Impact of Digital Technologies on Clinical Care for Adults with Cystic Fibrosis

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Abstract

The coronavirus disease 2019 pandemic accelerated the implementation of digital technologies, which have now become embedded as essential tools for the management of chronic disease, including cystic fibrosis (CF). Despite subsequent easing of restrictions and because of improved clinical stability resulting from the introduction of highly effective modulator therapy, digital technologies including video and telephone consultations and remote monitoring are likely to remain integral to the future delivery of CF health care. In this article, we explore some of the key developments in digital technologies, barriers to their adoption, and how the CF community is likely to embrace lessons learned from the recent pandemic to help modernize and reshape the future of CF care.

Keywords
- cystic fibrosis
- COVID-19
- video consultation
- telemedicine
- adherence

Digital technologies have transformed many sectors including the banking and online shopping industries. They have the potential to disrupt as well as significantly improve clinical efficiency, data quality, and patient engagement in health care. However, the actual uptake of digital technologies in the health care sector is still relatively limited, with often an over reliance on electronic versions of paper patients' records, which limits data flow, extraction, and accessibility, compared with digital approaches.

The coronavirus disease 2019 (COVID-19) pandemic was a powerful stimulus to the introduction of innovations in digital health technologies in day-to-day clinical practice and highlighted the limitations of traditional health care systems, based on paper notes and face-to-face models of care.[1] The implementation of infection prevention measures, social distancing, and shielding for the most vulnerable patients, including those with cystic fibrosis (CF), led to a shift toward a different model of care and increased the implementation of digital health technologies, in health services, worldwide.[1]

Many digital tools were available prior to the pandemic but health care services and providers faced financial and managerial barriers to service development and to the integration of digital health technologies into day-to-day clinical practice. The implementation of platforms that are clinician and patient centered, and allow true bidirectional connectivity in health care, is limited by the lack of resources, underinvestment in information technology (IT) infrastructure and the use of obsolete hardware and software systems, as well as the inherent complexity of having to connect to a large number of legacy systems which are often incompatible.[2] Many of these barriers were removed at the start of the COVID-19 pandemic, allowing clinicians more freedom to develop and expand alternative care pathways to ensure adequate provision of care.

The advice that people with CF (pwCF) should shield at the start of the COVID-19 pandemic provided the necessary stimulus for units to introduce and embrace varying formulas of remote patient care.[3–5] Despite subsequent easing of restrictions and because of improved clinical stability resulting from the introduction of elexacafor/tezacaftor/ivacaftror therapy,[6–8] video and telephone consultations and remote monitoring are likely to remain an integral part of future health care delivery in combination with face-to-face consultations.

In this review, we discuss the development, application, and impact of digital technologies in the care of pwCF. We

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discuss advancements in electronic patient records (EPRs), remote monitoring of adherence, telemedicine for the remote provision of clinical services, and the use of remote monitoring and wearable systems. We also explore some of the main barriers to adoption of these technologies and how they may help modernize and reshape the future of CF care.

Electronic Patient Records, Registries, and Big Data

EPRs can provide a foundation for the accurate, reliable capture of clinical measures, interventions, and epidemiological trends, as well as improve efficiency and adherence to standards of care.[2,9]

While most CF units use their hospital EPR platform, the reach and value of these systems can be restricted by several factors, including a lack of disease-specific functionality, limited data extraction, and an absence of clinically relevant graphical display capabilities. Barriers limiting functionality can also derive from the misconception that "one system fits all," development and running costs and investment in essential integration. Inadequate coding functionality for accurate capture of patient clinical information, and insufficient extraction and processing tools can also impact research and audit functionality, essential features for the delivery of evidence-based care.

While standalone functionalities continue to improve, integration with home monitoring devices, such as spirometers, weighing scales, and oximeters, is often absent or suboptimal, due to the lack of effective and standardized application programming interfaces (APIs). Generic linkage of monitoring devices and their respective apps are often available through platforms such as Apple Health and Google Fit. Secure generic linkage between these platforms and EPR systems could provide a cost-effective solution which would empower health care professional and patients alike. In the United Kingdom, there have been recent announcement that the National health Service (NHS) application will be significantly revamped to improve joined up care. Will this be the start of a revolution or a missed opportunity?

Coding

Collecting and storing data in a predefined format, using vocabularies of codes, provides a more standard approach to data collection and sharing through APIs.[10] Structured data collection lends itself to artificial intelligence (AI) and the monitoring and prediction of disease pattern in condition such as CF.[11]

Registries

The expansion of high-quality national and international registries has dramatically improved the quality of prospective data capture, the power of epidemiological studies, and postmarketing safety surveillance of new therapies. Registries are also now being used to undertake clinical trials, and the resulting expansion in big data provides real opportunities for the implementation of AI, to advance our knowledge of disease patterns and predictors of health outcomes.

Registries rely on the input of high-quality and repeatable data using clearly defined data fields, often relating to encounters or outcomes. Unfortunately, many registries still rely on manual data entry due to limitation in the integration and digital data capture. Registries should not be considered as replacements for clinical records or be confused with EPR functionality, which provide a wider array of data collection throughout the clinical history of each patient. In the not too distant future, EPR data will automatically stream to registries, but work is needed to standardize coding structures, improve accuracy of data entry, and ensure interoperability between systems.[12]

Unstructured health data, such as free text and voice recordings, can encapsulate rich information through narratives which can be critical to the understanding of a patient's condition. The extraction of such unstructured medical data are less straightforward and requires the use of complex algorithms and machine learning.[10] Natural language processing has been piloted in CF to automatically retrieve phrases associated with medication, dose, therapies, symptoms, bowel movements, and nutrition information.[10]

Adherence Monitoring Platforms

pwCF have a high treatment burden, and adherence to medications, in particular nebulized therapies, can be poor.[11,13] Self- and clinician-reported measures often overestimate adherence with a positive self-report bias.[13] Digital technologies can provide more accurate information on adherence and have the potential of supporting proactive approaches to improve concordance with treatment and clinical outcomes.

As an example, early work on electronic monitoring through the I-neb nebulizer demonstrated how digital data provided a more accurate assessment of adherence to nebulized therapy and highlighted the wide discrepancy between electronic monitoring and self- and clinician reports.[14] Indeed, physician assessment of adherence was remarkably inaccurate and was often no better than chance.[13,14] In a small study using data-logging of the I-neb device, overall adherence to inhaled therapies was found to be reasonable.[15] However, there was a significant reduction in adherence during holiday periods as well as at weekends during term time, highlighting the need to support families, personalize frequency of therapies and support structured daily routines to optimize adherence to long-term therapies.[15]

A growing number of platforms such as projects Fizzyo and CFHealthHub which remotely captures and analyzes adherence data and clinical outcomes such as airway clearance and nebulizer usage will in the future support intervention studies to improve the health care of pwCF.[16,17]

A more recent retrospective multicenter observational study of 318 adults with CF used data capture of nebulizer usage through the CFHealthHub platform.[18] The low real-world adherence to therapy was confirmed, with half of the study population having objective adherence of less than one in three.[18] This type of data is impactful and highlights the need to develop effective strategies which can positively influence concordance to evidence-based therapies.[13]

Remote Care and Telehealth

Prior to the COVID-19 pandemic, telehealth and remote monitoring were used sporadically in the care of pwCF. Experience was initially limited to those countries where traveling distances led to difficulties in accessing specialist services, such as Canada and Australia, or to specific pilot trials.[19,20] In these contexts, telehealth showed a good uptake and led to increased utilization of health care services, with good patient satisfaction and engagement[19]

Shortly after the onset of the pandemic, nearly all CF centers in the United States and in the United Kingdom commenced telehealth services at scale, with 97% of centers in the United States delivering some form of telehealth service.[21] To meet these demands, increased support and resources were made available and enabled clinicians to overcome some of the barriers which had previously been hindering the use of digital technology. Examples included wide access to communication software such as Teams, Accurx, AttendNow, WebEx, Skype, and Zoom as well as home spirometers.[3,5]

This unprecedented acceleration in service development resulted in some pitfalls. Not all platforms were secure or configurable for the virtual clinic, and there was often inadequate support in terms of operating systems, internet connectivity, and resources needed for the delivery of high-volume remote care.

Those centers with well-developed IT infrastructures had, therefore, an advantage. In the United States, the cystic fibrosis learning network (CFLN), which was embedded prior to the pandemic and comprises 39 multidisciplinary CF Foundation accredited pediatric and adult CF centers,[22] showed that shared learning through a collaborative, data-driven process led to standardized interdisciplinary telehealth, achieving reliable and sustainable processes which could be reproduced by other networks.[22] Despite the network being built and set up prior to the onset of the pandemic, many centers in the CFLN reported that staff access to technology remained a barrier to the delivery of appropriate interdisciplinary care.

Likewise, in our center (Leeds Regional Adult CF Centre), the prior deployment of full EPRs (EMIS Web) in 2007 enabled the delivery of remote care from any location using desktops, laptops, and mobile devices.[23] In addition, NHS-funded AccuRx software was used at the start of lockdown to increase EPR functionality. AccuRx, and similar alternatives, allows a secure bidirectional communication between health care professionals and patients, integrates with the EPR, enables documents and image sharing, and provides secure access to video and phone consultations, in compliance with the data protection act. These digital tools empowered the team to deliver regular and high-quality remote care to our patient cohort throughout the pandemic.[24] It also allowed clinically extremely vulnerable staff and those self-isolating to work remotely from home.[24]

Clinicians and Patients' Perception

Telehealth has been widely accepted during the COVID-19 pandemic, with care team members feeling comfortable using this technology.[21,25] A survey of 80 CF clinicians in the United States found that 90% of respondents had never used remote consultation before the pandemic. However, the satisfaction with telehealth was at 89%, with clinicians reporting a positive impact on the clinician–patient relationship as well as improved efficiency.[25]

Similarly, pwCF and their parents/carers have also responded positively, although perceived benefits and uptake of these services are influenced by the perception of quality and age.[26]

In the prepandemic era, a small study in rural Australia reported good uptake and a high satisfaction with telehealth in adults with CF resulting in an increased attendance to clinic.[19] Several larger and more recent studies report positive patient satisfaction with remote care which appears convenient and efficacious, although true outcome measures are difficult to interpret within the milieu of all the significant changes which have taken place over the last 2 years. pwCF also reported important barriers to remote consultations including, access and use of technology, reduced contact with the full MDT (3), and limited assessments of "objective" measurements such as lung function and sputum microbiology (8).

During COVID-19, the introduction of telehealth services for the management of children with CF was associated with reduced patient and parental anxiety and increased level of confidence in managing complications.[27] However, some pediatric centers have found that remote consultations can sometimes be less effective, especially with regard to the engagement of teenagers and safeguarding issues. In addition, children can on occasion be absent from the consultations, which is undesirable.

The CLIMB-CF study investigated the feasibility and potential obstacles related to regular home monitoring.[28] Children and adolescents with CF and their parents were linked to an application and asked to complete a variety of daily or twice weekly measurements as well as questionnaires assessing anxiety, depression, and quality of life. While the home monitoring and the interaction with the application did not negatively impact patients' lives, depression, anxiety, or quality of life over the 6-month period, median data completeness was only 40.1% and uptake was variable and not sustained over time, especially among adolescents.[28]

Their adoption of telehealth has the potential of reducing health care spending, improving convenience, and minimizing travel costs, and reducing the burden for those in education and employment.[29]

In lower income countries with limited access to hardware and the internet, telephone consultation can be an effective alternative. It has proved effective in the short term during COVID-19 to monitor patients' health condition and adherence to physiotherapy and physical exercise.[30]

Health Care Monitoring

There are little data on the clinical effectiveness of remote care in pwCF. Many studies have been undertaken on the backdrop of COVID-19, where pulmonary exacerbations may

have been minimized by infection control measures and the introduction of highly effective cystic fibrosis transmembrane conductance regulator (CFTR) modulators."

A relatively outdated systematic review of telehealth in CF from 2012 concluded that there was insufficient evidence to reach a firm conclusion about the benefits of telehealth in pwCF.[31] These results are unlikely to reflect the potential of digital health in the postmodulator era.

Microbiology

Over the last 2 years, the impact of the COVID-19 pandemic and the introduction of highly effective CFTR modulators have inadvertently reduced the frequency and quality of sputum samples which are routinely used in the surveillance of pulmonary pathogens.[32–35] Some units have developed various processes for collecting samples, including drop-off points, curbside appointment, and postal service.[32] Continued microbial monitoring remains essential to improve our understanding of the impact of modulators on lung microbiology and to ensure adherence to appropriate standards of care.

Lung Function

Lung function is routinely undertaken to assess clinical stability and the impact of pulmonary exacerbations.[36] In pwCF, variation in lung function may also be a useful marker of adherence to both oral and inhaled medication.[11] In the prepandemic era, uptake of home monitoring systems was low, due to limited patients' engagement, lack of equipment, and inconsistency between home and clinic spirometry values. The COVID-19 pandemic and its associated restrictions necessitated the need for remote lung function monitoring, and as a result, home spirometers were made available to pwCF in most countries.

Issues relating to remote spirometry include the lack of standardization of devices and device platforms, integration with EPR and costs. There has also been a lack of focus in the development of codes differentiating home physiological measurements from those undertaken in hospitals. This is surprising in view of exponential expansion of mobile devices and home care and is relevant to future data capture as home and hospital measurements are not directly comparable.[37]

While unsupervised portable spirometry can generate acceptable and repeatable results, physiological measurement may alter according to technique, quality of equipment, and engagement.[38] However, in such circumstances, the rate of change may be a more accurate measure of stability.[37] Effective coaching and support may also improve the quality and reproducibility of home spirometry in CF.[37]

Telerehabilitation: Physiotherapy and Exercise

Airway clearance, together with exercise, is a mainstay of treatment for pwCF. Over the last decade, telerehabilitation has emerged as an important element of telemedicine and resulted in an expansion in the use of apps, portals, and digital systems which can deliver high-quality, accessible, cost-effective, and efficient physiotherapy and rehabilitation services, for chronic disease, including CF.[39,40] In CF, the provision of rehabilitation, physiotherapy, and guidance to exercise can range from simple online video calls using platforms such as Skype or Zoom to more structured programs.[39–42] These solutions provide patients with the opportunity to engage in physiotherapy-led exercise programs with varied intensity, the level of which can be adequately assessed remotely.[43] In addition to enhancing physical health, the application of digital health technologies in the context of CF has the advantage of providing remote social contact and peer support in a group of people whose interactions are limited due to segregation policies and risk of cross-infection.[40]

Wearable Devices

There is an ever-increasing array of wearable devices and sensors which are freely available to consumers and are routinely used in day-to-day life. Examples include the mobile phone, activity trackers and continuous glucose and electrolytes monitoring systems.

Fitness Devices

Appropriate physical activity is essential for pwCF. Subjective measures of physical activity, such as questionnaires and recall techniques, are inexpensive and easy to use, but often prone to over-reporting activity levels and underreporting sedentary behavior.

In recent years, there has been a significant increase in the number of available wearables ranging from mobile phones and watch-like devices (such as Fitbit, Apple Watch, Garmin, etc.) to research-grade accelerometers, both of which allow longitudinal tracking of physical activity levels, for monitoring purposes and potentially to tailor advice and recommendation.

Watch-like wrist-worn devices have gained popularity and are widely used in the general population.[44] They are perceived as easy to use and acceptable among pwCF.[45] Evidence on the use of fitness devices in CF is limited to a few small-scale studies that investigated the accuracy of consumer-grade wearable technology in comparison to research-grade accelerometers. These showed that while there might be an underestimation of the step count, these consumer-grade devices provided valid and reproducible step-count measurements but were not consistently reliable in assessing heart rate as an indicator of exercise tolerance.[46–48] The use of such technology is likely to expand and become integral data for the monitoring of future health.

Electrolyte Monitoring and Sweat Test

Sweat chloride measurement remains the gold standard assay for the diagnosis of CF and more recently has been shown to be helpful in monitoring individual response to CFTR modulator therapy.[49,50] While noninvasive and relatively easy to measure, sweat collection is a multistep process that requires induction, collection, and laboratory analysis.

Recently, there has been a push toward the development of wearable sensors that could enable real-time measurements

of sweat chloride concentration.[51,52] These new techniques appear to be reliable when used during moderate exercise and may provide an indirect biomarker for assessing response to CFTR modulators over time and the need for electrolyte replacement during exertion and heat exposure[53,54].

Continuous Glucose Monitoring and Diabetes Management

The use of digital health technologies in the care of people with diabetes has been widespread for several decades. This includes the widespread use of telehealth intervention by the multidisciplinary team and through the introduction of wearable sensors to allow continuous monitoring of blood glucose levels (such as Freestyle Libre, Medtronic Guardian, and Dexcom). Telehealth-based intervention in this population has been shown to be clinically beneficial and associated with improved diabetes control in people with all forms of diabetes and at various ages, although more significant and relevant among younger patients.[55]

CF-related diabetes (CFRD) is one of the most common extrapulmonary complications of CF, and its incidence is likely to increase further with the aging of the population. While most continuous glucose monitoring (CGM) systems are not approved as a diagnostic tool for diabetes, an increasing number of CF centers are using these technologies to aid the diagnosis of CFRD. There is in fact a strong correlation between CGM and blood glucose values during oral glucose tolerance test, and dysglycemia on CGM traces correlates with early dysfunction in insulin secretion, decline in pulmonary function, and weight loss.[56,57]

The use of CGM systems is widespread among people with CFRD, despite only limited evidence on the outcomes and perception of telehealth in the management of people with CFRD.[58] In a small-scale study,[59] the degree of satisfaction for telehealth was high in both patients and providers, especially as a time-saving tool, leading to improved attendance rates. In addition, individuals with CF and CFRD have reported a high degree of satisfaction as CGM systems can provide information on trends and have set alarms for dysglycemia, allowing for adjustment and/or anticipatory treatment of episodes of hypo- or hyperglycaemia[60]. Finally, CGM systems allow secure data sharing with the clinical team, so that data can be reviewed to support medical decision-making.[61] Clinicians, however, expressed concerns for the lack of regular weight measurements and laboratory testing for HbA1C.[59]

In addition to the use of digital technologies to monitor diabetes, the introduction of insulin pumps, which provide a continuous subcutaneous insulin infusion in a programmed way, has helped improve diabetes control in people with type 1 diabetes. Despite the lack of specific evidence in CFRD, insulin pumps are often used as they allow for easier and more convenient insulin delivery. Sensor-augmented pumps integrate CGM data to facilitate insulin dosing but do not automatically adjust it. More recently, automated insulin delivery systems have been introduced which have closed-loop control systems which can change the insulin delivery rate according to glycemic excursion[58] These systems have been shown to improve control and reduce the burden of care in people with type 1 diabetes, and studies on people with CFRD are currently ongoing.

The Future of Telehealth in Cystic Fibrosis

While the COVID-19 pandemic significantly increased the number of providers offering telehealth services, we are now seeing an increase in face-to-face consultations following the relaxation of infection prevention measures.[21,24] In the United States, during the first wave of the pandemic, 57% of patients exclusively received in-person care, 36% telehealth by phone or video, and 8% of patients received telephone only care. The proportion of in person consultation increased to 80% after 8 months.[21]

While remote monitoring and telehealth have been accepted as a mechanism for delivering CF care during the pandemic,[62] further research is now needed to better understand the longer term engagement, adherence, and clinical outcome of routine use of these technologies and digital platforms. The introduction and availability of highly effective CFTR modulators have improved clinical stability and have resulted in a change in the landscape of health care provision, with a subsequent reduction in admissions and the expansion of a more outpatient-focused service, which is better suited to remote care.[3]

It was recently noted that 10% of patients with CF in the United States do not attend hospital appointments due to transportation and costs. In view of the recent increase in the cost of living, this could become an even greater issue in the future.

Digital and remote health is not suitable for all patients. A sizeable proportion of patients do not engage, respond to consultations, or provide clinical measurements such as lung function and weight when using these systems.[3] There is a need to empower pwCF to self-monitor and adjust treatment as and when needed, with appropriate high-quality input from their CF centers. Continuous monitoring may prove popular with clinicians and researchers, but a balance needs to be struck with patients allowed to live their life to the full while minimizing interventions and excessive monitoring.

Trials are currently ongoing to further evaluate the impact of digital health technologies in the care of pwCF. In particular, the impact of telemonitoring, self-management apps, coaching on adherence and exercise, identification of pulmonary exacerbations, and impact on quality of life are currently assessed[63–65]

Connectivity and Education

During the COVID-19 pandemic, communication between health care professionals gradually moved online, with increased accessibility and sharing of information. Examples of this shift include the temporary conversion of international, well-attended conferences to fully digital models, the expansion of online education platforms, and the provision of digital seminars. While many miss the face-to-face

interactions, a balance will be found which will encompass digital communication which will evolve significantly and provide an important platform for the CF community.

Barriers to the Implementation of Digital Health Technologies

While the COVID pandemic provided a valuable opportunity to accelerate the implementation of telehealth and digital technologies in the care of pwCF and other chronic conditions, barriers remain. These barriers are surmountable and need to be challenged effectively by the clinical workforce. They include access to appropriate technology, including high-speed internet, conflicting health system priorities, lack of will, resistance to change, and a lack of resources and infrastructure.[5,21,33,34]

The functionality and quality of "dedicated" platforms are often an issue and do not reflect the needs of users and clinicians.[9,21,66] Development of these technologies should be patient and clinician centered, with an open communication link between stakeholders and developers. This would reduce the risks of developing top-down projects which fail to achieve their proposed scope, such as the ambitious National Program for Information Technology in the United Kingdom, which cost over £10 billion and failed to deliver national integrated EPRs.[2]

In addition, clinicians, especially in programs with lower perceived quality of telehealth, have expressed concerns such as lack of physical examination and available data to monitor patients.[21,25,66]

Patient-related barriers should be considered when assessing the uptake and effectiveness of digital technology and remote consultations. These include an absence of perceived advantage over face-to-face care, internet access, financial concerns, and computer literacy, as well as socioeconomic status, race, and ethnicity (2, 7, 10, 30, and 31). These factors should be addressed to deliver equitable, high-quality care to all.[67] In contrast visualization of the home environment through remote video consultations can have a surprisingly positive effect, such as improving the personal connection between patients and health care providers by opening their eyes to the home environment, including beautiful countryside and frank poverty.[68]

Conclusion

While there have been and still are many obstacles relating to the implementation and use of electronic information and telecommunication technologies to deliver care to pwCF, most units have embraced these new digital tools. There remains an urgent need for integration and linkage between systems including EPRs and remote monitoring platforms and devices. Face-to-face interactions will continue to provide an important component of long-term care and help maintain the important rapport between patients and their clinical teams.

The accelerating change in digital technology is exciting and is likely to result in advances in seamless digital care which will hopefully be more intuitive, automated, and both patient and health care centric. There will however be many challenges and the focus must be to ensure future developments improve the quality of life and clinical outcomes for pwCF.

Conflict of Interest
None declared.

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