DO CURRENT CLINICAL TRIALS IN CYSTIC FIBROSIS MATCH THE PRIORITIES OF PATIENTS AND CLINICANS? A SYSTEMATIC REVIEW.

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Abbreviations:

JLA: James Lind Alliance

PSP: Priority Setting Partnership

ABSTRACT

There are many uncertainties regarding Cystic Fibrosis (CF) treatment. Recently, the first James Lind Alliance (JLA) Priority Setting Partnership (PSP) in CF was completed, bringing clinicians, patients and carers together to identify the Top 10 research priorities. Here we investigate how well the current clinical trials landscape reflects these priorities. Trials in CF were identified through searches of research databases (Pubmed, ANZCTR, EU clinical trials register, ClinicalTrials.gov and ISRCTN). Trials meeting inclusion criteria of registered intervention studies in CF published between 01.01 2016 to 11.09.2017 were matched to the Top 10 priorities. We identified 259 trials, with 193 fulfilling the inclusion criteria. Only 63 (33%) of these matched one or more of the JLA priorities showing that current clinical trials poorly reflect the JLA Top 10. By increasing awareness of the Top 10 priorities, it is hoped that this will fuel future research in areas important to the CF community.

KEYWORDS

Clinical trial, research priority, cystic fibrosis

SYSTEMATIC REVIEW PROTOCOL

http://eprints.nottingham.ac.uk/id/eprint/52745

INTRODUCTION

Knowledge of CF genetics has led to the development of many new therapies targeting CFTR dysfunction[1], however currently the majority of treatment for CF is aimed at treating downstream consequences of the CFTR defect. There are still many uncertainties regarding symptomatic CF treatment[2]. Conventional therapies for persistent airways infection are still required and yet we do not have definitive evidence to guide the choice of many routine treatments (such as airway clearance). Through undertaking well-designed clinical trials, these treatment uncertainties could be answered.

Clinical trials should focus on questions which are important to patients and clinicians; however, until now, research agendas have been determined by researchers choosing topics that are of personal interest or of interest to funders such as the Pharmaceutical Industry. The National Institute for Health Research (NIHR) in the UK supports and facilitates patient and public involvement in research [3]. The NIHR James Lind Alliance (JLA)[4] brings patients, carers and clinicians together in Priority Setting Partnerships (PSP) to agree on a prioritised 'Top 10' list of research questions, as a stimulus to future research.

In January 2017, the first JLA PSP in CF was completed, giving a list of Top 10 research priorities for treatment of CF[5]. During the JLA PSP process all priorities were checked to make sure we did not already know the answer using a systematic review identifying evidence gaps in treatment decisions in CF[2]. To investigate how well the current clinical trials landscape reflects the JLA Top 10 priorities for CF, we matched current clinical trials in CF to the JLA Top 10 priorities.

METHODS

We carried out a systematic review to identify ongoing trials in CF, following a published study protocol[6]. Pubmed, Australian New Zealand Clinical Trials Registry (ANZCTR), EU clinical trials register, ClinicalTrials.gov and ISRCTN ('International Standard Randomised Controlled Trial Number'; however, this registry now includes more than just randomised controlled trials) were searched with strategy adapted for each database, as shown in Appendix A. Other studies were identified by emailing experts in the field (Appendix B).

Search results were collated and duplicates excluded. Inclusion criteria were completed or registered intervention studies conducted with people diagnosed with CF and published in English between January 1, 2016 to September 11, 2017. Trials that did not meet the predetermined inclusion criteria were excluded (for full inclusion criteria see Appendix C). Included studies were matched to one or more of the Top 10 priorities by first reviewer (IK) and

recorded on a database then checked by second reviewer (NR) to ensure accuracy. A third reviewer (SS) was available should disagreements occur.

RESULTS

We identified 253 trials through the database searches and an additional six studies through contact with study investigators. After removal of duplicates, this gave 252 trials for filtering of which 193 studies fulfilled the inclusion criteria and 59 were excluded. Figure 1 shows a Prisma flow diagram of the study selection process.

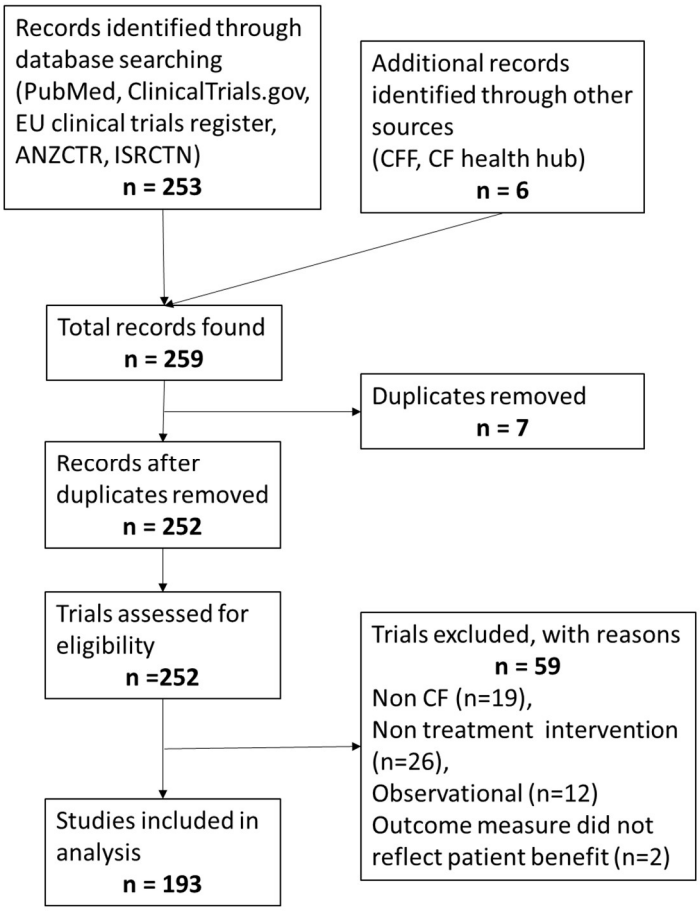

Figure 1. Prisma flow diagram of study selection process

Only 63 of 193 trials (33%) matched one or more of the Top 10 priorities. The number of ongoing trials matching each priority varied widely. There were only two studies addressing priority 3, treatment of lung infection due to non-tuberculous mycobacteria (NTM) – an antibiotic resistant infection which causes severe lung damage. In contrast,

there were 25 studies linked to priority 6, adherence to treatment. See Table 1. Appendix D gives a full list of trial titles and the priorities they were matched to.

Priority question	Number of trials matching
1. What are the effective ways of simplifying the treatment burden of people with Cystic Fibrosis?	10
2. How can we relieve gastro-intestinal symptoms, such as stomach pain, bloating and nausea in people with Cystic Fibrosis?	3
3. What is the best treatment for non-tuberculous mycobacterium (NTM) in people with Cystic Fibrosis (including when to start and what medication)?	2
4. Which therapies are effective in delaying or preventing progression of lung disease in early life in people with Cystic Fibrosis?	4
5. Is there a way of preventing Cystic Fibrosis related diabetes in people with Cystic Fibrosis?	7
6. What effective ways of motivation, support and technologies help people with Cystic Fibrosis improve and sustain adherence to treatment?	25
7. Can exercise replace chest physiotherapy for people with Cystic Fibrosis?	2
8. Which antibiotic combinations and dosing plans should be used for Cystic Fibrosis exacerbations and should antibiotic combinations be rotated?	6
9. Is there a way of reducing the negative effects of antibiotics e.g., resistance risk and adverse symptoms in people with Cystic Fibrosis?	3
10. What is the best way of eradicating Pseudomonas aeruginosa in people with Cystic Fibrosis?	8

Table 1.The number of clinical trials matching to each of the Top 10 priorities. *Priority questions are in the number order they were ranked during the JLA PSP. Some trials were matched to more than one priority.*

All five of the clinical trials identified through contact with study investigators matched to Priority 6 ("What effective ways of motivation, support and technologies help people with cystic fibrosis improve and sustain adherence to treatment.")

DISCUSSION

This study found that a very high proportion (67%) of the current trials in CF do not match any of the James Lind Top 10 priorities. This indicates a mismatch between the current clinical trials landscape and the priorities of the CF community. The James Lind top 10 priorities were derived from engagement with participants throughout the world and informed by a systematic review of existing gaps in the published research literature and so it is disappointing that ongoing research will not fill these gaps at present [2]. Our findings suggest a failure of the current arrangements for prioritising clinical trials. Similar studies in conditions other than CF also found a mismatch between their PSP

priorities and trial landscape [8, 9, 10]. One study[8] identified the treatments described in prioritised research questions generated by the first 14 JLA PSPs and compared them to the treatments described in ongoing clinical trials over the same time period. The results highlighted that although the research of non-drug treatment was prioritised by the PSPs, the ongoing research mostly involved evaluations of drugs. Another study also found a mismatch between Top 10 priorities for Palliative and End of Life care and research in progress[11].

To date, there have been no studies that have investigated how well the current clinical trials landscape reflects the research priorities of the CF community.

One of the most active areas of pharmaceutical research in CF is on modulators of the cystic fibrosis transmembrane conductance regulator (CFTR). Several CFTR modulators have received a marketing authorisation in recent years and many more are undergoing clinical trials. It is of interest that questions on CFTR modulators were absent from the Top 10. During discussions at the final workshop of the JLA PSP in CF, participating patients and clinicians said they believed that research regarding CFTR modulators will progress whether prioritised or not and so they did not propose them for the JLA top 10.

The lack of ongoing trials in some JLA priority areas may be due to a lack of suitable interventions, which could be evaluated in a clinical trial (e.g. gastrointestinal problems or NTM). Increased awareness of the importance of these issues to the CF community may lead to discovery science, to understand disease mechanisms and suggest "druggable targets" or to trials of repurposed drugs.

One strength of this study is the large number of current trials found in CF in countries worldwide, representing the current global clinical trial landscape in CF. Additional non-database searches were used to find all current and relevant trials in CF. A matching check by a second reviewer was carried out to ensure accuracy. Reproducible methods were used to systematically search, match and analyse and were described allowing for the future accurate replication. These were then matched to the JLA top 10 priorities which were derived from engagement with participants throughout the world[5].

By identifying and highlighting the mismatches between the current clinical trials in CF and the JLA Top 10 priorities, we hope that researchers will be made aware that their agendas currently do not meet the priorities of the people who are in the greatest need of relevant research evidence. This is an important step towards "co-production" of research[3]. The research landscape is starting to change in response to the Top 10 with the NIHR supporting research based on the top 10 research priorities in CF. Using the methodology described in this study, further research could explore how future clinical

trials in CF match to the priorities of the clinical and patient communities and how the Top 10 priorities for CF alter the research landscape further.

Declarations

Conflict of Interests Statement

NJR has given lectures at meetings sponsored by TEVA. AS 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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Authors' contributions

All authors were involved in the study design process and contributed in preparation of the manuscript.

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Appendix A: Search strategies used in the systematic review

ClinicalTrials.gov

Condition or disease: 'cystic fibrosis', Study Type: 'Interventional Studies', First posted: '01/01/2016' to '09/11/2017'

ISRCTN

Condition: 'cystic fibrosis', Date applied '01/01/2016' to '09/11/2017' and Overall trial start date '01/01/2016' to '09/11/2017'

EU CLINICAL TRIALS REGISTER

Search term 'cystic fibrosis', Date range '2016/01/01' to '2017/11/09'

Pubmed

'cystic fibrosis' in title/abstract, Date- Publication '2016/01/01' to '2017/11/09'

Article types: 'Clinical trials'

(cystic fibrosis[Title/Abstract]) AND ("2016/01/01"[Date - Publication] : "2017/11/09"[Date - Publication])

ANZCTR

Search term 'cystic fibrosis', Study type: 'Interventional', Trial start date '01/01/2016' to '09/11/2017' and registration date '01/01/2016' to '09/11/2017'

Appendix B: Experts contacted

Additional studies were found by emailing experts in the field of research in CF who were asked if they were aware of any ongoing studies of interventions which might help address any of the Top 10 priorities. Responses were received from Aliza Fink and Alexandra Quittner and both provided information on the Success with Therapies Research Consortium (STRC). Through Aliza Fink, contact was made with Cindy George who leads the STRC at CFF who gave information regarding current studies run by the STRC.

Appendix C: Criteria for the inclusion of studies for the review

	Inclusion criteria	**Exclusion criteria**
Types of study	Interventional studies published in English. Studies published since 01/01/16 to present and ongoing and also registered to take place trials.	Qualitative studies/observational studies
Participants	Participants diagnosed with CF (through genetic testing or sweat testing) and of any age. Studies including other conditions but where CF patients were analysed as a specific subgroup were included if they met the rest of the inclusion criteria.	Patients who are screen positive for CF but with no firm diagnosis
Intervention	Any treatment intervention actively involving participants with the potential to benefit participants directly. Studies involving trials of combinations of interventions, timings and duration of intervention and stopping interventions were included. The interventions were expected to fall into these categories: drugs interventions (antibiotics and CFTR modulators), behavioural interventions (supportive care etc), dietary interventions (vitamin D, fibre etc), device or web based interventions (trackers, smartphone apps or virtual reality etc) and other interventions such as home monitoring and exercise for example.	Studies covering diagnosis, newborn screening or those concerning diagnostic test accuracy as well as those concerning policy, evaluation of the training of physicians or organisation of care. Interventions involving miRNAs isolation from blood samples, diagnostic tests, measurement of sputum rheological properties, measure of endothelial function etc
Outcomes	Any clinically meaningful outcome measure or those that reflected patient benefit.	Those that did not reflect patient benefit ie studies aiming to assess outcome measures such as: bioavailability or pharmacokinetics,

	The outcomes were expected to fall into the categories listed: * Lung Function (e.g. FEV1,FVC, Lung clearance index etc) * Health-related quality of life validated measures (e.g. Cystic Fibrosis Questionnaire (CFQ) 26) * Respiratory symptom outcomes (e.g. Respiratory and Systemic Symptoms Questionnaire RSSQ) * Hospitalisation (e.g. number of nights inpatient) * School/Work attendance (e.g. number of days missed) * Nutrition & Growth (e.g. weight gain, height, fat) * Radiological (e.g. bone mineral density) * Sputum properties * Pulmonary exacerbations (measured by frequency of exacerbation or time to next exacerbation etc) * Antibiotic use (e.g. number of courses, combinations, delivery method) * Adverse effects (toxicity & allergy, microbiology, complication of delivery) * Exercise tolerance * Sweat chloride as a measure of CFTR function * Mucus clearance * Nasal symptom scores * Bowel symptoms (e.g. stool frequency, abdominal pain etc) * Treatment burden * Treatment adherence * Cost	clearance, volume of distribution, DNA methylation etc

Appendix D. Table showing trial titles and which research priority they matched with.

References to clinical trials follow table.

	DOES THE TRIAL MATCH ANY OF THE TOP 10 RESEARCH PRIORITIES?									
Trial Title	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
1. Integrating Supportive Care in Cystic Fibrosis	YES					YES				
2. Evaluation of Short Antibiotic Combination Courses Followed by Aerosols in Cystic Fibrosis								YES		
3. Nutritional Intervention and Glycemic Improvement in Patients With Pre-diabetic Cystic Fibrosis.					YES					
4. Evaluation of (R)-Roscovitine Safety and Effects in Subjects With Cystic Fibrosis, Homozygous for the F508del-CFTR Mutation										YES
5. A Study of Home Monitoring in Adults With Cystic Fibrosis (HOMECF)	YES									
6. Inhaled Sodium Nitrite as an Antimicrobial for Cystic Fibrosis										YES
7. An Efficacy and Safety Study of Ivacaftor in Patients With Cystic Fibrosis and Two Splicing Mutations			YES							
8. Study of Safety, Tolerability & Efficacy in Cystic Fibrosis Patients With Abnormal Glucose Tolerance					YES					
9. A Rollover Safety Study of Lumacaftor/Ivacaftor in Subjects Aged 2 Years and Older With Cystic Fibrosis, Homozygous for the F508del-CFTR Mutation				YES						
10. Simplification of CF-related Diabetes Screening at Home	YES					YES				
11. Does exenatide improve post prandial glycaemic control in young people with cystic fibrosis related diabetes or impaired glucose tolerance?					YES					
12. The effect of low glucose load diet on glycaemic control in patients with cystic fibrosis					YES					
13. The Effect of Soluble Fiber to Reduce Post-prandial Glycemic Excursion in Adults With Cystic Fibrosis					YES					
14. Interactive Mobile Health Information to Enhance Patient Care at a Cystic Fibrosis Center						YES				
15. The Use of Home Oral Glucose Tolerance Test Kit in Screening Cystic Fibrosis Related Diabetes	YES					YES				
16. Increase Tolerance for Exercise and Raise Activity Through Connectedness Trial						YES				
17. Improving Therapeutic Adherence With a Co-constructed Program Involving Both Patients and Health Care Professionals						YES				
18. Inhaled Nitric Oxide for Cystic Fibrosis Patients With MABSC			YES							
19. Saline Hypertonic in Preschoolers + CT				YES						
20. Impact of Telerehabilitation Training on Pediatric Cystic Fibrosis Patients: An Exploratory Study						YES				
21. A Study of the Dosing, Efficacy, and Safety of Oral Cysteamine in Adult Patients With Cystic Fibrosis Exacerbations								YES		
22. Virtual Reality for the Reduction of Pain During Venipuncture in Children With CF						YES				

23. Virtual Care in CF (VIRTUAL-CF) Study						YES				
24. A CFit Study - Acute Exercise					YES					
25. Safety and Efficacy of 2 Treatment Regimens of Aztreonam for Inhalation Solution in Children With Cystic Fibrosis and New Onset Pseudomonas Aeruginosa Infection										YES
26. Aztreonam for Inhalation Solution (AZLI) for the Treatment of Exacerbations of Cystic Fibrosis								YES	YES	
27. Do More, B'More, Live Fit	YES					YES				
28. IV Colistin for Pulmonary Exacerbations: Improving Safety and Efficacy								YES		
29. A Pilot Study to Evaluate the Use of Smart Adherence Technology to Measure Lumacaftor/Ivacaftor Adherence in CF Subjects Homozygous for the F508del CFTR Mutation						YES				
30. Standardized Treatment of Pulmonary Exacerbations II								YES		
31. Adherence to Airway Clearance. Novel Approaches to Improving Adherence						YES				
32. Project UPLIFT to Reduce Anxiety and Depression in CF Patients						YES				
33. SPI-1005 for Prevention and Treatment of Aminoglycoside Induced Ototoxicity									YES	
34. The cystic fibrosis (CF) anti-staphylococcal antibiotic prophylaxis trial (CF START): A randomised registry trial to assess the safety and efficacy of flucloxacillin as a longterm prophylaxis agent for infants with CF				YES						
35. Development and evaluation of an intervention to support Adherence to treatment in adults with cystic fibrosis: A feasibility study comprised of an external pilot randomised controlled trial and process evaluation						YES				
36. Randomised trial of a web-based intervention for adherence in cystic fibrosis						YES				
37. Effects of inhaled hypertonic saline in children with cystic fibrosis				YES						
38. Aztreonam for inhalation for the treatment of acute exacerbations in cystic fibrosis. An open-label, randomised, cross-over pilot study of AZLI plus intravenous Colistin versus standard dual intravenous therapy.								YES		
39. Tobramycin Inhalation Powder (TIP) Administered Once Daily Continuously Versus TIP Administered BID in 28 Day on / 28 Day Off Cycles										YES
40. A Phase 3, Randomized, Open-Label, Assessor-Blind, Non-Inferiority, Active-Comparator Study Evaluating the Efficacy and Safety of Liprotamase in Subjects with Cystic Fibrosis-Related Exocrine Pancreatic Insufficiency		YES								
41. Randomized, Double-Blind, Phase 3B Trial to Evaluate the Safety and Efficacy of 2 Treatment Regimens of Aztreonam 75 mg Powder and Solvent for Nebulizer Solution / Aztreonam for Inhalation Solution (AZLI) in Pediatric Subjects with Cystic Fibrosis (CF) and New Onset Respiratory Tract Pseudomonas aeruginosa (PA) Infection/Colonization										YES
42. An Open-Label Study Evaluating the Efficacy and Safety of Liprotamase in Subjects with Exocrine Pancreatic Insufficiency due to Cystic Fibrosis		YES								

43. Trial of Optimal Therapy for Pseudomonas Eradication in Cystic Fibrosis										YES
44. A Phase 4, Open-label Treatment, Randomized, Multicenter, 2-arm, Parallelgroup, Pilot Study of Adherence to Lumacaftor/Ivacaftor in CF Subjects Homozygous for the F508del-CFTR Mutation						YES				
45. Combined Effect of CFTR Modifiers and Intensive Antibiotic Treatment										YES
46. In adults with cystic fibrosis, what is the effect of a smartphone application used to report symptoms versus usual care on exacerbations requiring intravenous antibiotics, healthcare utilisation, lung function, quality of life, anxiety and depression, nutritional status, medication adherence and absenteeism and presenteeism.						YES				
47. Exercise alone versus exercise and positive expiratory pressure as a form of airway secretion clearance in adults with mild cystic fibrosis-related respiratory disease - a feasibility study	YES						YES			
48. Musculoskeletal clinical outcomes of Whole Body Vibration Training as an adjunct to physiotherapy in children with Cystic Fibrosis: a comparison of telehealth and face to face therapy delivery	YES									
49. A randomised controlled trial of a novel web-based intervention to promote physical activity participation in young people with cystic fibrosis						YES				
50. CyFiT Telerehabilitation: Investigation into the efficacy of a telehealth physiotherapy intervention on quality of life and community participation for school-aged children with cystic fibrosis, a randomised controlled trial	YES					YES				
51. Effects of high intensity interval training on exercise capacity in people with cystic fibrosis: a randomised controlled trial	YES									
52. Home Monitoring of Patients with Cystic Fibrosis to Identify and Treat Acute Pulmonary Exacerbations. eICE Study Results	YES									
53. Effects of treadmill exercise versus Flutter® on respiratory flow and sputum properties in adults with cystic fibrosis: a randomised, controlled, cross-over trial.							YES			
54. Combined Exercise Training Improves Glycemic Control in Adult with Cystic Fibrosis					YES					
55. Safety and Efficacy of a Novel Microbial Lipase in Patients with Exocrine Pancreatic Insufficiency due to Cystic Fibrosis: A Randomized Controlled Clinical Trial.		YES								
56. Gaseous nitric oxide to treat antibiotic resistant bacterial and fungal lung infections in patients with cystic fibrosis: a phase I clinical study.									YES	
57. One-year safety and efficacy of tobramycin powder for inhalation in patients with cystic fibrosis.										YES
58. Web-Based Intervention for Nutritional Management in Cystic Fibrosis: Development, Usability, and Pilot Trial.						YES				
59. Standardized Measures of Barriers to Treatment Adherence						YES				
60. Design CF: Developing e-Health Systems to Improve Growth and Nutrition in CF						YES				

61. Video-Based Tele-coaching to Promote Treatment Adherence						YES				
62. A Mobile Medication Planning Application, MedActionPlan® (MAP), to Encourage Self-Management						YES				
63. Chipped eTrack Devices to Collect Objective Measures of Adherence						YES				

1. NCT02668575 Integrating Supportive Care in Cystic Fibrosis. https://www.clinicaltrials.gov/ct2/show/NCT02668575 First posted 29th January 2016
2. NCT03066453 Evaluation of Short Antibiotic Combination Courses Followed by Aerosols in Cystic Fibrosis https://www.clinicaltrials.gov/ct2/show/NCT03066453 First posted 28th February 2017
3. NCT03205904 Nutritional Intervention and Glycemic Improvement in Patients With Pre-diabetic Cystic Fibrosis. https://www.clinicaltrials.gov/ct2/show/NCT03205904 First posted 2nd July 2017
4. NCT02649751 Evaluation of (R)-Roscovitine Safety and Effects in Subjects With Cystic Fibrosis, Homozygous for the F508del-CFTR Mutation https://www.clinicaltrials.gov/ct2/show/NCT02649751 First posted 7th January 2016
5. NCT02994706 A Study of Home Monitoring in Adults With Cystic Fibrosis (HOMECF) https://www.clinicaltrials.gov/ct2/show/NCT02994706 First posted 16th December 2016
6. NCT02694393 Inhaled Sodium Nitrite as an Antimicrobial for Cystic Fibrosis https://www.clinicaltrials.gov/ct2/show/NCT02694393 First posted 29th February 2016
7. NCT02934698 An Efficacy and Safety Study of Ivacaftor in Patients With Cystic Fibrosis and Two Splicing Mutations https://www.clinicaltrials.gov/ct2/show/NCT02934698 First posted 17th October 2016
8. NCT02955888 Study of Safety, Tolerability & Efficacy in Cystic Fibrosis Patients With Abnormal Glucose Tolerance https://www.clinicaltrials.gov/ct2/show/NCT02955888 First posted 4th November 2016
9. NCT03125395 A Rollover Safety Study of Lumacaftor/Ivacaftor in Subjects Aged 2 Years and Older With Cystic Fibrosis, Homozygous for the F508del-CFTR Mutation https://www.clinicaltrials.gov/ct2/show/NCT03125395 First posted 24th April 2017
10. NCT03227094 Simplification of CF-related Diabetes Screening at Home https://www.clinicaltrials.gov/ct2/show/NCT03227094 First posted 24th July 2017
11. ACTRN12615001029583 Does exenatide improve post prandial glycaemic control in young people with cystic fibrosis related diabetes or impaired glucose tolerance? https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?ACTRN=12615001029583 First posted 1st October 2015
12. ACTRN12616001159448p The effect of low glucose load diet on glycaemic control in patients with cystic fibrosis https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=371203 First posted 25th August 2016
13. NCT02810691 The Effect of Soluble Fiber to Reduce Post-prandial Glycemic Excursion in Adults With Cystic Fibrosis https://www.clinicaltrials.gov/ct2/show/NCT02810691 First posted 23rd June 2016

14. NCT03052231 Interactive Mobile Health Information to Enhance Patient Care at a Cystic Fibrosis Center https://www.clinicaltrials.gov/ct2/show/NCT03052231 First posted 14th February 2017
15. NCT02703155 The Use of Home Oral Glucose Tolerance Test Kit in Screening Cystic Fibrosis Related Diabetes https://www.clinicaltrials.gov/ct2/show/NCT02703155 First posted 9th March 2016
16. NCT02700243 Increase Tolerance for Exercise and Raise Activity Through Connectedness Trial https://www.clinicaltrials.gov/ct2/show/NCT02700243 First posted 7th March 2016
17. NCT03226795 Improving Therapeutic Adherence With a Co-constructed Program Involving Both Patients and Health Care Professionals https://www.clinicaltrials.gov/ct2/show/NCT03226795 First posted 24th July 2017
18. NCT03208764 Inhaled Nitric Oxide for Cystic Fibrosis Patients With MABSC https://clinicaltrials.gov/ct2/show/NCT03208764 First posted 6th July 2017
19. NCT02950883 Saline Hypertonic in Preschoolers + CT https://www.clinicaltrials.gov/ct2/show/NCT02950883 First posted 1st November 2016
20. NCT02715921 Impact of Telerehabilitation Training on Pediatric Cystic Fibrosis Patients: An Exploratory Study https://www.clinicaltrials.gov/ct2/show/NCT02715921 First posted 22nd March 2016
21. NCT03000348 A Study of the Dosing, Efficacy, and Safety of Oral Cysteamine in Adult Patients With Cystic Fibrosis Exacerbations https://www.clinicaltrials.gov/ct2/show/NCT03000348 First posted 22nd December 2016
22. NCT02802839 Virtual Reality for the Reduction of Pain During Venipuncture in Children With CF https://www.clinicaltrials.gov/ct2/show/NCT02802839 First posted 16th June 2016
23. NCT03069651 Virtual Care in CF (VIRTUAL-CF) Study https://www.clinicaltrials.gov/ct2/show/NCT03069651 First posted 3rd March 2017
24. NCT03237767 A CFit Study - Acute Exercise https://www.clinicaltrials.gov/ct2/show/NCT03237767 First posted 3rd August 2017
25. NCT03219164 Safety and Efficacy of 2 Treatment Regimens of Aztreonam for Inhalation Solution in Children With Cystic Fibrosis and New Onset Pseudomonas Aeruginosa Infection https://www.clinicaltrials.gov/ct2/show/NCT03219164 First posted 17th July 2017
26. NCT02894684 Aztreonam for Inhalation Solution (AZLI) for the Treatment of Exacerbations of Cystic Fibrosis https://www.clinicaltrials.gov/ct2/show/NCT02894684 First posted 9th September 2016
27. NCT03109912 Do More, B'More, Live Fit https://www.clinicaltrials.gov/ct2/show/NCT03109912 First posted 12th April 2017
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