The Role of the Physical Therapist in Cystic Fibrosis Care

Physical Therapy in CF: A Look Back, A Look Ahead

Cardiovascular/Pulmonary

Perspective

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[H1]Abstract

In looking back on 2020 and 2021, this Perspective reflects on the monumental impacts of the rollout of cystic fibrosis (CF) transmembrane conductance regulator highly effective modulator therapies and the COVID-19 pandemic on the management of CF. Advancements in the clinical management of people with CF have been both enormous and rapid, and physical therapists specializing in the care of people with CF have been at the forefront of driving this evolution in care. This year sees the thirtieth anniversary of the UK Association of Chartered Physiotherapists in Cystic Fibrosis and, as is inevitable in reaching such milestones, thoughts have turned to origins, role, impacts, and the future. With the changing demographics of the population of people with CF after the introduction of highly effective

modulator therapies, potentially with fewer secondary complications, the future role of the physical therapist who specializes in CF is in question. This Perspective reflects upon and highlights the role of physical therapy within CF and provides insights into how physical therapists and respiratory therapists can evolve their roles to ensure relevance for the future.

[H1]Introduction

[H2]The Past: Where Have We Come From?

The history of respiratory physical therapy long predates the first descriptions of the disease later known as cystic fibrosis (CF). Breathing exercises, then named "medical gymnastics," were promoted for general health from as early as 3000 BC in China and ancient Greece.[1-3] Nineteenth century publications advocated "judicious respiratory exercises" to enhance the lung function of healthy individuals.[4] Breathing exercises,[5-7] postural drainage,[6,8] and manual percussion[9] to the chest wall for the treatment of excessive bronchial secretions were described in the early 1900s.

In 1938, CF was initially described as "cystic fibrosis of the pancreas,"[10] with reports of pulmonary infections and respiratory tract obstructions appearing later in the 1940s.[11] Prevention of secondary complications such as chest infections was advocated in 1946 to improve outcomes,[12,13] leading to the introduction of physical therapy into CF management.[13,14] Postural drainage with percussion was adopted as the main airway clearance technique (ACT) used by physical therapists,[13,15] and was described by Reed[16] as "the most effective form(s) of mechanical stimulus to eliminate secretions." In 1964, 3 pillars of CF treatment were described—nutritional repletion, antibiotic therapy for lung infection, and relief of airway obstruction[17]—establishing the physical therapist firmly as a stalwart of CF care. Since then, ACTs have been developed to provide options for independent sputum clearance, an adaptation driven by the increasing numbers of adults with CF (Fig. 1). These options include breathing techniques such as active cycle of breathing techniques[18] and autogenic drainage[19] or adjuncts such as the positive expiratory pressure (PEP) mask[20] and oscillating devices (intrathoracic and extrathoracic oscillation) (eg, Acapella DM & DH Vibratory PEP Therapy System [Smiths Medical, Dublin, OH, USA]; The Vest Airway Clearance System [Hillrom Holdings Inc, Chicago, IL, USA]).[21] Although there are some international differences in ACT practice—for example, vest therapy using high-frequency chest wall oscillation is the most widely used ACT in the United States,[22] with PEP being the most frequently used in the United Kingdom[23]—current US, UK, and European guidelines for the care of people with CF all recommend ACTs as part of the management of CF.[24-26]

To support the growing number of physical therapists treating people with CF, national and international networks for CF physical therapists were created; these include the International Physiotherapy Group for Cystic Fibrosis in 1986[27] and the UK Association of Physiotherapists in Cystic Fibrosis (now known as the UK Association of Chartered Physiotherapists in Cystic Fibrosis [ACPCF]) in 1992. These organizations have been instrumental in promoting all aspects of physical therapy which could be beneficial to people with CF. In 2002, the first ACPCF standards of care for the physical therapist management of CF published in conjunction with the UK CF Trust,[28] included practical guidance on physical therapist techniques similar to the International Physiotherapy Group for Cystic Fibrosis Blue Booklet (first published in 1993)[21] with additional staffing and service recommendations. Since their creation, these standards have been influential in key service reviews[29-32] and national and international guidelines for CF care,[33,34] with the most recent (2020) edition being placed within the top 10 UK CF Trust downloads.[35]

[H2]The Present: Where Are We Now?

Since the early 2000s, when CF national and international standards recommended multidisciplinary team (MDT) care, including physical therapists and respiratory therapists,[25,33] physical therapist input into CF teams has increased; therapists are now one of the largest staffing groups in UK CF centers alongside nurses, physicians, and dietitians.[36] With >10,800 people with CF in the United Kingdom and CF care spread over 57 regional centers, 4 stand-alone centers, and 72 network clinics,[23] the ACPCF network has expanded from a small support group of CF Trust–sponsored physical therapists to >240 members in 100 different locations. The spread of care within the United States is similar, with >130 specialist CF care centers nationwide caring for over 31,400 people with CF[22] and respiratory therapists and increasingly also physical therapists being integral to care teams.[37]

The role of the CF physical therapist has evolved since it was first described in the 1950s, and the ACPCF standards of care (now on the fourth edition) and the International Physiotherapy Group for Cystic Fibrosis Blue Booklet have been updated to reflect changes in practice.[21,38] Although ACTs have remained integral, the profession has reacted to the changing demographics of the population of people with CF and adapted guidance as necessary. For

example, following the introduction of UK newborn screening for CF, the ACPCF network of specialists created a Delphi consensus document to provide guidance to clinicians on whether to routinely recommend ACTs in this cohort.[39]

The population of people with CF now has more adults with CF than children, and the average age is increasing[22,23] (Fig. 2). With this, an increase in associated comorbidities has also been seen. In order to ensure physical therapy as a profession changes with the landscape of CF management, CF physical therapists have expanded their treatment toolbox to address the joint or muscle problems of an older population combined with CF-specific issues related to low bone mineral density, stress incontinence or poor posture.[40] With over 64% of the UK and US populations of people with CF in work or study,[22,23] physical therapists as part of the MDT need to provide advice on lifestyle management regarding minimizing treatment burdens, maximizing adherence, and tailoring regimens to individual requirements (such as travel and independence) to help people with CF live their lives to the fullest.

Since the first ACPCF guidance on nebulized therapies were published in 1995[41] the scope of inhalation therapies have greatly expanded. With advancement in technology, both adaptive aerosol delivery and vibrating mesh technology, and changes in aerosol deposition, physical therapists and respiratory therapists are instrumental in the optimization of medication delivery, timing, and adherence to support ACTs. Extended roles into supplemental and independent prescribing for CF physical therapists have been and continue to be created,[38] with development of the ever-expanding ACPCF nonmedical prescribing group for peer support and continual professional development.

Previously an adjunct to care, increasing evidence of beneficial effects on physical and mental health,[42,43] has brought exercise advice and prescription to the forefront of physical therapist interventions. CF MDTs have expanded to include physical therapists and practitioners specializing in exercise, and the ACPCF have held combined educational events with the CF & Exercise Network[44] to optimize collaborative working.

Throughout 2020 the COVID-19 pandemic necessitated radical changes in CF care provision[45,46] to reduce the strain on health care systems and to support shielding of the population of people with CF identified as clinically extremely vulnerable. Physical therapists and respiratory therapists internationally have demonstrated flexibility and made swift changes coincident with the global environment. Hospital visits were replaced by virtual clinics, self-monitoring of lung function was introduced, digital monitoring was increased, and home treatments, including home intravenous antibiotic therapy were encouraged whenever possible. MDTs needed to create digital services, with therapists providing virtual ACT assessments and exercise sessions. Scaled back inpatient services embraced full personal protective equipment for aerosol-generating ACTs.[47] Although COVID-19 did fast-track the use of telehealth, the potential for virtual monitoring and interventions had been led by and embraced by CF physical therapists and the wider community earlier[48,49] with work such as the CFHealthHub learning health system[50] and SmartCareCF[51] investigating self-monitoring, alongside the creation of international online exercise platforms, such as Beam Feel Good,[52] which was developed by a CF physical therapist.

[H2]The Future: Where Are We Going?

Throughout 2020, the rollout of CF transmembrane conductance regulator (CFTR) highly effective modulator therapies (HEMTs)—particularly the compound elexacaftor/tezacaftor/ivacaftor (Kaftrio [the brand name used in Europe]/Trikafta [the brand name used in the United States; Vertex Pharmaceuticals, Boston, MA, USA)—potentially suitable for 80% to 90% of the population of people with CF[53] began. These medications are dramatically changing the outlook for people with CF for the future[54,55] by targeting the CF defect at a protein level, correcting abnormal ion transportation across cell membranes,[56] thus preventing airway dehydration within the lungs and limiting amounts of sticky mucus. Although long-term data are currently lacking for elexacaftor/tezacaftor/ivacaftor, early short-term data indicates reductions in pulmonary exacerbations and antimicrobial medication usage.[55] Longer-term data for up to 5 years are currently available for the single agent ivacaftor, with results indicating sustained reductions in pulmonary exacerbations, health care utilization, and enhanced quality of life.[57]

It is thought that although the early introduction of CFTR HEMTs will limit the development of CF lung disease, it will not be possible to correct established lung damage,[54] and sputum will still be produced in those individuals with existing bronchiectasis. However, in many individuals, sputum after the use of CFTR HEMTs appears to be smaller in quantity and easier to clear, potentially reducing the need for daily ACT regimens to facilitate clearance. However, experience with ivacaftor, where a retrospective 5-year study showed that annual rate of lung function decline of people with CF taking ivacaftor was unaltered,[58] suggests that this is not the end for ACTs and CF. Therapists must use skilled assessment to advise people with CF as to when the ACT is required, for example, during pulmonary exacerbations or for those with limited responses to HEMTs. Physical therapy research is under way to identify the best assessment tools[59] to ensure that optimal and relevant ACT regimens are created in partnership with individuals. We must also not forget the cohort of people with CF (approximately 10%) for whom CFTR HEMTs at present do not work; those who are unable to tolerate these medications; the underserved population of people who have CF but who may not have access or adhere to HEMTs; and those in lower- to middle-income countries who do not yet have access to these medications and so who have "traditional" CF, more likely requiring regular ACTs.

Sputum surveillance to identify and enable early treatment of harmful pathogens has long been a key part of CF management,[60] with physical therapists and respiratory therapists often taking a lead role in sample collection. The amount of sputum produced after CFTR HEMT seems to decrease for many people with CF, making obtaining regular samples more challenging. The best ways to induce or replace sputum samples for monitoring is currently unknown, more innovation and research is required in this area.

With the regular ACT, one of the mainstays of CF physical therapy in question, physical therapists need to help the CF community address how best to assess the ACT needs of people with CF. Research needs to answer questions such as whether other interventions such as cardiovascular exercise or yoga can replace the ACT and potentially reduce the therapy burden, 2 of the research priorities highlighted by an international 2017 CF James Lind Alliance survey.[61] People with CF are independently taking steps to replace the ACT with

exercise[62] or to stop the ACT; robust evidence to support or negate this move, alongside evidence for different forms of physical activity, is required.

The changing landscape of CF care provides many important clinical questions which require research to enable evidence-based practice for people with CF. The Table summarizes questions which the authors believe to be key questions which require answering, these questions have been influenced by research priorities identified by the CF community as part of a James Lind Alliance survey,[61] and also an international 2021 online survey of CF physical therapists and respiratory therapists.

Research into physical therapist interventions can be problematic to achieve because of issues with trial design and methodology. It is often difficult to control for all external forces which are influencing participants, and researchers need to consider other therapies and their effects when designing trials. Interventions such as the ACT or exercise take effort from people with CF to complete, and many have strong preferences for certain regimens. As a result, randomized controlled trials where people may be asked to complete an alternative treatment for a significant period often have difficulty recruiting or retaining participants.[63,64] Alternative methods such as long-term observational studies of large cohorts may be required to gain insights into physical therapist interventions in the future.

A long-standing issue with airway clearance research is the lack of validated, robust and relevant endpoints,[65] traditional outcomes of forced expiratory capacity in 1 second[66] and sputum weight will lack sensitivity in this more stable, minimal-secretion population. Emerging outcomes such as the Lung Clearance Index derived from the multiple breath washout test, shown to be a sensitive and reliable endpoint especially in mild CF lung disease,[67,68] needs questions such as what is a clinically meaningful change[68-70] to be investigated alongside its use in the specific context of ACT research.

Long-term outcomes which are impactful for people with CF such as quality of life or other patient reported outcomes, hospitalizations or frequency of exacerbations should also be considered.[64] CF physical therapists are working collaboratively and engaging in multicenter/multiprofessional studies to deliver high quality research outputs to influence

clinical interventions and use network links such as the ACPCF to achieve this goal. Now should be the time to embrace investigations into withdrawal or replacement of the regular ACT, something which has previously been discouraged because of the integral nature of the ACT within traditional CF management, but something that has come to the fore with changed health status because of CFTR HEMTs.

CF therapists need to advise and alter management strategies based upon the altered health status of people with CF after CFTR HEMT, but also for the additional comorbidities that the aging population experience which may require specialist physical therapist management such as CF related liver disease and some cancers which have an increasing incidence in people with CF.[71]

With improved health status and expected improvements in life expectancy, more women with CF are becoming pregnant[72] which requires adaptation of physical therapist interventions to ensure optimal management and safe gestation. Parenthood, for women and men with CF, offers its own challenges and therapists need to offer flexible and realistic advice for regimens balanced with child care responsibilities.

Telehealth offers opportunities for physical therapists to deliver education on all aspects of clinical care to people with CF with wide-ranging needs, including delivery of remote spirometry and management strategies. Access to sessions and advice has also been widely expanded allowing access to people who previously could not attend classes because of illness, location, finances or time constraints due to child care or work. A huge benefit of telehealth is the possibility of offering people with CF group sessions enabling peer support network which was previously impossible because of the risk of cross infection. One person with CF told us the following:

> "As a 39-year-old with CF, I have had almost no interaction with another CF patient since childhood in the days before segregation. But through the online classes and the removal of the risks of cross-infection, to be able to see, talk, and exercise with others for the first time in approximately 25 years was really mind blowing. It has been super motivational to see other people with CF … this social element benefit to the classes and teaching should not be underestimated."

Exercise evaluation and progression via online supervised activity with trained staff aware of any CF-specific exercise needs is now possible, and feedback from people with CF for early adopters of online exercise has been positive.[73,74] One person with CF stated the following:

> "The exercise program has been really enjoyable and varied, and to have it led by our own CF physio team, so familiar with our condition and our own personal stories, made the classes extra special. Exercising felt safe as there was constant awareness of potential CF issues (like shortness of breath/reflux/joint pain/diabetes) and how exercises might need to be altered. I can feel the benefit of working through the program and feel fitter than at the beginning."

Further participant feedback regarding online exercise sessions can be found in the Supplementary Appendix.

Social media such as Twitter, Instagram, or TikTok can engage people with CF of all ages, promoting sessions and creating center challenges enhancing the feeling of community. Physical therapists can use their role within the CF MDT to promote fitness and activity, while ensuring the safety of interventions for their individual patients.

Social media also allows the sense of community and engagement to be not just local to each center, but national and international with the potential for benefits for people with CF and clinicians. The ACPCF is currently finalizing collaborations with CF physical therapy organizations across the globe to provide educational online webinars for physical therapists ranging from basic ACT skills for those in locations with limited training and resources, to forums discussing current practice and planning international research collaborations.

Although telehealth and online interventions have been widely well received and do offer opportunities of access and socialization that were previously unavailable, therapists must be aware that remote monitoring or interventions may not suit all for all consultations.[46,75] Some individuals will require or prefer face-to-face in-hospital or community consultations and physical therapists must plan to incorporate varied contact options to ensure optimal and equitable management for all people with CF.

Further issues raised by the introduction of CFTR HEMTs include whether the use of inhaled antibiotics and mucoactive agents by people who have CF and have used modulators will be required or appropriate in the future. Inhaled mucoactive agents such as hypertonic saline

and mannitol may be more irritable to clearer airways, limiting tolerance, while the evidence for the use of deoxyribonuclease (or dornase alfa) in people with non-CF bronchiectasis, which might be mirrored by people who have CF and have used HEMTs, is unfavorable.[76] Physical therapists' experience and involvement with clinical trials, such as CF STORM (NIHR131889) and SIMPLIFY (NCT04378153), investigating the rationalization of inhaled mucoactive agents, will be key in clinical decision making.

The UK CFHealthHub learning health system,[77] with the involvement of physical therapists, includes monitoring of nebulizer taking via digital downloads and offers insights into the adherence of people with CF to medications. The CFHealthHub and CFDigicare (a collaborative approach to improving CF care via digital learning and real-time data)[77] are continuously developing to help clinicians support people with CF and will help to shape the evolution of CF management. The National Efficacy-Effectiveness CFTR Modulators Optimization (NEEMO) programme is nested within the CFHealthHub learning health system and is using long-term inhaled therapy adherence data to understand the impacts of coadherence to inhaled therapy and HEMTs on clinical outcomes of people with CF who are taking elexacaftor/tezacaftor/ivacaftor.

The introduction of CFTR HEMTs, especially elexacaftor/tezacaftor/ivacaftor, has altered the health status for many people with CF, with emerging evidence of decreased infections and lower antimicrobial usage[55]; however, because of its recent introduction, there is limited data on long-term effects. A comparison of US and UK CF registry data from the first available CFTR HEMT, ivacaftor, versus matched controls after 4 to 5 years of usage highlighted consistently favorable clinical outcomes, including lower risk of death, pulmonary exacerbations and hospitalization for those taking ivacaftor.[78] With these potential changes in health status in mind, alterations to physical therapy regimens and advice are being considered, however, recent evidence from the ivacaftor cohort showed the potential for improvements in lung function to return to baseline after 5 years.[57,58] The potential for nonadherence to medications should also be considered, as highlighted by Mitchell et al who reported adherence to ivacaftor, declined over a 5-year period, especially in young adults.[58] The unknown long-term effects and adherence to HEMTs highlights the need for long-term evidence before altering management, changes should be made cautiously with close

monitoring to ensure continued improved health status for people with CF with as low a treatment burden as possible.

The COVID-19 pandemic saw a significant change in day-to-day CF clinical services some of which such as remote monitoring and virtual clinician reviews, are unlikely to completely reverse. The new landscape of CF offers the opportunity for CF physical therapists and respiratory therapists to reassess their role to ensure it is fit for purpose moving forward. Interventions can be reassessed for both efficacy and mode of delivery to ensure that physical therapy remains at the forefront of excellent CF clinical care, and that it can be delivered effectively within this new digital and post–CFTR HEMT world. Partnerships between physical therapists and people with CF are now more important than ever to ensure individualized, optimal physical therapist management strategies in terms of the ACT, exercise, and inhaled therapies, taking into account the lifestyle and commitments of every individual with CF. Physical therapists and respiratory therapists have the opportunity to address current priorities for CF care and create modern roles for themselves after CFTR HEMTs; these roles could focus on key areas such as physical activity, well-being, and function, with specialized assessment that could complement the work of the larger CF MDT.

[H1]Conclusion

From soon after CF was first described in the 1930s, physical therapy has been a key part of its management, with a review of the decade from 1990 to 2000 putting good physical therapy as a mainstay to clinical well-being in CF.[79] Physical therapists have evolved throughout the decades to provide for the needs of the changing population of people with CF, adapting care for increasing numbers of adults with CF and the needs of asymptomatic infants diagnosed through newborn screening, and have embraced and suggested new therapies and technologies. The recent impacts of the COVID-19 pandemic and the rollout of CFTR HEMTs, have necessitated monumental changes to CF MDT care provision as a whole. Physical therapists and respiratory therapists have the opportunity to self-evaluate and evolve practice, embracing new opportunities for research and clinical practice to create a new era of CF physical therapy.

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Disclosure

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[H1]References

1. Gordon B. *Medicine Throughout Antiquity.* Phildephia, USA: F.A Davies Company; 1949.
2. Tipton CM. The history of "Exercise Is Medicine" in ancient civilizations. *Advances in Physiology Education.* 2014;38(2):109-117.
3. Innocenti D. An Overview of the Development of Breathing Exercises into the Specialty of Physiotherapy for Heart and Lung Conditions. *Physiotherapy.* 1996;82(12):681-693.
4. Gardner-Smith J. TYPES AND METHODS OF RESPIRATION. *Medical Record (1866-1922).* 1894;46(3):67.
5. MacMahon C. Breathing and physical exercises for use in cases of wounds in the pleura, lung and diaphragm. *The Lancet.* 1915;2:769-770.
6. Ewart W. The Treatment of Bronchiectasis and of Chronic Bronchial Affections By Posture and By Respiratory Exercises. *The Lancet.* 1901;158(4063):70-72.
7. Pryor JH. Deep Breathing as a Therapeutic and Preventive Measure in Certain Diseases of the Lungs. *Trans Am Climatol Assoc.* 1906;22:251-261.
8. Nelson HP. Postural Drainage of the Lungs. *Br Med J.* 1934;2(3840):251-255.
9. Mennell JB. *Massage: its principles and practice / by James B. Mennell.* Philadelphia: Blakiston; 1917.
10. Andersen DH. CYSTIC FIBROSIS OF THE PANCREAS AND ITS RELATION TO CELIAC DISEASE: A CLINICAL AND PATHOLOGIC STUDY. *American Journal of Diseases of Children.* 1938;56(2):344-399.
11. Farber SSHM, C. L. PANCREATIC FUNCTION AND DISEASE IN EARLY LIFE. I. PANCREATIC ENZYME ACTIVITY AND THE CELIAC SYNDROME. 1943(0021-9738 (Print)).
12. Andersen DH H, R. G. Celiac syndrome; genetics of cystic fibrosis of the pancreas, with a consideration of etiology. (0096-8994 (Print)).
13. Littlewood J. The History of Cystic Fibrosis. 2009-2016; http://www.cfmedicine.com/history. Accessed 16/9/2020, 2020.
14. McIlwaine MP, Lee Son NM, Richmond ML. Physiotherapy and cystic fibrosis: what is the evidence base? *Current Opinion in Pulmonary Medicine.* 2014;20(6).
15. Pryor J. Airway clearance in the spontaneously breathing adult – the evidence. *Physical Therapy Reviews.* 2006;11(1):5-10.
16. Doershuk CF e. *Cystic fibrosis in the 20th century, people, events, and progress. .* Cystic fibrosis in the 20th century, people,

events, and progress. : AM Publishing; 2001.

17. Matthews LW, Doershuk CF, Wise M, Eddy G, Nudelman H, Spector S. A therapeutic regimen for patients with cystic fibrosis. *Journal of pediatrics : devoted to the problems and diseases of infancy and childhood.* 1964;65(4):558-575.
18. Webber BA. The Active Cycle of Breathing Techniques. *CF News.* 1990;August/September:10-11.
19. Dab IA, F. The Mechanism of Autogenic Drainage Studied With Flow Volume Curves. *Monographs of paediatrics* 1979;10:50-53.
20. Fagevik Olsén M, Lannefors L, Westerdahl E. Positive expiratory pressure – Common clinical applications and physiological effects. *Respiratory Medicine.* 2015;109(3):297-307.
21. Fibrosis IPGfC. Physiotherapy for People with Cystic Fibrosis: from Infant to Adult. In: IPG/CF, ed. https://www.ecfs.eu/sites/default/files/general-content-files/working-groups/IPG%20CF_Blue%20Booklet_7th%20edition%202019.pdf2019.
22. Foundation CF. *2020 Annual Report.* https://www.cff.org/About-Us/Assets/2020-Annual-Report.pdf: Cystic Fibrosis Foundation;2021.
23. Trust CF. *UK Cystic Fibrosis Registry 2020 Annual Data Report.* https://www.cysticfibrosis.org.uk/sites/default/files/2022-03/2020%20Annual%20data%20report%20-%20Version%203.pdf March 2022 2020.

24. Flume PA, Robinson KA, Sullivan BP, et al. Cystic Fibrosis Pulmonary Guidelines: Airway Clearance Therapies. *Respiratory Care.* 2009;54(4):522.
25. Trust CF. Standards for the Clinical Care of Children and Adults with Cystic Fibrosis in the UK. 2011.
26. Smyth AR, Bell SC, Bojcin S, et al. European Cystic Fibrosis Society Standards of Care: Best Practice guidelines. *J Cyst Fibros.* 2014;13 Suppl 1:S23-42.
27. European Cystic Fibrosis S. Introduction - International Physiotherapy Group - CF. 2013; https://www.ecfs.eu/ipg_cf. Accessed 31/1/21, 2021.
28. Fibrosis AoCPiC. Clinical Guidelines for the Physiotherapy Management of Cystic Fibrosis 2002.
29. Trust CF. Cystic Fibrosis Trust website. 2021. Accessed 31/01/2021, 2021.
30. Morrison L, Duncan N. P133 Re-audit of the UK ACPCF Physiotherapy National Standards of Care. *Journal of Cystic Fibrosis.* 2018;17:S96-S97.
31. England N. *National service specification(s) for the provision of cystic fibrosis treatment for children and/or adults*

. https://www.england.nhs.uk/wp-content/uploads/2018/07/a01Sb-spec-cystic-fibrosis-child.pdf: NHS England;2012.
32. Team DoHPBR. *Payment By Results Guidance 2012-2013.* 2012.
33. Kerem E, Conway S, Elborn S, Heijerman H. Standards of care for patients with cystic fibrosis: a European consensus. *Journal of Cystic Fibrosis.* 2005;4(1):7-26.
34. Excellence NIfHaC. Cystic fibrosis: diagnosis and management. NICE guideline. 2017.
35. Ali J. ACPCF standards of care and good clinical practice download statistics. In: Stanford G, ed. Email communication ed2021.
36. Tracy Turc-Milloy SL, Rebecca Cosgriff. *UK cystic fibrosis service resourcing 2019 - Preliminary report.* Cystic Fibrosis Trust; September 2020 2020.
37. Foundation CF. Your CF Care Team 2022. Accessed 20/4/2022, 2022.
38. ACPCF. Standards of care and good clinical practice for the physiotherapy management of cystic fibrosis. Cystic Fibrosis Trust; 2020.
39. Prasad SA, Main E, Dodd ME. Finding consensus on the physiotherapy management of asymptomatic infants with cystic fibrosis. *Pediatric Pulmonology.* 2008;43(1099-0496 (Electronic)):236-244.
40. Tattersall R, Walshaw MJ. Posture and cystic fibrosis. *Journal of the Royal Society of Medicine.* 2003;96 Suppl 43(Suppl 43):18-22.
41. Association of Chartered Physiotherapists in Cystic Fibrosis CFNS. Practical guidelines for the use of nebulisers in cystic fibrosis. 1995. 1995.
42. Radtke T, Nevitt SJ, Hebestreit H, Kriemler S. Physical exercise training for cystic fibrosis. *Cochrane Database of Systematic Reviews.* 2017(11).
43. Dwyer TJ, Elkins MR, Bye PTP. The role of exercise in maintaining health in cystic fibrosis. *Current Opinion in Pulmonary Medicine.* 2011;17(6).
44. Douglas H, Tomlinson O, Ahlquist A, Shelley J. An update from the UK Cystic Fibrosis and Exercise Network. 2020.
45. Colombo C, Burgel P-R, Gartner S, et al. Impact of COVID-19 on people with cystic fibrosis. *The Lancet Respiratory Medicine.* 2020;8(5):e35-e36.
46. Dixon E, Dick K, Ollosson S, et al. Telemedicine and cystic fibrosis: Do we still need face-to-face clinics? *Paediatric Respiratory Reviews.* 2021.
47. Thomas P, Baldwin C, Bissett B, et al. Physiotherapy management for COVID-19 in the acute hospital setting: clinical practice recommendations. *Journal of Physiotherapy.* 2020;66(2):73-82.
48. Ketchell RI. Telemedicine is the way forward for the management of cystic fibrosis - the case in favour. (1526-0550 (Electronic)).

49. Calthorpe RJ, Smith S, Gathercole K, Smyth AR. Using digital technology for home monitoring, adherence and self-management in cystic fibrosis: a state-of-the-art review. *Thorax.* 2020;75(1):72.
50. Hub CH. CF Health Hub. 2021. Accessed 16/3/21, 2021.
51. Trust CF. SmartCareCF. 2015. Accessed 16/3/21, 2021.
52. Good BF. Beam 2022. Accessed 8/9/22, 2022.
53. Mahase E. Cystic fibrosis: triple therapy shows promising results. *BMJ.* 2019;367:l6347.
54. Nissenbaum C, Davies G, Horsley A, Davies JC. Monitoring early stage lung disease in cystic fibrosis. *Current Opinion in Pulmonary Medicine.* 2020;26(6).
55. Miller AC, Harris LM, Cavanaugh JE, et al. The rapid reduction of infection-related visits and antibiotic use among people with cystic fibrosis after starting Elexacaftor-Tezacaftor-Ivacaftor. *Clinical Infectious Diseases.* 2022:ciac117.
56. Lopes-Pacheco M. CFTR Modulators: The Changing Face of Cystic Fibrosis in the Era of Precision Medicine. *Frontiers in Pharmacology.* 2020;10:1662.
57. Duckers J, Lesher B, Thorat T, et al. Real-World Outcomes of Ivacaftor Treatment in People with Cystic Fibrosis: A Systematic Review. LID - 10.3390/jcm10071527 [doi] LID - 1527. (2077-0383 (Print)).
58. Mitchell RM, Jones AM, Stocking K, Foden P, Barry PJ. Longitudinal effects of ivacaftor and medicine possession ratio in people with the Gly551Asp mutation: a 5-year study. *Thorax.* 2021;76(9):874.
59. Stanford G, Davies JC, Usmani O, et al. Investigating outcome measures for assessing airway clearance techniques in adults with cystic fibrosis: protocol of a single-centre randomised controlled crossover trial. *BMJ Open Respiratory Research.* 2020;7(1):e000694.
60. Castellani C, Duff AJA, Bell SC, et al. ECFS best practice guidelines: the 2018 revision. *Journal of Cystic Fibrosis.* 2018;17(2):153-178.
61. Alliance JL. Cystic Fibrosis Top Ten Prioirities. 2020; https://www.jla.nihr.ac.uk/priority-setting-partnerships/cystic-fibrosis/top-10-priorities.htm. Accessed 5th November 2020, 2020.
62. Ward N, Stiller K, Holland AE, et al. Exercise is commonly used as a substitute for traditional airway clearance techniques by adults with cystic fibrosis in Australia: a survey. *Journal of Physiotherapy.* 2019;65(1):43-50.
63. McIlwaine M, LT. W, M. C, Davidson GF. Long-term comparative trial of two different physiotherapy techniques; postural drainage with percussion and autogenic drainage, in the treatment of cystic fibrosis. (1099-0496 (Electronic)).
64. Main E. Airway clearance research in CF: the 'perfect storm' of strong preference and effortful participation in long-term, non-blinded studies. *Thorax.* 2013;68(8):701.
65. Bradley JM, Moran FM, Elborn JS. Evidence for physical therapies (airway clearance and physical training) in cystic fibrosis: an overview of five Cochrane systematic reviews. *Respir Med.* 2006;100(2):191-201.
66. Horsley A, Siddiqui S. Putting lung function and physiology into perspective: cystic fibrosis in adults. *Respirology.* 2015;20(1):33-45.
67. Kent L, Reix P, Innes J, et al. Lung clearance index: evidence for use in clinical trials in cystic fibrosis. *Journal of Cystic Fibrosis.* 2014;13(2):123-138.
68. Hatziagorou E, Kampouras A, Avramidou V, et al. Toward the Establishment of New Clinical Endpoints for Cystic Fibrosis: The Role of Lung Clearance Index and Cardiopulmonary Exercise Testing. *Frontiers in Pediatrics.* 2021;9.
69. Short C, Saunders C, Davies JC. Utility of lung clearance index in CF: What we know, what we don't know and musings on how to bridge the gap. *Journal of Cystic Fibrosis.*
70. Stanojevic S, Ratjen F. Physiologic endpoints for clinical studies for cystic fibrosis. *Journal of Cystic Fibrosis.* 2016;15(4):416-423.

71. Maisonneuve P, Lowenfels AB. Cancer in Cystic Fibrosis: A Narrative Review of Prevalence, Risk Factors, Screening, and Treatment Challenges: Adult Cystic Fibrosis Series. *Chest.* 2022;161(2):356-364.
72. Taylor-Cousar JL. CFTR Modulators: Impact on Fertility, Pregnancy, and Lactation in Women with Cystic Fibrosis. *Journal of Clinical Medicine.* 2020;9(9).
73. Wilkinson E. The NHS virtual gym boosting fitness and social connections for cystic fibrosis patients. *BMJ.* 2020;371:m4063.
74. McCrea G, Morrison L, Palmer S. EPS1.08 Exercising online a Beaming good initiative. *Journal of Cystic Fibrosis.* 2021;20:S31.
75. Morrison L, McTavish D. WS07.1 Evaluation of video conferencing consultations in the West of Scotland Adult Cystic Fibrosis unit. *Journal of Cystic Fibrosis.* 2020;19:S11.
76. T Hill A, L Sullivan A, D Chalmers J, et al. British Thoracic Society Guideline for bronchiectasis in adults. *Thorax.* 2019;74(Suppl 1):1.
77. CFHealthHub. CFHealthHub Publications. 2022; https://www.cfhealthhub.com/resources/publications/. Accessed 21st February 2022, 2022.
78. Higgins M, Volkova N, Moy K, Marshall BC, Bilton D. Real-World Outcomes Among Patients with Cystic Fibrosis Treated with Ivacaftor: 2012-2016 Experience. (2364-1746 (Electronic)).
79. Jaffé A, Bush A. Cystic fibrosis: review of the decade. (1122-0643 (Print)).
80. Davis PB. Cystic Fibrosis Since 1938. *American Journal of Respiratory and Critical Care Medicine.* 2006;173(5):475-482.

Table

Table. Key Questions for Physical Therapy Research[a]

High-Priority Research Question	Including:
Can exercise replace airway clearance for people with CF?	In times of health stability In times of pulmonary exacerbations Different levels of clinical status Type/duration/intensity of exercise required Effect on quality of life
What mucoactive medications are required for people who have CF and are taking CFTR HEMTs?	Deoxyribonuclease Mannitol Hypertonic saline
How can treatment burdens and physical therapy regimens be reduced for people with CF?	People who have CF and are taking CFTR HEMTs People who have CF but are not taking CFTR HEMTs Combinations of treatments Replacements/withdrawal of treatments
Are telehealth interventions as effective as face-to-face consultations?	Effectiveness of virtual assessments Satisfaction of people who have CF with telehealth interventions
What physical therapist interventions enhance well-being and quality of life for people with CF?	Effect of physical therapy regimens Investigations into specific interventions
How best can the effects of treatments be assessed?	Best outcome measures for assessment of exercise Best outcome measures for assessment of the airway clearance technique How to assess the quality of interventions
What are the barriers and enablers to interventions?	Physical activity and exercise Airway clearance Inhaled medications

What are the specific groups within CF?	Effect of exercise on airway clearance technique for people not taking CFTR HEMTs How best physical therapists can support people who have CF and are transitioning from pediatric to adult services and their independence with physical therapy regimens Best practice to support pregnancy and parenthood for people with CF

[a]CF = cystic fibrosis; CFTR = CF transmembrane conductance regulators; HEMTs = highly effective modulator therapies.

Figure Legends

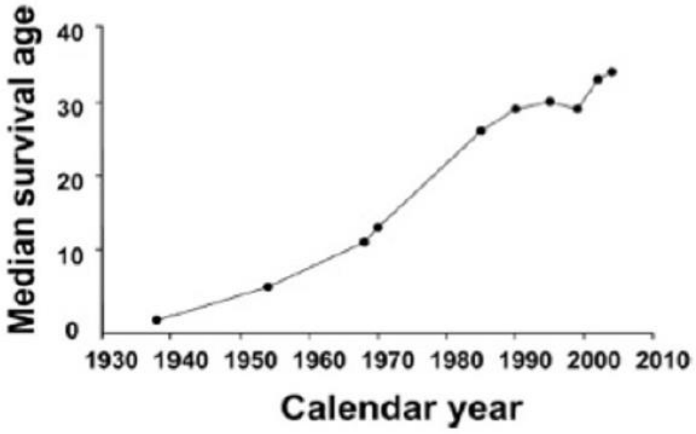

Figure 1. Median survival age for people with cystic fibrosis (CF) in the United States. Data from before 1970 were gleaned from the then-current literature. Data since 1985 were taken from the Cystic Fibrosis Foundation Data Registry and represent projections of median survival age for a child born with CF in that year. Reproduced with permission of author Pamela B. Davis.[80]

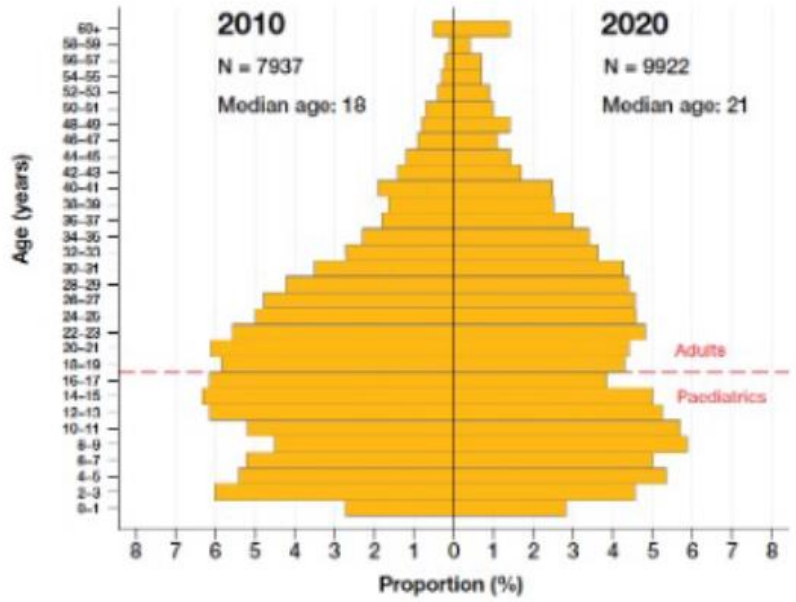

Figure 2. Age distribution of the population of people with CF in the United Kingdom in 2010 versus 2020. Reproduced with permission of the Cystic Fibrosis Trust from the *UK Cystic Fibrosis Registry 2020 Annual Data Report*.[23]