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Unique patient challenges and support solutions in rare disease

IN THIS ISSUE:
- Patient stories
- Health psychology insights
- Pharma insights
- Predictors of non-adherence
- Interventions to improve adherence
- Clinical literature overview

Living with any chronic health condition can be demanding, but rare diseases bring a unique set of challenges for patients. These can range from diagnosis difficulties to limited information and support, a lack of knowledge – even within medical services – and social stigma. Such challenges negatively impact patients and carers – preventing the best possible health outcomes from being achieved.

To better understand the unmet support needs of such patients along with the solutions to address these, we asked people who have been diagnosed with a rare disease to share their stories, interviewed a pharmaceutical executive and health psychology researcher and reviewed the most recent and relevant adherence and self-management research in rare disease.

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Executive summary

Rare diseases bring a unique set of challenges, ranging from diagnosis difficulties to limited information and support, a lack of knowledge – even within medical services – and social stigma.

As with more common diseases, rates of non-adherence to treatment recommendations appear to be sub-optimal. To date, there has been little research into the specific determinants of non-adherence among people with rare diseases. However, some studies have shown that for children with rare genetic conditions, there is an increased risk of non-adherence during the transition from childhood to adolescence, suggesting the need for increased support over this period.

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Whereas among adults, predictors of non-adherence identified in the literature include perceptual barriers, such as a lack of perceived need for treatment, perceived lack of benefit and the experience of side effects. Psychological barriers, including depression, avoidance and denial, and practical barriers such as forgetting, a lack of time and unstructured daily routines, were the other key predictors of non-adherence in rare disease.

There is evidence that adherence to dietary requirements among children with rare genetic disorders may be enhanced through behavioural and educational strategies, though it is not clear which components of these interventions are most effective. There remains a need for the development of interventions to support self-management and enhance adherence to medication and treatment recommendations among people with rare diseases.

Increasing numbers of people with rare diseases obtain information and support from Internet resources and online communities that share their condition. Therefore, the Internet may provide a useful tool for both the recruitment of isolated patients in order to develop further research in this area, and also as a channel for the delivery of evidence-based interventions to enhance the self-management of rare diseases.

Introduction

Rare diseases are defined as those that affect fewer than five in 10,000 of the general population[1]. There are currently between 6,000–8,000 rare diseases and this number is rising as new rare diseases are discovered[2]. Some of the most well-known rare diseases are Huntington's disease, cystic fibrosis and sickle cell anaemia. Rare diseases also include some autoimmune diseases and rare cancers including childhood cancers. When considered together, rare diseases are not so rare: in the EU, one in 2,000 people have a rare disease, while in the USA, one person in 1,500 is affected[2].

Despite the diverse range of rare conditions, there are common issues, such as the burden this kind of diagnosis places on patients and their families. An online survey conducted by a national patient organisation (Rare Diseases UK) identified a range of difficulties experienced by people with a rare disease, including delays in receiving a diagnosis, experiences of being misdiagnosed and problems obtaining specialist care and treatment[2].

Eighty percent of rare diseases have a genetic component[2], so the majority of people diagnosed with a rare disease will have this for their entire life from birth. The transition from childhood to adulthood can be particularly difficult for people living with a chronic genetic condition[3]. The Rare Diseases UK report highlighted a wide range of problem areas, including medical challenges, a lack of knowledge about the rare disease within adult services and a lack of communication between specialists and also with the patient and their family. Furthermore, limited availability for specialist consultations was another challenge. Psychological challenges included those stemming from a different approach to care within the adult service and limited availability of psychological support for those with a rare disease. Provision of social support and information about the financial support available to patients were also lacking[2].

People living with rare diseases often experience psychosocial difficulties including depression, feelings of isolation, body image concerns, low self-esteem and stigma[4]. Stigma may be associated with having visible signs of the disease, feeling different, or feeling socially ostracised[5]. Adults with Moebius syndrome, a rare genetic condition characterised by paralysis of the face, reported experiences of prejudice, discrimination, teasing and bullying[6]. Parents of children diagnosed with mitochondrial disease perceived stigma because of their child's illness[7]. Moreover, those with higher perceived stigma scores reported poorer psychological wellbeing (depression and stress)[7]. It has been argued that there is a need to raise the profile of rare diseases in order to facilitate inclusion and help to combat stigma[8].

Healthcare professionals (HCPs) have an important role in terms of providing medical advice, information and support for people with rare diseases. The European Commission and European Council identified the absence of reliable information for both patients and HCPs as a key unmet need[9,10]. Patients with rare diseases require both medical and emotional support. While two-thirds of men with congenital hypogonadotropic hypogonadism reported that their HCP understood the medical aspects of their condition, only 38 percent believed that their HCP understood the emotional aspects of their condition[4]. Patients with scleroderma revealed that the quality of care varied widely across treatment centres, suggesting the need for a standardised approach[11].

There is little research into self-management among people with rare diseases. Studies suggest that as with more common chronic diseases, non-adherence to treatment recommendations may be a problem. Reported rates of medication adherence range from 58 – 65 percent among patients in the rare conditions reviewed; 58 percent adherence is reported in systemic scleroderma,[12] 63 percent among men with hypogonadotropic hypogonadism[4] and 65 percent among patients with sickle cell disease[13]. This data should be interpreted with caution because of differences between studies in the measurement and definition of non-adherence. Non-adherence has also been associated with poor clinical outcomes and higher healthcare costs[13].

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80%
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Reported rates of medication adherence range from
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Patient insights

In 2004, Jane (pseudonym) was diagnosed with relapsing polychondritis, lupus (SLE) and Sjögrens syndrome. She explained that it took almost five years to find a combination of medicines that suited her – she now takes prednisolone, hydroxychloroquine and mycophenolate mofetil, plus lansoprazole and calcitriol.

Jane described how difficult it was for her to access accurate information following her diagnosis:

"I was told at the time that it (the rare condition) affected one in a million people so I knew that it was very, very rare, and there were no information leaflets. I'd say there was a distinct lack of information in terms of what the hospital gave me when I was diagnosed.

The consultant sat next to me and she gave me a leaflet that was actually about lupus and she'd written on the back page 'relapsing polychondritis' and she'd just written the definition of it because there wasn't even a leaflet about it. I think that's the worst thing with RP. An awful lot of the information on the Internet is out of date and it gives some really frightening statistics, and I think that in itself is awful because you don't get any leaflets from your doctor, and then you go on the net and all the information is out of date."

On the whole, Jane takes her medicines as prescribed. She explained how she balances the risk of disease progression against her concerns about side effects and potential adverse effects:

"It's not much fun to take them (treatments) with all the side effects and everything, so I've had to balance it out – would I rather risk it and let the disease progress potentially faster and shorten my life expectancy, or take the meds and just risk it (adverse effects) really. So I've chosen to go with taking the meds and seeing what happens, but in all honesty I hate being on the medication.

I know that they are quite powerful medications. I think that, especially since I started taking them so young and it looks like I am going to be on them for the rest of my life, it does worry me in the sense that, OK, it may be suppressing the illness but what else is it doing to my body? Do the doctors really know everything that these medications do? OK, they do clinical trials but then sometimes side effects and things don't come up until 10 years later. So it does worry me."

Jane emphasised how difficult it was for her to get her psychological support needs met, often leading to a sense of isolation:

"Definitely in terms of the psychological side, it's been poor, really poor. I think because there is so much focus on the physical side of the disease, the psychological is so neglected. I think one of the things for me is that I look well, and I think that makes it very difficult for friends, family, even doctors to understand that you are in so much pain. I'm surrounded by friends who don't have an autoimmune disease – their lives feel very different to mine and it makes me feel very isolated and alone."

Jane turned to the Internet and found an invaluable source of information and support:

"There is a Yahoo support group – they are absolutely fantastic. I don't know what I would have done without them. They were amazing when I was first diagnosed. I'd post a message saying, 'This is how I'm feeling, what are your experiences of this?' And the members would post back and say, 'Don't worry' and 'This happened to me' and you know 'We're all here for you' and 'Things will get better'. They just tried to make helpful suggestions. I knew that they understood."

"Do the doctors really know everything that these medications do? Ok, they do clinical trials but then sometimes side effects and things don't come up until 10 years later. So it does worry me."

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Di was diagnosed with scleroderma two years ago and is using Quinoric (400mg daily). She described the frustrating and lengthy process of getting a diagnosis, requiring numerous visits to different healthcare professionals over approximately five years.

"I saw my then GP and mentioned it (symptoms) to her. She said don't worry about that, and said don't go Googling it because you will read about some very nasty disease that affects your throat and lungs and God knows what else. But it turned out to be the disease that she told me not to look up! I had Raynaud's – which my doctor knew I had and which is another indicator of scleroderma that she missed – she didn't put them together. Then gradually I had blood tests. Then I was told I had lupus, then I was told I had mixed connective tissue disease – these things often overlap. But all the markers in my blood say I've got limited scleroderma."

Di takes medication daily and is highly adherent to the treatment regimen. She does, however, have concerns about her treatment, and the lack of medical monitoring for adverse effects:

"It makes you feel incredibly sick. It's given me tinnitus, it can affect your eyesight, and they are quite unpleasant drugs really. They can badly affect your eyesight and it has. I'm more concerned that I'm not being monitored because I was told initially that I would need to be monitored regularly, have regular blood tests, regular urine tests and so on and be checked, and I haven't been."

Di explained the major impact the disease has had on her life:

"I have always been a very lively, outgoing kind of person, and then when something like this happens, it changes every single aspect of your life. The doctor wanted to put me on Prozac. Most people with autoimmune diseases are on an antidepressant of some kind because it is an incredibly depressing thing to have. I have got so low and so isolated I've thought what's the point? I can't have my life any more, I can't work any more, I can't earn any money."

In particular, she highlighted the sense of isolation resulting from having a rare disease:

"The fatigue is overwhelming, there's a lot of joint pain, brain fog – it is incredibly debilitating. It's difficult to get through the day, physically. Mentally it is very draining, especially when you are so isolated because nobody has heard of scleroderma. A few people have heard of lupus but generally no one has even heard of it. So it's a very isolating condition."

Health services alone have not been able to adequately meet Di's needs:

"Unfortunately there is just so much ignorance and negativity within the medical profession. People aren't getting the help that they need."

Like Jane, Di valued the information and support offered by online groups and patient organisations:

"I have found information from the Scleroderma Foundation, Lupus Support and various other sites – mostly from Facebook and Google and stuff. I've got a lot of online friends who, bizarrely, have become very good friends because they understand and they give a lot of support. I chat with people, I feel like I know them. We talk very candidly about how we are feeling. It's not all doom and gloom – we have a laugh, but we have this one thing in common – and it does really help."

"I have always been a very lively, outgoing kind of person, and then when something like this happens, it changes every single aspect of your life."

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We also spoke to Wallace Chapman, a prominent broadcaster in New Zealand who was diagnosed with Gaucher's disease at age twenty-four – a rare enzyme deficiency disorder. Wallace tells us about his journey, including the shock of diagnosis, the fight for treatment and insights to why community is so important.

After a prolonged period of misdiagnosis, Wallace's initial reaction was shock when he was diagnosed with Gaucher's disease:

"When the haematologist sat down with me and said, "This is what you've got," it was a shock, but in a way it was good to put a name on it because I was misdiagnosed for about six or eight months. I was a long distance runner and I thought I had some physiological thing like hip capsulitis. I went to a physio and they tried to bend my leg into shape. Really, it was completely the opposite of what I needed, it was doing worse damage. By this stage I was on a walking stick. Then they came back with this rare disease diagnosis, so, the first reaction was real shock and I remember going and sitting in the hospital church for the afternoon just crying."

Once the diagnosis was made, Wallace and his family faced a number of challenges. The first was the fight to access the drugs needed to treat Gaucher's disease. After undergoing a partial splenectomy Wallace was advised by a specialist from Australia that there was a medication that could help, but it was not available in New Zealand and it was incredibly expensive:

"The challenges were significant. What happened is that I got diagnosed with this rare disorder, Gaucher's disease, and the next step was, what do I do? What happens? They gave me a walking stick, because my leg by then was pretty much gone and I was really struggling. I went on the disability benefit – WINZ – took taxis everywhere, and that was a financial struggle as well. The next challenge was I had a massive spleen. It should've been the size of a small fish, but my spleen was the size of a one and half litre bottle of milk, and that was sitting inside my tummy. So, I had a huge spleen and it was very dangerous.

They suggested a very rare operation they hadn't done before and got a HCP from Sydney to give me a partial splenectomy – to cut it in half and sew it up, because it's like a balloon. They did that and it was successful, but the next step was ongoing medical treatment. My HCP said to me "Wallace, there is actually a drug for your condition." I said, "Really?" He goes, "Yes, it is. It's called Ceredase. It's made by Genzyme in Boston," and I was like, "Oh, my God, that was fantastic." They said, "There's two small problems – one, it's not in New Zealand, and two, it's the world's most expensive drug (at the time)," and I said, "I'll save up, don't worry, we can somehow do it." He said, "The problem is it will cost around a million dollars a year." I said, "Okay."

After some homework Wallace discovered that a smaller dose of this treatment could be just as effective. This was encouraging news given that his health was quickly deteriorating, however, the treatment was still not available in New Zealand:

"...A major study came out of Holland by Dr Carla Hollak, which said if you take a smaller dose it can be just as effective. In fact, a tenth of the dose is found to be still quite effective taken in a different regimen, three times a week. That study was peer reviewed and that led the basis for us to say, "We want the drug here." By this time I was very sick and Mum, she'd just lost her husband, a housewife at home, she stepped up and she got the information together and she went around the country lobbying politicians. Flew around the country. Extraordinary, what she did. She met with Jenny Shipley (Prime Minister at the time), she met with clinicians and she met with the highest level of hospital boards. She said, "My son needs the drug. This is the research."

Anyway, she did get the ear of Jim Anderton (a member of Parliament), who brought it up at the house. So, a long story short, after maybe two and a half, three years the drug got funded in New Zealand. So, it was quite a fight because when you have a rare disease you're the forgotten people. You are the forgotten ones... Unlike other drugs where say, for example, breast cancer, it's a big issue, big profile, affects many thousands of people. But Gaucher's disease affects a small number of people, so, the question in the public's mind is why should I give you this money every year? So, that is what we fought against – the right to have this drug. So, that was the long road to getting Ceredase, or now it's called Cerezyme."

Wallace encourages others diagnosed with a rare disease to keep in touch with the international community – to build a support network and to keep abreast of the latest medical research:

"Networks and support are essential. Talking. Knowledge is just absolutely vital. And be wise with knowledge. It's not about Doctor Googling and self-diagnosing – I think it's a mix. I was ready to hear some sober information, too, with my clinicians, saying, "This may not work, or this might not work, this route."

Wallace was able to help another person with Gaucher's disease he'd met by reaching out to the wider community:

"His started in his spine, and his spine started fracturing and then his hips just – boom – gave out while he jumped into a ditch – then it progressed very fast. So, five months on he had no hips, he was walking on two pins. Gosh, his pain level is something else. White with pain.

He was in a terrible way. So, I contacted, again through networks, I found out about a HCP called Dr Ari Zimran, who was a specialist in orthopaedic procedures. I emailed him and I think I actually asked the haematologist to email the scans over. He ended up agreeing to operate the hip replacement surgery, and the result? He can now take his children to the playground again. So, this is an example of using the networks to help bolster information and help bolster the clinicians' information, to help them find the confidence to treat patients with rare diseases."

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Health psychology expert interview

We spoke with Dr. Sumaira Malik, a health psychology specialist, about her research into the management of a very rare genetic disease.

While in the past those born with this condition rarely survived childhood without a liver transplant, it can now be managed longer-term through medication and a low-protein diet. This means that people with the condition are making the transition from childhood to adulthood – although, as Dr Malik explained, this may be a complex journey.

Dr Malik's research has explored many of the challenges faced by patients and their families in adhering to the treatment and lifestyle requirements:

"The diet aspect of the treatment is particularly challenging. Some of the special foods don't taste very nice so it can be hard to encourage children to eat them. Often parents have to make different meals for different members of the family, which can be inconvenient. Also, if the child is left with others – grandparents or friends – they may have different ideas about which foods are acceptable."

In addition to the practical challenges facing patients and their carers, Dr Malik highlighted the need to consider the emotional impact of the condition. For example, she found that the stigma associated with being 'different' has a major impact on both the young people and their carers:

"A lot of children said that they just didn't want to be different any more – they just wanted to eat what their family and friends were eating... There were some instances where parents wouldn't prepare special food for their children when they went to social events because they didn't want their children to stand out. They would rather they ate something they shouldn't and fit in."

It was clear from Dr Malik's research that patients' support needs are likely to change over time, with the initial emphasis being on helping the parents come to terms with the diagnosis, and get to grips with the treatment, followed by a gradual shift in emphasis towards supporting the young people themselves. Adolescence was highlighted as a particularly challenging period, as young people become responsible for managing their own health at a time of heightened desire to 'fit in' and increased tendency to engage in risk-taking behaviour. Some health professionals reported that they encountered young people who deliberately deviated from treatment recommendations as a form of teenage rebellion:

"Non-adherence can sometimes be used by teenagers as a mechanism to rebel against their parents – it's a way to wind up their parents because they know that not adhering will get to them."

Interventions to support people affected by this condition clearly need to be long-term and flexible, to meet the family's changing needs over the life course:

"There's obviously a real need to educate parents at the beginning when their child's diagnosed but the importance of the diet and medication then needs to be reinforced over time. It's got to be a continuous process. It's also important to work directly with the children to help them take control of their condition early on, while they've still got a support network around them. They may need additional focused support around adolescence, given the extra challenges at this time."

Patients and carers interviewed by Dr Malik stressed their desire for greater peer support:

"One of the things that young people and their parents seem to want is more peer support – being able to talk with others going through a similar thing. Peer support can not only provide education and practical advice but also vital emotional support – it enables people to connect with others who can empathise with what they are going through. There are patient days run by the hospital, which are quite popular, but they are relatively infrequent and not everyone can access them."

Given the rare nature of this condition, online support networks may be a particularly promising area of development:

"An online community would be great – particularly when you're dealing with a very rare disease, where in some countries there may only be a couple of families affected by the condition. Even if you don't want to communicate directly with others, it can be really powerful to see that there are other people out there going through something similar."

Interestingly, Dr Malik did not feel that such communities would need to be disease-specific, but that people with different rare diseases could support and learn from each other:

"Making links to those with other rare diseases is really important – it may be that someone has a different rare disease than you but some of the issues around it may be very similar, such as feeling different or stigmatised, feeling guilty about passing on a genetic condition or issues around necessary lifestyle changes."

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Insights from the pharmaceutical industry

Genzyme, a pioneering company belonging to the Sanofi Group, specialises in the development of patient-centred treatments for rare diseases. We spoke with Fernando Royo, Chair of the Genzyme Foundation in Spain, about the work they are doing.

"One of the main aims of the Genzyme Foundation in Spain is to support people with rare diseases to have a fuller life, with the same rights and opportunities as others. Being recognised and accepted are key challenges. There was a campaign in Spain some years ago centred around the message: 'We are three million and still we feel alone'. This epitomises what patients with rare diseases feel, so trying to overcome this is a core activity."

He described a project they are involved in with the Spanish Federation of Rare Diseases that aims to reduce barriers to education through tackling stigma in schools:

"It's true that children with rare diseases are different, but this doesn't have to be in a negative way. We need to enhance awareness and acceptance by their peers. One of the elements of the campaign involves people with rare diseases going into schools to help increase understanding among students and teachers. We're finding that as a result of this work, people become more aware of the extra challenges faced by children with rare diseases and instead of rejecting them, they value them more."

Fernando reported that treatment adherence is generally high in the rare disease populations Genzyme works with, highlighting how the personal relationship formed between HCPs and patients may support adherence:

"Compliance with orphan drugs [drugs developed for rare diseases] is probably much higher than in more common diseases. If there's something you want and you can just go out and get it, surely you value it less than something you have to really fight for. Many of the orphan drugs are administered in hospital, so there's going to be a specialist team who will call you to arrange treatment. It would be a rejection of one's medical care not to accept such medication."

While adherence is generally high, Fernando described a specific context in which patients may not take their recommended dose of medication:

"The only time we see a trend of non-compliance is during the holiday season – not in the early stages when the patient is in a critical situation, but once everything is stable then patients may miss some infusions. The system will not usually provide them with the treatment outside of their home country, or even the specific area where they live, so they have a choice of either foregoing a trip away or missing an infusion. It's a departure from the regime, and it's not ideal, but it's humanly understandable."

One solution to this is to develop a more flexible approach to delivering medication:

"Some hospitals may allow the products out of their premises to be administered wherever the patient is. We've been running a programme for some time now that enables patients to receive their treatment at home. In some cases it may even be possible to get the treatment to where the patient is having their holiday."

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Barriers and facilitators of adherence

There is a lack of published research on determinants of non-adherence to orphan drugs and other treatment recommendations for patients with rare diseases.

The Capability, Opportunity and Motivation model of Behaviour (COM-B) has been applied to medication taking and suggests that key influences on patients' adherence behaviour include their psychological and physical capacity to adhere (Capability), their physical and social environment (Opportunity) and their brain processes that direct behaviour (Motivation)[14].
Table 1 lists predictors of adherence identified in a systematic review in cystic fibrosis (CF) and individual studies in CF, sickle cell disease and chronic myeloid leukaemia. These predictors fall into the Motivation and Opportunity categories.

Table 1: Predictors of non-adherence to treatment for rare diseases

Motivation	**REFLECTIVE:** • Doubts about the need for treatment[15, 20] • Belief that it is okay to miss doses[15,22] • Decreased symptoms[15] • Risks outweigh benefits of treatment[15] • Less acceptance and greater feelings of hopelessness[15] • Less worry about illness[15] • Avoidance and denial[15] • No perceived benefit of treatment[18] • Planned non-adherence[18] • Depression[19] • Side effects[21,22] **AUTOMATIC:** • Change to routine/diversion from planned activities[22] • Weekends and holidays[15,16]	
Opportunity	**PHYSICAL:** • Lack of time (for nebulised treatment)[15] • Socialising[22] • Treatment burden[18] • Low social support[18] • Not having medicines on person[21] • Medicines running out[21] • Bad taste or smell[21,22] • Conflicted relationships at home[15,18]	

Demographic variables including older age children and adolescents[15,17], the transition from childhood to adulthood[15] and female gender[15] have also been associated with non-adherence, however the mechanism through which these variables influence adherence is unclear. For example, the transition from childhood to adolescence may be a barrier to adherence because the patient has limited capacity to plan (Capability), does not believe that treatment is necessary (Motivation), lacks previously available social support for adherence (Opportunity), or a combination of these factors. In addition, forgetting has often been associated with non-adherence[15,18,21,22] but is arguably a non-adherence behaviour rather than a predictor of non-adherence. As with the above example, forgetting may be due to Capability, Motivation or Opportunity factors.

Implications for interventions to enhance adherence

Based on the predictors of non-adherence identified, interventions to help patients get the most from their medicines could include:

- Strategies to address perceptual barriers to adherence, such as ensuring a thorough understanding of the rationale for treatment, demonstrating tangible benefits of treatment, informing patients of the risks of non-adherence and strategies to detect and manage treatment side effects.
- Strategies to address practical barriers, including simplification of the treatment regimen and strategies to prevent forgetting (eg organisers, text reminders, linking treatment with daily activities).
- Support to prepare patients to appropriately manage the transition from child to adult services.
- Support to help individuals and families to cope with changes to established routines, including weekends and holidays.
- Strategies to provide psychosocial support, including those that aim to provide social support (such as peer support, or family support for adherence) and strategies to detect and manage depression.

Interventions that work

A literature search revealed very few published interventions to improve adherence among people with rare diseases. However, the majority of interventions have been in cystic fibrosis (CF)[22,23].

CF causes the body to produce a thick mucus, particularly affecting the lungs and digestive system[24]. Treatment consists of medicine, modified diet and airway-clearance techniques. A meta-analysis across chronic childhood conditions[23]showed that educational interventions had a small effect, while behavioural and multicomponent interventions had a medium effect. The average effect of interventions on adherence was greater for paediatric patients with CF than with more common diseases such as asthma and diabetes[23].

Adherence to medication in CF

A randomised controlled trial of a 10-week educational programme 'Airways', showed significantly improved self-management of aerosol and airway-clearance treatments for children with CF, with effects maintained over 12 months[25]. The programme was completed by children and their caregivers at home, and contained the following components:

- Information about the disease and its treatment
- Decision-making skills
- Strategies to overcome barriers to adherence
- Behavioural exercises
- Cognitive behavioural therapy.

Adherence to dietary recommendations in CF

Since younger children are dependent on their parents to administer their complex treatment regimens, these interventions were focused on supporting the parents of children with CF. Successful interventions to improve adherence to recommendations for calorie intake[26-30] included the following components:

- Parent nutritional education
- Parent behaviour modification (praising appropriate behaviour, ignoring inappropriate behaviour, contingency management, where a child earns points for eating specified amounts of food, implementation of a token economy)
- Child nutritional education at an age-appropriate level
- Relaxation for children to ease stomach pain following eating.

Increases in adherence to caloric intake requirements were sustained over time (including a two-year follow-up)[28]. The results of these studies are encouraging, though it should be noted that sample sizes were small, and several different behavioural change techniques were used. Therefore it is not clear which technique or combination of techniques contributed most to the success of the intervention[22].

Use of web-based strategies as a platform for recruitment and delivery of self-management interventions

The Internet is likely to be an effective way of recruiting patients with rare diseases to research studies[31]. Patients with rare diseases consult the Internet for basic disease information, details about their treatment, to seek a diagnosis for their symptoms and access to specialists. They will also consult the Internet to better understand and supplement information discussed in medical consultations[32]. Social media is widely used by people with rare diseases for accessing information and social support, and may therefore be relevant to the development of accessible self-management interventions.

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Conclusions

- People with rare diseases are adversely affected by delays in diagnosis, a lack of information, including about available support groups, and a lack of psychological support.
- Obtaining accurate and up-to-date information about their condition is a key unmet need of patients with rare diseases.
- Rates of non-adherence to treatment recommendations appear to be comparable to those of patients with more common conditions.
- There is a lack of active research studies in rare diseases and consequently little is known about the specific barriers to adherence in these populations.
- Interventions to enhance self-management, including adherence to treatment recommendations, should be targeted to address specific barriers in individual patients.
- For people with rare genetic conditions, the transition from childhood to adulthood may be particularly challenging. There is a need for the development of interventions to support patients to manage their condition effectively over this time.

- Establishing effective communication between patients, their families and HCPs is also a priority.
- Many patients with rare diseases use the Internet, including social media, for disease information and support.
- The Internet may therefore be a useful tool for providing people with rare diseases with information about research studies and delivering self-management interventions.

> *Interventions to enhance self–management, including adherence to treatment recommendations, should be targeted to address specific barriers in individual patients.*

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