to health data (81%), better overview of the course of the disease (80%), better understanding of the disease (70%) and faster detection of drug side effects (64%). only the minority of patients believed that an app could help to improve quality of life (21%), reduce fears associated with the disease (24%), reduce mistakes in taking medication (32%) or improve medication adherence (37%) (Fig. 3). Significantly desired features were information on new developments (93%), access to one's own medical records (89%), notifications to practitioner in case of concerns (84%), automatic ordering of follow-up prescriptions (81%), information on clinical trials (79%), disease information (79%) and recording of health concerns with symptom trackers (73%). In contrast, significantly undesired features were gamification or reward system (5%), networking (27%) and comparisons (35%) with other persons affected (Fig. 3). Did not all match with HCP responses.
61	Sottilotta G, et al. The HEMONLINE project: Preliminary results. Haemophilia. 2012;3):77.	2012	Italy	Haemophilia	HEMONLINE	Research	Conference abstract	Distance to treatment centre burdensome and results in expenses including loss of wages.		telehealth	Not given	Web-cam and internet connection provided to patients to allow them to contact HCPs in addition to in person home visits by the MDT	In progress but suggests better use of health services and patient satisfaction

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62	Stevenson Won A, et al. Assessing the Feasibility of an Open-Source Virtual Reality Mirror Visual Feedback Module for Complex Regional Pain Syndrome: Pilot Usability Study. J Med Internet Res. 2021;23(5):e16536.	2021	USA	Complex regional pain syndrome (CRPS)	Virtual Reality Visual Feedback Module	Research	Journal article	Few treatment options for CRPS.	Mirror visual feedback therapies promising. Can be delivered using VR but costly and not so far popular. Now cheaper and HCPs developing skills to deliver it	Website active	Not reported	HCP led VR sessions in a clinic with a view to extending it to home use. Provides therapy platform and information.	Did not improve pain but usability, feasibility and all good.
63	Storf H,et al. Vision and challenges of a cartographic representation of expert medical centres for rare diseases. Studies in health technology and informatics. 2014;205:677-81.	2014	Germany	Rare diseases	se-atlas	Research	Journal article	Difficult for people with rare diseases to find appropriate specialist centre in Germany		website active	Not given	Interactive map and list	
64	Timmer AM, et al. A Blended Physiotherapy Intervention for Persons With Hemophilic Arthropathy: Development Study. J Med Internet Res. 2020;22(6):e16631.	2020	Netherlands	Haemophilia	e-Exercise HA	Research	Journal article	Few PTs understand haemophilic arthropathy and so accesss to one is difficult for this common complication; Cost of specialist physio	most critical barriers to adhering to physiotherapy were the limited reimbursement by the health insurance, execution of boring exercises, and stubbornness of the patients to accept advice. The patients mentioned that a good relationship with their physiotherapist facilitated their adherence to the physiotherapy treatment.	website active	Not given	A 12-week blended intervention was developed, integrating face-to-face physiotherapy sessions with a web-based app.The intervention consists of information modules for persons with HA and information modules for physiotherapists, a graded activity program using a self-chosen activity, and personalized video-supported exercises. The information modules	
65	Verkleij M, et al. Development and evaluation of an internet-based cognitive behavioral therapy intervention for anxiety and depression in adults with cystic fibrosis (eHealth CF-CBT): An international collaboration. Internet Interventions. 2021;24.	2021	Netherlands	Cystic fibrosis	eHealth CF-CBT	Research	Journal article	Anxiety and depression in people with CF common and can affect adherence, health and QoL	Access to evidence-based mental health care can be limited adding to the cost and burden of care for people with CF.	website active	English and Dutch	Internet delivered CBT sessions guided bya therapist. Trialled with 16 people with CF	high levels of acceptability and usability
66	Verkleij M, et al. Development of a therapist-guided internet-delivered cognitive behavioral therapy intervention for anxiety and depression in adults with cystic fibrosis (e-Health CF-CBT): An international collaboration. Pediatric Pulmonology. 2019;54(Supplement 2):406-7.	2019	Netherlands	Cystic fibrosis	eHealth CF-CBT	Research	Conference abstract	Anxiety and depression in people with CF common and can affect adherence, health and QoL	Access to evidence-based mental health care can be limited adding to the cost and burden of care for people with CF.	website active	English and Dutch	Pilot Internet delivered CBT sessions guided by a therapist	
67	Verkleij M,et al. Development and evaluation of an internet-based cognitive behavioral therapy intervention for anxiety and depression in adults with cystic fibrosis: An international collaboration. Pediatric Pulmonology. 2020;55(SUPPL 2):267.	2020	Netherlands	Cystic fibrosis	eHealth CF-CBT	Research	Conference abstract	Anxiety and depression in people with CF common and can affect adherence, health and QoL	Access to evidence-based mental health care can be limited adding to the cost and burden of care for people with CF.	website active	English and Dutch	Internet delivered CBT sessions guided bya therapist. Trialled with 16 people with CF	High levels of acceptability and usability
68	Wagner B,et al. Establishing an online physical exercise program for people with hemophilia. Wiener Klinische Wochenschrift. 2019;131(21-22):558-66.	2019	Germany and Austria	Haemophilia	online exercise program	limited availability	Journal article	Distance to attend exercise program at the specialist centre not feasible		website passive	Not given	Online exercise lessons for adults and young people conducted by physician. Also have consultation hours (? Online) when you can speak to someone at the clinic about the program)	

	A	B	C	D	E	F	G	H	I	J	K	L	M
69	Walker KK. Cognitive and affective uses of a Thoracic Outlet Syndrome Facebook support group. 2014	2014	USA	Thoracic Outlet Syndrome (TOS)	Thoracic Outlet Syndrome (TOS) Awareness Facebook group	publicly available	Journal article	Finding reliable information difficult for people with a rare disease	HCPs may not be knowledgable. Support from peers difficult due to rarity.	social platform	Not given	Facebook group for people with TOS	Analysis of cognitive needs indicated TOS patients used the site more to share information about their own TOS symptoms and journey with diagnosis than to seek information. Analysis of affective needs found patients were more likely to use the site to give support and encouragement to others than to express concerns and complaints. The complaints they did express were primarily related to their frustration with the general medical community's perceived inability to diagnose and understand their disease or to question a specific doctor's diagnosis/recommendation
70	Wittmeier K, et al. Analysis of a Parent-Initiated Social Media Campaign for Hirschsprung's Disease. J Med Internet Res. 2014;16(12):e288.	2014	Canada	Hirschsprung's Disease	Social media campaign "Shit happens"	publicly available	Journal article	Families of children with rare diseases can feel isolated and unsupported		social platform	English	Social media campaign to raise awareness and provide support for families dealing with Hirschsprung's disease. Facebook, Twitter, Blog posts and question and answer style postings. Very engaging for the community	Analytics showed 5400 views of the blog from 37 countries. Across platforms - within 2 hours of posting a question could get 143 views, 20 responses increasing to 30 responses within 5 hours.
71	Wood J, et al. A smartphone application for reporting symptoms in adults with cystic fibrosis improves the detection of exacerbations: Results of a randomised controlled trial. Journal of Cystic Fibrosis. 2020;19(2):271-276.	2020	Australia	Cystic fibrosis	Not given	Research	Journal article	Delayed reporting of symptoms can result in more severe exacerbations and worse outcomes.		App	Not reported	12 questions re symptoms associated with exacerbation that alert a nurse if respondents answer yes.	No change in IV antibiotic use. Number of courses of oral antibiotics increased and the median (IQR) time to detection of exacerbation requiring oral or IV antibiotics was shorter in the intervention group compared with the control group. No detectable change in lung function.
72	Wood J, et al. High usability of a smartphone application for reporting symptoms in adults with cystic fibrosis. J Telemed Telecare. 2018;24(8):547-552.	2018	Australia	Cystic fibrosis	Not given	Research	Journal article	Delayed reporting of symptoms can result in more severe exacerbations and worse outcomes.		App	Not reported	12 questions re symptoms associated with exacerbation that alert a nurse if respondents answer yes.	Study looked at HCP response to the app questions using 45 clinical scenarios. Excellent usability and near-perfect agreement interpreting the app responses.