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Title: Using digital technology for home monitoring, adherence and self-management in cystic fibrosis: A state of the art review

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Abstract

Digital healthcare is a rapidly growing healthcare sector. Its importance has been recognised at both national and international level, with the World Health Organisation recently publishing its first global strategy for digital health. The use of digital technology within cystic fibrosis (CF) has also increased. CF is a chronic, life limiting condition, in which the treatment burden is high and treatment regimens are not static. Digital technologies present an opportunity to support the lives of people with cystic fibrosis. We included 59 articles and protocols in this state of the art review, relating to 48 studies from 1999 until 2019. This provides a comprehensive overview of the expansion and evolution of the use of digital technology. Technology has been used with the aim of increasing accessibility to healthcare, earlier detection of pulmonary exacerbations and objective electronic adherence monitoring. It may also be used to promote adherence and self-management through education, treatment management Apps and social media.

Introduction

The digital technology sector is a rapidly growing industry, with recent estimates suggesting digital technology is worth £184 billion to the UK economy[1] and $1,351 billion to the US economy.[2] Digital technology has become more accessible than ever before, especially amongst children and young people, with the Royal College of Paediatrics and Child Health describing this generation as "digital natives"; growing up surrounded by digital information. It is also an emerging field within the healthcare sector. It is widely used amongst the general population to track and promote health changing behaviours with devices such as exercise trackers and fitness Apps. Disease specific interventions are also emerging. In chronic obstructive pulmonary disease and asthma, there has been a move towards the use of digital technologies in the ongoing monitoring of disease and adherence promotion. Strategies include text messaging reminders and web-based and mobile applications to monitor and record symptoms.[3,4] Its importance has been recognised by the World Health Organisation who recently published its first global strategy for digital health. This brought together evidence for digital health interventions currently in use and provided recommendations for future development.[5]

Cystic fibrosis (CF) has also seen the application of digital technologies. CF is an autosomal recessive, multisystem disorder. In the UK there are around 10,000 people living with the condition, of which 40% are under the age of 16.[6] In the US around 34,000 people have CF,[7] with the predicted life expectancy of 46 years for those born in 2017.[8] CF is caused by abnormal functioning of the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR), responsible for the transport of chloride and

regulating the movement of water and ions across epithelial surfaces. Based on the CF pig model, a defect in the CFTR protein may lead to abnormal mucous pH in the periciliary fluid and mucous stasis which is primarily responsible for the multisystem manifestations of CF.[9,10] Specialist CF centres in conjunction with developments in treatments, improvements in antibiotic therapy, and better nutrition have improved outcomes for people with CF (pwCF).[11] However, treatment regimens have become increasingly complex, with many patients prescribed daily airway clearance techniques (ACTs), exercise, inhaled and nebulised medications, pancreatic enzyme replacement (PERT) and dietary supplementation. Intravenous antibiotics are required for acute pulmonary infections, often more frequently as patients get older.

Despite the complexity of CF therapies, much of the regimen can be completed in the patient's home, allowing the integration of treatments into everyday routines, with regular monitoring from the CF team. However, treatments are tiring, time-consuming and burdensome; the average time spent on treatments for children in the UK is 137 minutes per day and 150 minutes in adults.[12] In addition, the routines of adults and families of children with CF are not static; managing the condition is a dynamic process involving ongoing adaptation and readjustment.[13] Managing treatments alongside daily life activities can therefore be challenging and restrictive. Digital technologies present an opportunity to support and improve the lives of pwCF. Indeed, pwCF and parents acknowledge the role of technology and there are a range of applications and platforms that have been designed by them for pwCF.

The aim of this state of the art review is to provide comprehensive overview of the evolution of CF-specific digital technologies and their effectiveness in the promotion of home monitoring, adherence or self-management in what is a rapidly changing area of medicine.

Methods

We conducted a systematic literature search of electronic databases and clinical trials registers from 1/1/1999 to 14/02/2019. The protocol with full search strategies and inclusion criteria can be found at https://nottingham-repository.worktribe.com/output/2044553. Broad search criteria were used and full text, article abstracts, conference abstracts and trial protocols were considered for inclusion in order to increase sensitivity. Once duplicates were removed, a total of 1968 electronic search results were identified which were imported into Covidence[14] and considered for inclusion. The search results were reviewed independently by two reviewers. We excluded 1,665 articles on title alone, leaving 303 for full text screening, of which 51 articles met criteria for inclusion. Searches of clinical trials registered over the same time period identified 48 protocols, which following duplicate removal and screening, identified a further 8 studies. Once the final articles had been identified, data were independently extracted by both reviewers with results collated into MS Excel. We included 59 articles

and protocols (online table 1), relating to 48 studies. The general quality of the evidence was low; mainly consisting of small interventional and before after studies with only three full text randomised-control trials (RCTs) and one systematic review. Figure 1 highlights the expansion of technology over the last twenty years. Although for the purposes of this review technology has been assessed for its role within either home monitoring, measuring adherence or self-management we recognise that in practice these are often inter-related concepts in relation to CF.

Digital technology used for home monitoring

Increasing accessibility to healthcare

Centralisation of care means that many patients do not live in close proximity to their CF centre which potentially becomes a barrier to accessing healthcare. Therefore, digital technology has been explored as an option for remote delivery of care. Videoconferencing has been used for delivery of routine appointments, annual assessments and multidisciplinary team (MDT) discussions,[15] with more recent studies also able to share imaging, educational slides, lung function and microbiology results. Although there was no significant difference in Forced Expiratory Volume in one second (FEV_1) results reported with teleconferencing, one study described positive patient satisfaction and 63% felt it was as good as a face to face review.[16] It has also been used more widely for delivering mental health services to pwCF online.[17] These studies again were small interventional studies and larger RCTs are required to fully assess the impact on telehealthcare in remote delivery of care. An ongoing RCT, VIRTUAL-CF is using videoconferencing to the CF MDT with remote spirometry and oxygen saturation measurements for patients receiving intravenous antibiotics in the community. It is assessing whether this approach promotes health-related quality of life compared to standard community intravenous antibiotics care.[18]

Home monitoring for early detection of pulmonary exacerbations

Despite life expectancy improving, the majority of deaths in CF are still attributable to respiratory failure secondary to recurrent pulmonary exacerbations. Exacerbations also contribute to morbidity; worsening CF related diabetes and reducing health-related quality of life.[19-21] Therefore, the use of digital technology has been evaluated to determine if it can lead to the earlier detection of exacerbations and subsequently reduce the rate of respiratory decline. One of the first uses of digital technology in this context was in the 1980s for home monitoring of respiratory symptoms and lung function.[22] This, along with other earlier studies, used a combination of home spirometry, measuring physical parameters such as heart rate and oxygen saturations, blood glucose levels and respiratory symptom scoring with the results collated and sent via modem internet to the CF centre.[23] In more

recent work, advances in technology have allowed streamlining of data transmission via Wifi or Bluetooth. A small non-randomised interventional study showed promising results in FEV_1 status. Data collected from a Spirotel™ device (Medical International Research, Rome, Italy) were sent via email to the CF centre, with patients contacted if they met intervention criteria for an exacerbation based on FEV_1 decline or oxygen saturations.[24] A significantly smaller decline in annual FEV_1 status was noted in the telehealth group over a 4.5 year period. However, these results were not subsequently supported by a large multi-centre RCT, the Early Intervention in Cystic Fibrosis Exacerbation (eICE) trial.[25,26] Using twice weekly home spirometry (Viasys AM2 device, CareFusion, California, USA) and respiratory symptom scoring, patients were contacted by the CF team if a reduction in FEV_1 greater than ten percent or an increase in respiratory symptoms was seen. The early intervention group had a shorter time to first exacerbation and more exacerbation treatments compared to the control group, however this was not associated with a slower FEV_1 decline. The trial was stopped early for futility, as completing the trial was unlikely to show a difference in primary end point.[27]

However, the eICE study highlights the issue of adherence. In a condition where treatment burden is already high, home monitoring adds an additional task for the patient to complete. Home monitoring studies have required data entry from once a month to three times a week.[28,29] Adherence to telemonitoring in the eICE trial over 52 weeks was suboptimal; 50% of patients transmitted data once per week and only 19% twice per week as per the protocol, with an increased treatment burden score in the early intervention telemonitoring group.[26]

Ongoing studies

Current studies are assessing the use of smartphone applications for the earlier recognition of exacerbations through changes in respiratory symptoms. They hope to establish whether having monitoring which is less restrictive and more mobile would improve adherence and therefore outcomes.[30,31] Unfortunately, preliminary data from RCT (ACTRN12615000599572) suggests that the use of a smartphone for symptom reporting had no effect on the number of courses of antibiotics or days of antibiotic treatment, with full results awaited.[32]

Digital technology for monitoring and promoting adherence and exercise

Home monitoring for supporting adherence

Adherence monitoring enables treatment guidance and allows clinicians to differentiate if changes in a patient's condition are related to disease progression, attributable to poor adherence or a combination of the two. The impact of home monitoring on treatment adherence in adolescents and young adults has been explored in a before and after study using once weekly home monitoring and adherence monitoring using medication prescription refill data to calculate the medication possession ratio (MPR).[33] In comparison to Lechtzin's eICE study, adherence to weekly spirometry monitoring was 59% which may reflect the impact of parental supervision in this population group. Less frequent monitoring may have lessened the treatment burden to patients. There was a small associated overall increase in medication adherence; MPR was 60% in the year prior to study enrolment, and 65% during the 12 month study period (p=0.038). These authors found no change in the number of exacerbations or FEV_1 decline between groups across the study period.[33]

Digital technologies for adherence

Self-monitoring also helps patients better understand and self-manage their condition. However, self-reporting of adherence is notoriously inaccurate and so alternative ways for adherence monitoring are being pursued. Prescription refill data and MPR is a valid and inexpensive way of monitoring adherence however, this is still prone to inaccuracies, as it is based on the assumption that all of the medications refilled are always taken.[33] Hence digital technologies are being developed to more accurately record treatment adherence.[34]

One small intervention study compared self versus digital electronic adherence recording of a high-frequency chest wall compression vest (Vest System, Hill-Rom, Indiana, USA). Although the results showed a high variability in self-reporting, it supported the view that patients over-estimate treatment duration; by 127% in adults and 26% in parents of children wCF over a 2 week period. Overall average treatment adherence was 69%.[35]

An established digital technology for adherence monitoring in CF is the data logging nebuliser device which combines routine nebuliser treatment with accurate adherence logging, via an electronic data capture facility. This gives an insight into how often and how long treatments are taking to build a picture of adherence. One such device is the I-Neb™ (Respironics, Chichester, UK). It is an adaptive aerosol delivery system which adapts medication delivery to the patient's breathing pattern, delivering only during inspiration.[36,37] It also provides patients with visual and audio feedback whilst they undertake their treatments. Its data capturing facility allows trends to be identified. For example: although one study found adherence was maintained between 60-70% over one year, diurnal

variation was also noted; evening 70% vs 58% morning (p=0.012).[36] This allows for more realistic joint goal setting and changes to treatments based on the results.[35,36] However, this device is currently only available to a subset of patients prescribed Promixin™ (colistimethate sodium, Profile Therapeutics plc, West Sussex, UK) and although data logging devices may provide useful information to the CF team regarding adherence, some patients may find this level of monitoring intrusive.

Insight Online™ (Respironics, Chichester, UK) has been developed to be used alongside the I-Neb™. It is a home monitoring telehealth interface, where patients upload data from the I-Neb™ to a server. The data are then analysed and presented for patients and clinicians to view. Patients are encouraged to set treatment targets, against which they can self-monitor their progress. Data presented from a small intervention study had mixed results. This showed that for the patients who did engage it improved adherence, however over 50% of the participants failed to upload regularly.[38] This result again raises the issue of increased treatment burden on patients, and that CF teams' perceived benefit of technology may not be shared by all patients.

Digital Technologies for exercise

The video gaming industry is a continuously growing global industry accessed by 64% of the US population. Of those using game consoles, 76% played for at least 3 hours a week with the majority using it for significantly longer.[39] Exercise is a key treatment in CF and, given the popularity of gaming technology, incorporating exercise through gaming has been explored as a strategy to help people to engage and self-monitor exercise. There have been small interventional studies using games consoles for promotion of home-based exercise.[40] A RCT used the Nintendo Wii EA Sports Active 2 to deliver a six week training programme of 30-60 minute sessions, five days a week, monitored by a virtual personal trainer, with participants followed up for 12 months following the intervention.[41,42] Unfortunately this did not support the use of video gaming. Although both control and intervention groups showed a significant difference between physical parameters pre and post study, there was no difference between groups. In addition, although short term adherence was good, with 95% adherent at 6 weeks, this was not sustained and reduced to 35% using the game twice a week by 12 months, with 65% not using it at all.[41] A potential reason is that if games are played frequently over an extended time period there is an element of monotony, similar to treatment regimens.

Fitness trackers have been used within the general population for some time to promote exercise, with CF-specific trials focused mainly from 2017 onwards. A RCT by Bishay compared a fitness tracker with a personalised exercise prescription and social media platform to exercise prescription alone over a 12 month period.[43] This study did not support the use of fitness trackers in CF with no significant

difference between the two groups in terms of exercise tolerance, pulmonary function or patient reported outcomes.

There are other examples of social media and web-based platforms for exercise promotion. A small interventional pilot study used a closed Facebook group to promote a 30 day exercise challenge to increase daily exercise.[44] Pactster in the UK (developed with the CF Trust) provided online exercise classes and included instructors who have CF.[45] "CFYOGI" in the USA[46] is an exercise web platform co-founded by a pwCF and a parent of children with CF in partnership with Social Good Fund. It includes livestreamed and recorded fitness videos led by instructors with CF and has community features allowing patients to share progress and fitness goals while avoiding cross-infection risks.

Ongoing studies

The development of data-tracking nebulisers has led to the development of CFHealthHub observatory,[47] a large scale data observatory which aims to recruit 6,000 pwCF over the period 2017-2021 and collect observational data using patients' data tracking nebulisers. In addition, it will be used as part of a large multicentre RCT (ISRCTN55504164)[48] which will combine the use of data captured from data tracking nebulisers with behavioural change interventions available via a web portal, CFHealthHub. Data is available to be viewed by both clinicians and pwCF, with the primary outcome of the study being number of exacerbations. Secondly, a non-randomised cross over study (NCT02700243) is exploring the use of video games in improving adherence to ACTs using a positive expiratory pressure (PEP) device. Electronic versus self-reporting of adherence will be monitored over a 4 month period, following which a video game will be integrated into the PEP device operated by the patient performing their therapy correctly. Primary outcome is adherence to therapy, with change to pulmonary function a secondary outcome.[49]

There are several ongoing studies in relation to exercise.[50] ACTIVATE-CF,[51] is using pedometers and daily web-based logging of exercise activities in addition to the standard care of 3 monthly counselling sessions to promote physical activity. Patients are encouraged to exercise 3 hours a week, with FEV_1 status being the primary outcome. Another RCT (NCT03672058) combines the use of Fitbit™ exercise trackers (Fitbit, Inc. California, USA) with an online activity monitoring system (Fitabase) and personalised feedback on activity levels and progress, compared to the use of a Fitbit alone on steps per day and FEV_1 status.[52] Finally, project Fizzyo combines their use with ACT devices to assess activity levels, with chipped ACT devices used to capture daily adherence data.[53] Data transmission appears more streamlined compared to other studies, with the results sent automatically once the ACT device

is synchronised with a tablet computer. In addition, computer games have been developed in conjunction with patients to be used at different intervals within the study to assess the impact of gaming on adherence.[53]

Digital technology for education and self-management

Self-management is key to successful management of chronic conditions such as CF. Self-management has been described as the process of helping patients and their families to choose, monitor and adjust their treatment requirements in relation to their condition and the effect it has on their lives.[54]

Education

Multiple digital technology platforms have been explored to promote self-management through education delivered as either self-guided sessions or mentor-supported individual or group web-based sessions. Whilst they may provide educational opportunities for participants, the self-management education and digital technologies themselves have had limited success, so far, in relation to patient outcomes. This is in keeping with a Cochrane review that suggested self-management education in CF could provide limited positive change for a small number of self-management behaviours.[54]

Early education strategies explored education delivery via a CD-Rom, combining a computer game with education.[55] Several platforms have since been developed. Web based education has increased in popularity, and the use of smartphones and Apps has been developed.[56] CFfone provided access to the CFfone website via a smartphone, which contained educational materials and social support through inspirational stories and communication with peers in an online community.[57] The BeInCharge study for parents of children with CF combined an education programme on dietary education, personalised calorie intake goals and behaviour techniques with a daily diet tracker App. Use of the App resulted in no significant increase in weight gain in the intervention group and indeed the App was less successful in achieving weight gain compared to the face-to face delivery used previously.[58]

Individual education delivery for both children and adults guided by a mentor or physio has been explored. Patients in a small RCT, with two intervention treatment arms, used an online mentor-guided self-efficacy programme with or without an App to monitor their symptoms and quality of life, compared to the control group.[59] Results were limited by the small sample size although patients reported being confident in using digital technology. An increase in self-efficacy was seen across the intervention groups; however, this was similar in both groups with and without the use of the App.

Similarly, group sessions in CF have been limited to small interventional trials.[60] Results of larger studies are required, one of which has recently been completed.[61] This delivered 6 online modules relating to nutrition, medications and respiratory and liver disease. Patients also completed tasks and had access to videos of patients sharing their experiences. Preliminary data at 6 months show mixed results, with adherence data awaited. Significant improvements in body mass index and ADE vitamin levels were seen, however this did not translate to a reduction in lung function decline.[61,62]

Ongoing studies using education

Two large RCTs addressing this issue are due to be completed in 2019. Project UPLIFT provides group web-based education and intervention programme focusing on improving anxiety and depression in pwCF.[63] Adherence is a secondary outcome. It focuses on education on depression and CF; coping strategies such as cognitive behavioural therapy and mindfulness; and relaxation techniques. An Australian project CyFiT, [64] encompasses several aspects of digital healthcare delivery. It combines the delivery of outpatient physiotherapy via videoconferencing, with additional multimedia and educational features. Participants are also given an activity tracker to record sleep and physiological parameters to guide exercise prescriptions and the telehealth sessions. The primary outcome is pulmonary function and the comparator is standard physiotherapy. Finally, a pilot study for a RCT (NCT03637504) plans to evaluate the feasibility of MedActionPlan™ (MedActionPlan, Peapack, USA); a web-based medication management App which uses education about treatment regimens to encourage self-management and adherence. Adherence is assessed using eTrack nebulisers and AdhereTech™ pill bottles (AdhereTech, New York, USA).[65]

Digital technology for self-management of treatments

Digital Apps are being used in a variety of contexts within CF including symptom monitoring, education and diet tracking. A newer area of interest is the development CF-specific Apps to help manage treatment regimens. “Genia” is a Swedish based treatment management App developed by a father and his daughter, who has CF,[65] which allows pwCF to track their condition as well as providing the option to share information with care teams about symptoms, daily activities and medications, as well as sharing updates with family and friends.

Ongoing Studies

In the context of pancreatic insufficiency, smartphone Apps are under development which will be capable of calculating patient specific PERT requirements.[66-68] MyCyFAPP is a multicentre, multidisciplinary development currently being tested which aims to allow patients to better self-manage their PERT and nutrition. Importantly, parents and patients of various ages were involved in

the development phase as part of interviews and focus groups. The protocol describes a number of expected features of the App including education through games, food and symptom scoring records and a handbook containing nutritional information, in addition to calculating optimal PERT dosing. These data are also accessible to clinicians with alerts for suboptimal treatment, with the aim of promoting more focused and realistic goal setting at follow ups.[68]

The use of social media for self-management in cystic fibrosis

Social support is known to improve self-management and therefore the use of social media to provide social support has been explored, although CF-specific research is limited. A thematic analysis undertaken on a CF charity website message board found that online support groups seem to supplement professional support in relation to self-management and self-esteem.[69] Social media has also been incorporated into projects such as CFfone (described previously). No larger CF-specific studies were identified.

Conclusion

Digital technology is a growing industry. We have highlighted the expansion and evolution of its use in CF over the last 20 years for supporting home monitoring, adherence and self-management. Despite the large number of articles, most were small pilot and intervention studies without comparators and there were very few full text RCTs. Although ongoing studies may yield some positive results, the majority so far have shown limited evidence to support the use of digital technology. An area of promise was electronic monitoring of adherence via data logging nebulisers to accurately capture adherence data. However, this does not address barriers to adherence. In addition, a potentially exciting area of development is the use of digital technology to assist in the self-management of medications, such as Apps providing patient-specific PERT dosing information. Future evaluation of the role of digital technology in CF will require well designed, adequately powered RCTs. Developers should be mindful that, in a condition where there is already a significant treatment burden, patients must find these technologies acceptable and sustainable. The benefits of digital technology must be carefully balanced against the investment of time needed to use them. Patient involvement in the design process is key. Furthermore, the benefits of treatment should be of benefit to the patient as well as the CF team.

List of Abbreviations

Airway Clearance Techniques (ACTs)

Early Intervention in Cystic Fibrosis Exacerbation (eICE)

Cystic Fibrosis (CF)

Cystic Fibrosis Transmembrane Conductance Regulator (CFTR)

Forced Expiratory Volume in one second (FEV_1)

Medication Possession Ratio (MPR)

Multidisciplinary Team (MDT)

Pancreatic Enzyme Replacement Therapy (PERT)

People with CF (PwCF)

Positive Expiratory Pressure (PEP)

Randomised Control Trials (RCT)

Contributorships

R Calthorpe and S Smith completed the systematic literature search and data extraction. Dr Calthorpe wrote the review with all authors commenting on the final manuscript. In addition, Dr Gathercole also contributed to the review by the inclusion of the patient's perspective throughout the article. Prof A Smyth was the supervising author on this review, and is the corresponding author.

Competing Interests

Prof. A Smyth has provided consultancy for Vertex and holds a current unrestricted research grant from Vertex. He has taken part in clinical trials sponsored by Vertex, Raptor and Insmed. He has given lectures at meetings sponsored by Teva and Vertex.

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Not applicable

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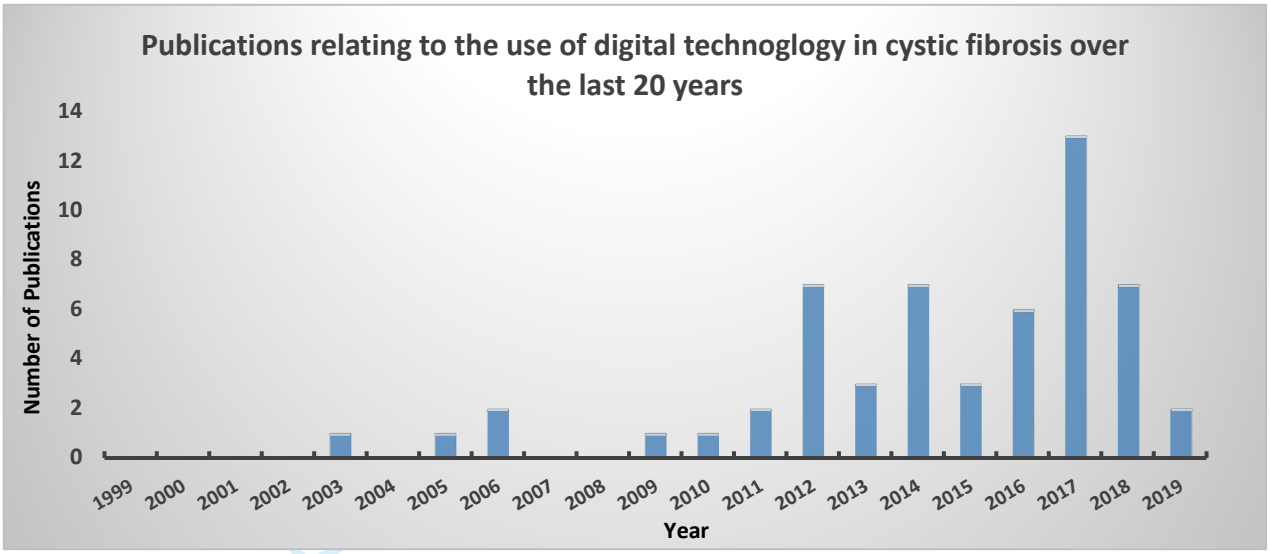

Figure 1: Publications relating to the use of digital technology in cystic fibrosis over the last 20 years.

Author and Year	Study and article type	Population and patient number	Intervention	Comparator	Outcome	Summary of findings	Grade and Description
Home Monitoring							
Increasing accessibility to healthcare							
Appiah-Kubi 2012[15]	Descriptive Conference abstract	Adults wCF 71 patients	Monthly videoconferencing session to main CF centre. Blood tests taken locally and the results faxed to the centre prior to session.	No comparator	Improve patient care and education. Cost	Improved patient care, reduced patient costs and improved inter-professional collaboration. Used for routine clinics, medication explanations and to treat patients on IV antibiotics.	Grade: Very low All three studies contributing data to this outcome were small and observational in design. Two of the papers were only available as an abstract and one of the studies had no comparator. The quality of the evidence for this outcome was downgraded accordingly.
Becerra 2017[17]	Observational cohort study Conference abstract	PwCF with mental health symptoms 10 patients	Telehealth interventions accessed by the patient in their home on relapse prevention, crisis management, CBT, emotional wellness, mental health coordination with an outside provider, assessment and linkage.	Not specified	Emotional functioning; mental health symptoms	Telehealth improved how patients assessed their emotional functioning and assisted them with overcoming negative thinking patterns and improved their usage of coping skills.	
Lester 2016[16]	Observational intervention study Conference abstract	Adults wCF 29 patients	Annual assessment delivered via videoconferencing with physio input, and shown educational slides, physical parameter trends and reports over 5 years.	Usual care: in clinic	Primary: improve understanding of ACT Secondary: how TM compared to face to face, and would they participate in future	There was no improvement in FEV_1 % after the TM call. Patients were satisfied with TM and would participate in other TM education opportunities (95%). 63% thought was as good as face to face.	
Bella 2017[75]	Observational cohort study Conference abstract	PwCF 50 patients	Various technologies to deliver home telemedicine over a 15 year period. FEV_1 monitored at home.	Unclear	FEV_1; adherence; pulmonary relapse	36% drop out, 68% of which was due to poor adherence. Benefits of using telemedicine identified were a better doctor-patient relationship and increased QoL.	
Ongoing studies							
NCT03069651 2017[18]	RCT Protocol	Adults wCF requiring community-delivered IV antibiotics 100 patients	VIRTUAL-CF: Community IV antibiotics. Patients perform spirometry and pulse oximetry twice weekly during videoconferencing with the CF MDT with community CF nurse if required as usual.	Usual care: MDT input at beginning of antibiotic course with CF nurse visit if required.	Primary: health related QoL Secondary: patient satisfaction, lung function, weight, economics	Ongoing trial Dec 2016 - Dec 2019.	Ongoing study
Home monitoring for early detection of pulmonary exacerbations							
Bell[71]	Editorial review Full text	PwCF (14yrs+) FEV_1 >25% 320 patients	As per eICE trial	As per eICE trial	As per eICE trial	Editorial review of eICE trial by Lectzin. Poor adherence to trial discussed.	
Cox 2012[70]	Systematic review Full text	PwCF 8 studies	Telehealth to monitor health symptoms, adherence or provide therapy via some form of user interface, i.e telephone, videoconferencing or electronic diary.	Different for each study	Monitor symptoms, assess adherence to prescribed therapies or provide therapy via some form of user interface	Patients were confident in their ability to use the technology. However, in many studies participants failed to provide data at the time points required. Insufficient evidence to reach a firm conclusion about the benefits of telehealth in PwCF. Most studies were small feasibility trials with limited external validity.	

Frost 2017[72]	Intervention study Conference abstract	Inpatient adults wCF 36 patient	Step counting via a smartphone activity tracker. Retrospective review of participants recorded steps for three seven day periods 1) before discharge 2) week before admission 3) a week when clinically stable	Comparison between the time periods	Whether using a smartphone step counter App can detect changes in health status	Those with better lung function trended towards increased steps. Step-count was significantly lower when an inpatient than when clinically stable (1292 vs. 3104) and significant decreased in the 5 days immediately prior to admission.	
Fischer 2003[23]	RCT Conference abstract	Adult wCF 51 patients	Twice weekly home spirometry, oxygen saturations, heart rate, blood glucose and QoL. Data transmitted via a modem connection to the CF centre to detect onset of deterioration and PE. Patients can follow their own lung function at home.	Regular care: 3 monthly visits in clinic	Hospitalisations, drug prescription rate; periods of disability; days out of work; lung function.	Ongoing study at abstract submission: too early to report lung function but trend toward improved motivation and lung function in telemedicine group. Some patients did not tolerate the frequent FEV_1 measurements. No follow up results identified.	Grade: Low Although two of the studies were RCTs, only one of these was published as a full paper. The quality of the evidence has been downgraded due to small numbers of participants in all but the full RCT and heterogeneity in the findings.
Lechtzin 2017[21,26,27,73,74]	RCT Full text	PwCF (14yrs+) FEV_1 >25%. 267 patients	EI arm (Home monitoring): Visay AM2 spirometry which recorded spirometry and 8 questions from the CFRSD twice weekly. Results uploaded to central database and contacted if FEV_1 decreased >10%, or declined in symptoms	Usual care	52 week change in FEV_1; CFQ-R; CFRSD; FEV_1 % predicted; FVC (L); FEF25-75; Time to first PE; time from end of first PE to start of subsequent PE; Number of hopsitailisations and days; prevalence of P.aeruginosa; prevalence of staph aureus; protocol burden.	Interim data (2014): 35% patients were >80% adherent.76% used device at least 1x week[74] Interim data (2015): 74% patients required alarm at 5 days to remind them to submit data, 51% were compliant of their weekly data transmission 20% managed 2 x week[73] Final article (2017): More PE and time to first PE shorter in EI group, but didn't result in slower decline in lung function with no difference in FEV_1 change. Once weekly data transmission 50%; 19% twice weekly. No change in Pseudomonas compared to baselines. The intervention was associated with an increased burden.[22]	
Murgia 2012 and 2015[24,75]	Non-randomised controlled intervention study Full text	PwCF 32 patients	Telehomecare: twice weekly remote transmission data via Spirotel (Home Vivitel Control Service spirometry) pulmonary symptoms and overnight pulse oximetry. Used as an adjunct to standard therapy.	Standard therapy	FEV_1 reduction >10%; worsening of symptoms; nocturnal pulse oximetry; oxygen saturations	Telemedicine group showed a significantly lower decline in FEV_1. Patients accepted the home telemonitoring, high number of daily responses and increased data transmission over time.	
Van Horck 2017[29]	Multicentre, observation cohort study Full text	PwCF (5 -19 years) 49 patients	Home spirometry and respiratory symptom monitoring via Handheld Jaeger home monitor three times a week, with data transfer to web-based portal once a week. Patients split into exacerbation (E=28 patients) and non-exacerbation (NE=9 patient) groups.	No comparator	Primary outcome: detection of PE FEV_1 (% predicted), RSS, adherence to home monitor	Increase in the RSS in the 2 weeks before a PE (p=0.051). No deterioration in FEV_1 % predicted in the 4 weeks before a PE. Mean FEV_1 % predicted and mean RSS of four weeks to one week before an PE resulted in good sensitivity 92.9% (CI 75.0–98.8%) and specificity 88.9% (CI50.7–99.4%) to predict a PE. 54% of the children had good to optimal adherence	

Wall 2011[28]	Intervention study Conference abstract	PwCF (7-17 years) >120 miles from CF centre 10 patients	Minimum monthly home spirometry, FEV_1 and 6 likert questions relating to respiratory symptoms via internet. Reponses reviewed by CF nurse within 24 hours and contacted via phone	No comparator	Responses leading to an intervention (starting oral abx, hospitalisation, call to come to clinic or advice). Number of interventions required.	40% of encounters led to an intervention. Patients were more likely to submit data when they experience symptoms. Major barriers were forgetfulness and denial	
Ongoing studies							
NCT02122289 2014[31]	RCT Protocol	PwCF (14 - 25 years) 45 patients	Weekly symptom scoring questionnaire via smartphone over 6 months. Creates an alert to identify a possible PE	No smartphone App	Primary: frequency of PE Secondary: user satisfaction of device and compliance	2014 - 2016. No results found.	Ongoing studies
ACTRN12615-000599572 Wood 2018[30]	RCT Conference abstract	adults wCF 60 patients	Smartphone app used weekly for symptoms reporting to CF team. Contacted by CF nurse if symptomatic for a PE	No App	Whether an App can early detect an PE, affects number of courses and days of IV abx.	The preliminary results had no effect on number of days or courses of antibiotics.	
Digital technology for monitoring and promoting adherence and exercise							
Home monitoring for supporting adherence							
Shakkottai 2018[33,78]	Pilot study and prospective interventional study Full text	PwCF (12-21 years) 39 patients	SpiroPD™ personal spirometer to measure lung function at home (1x week) and daily personal medication reminders. Prescription refill data collected.	Measurements from the year preceding the study	Adherence; perception of treatment burden via CFQ-R; PFTs; BMI; frequency of exacerbations requiring IV or oral antibiotics	Pilot study completed to test feasibility of equipment being used for the first time in this age group. Mean adherence to weekly spirometry 59.47%. Mean treatment burden: 68 at enrolment and 66 at study completion (P = 0.14). 30% had greater than 80% adherence. Medication adherence overall increased from 60% to 65% (p=0.038). No statistically significance in adherence to individual oral and IV medications, exacerbations or FEV_1 decline	
Digital technologies for adherence							
Thorton 2014[38]	Intervention study Conference abstract	PwCF (6 - 17 years) 28 patients	I-neb Insight online™: Record iNeb and symptom monitoring twice weekly and upload to Insight online. Patients receive prompts if fail to upload data regularly.	No comparator	If telehealth system (iNeb and Insight Online) promotes adherence to nebulised treatment	Group 1: independently uploaded, group 2: uploaded with prompts, group 3: failed to upload despite prompts. Group 1: adherence maintained >85%. Group 2: 38% baseline - 111% at 2 months Group 3: 71% baseline - 7% change at 2 months. on iNeb downloads. >50% failed to upload regularly.	
McNamara 2009[36]	Retrospective observational study. Full text	PwCF (2–15 years) with P. Aeruginosa infection 48 patients	Use of I-neb™ AAD with data logging facility.	No comparator	Treatment episodes. Adherence	Overall monthly adherence to nebulised therapy was 60-70% over one year. Considerable variation; evening better than morning adherence (75% vs 58%: p=0.012).	**Grade : very low** All studies had small numbers of participants and no comparator group therefore the quality of evidence has been downgraded.
Mikesell 2017[35]	Interventional study Full text	PwCF (6- 24 years) using HFCWC equipment 85 patients	The Vest System model 105™. Records data on time, duration of use, frequency of compressions and compression pressure intensity with data downloaded every 30 days.	No comparator although they did compare results for those who had	Compare self-reported to objective adherence measurements via HFCWC vest. How adherence	Average adherence was 69%; highest in children and those assisted with treatment (82%). Overestimation of therapy duration by adults (127%), 26.3% by parents. Average daily	

			3 cohorts: <13 years, 13-18 years, 19+ years	an exacerbation with those who did not.	correlates to baseline pulmonary functions and exacerbations	therapy time and adherence had significant positive associations with baseline FEV_1 percent of predicted and negative associations with PE.	
Thorton 2013[34]	Intervention study Conference abstract	PwCF (5 - 16 years) 15 patients,	Self-reporting vs iNeb reporting of adherence to nebulisers. Use of Insight Online telehealth home monitoring.	No comparator	Self-perceived vs electronic adherence (iNeb); Determine if the feedback from Insight Online optimises adherence	Inaccurate self-reported adherence; 6 patients within 10% accuracy of actual vs perceived adherence. When Insight Online used with the iNeb it maintained adherence in 3 out 4 children with adherence already above 90%. 6/11 children who's adherence <90% improved by a median of 22.3% over 4 weeks.	
Spencer 2012[77]	Observational intervention study Conference abstract	PwCF 49 patients	I-Neb™ ADD with data logging facility, with Insight Online, a telemedicine patient management system	No comparator	Resolution of treatment issues; adherence; compliance; treatment time	I-neb Insight Online adherence 69.4%. Mean TBM treatment time of 4.9 min, and a mean TIM treatment time of 2.9 min.	
Digital technologies for exercise							
Aquino 2006[82]	RCT cross-over design Conference abstract	PwCF (7 - 29 years) 13 patients	Physical exercise via PlayStation 2 - Eye Toy1. 4 minutes game followed by 3.5 minute break with 3 bouts of cough and sputum expectoration.	4 minutes PEP mask followed by 3.5 minutes break with 3 bouts of cough and sputum expectoration.	weight of sputum; SaO2%; VAS test	No significant difference in sputum production, resting saturations, peak oxygen desaturations between groups. Exercise as effective as PEP	
Bishay 2018[43]	RCT Conference abstract	Adults wCF 40 patients	A personalised exercise prescription provided by a physical therapist plus use of a wearable fitness tracker integrated with a social media platform.	Exercise prescription alone	Primary: mean level completed on a GXT after 12 months Secondary: change in GXT and FEV_1, mean FEV_1 at one year, anxiety and depression	Provision of a fitness tracker with an exercise prescription did not result in significant improvements in exercise tolerance, pulmonary function or patient reported outcomes compared to exercise alone. The results did not support routine use of fitness trackers in adults with CF.	Grade: Moderate The evidence for this outcome came from two RCTs which had small numbers of participants but compared the digital technology with usual exercise prescription.
Del Corral 2018[41,42,83]	Pilot study and RCT Full text	PwCF (7 - 18 years) Clinically stable 41 patients	6 week home training programme (30-60 minute sessions, 5 days a week using a Nintendo Wii™ with the game EA sports active 2, supervised by a virtual personal trainer. Training load increased weekly, along with weekly phone calls from physio. After the training programme, participants were asked to continue the program for a 12 month follow up period.	Normal care: usual exercise programme without Nintento Wii™	Primary: MSWT; Secondary: 6MWT; Horizontal jump test; medicine ball throw; hand grip; spanish version of the CFQ-R, HRQoL	Pilot study: improved exercise tolerance on 6 min walk test and shuttle test. Respiratory symptoms and physical tendency domains were statistically significant. No significant difference between the dyspnoea and fatigue perception.[63] RCT: Significant between-group differences in exercise capacity before versus after intervention. Good short term adherence (95%), Poor overall adherence at 12 months; 35% exercised 2 days a week, 65% patients didn't use Wii for exercise.[62]	

Smith 2015[44]	Observational intervention pilot study Conference abstract	PwCF 10 patients	Facebook challenge: Increasing the daily number of squats, press ups and sit ups. Participants encouraged to post their progress on social media	No comparator	Increase motivation to exercise	Half the patients found it maintained their motivation to exercise.	Grade: Very Low Small study with no comparator group
Ongoing studies							
ACTRN126130-009297072013[79]	RCT Protocol	PwCF 4-17 years) 36 patients	PEP PT: PEP with additional features including reminder alarm, screen display showing pressure curve to achieve ideal technique with gaming features, and point scoring which can be redeemed for rewards. Information stored to be used with clinicians to guide consultations.	PEP device that measures adherence and technique, without feedback function	Primary: adherence to PEP measured by PEP device Secondary: PEP technique	No follow up paper of results	Ongoing studies
Kiviet 2010[80]	Proposal. Conference abstract	Children wCF 200 patients	Patient-accessed E-portal connected to Electronic Patient Dossier	No comparator		Study not running yet	
Hind 2017[48,81]	RCT Conference abstract And protocol	PwCF (6+ years) 64 patients	Information on adherence using a chipped nebuliser with software platform (CFHealthHub). Web-based with strategies to empower self-management delivered online and in six face-to-face/telephone sessions over 5 months	Usual care	Primary: Number of PE Secondary: knowledge, skills and self-management (PAM-13), life chaos, generic health status, habit based behavioural patterns, QoL, HADS, adherence, medication beliefs, behaviour	Feasibility study completed, RCT in progress.	
Mcllwaine 2016[49]	Non-randomised interventional study Protocol	PwCF (6 - 12 years) 20 patients	First 4 months: adherence measured via digital manometer attached to PEP devices vs patients own self-reported adherence. Second 4 months: PEP device attached to video game	No comparator	Primary: adherence to therapy (electronic vs self-report). secondary: change in FEV_1 from 1st and 2nd 4 month block	Ongoing study	
NCT02700243 2016[50]	RCT Protocol	Adults wCF 40 patients	Interact: given Fitbit exercise tracker™ and are followed over the course of one year, completing surveys and exercise tests	Usual Care	Graded exercise test; HAES, FEV_1 change from baseline; FEF25-75; PE requiring IV antibiotics; CFQ-R; use of social media; Depression scale	Ongoing study	
ACTRN12617-001009303 2017[84]	RCT Protocol	PwCF (12-24 years) inpatients Recruiting target 150 patients	Online programme (ActivOnline) + usual care. Participants record their daily physical activity and exercise using online portal. Patients set goals, record physical activity using a pedometer (or other device) with data displayed graphically so participants can see their progress. Facility to message researchers and other participants.	Usual care: given details of online information website on physical activity	Change in physical activity participation; change in exercise capacity; FEV_1; CFQ-R; HADS; PSQI; time to first hospital admission; change in depression scale; HAES; number of hospital inpatient days	Currently recruiting	

NCT03672058 Cahalan 2018[52]	RCT Protocol	Adults wCF 61 patients	Both groups have fitness tracker linked to online monitoring system Fitabase (24 weeks). Personalised weekly text message on progress for 12 weeks, next 12 weeks no feedback.	Fitabase and exercise tracker.	FEV_1, maximal aerobic power, FVC, grip strength; BMI; muscle mass; % body fat; CFQ-R; subjective: physical activity; sleep quality; SoB; activity level; exacerbation frequency	Ongoing study	
Hebestreit 2018[51]	RCT Protocol	PwCF (>/= 12 years) and FEV_1 >/= 35% 292 patients	Weekly exercise regime (30 minutes strength, 2 hours aerobic) with regular monitoring and encouragement. Incorporates questionnaire, pedometer and daily logs. Centralised team monitors logs and contacts if inactivity for >3 days.	Instructed to keep physical activity constant over 12 months	Change in FEV_1 over 6 months; exercise capacity, physical activity, pulmonary function, exacerbations, QoL, HADS, compliance	Enrolment 2014 - 2018. No results yet.	
NCT02277860 2014[40]	Single group intervention study Protocol	PwCF age (19years+) with stable CF 11 patients	12 week exercise programme delivered using Nintendo Wii Fit™ for ≥ 30 min, ≥3 days/week with monthly phone calls (exercise counselling and motivation). Further 12 weeks using the Wii but without supervision.	No comparator	Primary: peak oxygen consumption VO_2 peak. secondary: nasal potential difference, HRQoL, habitual activity level	May 2015 - Dec 2017	
ISRCTN51624752 2018[53]	Intervention study	pWCF (6-16 years) 160 patients	Project Fizzyo: Daily use of FitBit exercise tracker™ and electronic chipped sensor for use with ACT devices. Data sent automatically when syncronised to a tablet device. Games also built into ACT devices and used at specific intervals in the study. Exercise test, spirometry and questionnaires completed at 3 time points.	No comparator	Primary: adherence to ACT. Physical activity. Secondary: types of physiotherapy, details of ACT, QoL, physical activity (steps and heart rate by Fitbit), lung function, exercise capacity	Data collection over 16 months Ongoing	
Digital technology used for self-management							
Education							
NCT00185549 2005[56]	RCT Protocol	PwCF (1 month - 21 years) 60 patients	Internet Access to the program CF.DOC. Aim to log on once a month and asked to set treatment goals and health measures. Program provides virtual visits, a personal health record, messaging with clinicians and several tools for monitoring self-care behaviours	Usual care	Primary outcome: improved nutritional status, improved CF QoL Secondary outcome: phone utilisation and analysis of program	No results available - completed sept 2005	Grade: Low Although there were four studies for this outcome, only one was a completed RCT. The descriptive study had no comparator and the other RCT was only presented as a protocol with no results available despite study completion.
Duff 2006[55]	Descriptive Full text	Children wCF 4 programs: 3-5yr, 6-8yr, 9-11yr, 12yr+	An interactive CD-rom computer game "Betterland" with games, videos and activities focusing on different treatment aspects.	No comparator	Patient carer feedback	Allows young people with CF to learn about their condition in an interactive and fun way.	
Stark 2016[58]	Technology assessment and Pilot study Full text	Parents of PwCF (4-9 years) BMI<50th centile 10 patients	BeInCharge: A web-based 7 module intervention program which included dietary education, a daily diet tracker App, personalised calorie intake goals and behaviour techniques.	Standard care: usual care through CF centre.	Weight change within each group; calorie intake; technical difficulties; adverse events.	Designed and assessed usability of equipment. Children had an increased in weight from baseline to week 10. BIC by 0.67kg (p=0.04), standard 0.41kg (p=0.1). Weight gain not as good in BIC web compared to results seen previously in face-to-face.	

Quittner 2013[57]	Controlled trial (randomisation unclear) Conference abstract	Adolescents and young adults wCF 95 patients	CFfone™: smartphone with access to CFfone website via smartphone or home computer. Website contained educational materials, quizzes, inspirational stories of peer role models, and a "chat" function in which they could post messages or communicate with peers	Educational website for PwCF	Knowledge of disease management; perceived adolescent social support, HADS; CFQ-R (treatment burden, social functioning, respiratory symptoms), adherence (Pharmacy refill data)	Increased knowledge of disease management and social functioning at 6 months but effect decreased 3 months post intervention. Improvement in the nutrition knowledge scale in intervention group at 3 months. No difference in HAD scores. Future analysis planned to assess adherence.	
Cummings 2011[59]	RCT Full text	PwCF with FEV_1>35% 20 patients	Mentorship and self-monitoring via a mobile phone and web-based application. Intervention 1: access to a mentor guided self-efficacy program Intervention 2: as per Intervention1 plus the provision of a mobile phone and web-based App allowing participants to monitor their daily symptoms and QoL.	Usual care	Primary: health status, self efficacy, FEV_1 and FVC. experiences of participants in study i.e. improving self-management behaviour and QoL	PwCF are confident to use ICT devices for self-monitoring. Both intervention groups had significant increase in self efficacy sustained at 12 months however was similar within both intervention groups, with mobile use reduced overtime.	Grade: Very Low These were three small studies, one of which had no comparator group. The results from the White study were preliminary results only.
Porco 2018[60]	Intervention study Conference abstract	PwCF 15 patients	Attain Health: Online weekly virtual meetings with Performance Coach and Integrative Health, group coaching sessions and educational webinars.	No comparator	FEV_1; BMI	Mean increase in FEV_1 was 3.3% (-2% to 15%) over 3 months. Improved BMI 10/15. 2 met a weight loss goal.	
White 2016[61,62]	RCT Protocol and conference abstract	PwCF (16 – 60 years) Target of 100 patients	Web based adherence intervention. Participants and clinicians jointly identify 1-3 treatment areas to focus on to improve adherence. 6 interactive online modules on nutrition, PERT, vitamins, liver and respiratory disease and antibiotics with incorporated interactive materials and patient videos	Usual care: information via fact sheets, discussion, and clinician explanation	Primary: Changes in adherence: pharmacy refill, self-reporting secondary: BMI, weight, height, vitamin levels, lung function, IV abx days, QoL and knowledge. (at 1 year)	Intervention group showed significant improvement in BMI, vitamin ADE levels. No difference in the rate of FEV_1 decline. No results reported on adherence but awaiting full analysis.	
Ongoing studies using education							
Lang 2019[64]	RCT Protocol	PwCF (8-18 years) 110 patients	CyFiT: wrist worn activity tracker to record health information, and telehealth outpatient physiotherapy with real-time image/video sharing, features such as a whiteboard for drawing diagrams, measurement tools for physiotherapy and videoconferencing to delivery group based sessions. CyFIT in addition to usual care.	Usual care: outpatient physiotherapy (face to face, telephone and/or standard telehealth).	Primary: pulmonary outcome; QoL Secondary: quality of care, cost effectiveness, participation in activities outside school, cough and activity, medical shuttle test	No results published yet	
NCT03637504, 2018[65]	RCT Protocol	PwCF (12 years+) 105 patients	Web based medication management App [MedActionPlan™ (MAP) to encourage self-management, education and adherence. Adherence measured by eTrack nebulisers and AdhereTech pill bottles™	Usual care	Feasibility and acceptability. Change in knowledge of disease management; CF medication beliefs; adherence; CF medication questionnaire	Study in progress: start 2018. Completion 2021.	
NCT03139266 2017[63]	RCT Protocol	PwCF (13+ years), score GAD-7 and/or a 5-19 PHQ-10 70 patients	Project UPLIFT: Group web-based intervention comprised eight hour-long sessions aim to increase knowledge about depression, CF, cognitive behavioural therapy (CBT), and mindfulness and skills related to CBT, mindfulness and relaxation techniques with homework.	Usual care: seek support from mental health services	Primary: anxiety and depression symptoms Secondary: QoL, satisfaction with life, adherence, self-efficacy, knowledge and self-	Ongoing - to be completed May 2019.	

					management of anxiety and depression		
Digital technology for self-management of treatments							
Breeding 2016[67]	Cohort study Conference abstract	Adults wCF with pancreatic insufficiency 5 patients	Smartphone App to calculate PERT needed, used for 7 days with symptom questionnaire pre and post App use.	No comparator	GI symptoms	Interim results: 1 patient completed the study at time of abstract. 100% reduction in symptoms. 47% reduction in bowel movements. Improved weight gain. No follow up publications	Ongoing trials.
Calvo-Lerma 2017[68]	RCT Protocol	PwCF (1-17 years) 200 patients	MyCyFAPP Project: Smartphone App to self-manage nutrition and PERT. Able to be viewed by clinicians - alerts to patients and teams if not meeting targets.	Not described	QoL; nutritional status; healthcare usage	The protocol is for design, development and implementation of the app including a multicentre RCT	
The use of social media for self-management in cystic fibrosis							
Kirk 2016[69]	Online ethnographical study Full text	PwCF and parents of PwCF 279 patients	Review of message boards on a charity website online forum for young people and parents over a 4 month period. discussion threads downloaded for analysis	No comparator	To explore how online peer support is used to support self-care in CF	Online support groups supplement professional support in relation to self-management and self esteem. Used to share experiences, strategies for living with CF, emotional support and social networking.	Grade: Very Low Although the ethnographic study had a large number of participants (n = 279), there was no comparator group and so it is unclear whether the effects seen were due to the intervention or other factors.

Abbreviations: Adaptive Aerosol Delivery (AAD), Airway Clearance Techniques (ACTs), Antibiotics (Abx), Be In Charge (BIC), Body Mass Index (BMI), Cognitive Behavioural Therapy (CBT), Confidence Interval (CI), Cystic Fibrosis Respiratory Symptom Diary (CFRSD), Cystic Fibrosis Questionnaire-Revised (CFQ-R), Early Intervention (EI), early Intervention in Cystic Fibrosis (eICE), Forced Expiratory Flow 25-75% (FEF25-75), Forced Expiratory Volume in one second (FEV_1), Forced Vital Capacity (FVC), Habitual activity estimation scale (HAES), Health related quality of life (HRQoL), High Frequency Chest Wall Compression (HFCWC) Hospital Anxiety and Depression Scale (HADS), Intravenous (IV), Modified Shuttle Walk Test (MSWT), Pancreatic Enzyme Replacement Therapy (PERT), People with Cystic Fibrosis (PwCF), Pittsburgh sleep quality index (PSQI), Positive Expiratory Pressure (PEP), Pulmonary exacerbation (PE), Pulmonary Function Tests (PFTs), Personal Trainer (PT), Randomised Control Trial (RCT), Respiratory Symptom Score (RSS), Shortness of Breath (SoB), Six Minute Stepper Test (6MST), Submaximal Graded exercise tolerance test (GXT), Target Inhalation Mode (TIM), Telemedicine (TM), Tidal Breathing Mode (TBM), Visual analogue scale (VAS)

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