

Investigating the predictors of physical activity maintenance in children and young people with cystic fibrosis

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Declaration

I, Helen Louise Douglas, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Abstract

Maintaining adequate levels of physical activity (PA) is important for the health and well-being of children and young people with cystic fibrosis (CYPwCF). Identifying who maintains adequate levels and who needs targeted support is difficult in the clinical setting. This mixed methods programme of research investigated the maintenance of PA in CYPwCF in 2 phases.

Phase 1 explored factors affecting maintenance of PA in 49 CYPwCF who had experienced the withdrawal of a supervised exercise intervention. A subgroup of 20 CYPwCF and their parents provided greater insight into the barriers to and facilitators for the maintenance of PA through semi-structured interviews. The results established that the supervised exercise intervention worked for some CYPwCF but not for others, and benefits only lasted as long as participation continued. An adult facilitator, sociability of activities, and praise and acknowledgement all helped overcome barriers. Self-efficacy for PA was an important factor in the maintenance of PA.

Phase 2 evaluated the relationships between exercise capacity, self-efficacy for PA and self-reported PA with objectively measured PA in 78 CYPwCF. The results demonstrated that patterns of PA were varied: some CYPwCF were able to maintain regular high levels, some maintained very little activity, and others were active sometimes but not routinely. These patterns were not predictable by 3 simple clinical measurement tools. Self-reported PA was not an accurate representation of actual PA, and whilst self-efficacy for PA is important for the maintenance of PA, it did not predict PA patterns. These findings are significant for CF clinical teams in allocating resources for optimal outcomes. Different CYPwCF need different support to maintain adequate levels of PA. Therefore, it is important to accurately identify PA maintenance patterns, and the factors affecting them, so that clinical teams can facilitate the right type and level of support for individual CYPwCF.

Impact statement

The primary impact of this clinical research will be directed to the current cystic fibrosis community. The key findings are: the maintenance of physical activity behaviours is complex and unpredictable, and physical activity patterns vary between children and young people with cystic fibrosis. These findings will be disseminated through publications, presentation at conferences and within the established clinical network. Clinical teams will then be able to facilitate appropriate assessment of the physical activity maintenance behaviours, and the factors affecting those behaviours, in their patient groups. By understanding the physical activity support requirements of each individual with CF, clinical teams will be able to identify the right personalised advice and support, and the health and well-being benefits of being physically fit and active could be experienced by all children and young people with cystic fibrosis rather than just a few. In an era where so much research has been directed to those who are eligible for highly effective modulator therapies, this clinical research will have a direct impact on all of the current cystic fibrosis community. Those people with cystic fibrosis who are eligible for modulator therapies may live well into adulthood, thus the public health problem of inactivity must be addressed. Those who are not on modulator therapies need as much support as possible to enable them to gain the benefits of being physically fit and active.

The confirmation that self-reported levels of physical activity are not an accurate representation of actual levels of physical activity should have a direct impact on clinical teams providing care to people with cystic fibrosis. Simply asking children and young people with cystic fibrosis how active they are provides no useful insight into levels or patterns of physical activity. Clinical teams should focus efforts on monitoring physical activity, preferably continuously, and developing a network of adult facilitators to support children and young people with cystic fibrosis to maintain activity. Providing social support, and praise and acknowledgement will empower many to combat their barriers to the maintenance of physical activity.

This research will also impact the academic community. The findings presented in this thesis demonstrate a novel method of collecting long-term continuous physical

activity data with personalised rather than generic thresholds of moderate-to-vigorous physical activity. This facilitated the description of the different patterns of physical activity in children and young people with cystic fibrosis. The method is feasible and reproducible, and could lead to a single standardised outcome measure. This would enable comparison of physical activity data between studies which has been limited to date by the variety of outcome measures and physical activity cut-points used. This is not limited to the cystic fibrosis population and will enable future academic research into the longer-term patterns of physical activity in any population. In the long term, a more widely available, validated outcome measure of physical activity will offer the opportunity to assess the impact of interventions aimed at increasing physical activity in any population. This will help to tackle the global public health problem of inactivity.

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Division of Labour Statement

- Chapter 1** HD all work
- Chapter 2** HD all work
- Chapter 3** HD all work
- Chapter 4** HD conceived and designed the analysis, recruited participants and collected the data
SD provided second coding for Phase 1 Part C study
INSPIRE-CF research team (GOSH) provided data collected during INSPIRE-CF
- Chapter 5** NF generated GEE
HD all other work
- Chapter 6** HD all work
- Chapter 7** HD conceived and designed the analysis, recruited participants and collected data
ER recruited participants and collected data
- Chapter 8** EM, ER, KK, NF, GT, HD developed PA tracker data processing pipeline
KK, NF, GT conducted PA tracker data processing
NF generated standardised residuals for 10m-MSWT, standardised by age
GT conducted LCGA
HD all other work
- Chapter 9** HD all work
- Chapter 10** HD all work

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Abbreviations

Abbreviation	Definition
ANCOVA	Analysis of covariance
ANOVA	Analysis of variance
ATS	American Thoracic Society
BMI	Body mass index
bpm	beats per minute
BPN	Basic psychological needs
CF	Cystic fibrosis
CFQ-R	Cystic Fibrosis questionnaire- revised
CFTR	Cystic fibrosis transmembrane regulator
cm	Centimetre
CPET	Cardiopulmonary exercise test
CPM	Counts per minute
CSAPPA	Children's self-perceptions of adequacy in and predilection for physical activity
CYP	Children and young people
CYPwCF	Children and young people with cystic fibrosis
ERS	European Respiratory Society
FEV ₁	Forced expiratory volume in 1second
GEE	Generalised estimating equation
GLI	Global lung function initiative
GMM	Growth mixture modelling
GOSH	Great Ormond Street Hospital NHS Foundation Trust
GPS	Global positioning system
HAES	Habitual activity estimation scale
HBM	Health belief model
HEMT	Highly effective modulator therapies
HR	Heart rate
HR _{peak}	Peak heart rate

HRQoL	Health related quality of life
HRR	Heart rate reserve
ICAD	International Children's Accelerometry Database
IMT	Inspiratory muscle training
IOC	International Olympic Committee
IQR	Interquartile range
kg	Kilograms
LCGA	Latent class growth analysis
LDA	Linear discriminant analysis
LPA	Light physical activity
m	Metres
M	Mean
MANOVA	Multi-variate analysis of variance
MCID	Minimal clinically important difference
MDC	Minimally detectable change
MPA	Moderate physical activity
MVPA	Moderate to vigorous physical activity
PA	Physical activity
PAM	Physical activity maintenance model
ppFEV ₁	Percent of predicted forced expiratory volume in 1second
PPIE	Patient and public involvement and engagement
RBH	Royal Brompton Hospital
RCT	Randomised controlled trial
RHR	Resting heart rate
RLH	Royal London Hospital
RPE	Rate of perceived exertion
SCT	Social cognitive theory
SD	Standard deviation
SE	Self efficacy
SOC	Stages of change

SRC	Strategic research centre
TPB	Theory of planned behaviour
TTM	Trans-theoretical model
VHPA	Very high physical activity
VPA	Vigorous physical activity
WHO	World Health Organisation
10m-MSWT	10metre modified shuttle walk test

1 Introduction

Cystic Fibrosis (CF) is the most common genetically-inherited and life-limiting condition in the UK, and currently affects about 10 500 people, 48% of whom are aged less than 20 years (UK Cystic Fibrosis Registry, 2020). The genetic fault occurs on the long arm of chromosome 7, and results in an encoding error in the production of cystic fibrosis transmembrane regulator (CFTR), an epithelial ion channel (Riordan et al., 1989). CFTR is expressed throughout the body and regulates the movement of sodium and chloride ions across the cell membrane. In CF, the absence of effective CFTR results in increased viscosity of mucus. In the respiratory tract, this leads to dehydration of the airway surface liquid layer and problems associated with recurrent and chronic infection, inflammation and obstruction (Horsley, 2015). Respiratory failure causes more than 70% of deaths in people with CF (UK Cystic Fibrosis Registry, 2020).

Treatment and care for people with CF has progressed in recent decades, resulting in an increase in median predicted survival age to 49.0 years for those born in 2019 (UK Cystic Fibrosis Registry, 2020). However, there are gender-related differences: the median predicted survival age for females is 45.7 years whilst for males it is 51.6 years (UK Cystic Fibrosis Registry, 2020). The reasons for this are still not fully understood.

Despite the considerable progress in the management of CF, it remains progressive and incurable, thus all treatment strategies aim to slow the rate of decline. Physiotherapy is a burdensome element of CF treatment, predominantly aiming to minimise the development, progression or complications of bronchiectasis. It includes the assessment and management of airway clearance, inhaled therapies, exercise, posture, stress incontinence and non-invasive ventilation (Cystic Fibrosis Trust, 2011). Physiotherapy is unpopular with people with CF and evidence has suggested that adherence to physiotherapy regimens by children and young people with CF (CYPwCF) is only about 50% (Goodfellow et al., 2015, Sawicki et al., 2015). The James Lind Alliance CF research priority setting programme identified that people in the CF community (people with CF, their relatives and carers, and CF

clinicians) considered that reducing the burden of physiotherapy was a key research priority. Research priority question 1 was: ‘What are the effective ways of simplifying the treatment burden of people with Cystic Fibrosis?’, and 7: ‘Can exercise replace chest physiotherapy for people with Cystic Fibrosis?’ (Rowbotham et al., 2017). The concept of treatment burden was investigated in more detail. Airway clearance techniques, and exercise and physical activity (PA), were rated in the top 5 most important treatments by both lay (people with CF and their relatives and carers) and professional (healthcare professionals) participants. Airway clearance techniques were rated as the most burdensome of all CF treatments by both lay and professional participants. Interestingly, exercise and PA were rated in the top 5 most burdensome treatments by the professional participants but not by the lay participants (Davies et al., 2019). This suggested that people with CF and their relatives and carers valued exercise and PA, and did not experience a sense of burden in the same way as with airway clearance techniques.

PA refers to any bodily movement generated by skeletal muscles that results in energy expenditure. Exercise is a subset of PA, and is defined by activity that is structured and organised with an end objective of improving or maintaining fitness (Caspersen et al., 1985), hence why this term is frequently used in CF research. Both terms will be used throughout this thesis. Exercise will be used when the aim was known to be maintaining or improving health and/or fitness. PA will be used when the aim of participation was not for maintaining or improving health and/or fitness, or was unknown. There remains a paucity of evidence of clinical efficacy for many aspects of physiotherapy, however exercise and PA have a strong and growing evidence base, and may be one of the most evidenced tool that the CF physiotherapist has. Despite this, the provision of exercise and PA support by UK CF services has been limited (Stevens et al., 2010). PA, including exercise, has been considered a key part of the CF treatment regimen, and therefore clinicians have a duty of care to assess and manage each patient individually, and provide personalised care and advice to enable each individual to maintain PA participation. It is important to be able to identify individual PA support requirements and thus deliver optimal care, by starting with the achievable (Fitzgerald, 2014).

This programme of research aimed to thoroughly investigate the maintenance of PA in CYPwCF in order to identify whether PA maintenance behaviours can be predicted by clinical teams. For the purpose of this thesis, the term maintenance refers to an individual regularly taking part in enough PA to continually experience the health and well-being benefits. A review of the literature was conducted to explore PA in CYPwCF (Chapter 2). A mixed methods study was developed (Chapter 3), comprising of 2 phases, in order to explore (Phase 1) and then confirm (Phase 2) the factors affecting the maintenance of PA in CYPwCF. Phase 1 of the research explored the factors affecting the maintenance of PA in a group of CYPwCF who had experience of a supervised exercise intervention in 3 parts (Chapters 4 to 6). This unique population was able to offer greater insight into how they behaved after the withdrawal of the supervised exercise intervention and the resultant impact on their health and well-being (Part a), why they did or did not maintain PA participation (Part b), and what they perceived as the barriers to and facilitators for the maintenance of PA (Part c). Phase 1 methods are presented in Chapter 4, with the findings presented in Chapter 5 and discussed in Chapter 6. Phase 2 identified objectively measured patterns of PA maintenance in CYPwCF, and investigated whether pattern of PA maintenance could be predicted by 3 simple clinical outcome measures. The methods used in phase 2 are presented in Chapter 7, with the main findings presented in Chapter 8 and discussed in Chapter 9. The final chapter assimilates the integrated interpretation of the different elements of this mixed methods programme of research and discusses the potential impact on clinical practice (Chapter 10).

2 Literature review

This literature review aimed to describe, review and explore the current evidence-base regarding PA for CYPwCF, why this is a point of relevance, what current patterns of PA behaviours appear to exist in CYPwCF, and what might predict those individual behaviour patterns. This chapter presents a review of the literature by considering:

- The impact of PA on CYPwCF,
- Levels of PA participation in CYPwCF,
- Barriers to and facilitators for PA participation,
- The effect of PA interventions,
- Maintenance of PA participation in this population.

This research was focused on the health and well-being outcomes associated with physical fitness in CYPwCF. Literature documenting this subject matter does not always make the distinction between specific exercise or more general PA, thus, for the purposes of this literature review, both exercise and PA were searched and explored. Where literature pertaining to CYPwCF specifically was limited then literature investigating adults with CF and children and young people without CF were also considered.

2.1 Literature search and review strategy

A number of literature searches were carried out to enable a comprehensive review of the literature addressing the aims of this chapter, details of which can be seen in Table 1. Each search was conducted in a number of databases: CINAHL, Medline, Embase, PubMed, Scopus and Cochrane database for systematic reviews. Papers were initially screened by title, then abstract and finally by full text. Included papers were reviewed using the methodologically appropriate Critical Appraisal Skills Programme (CASP) checklist.

Table 1: Details of the conducted literature searches including aims and the key words or phrases used for each search

Aims	Key words (PICO format)	Chapter section
To review the impact of PA on CYPwCF	P: People with CF I: Physical activity OR exercise O: Physical OR health OR mental OR well-being OR psychosocial AND benefits OR impact	2.2
To review the levels and patterns of PA participation in CYPwCF	P: <ul style="list-style-type: none"> • Children OR young people OR adolescent • people with CF O: Levels OR patterns AND PA OR exercise	2.3
To review the barriers to and facilitators for PA participation in CYPwCF	P: <ul style="list-style-type: none"> • Children OR young people OR adolescent • people with CF O: Barrier OR facilitator OR correlate AND PA OR exercise	2.3.1 and 2.3.2
To review the effects of PA interventions on CYPwCF	P: <ul style="list-style-type: none"> • Children OR young people OR adolescent • people with CF I: PA OR exercise AND intervention OR programme O: <ul style="list-style-type: none"> • Physical OR health OR mental OR well-being OR psychosocial AND benefits OR impact • Level OR pattern OR maintenance AND PA OR exercise 	2.4

Key: CF cystic fibrosis, CYPwCF children and young people with cystic fibrosis, PA physical activity, PICO population, intervention, comparison and outcome

2.2 The importance of being physically fit and active

The physical and emotional health and well-being benefits of being physically fit and active are well documented in both health and disease populations (World Health Organisation, 2010, Biddle and Asare, 2011, Mountjoy et al., 2011), and have been demonstrated in individuals with CF.

2.2.1 CF-related physical health benefits of exercise and physical activity

Early research in this area established the safety of regular exercise for CYPwCF (Godfrey and Mearns, 1971, Orenstein et al., 1981, Cerny et al., 1982, Cropp et al., 1982, Henke and Orenstein, 1984, Cerny and Armitage, 1989). Since then progress in the understanding of the CF disease process and the physiological effects of exercise has led to exercise, with the aim of improving or maintaining health, being considered a key part of the management of CF (Wilkes et al., 2009, Cystic Fibrosis

Trust, 2011, Rand and Prasad, 2012, Cerny, 2013). Evidence has shown that effective PA and exercise training can help maintain or possibly even increase lung function (Kriemler et al., 2013, Schneiderman et al., 2014, Hommerding et al., 2015). This can be explained by the mechanical breathing changes caused by exercise, for example hyperventilation and change in expiratory flow bias, leading to the mobilisation of sputum, as well as a change in the rheology of sputum resulting in improved ease of secretion clearance (Hebestreit et al., 2001, Paranjape et al., 2012, Dwyer et al., 2017). Furthermore exercise can prevent reduction in bone mineral density (Frangolias et al., 2003, Hebestreit et al., 2006, Tejero Garcia et al., 2011), and improve glycaemic control in people with CF (Beaudoin et al., 2017).

Research has also demonstrated that appropriate exercise training can result in improved physical function, improved cardiovascular performance and improved muscle strength in people with CF (Bradley and Moran, 2008, Radtke et al., 2017). Thus, in addition to experiencing the CF-specific health benefits, people with CF who take part in regular exercise training can improve their fitness, function and strength. This has been demonstrated irrespective of disease severity measured by lung function (Klijn et al., 2004, Schmidt et al., 2011, Moorcroft et al., 2004). Moreover, survival is linked to and predicted by exercise capacity in CYPwCF (Nixon et al., 1992, Pianosi et al., 2005), therefore improving physical fitness may have a direct impact on the life expectancy of an individual with CF.

In a Cochrane review examining the evidence around physical exercise training in CF, the authors identified 83 unique studies (Radtke et al., 2017). In spite of the quantity, quality of research in this field has continued to be moderate to low with only 15 studies meeting the strict inclusion criteria for the systematic review (Radtke et al., 2017). The majority (13 of 15) involved CYPwCF either exclusively (n = 7) or combined with adults with CF (n = 6), while the remaining 2/15 studies only involved adults with CF. The authors of the review noted heterogeneity of study design, especially in terms of intervention: exercise modality, level of supervision and duration. Nevertheless, they concluded that effect ranged from no effect to evidently positive, and that exercise training appeared to have a consistent

positive effect on exercise capacity measured by peak oxygen consumption (observed in 4 of 7 studies). However, the effects on lung function, measured by forced expiratory volume in 1 second (FEV₁) (2 of 11 studies) and health-related quality of life (HRQoL) (2 of 7 studies) were more variable. The wide heterogeneity of investigated interventions resulted in a continued lack of clear evidence supporting one type of exercise regimen over another. This perhaps indicated that any exercise intervention has the potential to have a positive impact on the health and well-being of CYPwCF. It has been suggested that a combination of aerobic and resistance work could be the most beneficial to health (Orenstein et al., 2004, Williams and Stevens, 2013).

2.2.2 Other benefits of physical activity and exercise

In addition to the physical health benefits for individuals with CF, PA and exercise also have a positive impact on psychosocial outcomes to the wider population (Biddle and Asare, 2011, Zahl et al., 2017). In a study carried out by Lovell et al. (2010), the researchers reported that psychological outlook was rated as the second highest benefit from exercising by participants surveyed using the validated Exercise Benefits/Barriers Scale. Whilst the sample was limited to 200 female university students, the findings supported those of previously published work thus adding strength to their credence. Considering only literature investigating children and young people (CYP), Biddle and Asare (2011) authored a 'review of reviews' paper synthesising the literature on PA and mental health. The authors suggested that quality of methodologies was weak for many of the studies. However due to the consistency of associations, albeit small, the authors concluded that PA was likely to have positive psychosocial effects.

Evidence also suggested that the psychosocial benefits of PA and exercise are available to individuals with CF (Orenstein et al., 1989). Hebestreit et al. (2014) investigated the associations between quality of life and PA and fitness in 76 young people and adults with mild to moderate CF. The authors concluded that aerobic fitness was directly positively associated with quality of life, as measured using a validated HRQoL tool. This study was limited to 2 centres, 1 in Germany and 1 in Switzerland, with participants aged 12 years and over, therefore generalisability of

the results was limited. However, given the similarities in findings with the international literature reviewed by Biddle and Asare (2011), and the lack of any evidence indicating a negative psychosocial impact of PA and exercise, it was sensible to consider the results of Hebestreit et al. (2014) as having value.

Corroborating other research findings, INSPIRE-CF, a two-year long supervised exercise intervention randomised controlled trial (RCT) (Ledger et al., 2017), reported that quality of life, as well as functional exercise capacity, improved in the CYPwCF who received the exercise training (n = 34) when compared to the control group (n = 32) who continued to receive standard CF care but no supervised exercise intervention. In addition, those who attended more than 50% of their training sessions experienced a positive effect on lung function (measured by FEV₁) (Ledger et al., 2017). These results suggested that the functional and psychosocial well-being benefits of exercise could be more readily achieved, but CF-specific health benefits on lung function may be more dependent on dose of exercise.

Despite the remaining gaps in knowledge about optimal type and dose of exercise, it was clear that PA and exercise are safe for people with CF (Ruf et al., 2010), and have an established and relevant role in the treatment of people with CF (National Institute for Clinical Excellence, 2017, Cystic Fibrosis Trust, 2017b, Cerny, 2013, Rand and Prasad, 2012, Wilkes et al., 2009). This component of treatment is significantly more cost-effective to deliver than many others. For example, new highly effective modulator therapies (HEMT) cost in excess of £100 000 per person per year, and have commonly reported adverse reactions (National Institute for Clinical Excellence, 2017). Indeed, some individuals with CF find the side effects of some therapy combinations to be intolerable and, despite the benefits to other aspects of health, stop therapy. By comparison PA and exercise are low-risk, low-cost and high-benefit. However, the benefits are only experienced if PA and exercise regimens are followed.

2.3 Activity and exercise behaviour patterns in children and young people

Adherence to all recommended CF treatments, including exercise, is often poor (O'Donohoe and Fullen, 2014, Goodfellow et al., 2015). White et al. (2007) explored

this in an Australian population of adults with CF. Their participants reported adherence to exercise as recommended by their clinical team to be 91.2% when well and 77.8% when unwell. However, self-reporting of adherence is notoriously inaccurate and often results in over-reporting (Daniels et al., 2011), thus participation in exercise may actually be lower in this sample.

A number of studies have examined participation in PA and exercise amongst CYPwCF. Selvadurai et al. (2004) used activity diaries and accelerometry to investigate activity levels in CYPwCF and classified participants by developmental stage. They found that the activity levels were equal between the two groups (CF group and non-CF control group) of the pre-pubescent participants, and noted that those with milder disease were, in fact, even more active than the healthy controls. There was no difference between girls and boys at this developmental stage. However, pubescent girls were found to be less active than pubescent boys. Again in the pubescent developmental stage, those with milder CF remained more active than the control group, but those with moderate-severe disease were less active when compared to healthy control. Baker and Wideman (2006) also noted that girls were less fit and less active than boys in their sample of CYPwCF aged 12-18 years. These findings were similar to those of Schneiderman-Walker et al. (2005) who again demonstrated that boys were more active than girls in their sample of 109 7-17 year olds with CF.

Whilst Britto et al. (2000) reported that PA levels did not differ much between adolescents with CF and age-matched controls, it is important to remember that PA levels begin to reduce in early adolescence in the healthy population (Blaes et al., 2011, Van Dijk et al., 2016), and more markedly in girls than boys (Sallis et al., 2000, Ruiz et al., 2011, Cooper et al., 2015).

Van Dijk et al. (2016) monitored levels of PA amongst adolescents in the Netherlands whilst exploring the associations between changes in PA and changes in depressive symptoms and self-esteem over 1 year. Participants were recruited from 2 school year groups (years 7 and 9, average age 13.6years at baseline) and wore a thigh-worn accelerometer for 1 week at baseline and a further week for follow-up 1 year later. Total number of steps per week was used as the outcome

measure for PA, with a minimum of 4 days (including both weekend days) and a maximum of 6 days included per participant. Depressive symptoms and self-esteem were measured by validated questionnaires at baseline and follow-up at 1 year. The authors concluded that there was no association between levels of PA and the mental health outcomes. However, the results of this study may have been impacted by a self-selection bias as adolescents experiencing more severe depressive symptoms may be less likely to participate in research. The authors also reported that PA fell by an average of 15.3% over the year. Participants in year 7 were more active at baseline but had a more substantial decline in PA (-20.7%) than those in year 9 (-5.0%). This might have indicated that levels of PA fall earlier on in adolescence and then remain more stable, or it may have occurred as a result of limitations of the study. For example, 440 participants were recruited from a population of 526, however only 158 participants provided full datasets for baseline and follow-up test points and were therefore included in analysis. Those participants who contributed full datasets at both baseline and follow-up may have been inherently more interested in PA and therefore have higher levels of PA than those who did not participate. Furthermore, there was no evidence that the outcome measure of steps per week was standardised by number of days of data included in the analysis. If a participant contributed the maximum of 6 days at baseline but only the minimum of 4 days at follow-up then the difference between these values may have been related to the number of days included rather than a difference in the levels of PA of that participant. Therefore, the change in PA and differences between year groups may have been impacted.

Van Dijk et al. (2016) reported that there was no statistically significant difference in change in PA over 1 year between male and female participants (-17.4% and -13.8% respectively). However, the values were not presented so it was not possible to understand if there were sex-based differences in levels of PA. Blaes et al. (2011) tracked PA in 361 CYP resident in 1 peri-urban, medium-sized town in France. The investigators aimed to analyse the changes in habitual PA in males and females from pre-school to junior high school. The participants were categorised into 3 age groups: pre-schoolers aged 4.5 years (n = 94), primary schoolers aged 9.2 years

(n=156) and junior high schoolers aged 12.4 years (n = 111). Participants were issued with a hip-worn accelerometer to be worn during waking hours for 7 days, including 4 school days and 3 free days. The raw accelerator counts per minute (CPM) were summarised into time spent in 4 different PA intensities (light PA (LPA), moderate PA (MPA), vigorous PA (VPA), very high PA (VHPA)), and the proportion of participants who achieved 60 minutes of moderate to vigorous PA (MVPA) on 5 days was calculated. The authors concluded that boys were more active than girls achieving, on average, 18 minutes less LPA and 11 minutes more MPA, 4 minutes more VPA and 2 minutes more VHPA. Furthermore, they identified an age-related fall in PA as PA recommendations (60 minutes of MVPA per day) were more frequently met by the younger participants than the older participants (pre-school: 95% males/73% females, primary school: 99% males/76% females, junior high school: 60% males/31% females). The sample in this study was limited to 1 small area and the authors identified homogeneity of social-economic status (all described as middle-class). This limited the transferability of the results, although findings were in line with other studies.

Ruiz et al. (2011) conducted a cross-sectional study to describe the levels of PA and sedentary time amongst 2,200 adolescents, aged 12.5-17.5 years, from 9 European countries. PA data were recorded by waist-worn accelerometers. Participants were asked to wear the accelerometers for 7 days but data were included in analysis if participants contributed a minimum of 3 days each with 8 hours of data. CPM data were summarised into mean CPM for the minutes of wear-time per participant and time spent in MVPA (defined by standard published cut-points), which was then dichotomised into <60minutes or ≥60minutes in line with PA recommendations. The investigators reported that males were more active than females with 56.8% of the male participants achieving ≥60minutes of MVPA compared to only 27.5% of female participants. The results also identified that the older male participants were less active than the younger male participants, but this age-related difference was not apparent in the female participants. Data collection took place across the year which may have led to a hidden seasonal- or weather-related impact on the levels of PA amongst the participants. Furthermore, the short duration of

accelerometer use may have resulted in participants behaving differently on the days that they wore the monitor. Participants may have increased levels of PA compared to their habitual levels knowing that they were being monitored. However, the relatively large sample size and varied geographical locations of the participants meant that the results were likely to be representative of the population of European adolescents.

Cooper et al. (2015) reported similar results following an analysis of accelerometer data from the International Children's Accelerometry Database (ICAD). This analysis included data from 20 studies across 10 countries which involved 27,637 participants, aged 2.8-18.4 years. This international database used common data reduction procedures which enabled the integration of data from different studies facilitating a sample of size, geographical variety and age range that would be difficult to achieve by any single study. Participants contributed at least 3 days of PA data with a minimum of 500 minutes per day. The authors reported that boys were less sedentary and more active than girls, and that levels of PA fell with age. After the age of 5 years, there was a decline of 4.2% of total PA with each additional year of age. This fall was mostly due to less light PA and more sedentary time, but time spent in MVPA, the intensity associated with more health benefits for CYPwCF, also reduced with age.

Jago et al. (2017) corroborated this message with their research considering longitudinal accelerometry data from a cohort of UK primary school children at 2 time points, 3 years apart (total n = 1837, Year 1 only n = 614, Year 4 only n = 538, data provided at both time points n = 685). The authors reported three measurements of activity: total activity measured by average CPM, average number of sedentary minutes per day, and average time spent in MVPA state in minutes per day (derived using population-specific accelerometer cut-points). Boys demonstrated higher activity levels and lower sedentary time than girls throughout this study. The data also showed a statistically significant fall in both CPM and MVPA minutes/day and an increase in sedentary time between Year 1 (aged 5/6 years) and Year 4 (aged 8/9 years) time points. This was apparent in both girls and boys, although change was noted to be more dramatic amongst the female

participants who demonstrated a fall of 11% (7minutes/day of MVPA) than the male participants (4%, 3minutes/day of MVPA), thus supporting previously published work.

Farooq et al. (2017) contested this concept. This research group conducted a longitudinal study collecting habitual PA data (total habitual activity in CPM and MVPA minutes/day) from the cohort at 4 time points, at 7, 9, 12 and 15 years of age. Data were included in analysis if an individual participant had provided accelerometry data twice (n = 545). A total of 217 provided data at each of the 4 time points. The investigators were able to identify different trajectories of daily minutes of MVPA, 4 for boys and 3 for girls. The majority of participants were in the lower 2 MVPA trajectories, 64% of males and 81% of females. They concluded that activity levels (both total activity and time in MVPA) did indeed drop as a child aged, but, in contrary to previously established views, this had already started by the age of 7 years and they did not observe a significantly greater decline once adolescence was reached. They also stated that activity decline was comparable between girls and boys, although females were less active than males at each assessment point. It should also be noted that around 19% of the males in their sample maintained fairly high MVPA levels across the 8 years of the study. This was not observed in the female participants. A total of 19% of females were in the highest MVPA trajectory although this still fell with age. In addition males demonstrated higher levels of activity (in both measurements) than females consistently across the study duration, so whilst rate of decline was comparable, activity levels were not. The sample was recruited from a different geographical area to the participants in the Jago et al. (2017) study, Northeast England and Southwest England respectively. BMI for the participants in the Jago et al. (2017) was slightly lower than that reported for the participants in Farooq et al. (2017), which might be as a result of the levels of PA being maintained for slightly longer in the Jago et al. (2017) study, therefore BMI remaining slightly lower. Both studies reported including participants from a range of socioeconomical backgrounds and collected PA data throughout the seasons. However, there may have been other inherent differences between

the 2 populations, such as access to leisure facilities and availability of sport in schools, that may have resulted in the different findings.

It was apparent, from the available literature, that the pattern of change in levels of PA in adolescents with CF was similar to those without CF: males being more active than females, and activity levels falling throughout childhood and during the transition from childhood to adulthood. This must be taken into account when considering a comparison of activity levels between those with CF and those without, and is of particular concern in CF where exercise and PA can have such a role in treatment, and where females already have a reduced life expectancy compared to males (UK Cystic Fibrosis Registry, 2020). The fall in PA levels that occurs in adolescence, and most dramatically in females and those with more severe disease in CF, threatens to limit the health of young people living with CF.

However, levels of PA and exercise participation amongst people with CF appeared to vary (Nixon et al., 2001, Selvadurai et al., 2004, Gruber et al., 2011, Douglas et al., 2016b). The mean overall attendance at training sessions by the participants of INSPIRE-CF was 60.7%, however this ranged from 16% to 93% for individual participants (Douglas et al., 2016b). This was supported by anecdotal reports from physiotherapists and other healthcare professionals working with CYPwCF, as it often appeared that some individuals within their patient cohorts were regularly physically active and exercising without evidence of effort or even awareness of barriers, whereas others were much more sedentary and seemed to experience barriers to even low levels of PA. Identifying and understanding these barriers and ranges in maintaining participation, and how they may differ from those experienced by CYP without chronic illness, is important, and an important step towards delivering effective support and interventions to enable all CYPwCF to experience the benefits of regular PA and exercise participation.

2.3.1 Barriers to and facilitators for physical activity and exercise

In an era where physical inactivity is considered to be a major public health concern (Department of Health and Social Care, 2019), much work has been done to explore and understand barriers to and facilitators for PA and exercise participation in

health and disease populations (Troost et al., 2014). Barriers, defined as internal or external challenges or obstacles to participation, exist on personal, inter-personal and community levels (Ontario Agency for Health Protection and Promotion (Public Health Ontario) et al., 2016). Lovell et al. (2010) reported that physical exertion was the most commonly cited barrier to exercise. Time taken to exercise, access to exercise facilities and negative impact of other people were also reported by their participants, but less frequently. Whilst the sample in this study was limited by age, gender and location (female students, aged 19.03 ± 1.06 years (mean \pm SD) from two universities in the south of England), the results reflected the findings of other studies (Happ et al., 2013).

In a population sample of adults with CF, White et al. (2007) identified barriers to taking part in exercise regimens as being too busy and too tired. Conversely, the authors noted that adherence to recommended programmes was higher in those in full-time work or study therefore raising doubt over those identified reasons. This suggested that those participants who had more constraints on their time, by work and study, were actually more able to maintain exercise participation, despite time and fatigue being reported as barriers. Those with fewer time commitments were also less able to maintain exercise participation. It is possible that research participants find it easier to identify more tangible reasons, such as time and fatigue, when trying to explain a lack of a certain positive behaviour, such as PA or exercise. There might be other barriers to exercise that participants were either unable or unwilling to cite to the researchers. The issue is likely to be more complex than merely time and energy taken to participate in a PA.

Lovell et al. (2010) investigated the relationship and impact of perceived barriers and benefits to exercise. Whilst a benefit of exercise is a slightly different concept to a facilitator for exercise, defined as a factor that aids or encourages participation, there is clearly some overlap thus the findings have relevance. Lovell et al. (2010) concluded that physical performance was the most frequently identified benefit of exercise, followed by psychological wellbeing and preventative physical health benefits. Notably, social interaction was much less frequently cited. This construct is often thought to be an important element of PA and exercise (Woods et al.,

2010). The limited sample may have resulted in bias and a lack of representation of, for example, CYPwCF. Alternatively, social interaction in relation to PA and exercise may not be as important and relevant as academics and researchers have described.

As part of a 4 phase action research project, Shelley et al. (2018) explored the barriers, facilitators and perceptions of PA among CYPwCF. The first phase of this project used semi-structured interviews with CYPwCF. The interview transcripts were analysed using a broad model of interpretative phenomenology and no new themes were identified after the 9th interview, thus the sample size remained at 9 participants. The CYPwCF interviewed in this study identified that parents/carers, peers and coaches all had a reinforcing influence on PA engagement. Whilst this sample was limited to CYPwCF recruited from a single CF centre in the UK, thus limiting transferability, the findings suggested that social interaction was indeed an important facilitator for PA participation amongst CYPwCF.

The non-exercising sample studied by Lovell et al. (2010) reported perceiving strong benefits to exercise, with comparatively less barriers, with benefit/barrier ratio of 1.33. This indicated that the presence of any barriers was sufficient to prevent this group of people from being more physically active, even when recognising the many benefits associated with exercise. These results corroborated those reported in adolescents with CF by Baker and Wideman (2006) where female participants, who had lower levels of PA, reported fewer barriers to participation and slightly more positive attitudes than male participants. This suggests that the complexities of psychosocial factors such as self-efficacy and the direct and indirect impact of others may compound both barriers and benefits. Consideration must be paid to these intricate factors that exist at personal, inter-personal and community levels.

2.3.1.1 Self-efficacy for physical activity

Self-efficacy, a concept described by Bandura (1977), is the strength of a person's conviction in their own effectiveness, and is often discussed in relation to behaviour change and coping. In relation to PA, it has been widely agreed that a person's perception of and confidence in their own abilities impacts whether they will even

try a particular activity (Harter, 1982, Hovell et al., 1989, Sallis et al., 2000, Spink et al., 2006, Campbell, 2012).

Hay (1992) discussed self-efficacy for PA, and resultant impact on participation in CYP. He suggested that CYP who consider themselves to be inadequate in an activity or behaviour would avoid situations where these short-falls would become apparent. Spink et al. (2006) conducted a questionnaire-based study exploring the correlates of structured (sport and exercise) and unstructured (physical activities) activities among sufficiently active CYP aged 12-17 years old. Interestingly, the researchers identified that 39% of their participants recognised perceived competence as being connected to participation in structured activities but only 3% suggested connection with unstructured activities. This indicated that informal PA (unstructured activities) would perhaps be more accessible to CYP with less confidence in their abilities than formal exercise. However, the small sample size (n = 198) was limited by the inclusion of only sufficiently active CYP. A total of 434 CYP were excluded because their activity levels were considered to be insufficient. It was possible that CYP who were less active would demonstrate different results.

Prasad and Cerny (2002) made reference to self-efficacy as an important concept when discussing the factors that influence adherence to exercise in CYPwCF. Whilst this construct has been explored in more detail in CYP with developmental coordination disorder (Hay et al., 2004, Cairney et al., 2005, Cairney et al., 2007), less is known about the impact of self-efficacy for PA on the levels of participation in CYPwCF. Street et al. (2016) explored the experiences of PA in 12 adults with CF using semi-structured interviews. The transcripts were analysed using an interpretative phenomenological approach to understand how the participants made sense of and derived meaning from their PA experiences. The authors reported that the participants who were regularly active tended to demonstrate greater self-efficacy for PA, and adjustment to and acceptance of their PA abilities. Those who were less active appeared less able to adjust or view themselves positively if their PA abilities were lower than they had been previously, or low in comparison to healthy peers.

Patterson et al. (2016) explored self-efficacy, barriers to PA and levels of participation in children aged 8 to 17 years old post-liver transplantation. Whilst there are notable differences between this population and CYPwCF, there are similarities, for example, chronicity, fatigue and significant daily treatment burden. Participants wore accelerometers for 7 days to generate PA data (daily step count and time in MVPA), and completed questionnaires measuring self-efficacy for PA, barriers and benefits to PA and HRQoL. The researchers concluded that the results demonstrated a significant correlation between self-efficacy for PA and activity levels. This remained even after controlling for confounding variables, such as fatigue, age and gender.

Self-efficacy was identified as a correlate of PA in CYP in a review of 102 relevant studies (Sallis et al., 2000). This was a weak correlate in studies involving children aged 3-12 years old but increased in both frequency of report and strength of correlation with PA participation in studies involving 13-18 year olds.

Methodological differences between studies resulted in limited analysis and therefore interpretation of these results. For example, different classification of variables led to themes of self-efficacy, self-esteem, perceived competence, and behavioural attributes and skills all being identified. The concept of self-efficacy could incorporate all of these themes together. This review also concluded that being male, parent support (direct and indirect), support from others, and opportunities to exercise were all significant correlates for PA in adolescents.

2.3.1.2 The role of parents and carers

It is logical to assume that a parent or other primary-carer will have a significant influence on the PA and exercise opportunities that are available to the CYP in their care. However, the direct relationship between child and parent levels of PA was less clear. A cross-sectional study carried out by Rodrigues et al. (2017) investigated the PA levels of 834 parents and association with their child's sport participation. Children were aged 6-10 years, and all attended participating elementary schools in central Portugal. The researchers concluded that both mothers' and fathers' own PA participation had an influence on children's participation in sport. For those families where one parent was more active, the influence appeared to be greater

for children of the same gender as the active parent. There was potential bias in the data as a self-report questionnaire was used and no objective activity monitoring took place. However, the authors stated that their findings were in line with studies that had used accelerometry to measure levels of PA in adults and children.

Solomon-Moore et al. (2018) used a mixed methods approach to explore parental influence on their child's level of PA in a UK-based sample. The authors identified higher child levels of PA, measured by accelerometry, in family units where parents shared responsibility for their child's exercise participation, which was established during interview. This was possibly more apparent in boys than girls, whereby parental influence appeared to be more substantial on levels of PA in boys than girls. Parent roles varied between midweek and weekend days, with mothers taking more of a lead responsibility for their child's levels of PA during the week and shared more equally with fathers at the weekend. Whilst this provided a useful insight into some aspects of the role that parents played, the geographically limited sample restricted transferability of the findings. In addition, only one parent from each family unit was interviewed, 72% being mothers. This may have resulted in biased interview responses. The authors acknowledged that they were unable to include information about family composition, again limiting how much the results can contribute to current knowledge. Despite these limitations it was clear from this study that parents played a significant role in their child's PA and exercise participation, and so must be considered when carrying out research in this area.

There has been little research exploring the relationship between parent levels of PA and those of CYPwCF. However, Fereday et al. (2009) carried out a qualitative study exploring the PA perceptions and experiences of CYP living with chronic disease, including CF, and those of their parents. The researchers used multiple techniques to collect data. The findings demonstrated that both CYP and their parents perceived that chronic disease was not a barrier to PA participation, and that levels were similar to their healthy peers, although this study did not involve any objective activity tracking element thus limiting the strength of this evidence. In addition, the researchers did not make reference to parent PA participation and any impact this may have on CYP participation. However the findings did establish that

parents play a significant role in facilitating their child's PA participation. Examples included providing transportation or attending with their child, despite involving a substantial distance or time commitment by the parent, and background planning to ensure that risks of exacerbating their illness were minimised.

It was clear from the available evidence that a parent or primary-carer could act as a facilitator in the PA and exercise participation levels of CYPwCF, and by contrast in some circumstances may also contribute to barriers to participation. When considering CYPwCF, the role that parents and carers play should not be underestimated (Prasad and Cerny, 2002, Rand and Prasad, 2012).

2.3.2 Correlates for physical activity and exercise

This review has identified a number of the most significant factors involved in PA and exercise for CYP, and how they exist at personal, interpersonal and community levels. Personal factors include self-efficacy, temperament, enjoyment, hope and feeling good (Sallis et al., 2000, Spink et al., 2006, Moola et al., 2012, Poobalan et al., 2012, Patterson et al., 2016, Janssen et al., 2017). Parental support and social support are significant interpersonal factors (Sallis et al., 2000, Spink et al., 2006, Moola et al., 2012), and access to facilities, influence of school and activity opportunities are community level factors all impacting on the levels of PA of CYP (Prasad and Cerny, 2002, Morgan et al., 2016). From the examined literature it appeared that correlates for PA participation in CYP included:

- Gender (being male) (Sallis et al., 2000, Farooq et al., 2017),
- Age (inverse correlation) (Sallis et al., 2000, Farooq et al., 2017),
- Positive self-perception of skills and abilities (Sallis et al., 2000, Spink et al., 2006, Moola et al., 2012, Patterson et al., 2016),
- Finding activities enjoyable/fun (Spink et al., 2006, Moola et al., 2012, Poobalan et al., 2012),
- Positive body image (Poobalan et al., 2012),
- Temperament- those who enjoy high intensity stimulus activities (high intensity pleasure) and are highly active, impulsive and quick to respond (high surgency) (Janssen et al., 2017),

- Parental support and facilitation (Sallis et al., 2000, Prasad and Cerny, 2002, Spink et al., 2006, Moola et al., 2012),
- Support from peers and others (Sallis et al., 2000, Prasad and Cerny, 2002, Spink et al., 2006),
- Activity provision at school and longer breaks (Morgan et al., 2016),
- Proximity to facilities (Prasad and Cerny, 2002, Spink et al., 2006).

Bauman et al. (2012) conducted a review of systematic reviews pertaining to correlates (defined as factors associated with PA) and determinants (defined as factors with a causal relationship) of PA. The authors identified 7 systematic reviews that involved CYP and concluded that male sex was a determinant of PA in children aged 4-9years, but over the age of 9years male sex was a correlate for PA. Level of parental activity was identified as a correlate to PA in children but not adolescents, and general social support was a determinant of PA in adolescents but not children. Self-efficacy for PA was highlighted as a determinant of and correlate for PA in CYP. These findings suggested that parents may have more impact on the levels of PA in younger children whereas peers have more influence during adolescence. However, level of PA participation and maintenance is affected by how much confidence a child or young person has in their own abilities to be physically active regardless of age. Prasad and Cerny (2002) and Wilkes et al. (2009) identified that CYPwCF had additional factors, on top of those common to all CYP. These included:

- Burden of disease and impact of complex treatment regimen, including physiotherapy and medications,
- Variable health status and impact of illness and infection,
- Decreasing exercise capacity,
- Vulnerable child syndrome, whereby parents of CYPwCF may perceive their child as being more vulnerable and thus limit their activities,
- Impact of CF clinicians,
- Social stigma associated with symptoms, such as coughing.

This highlights the complexities that exist for CYPwCF, all of which can impact on PA and exercise participation and maintenance. Research considering PA and exercise interventions in CYPwCF must respect and balance these factors and the interactions between them. This is particularly pertinent now that such a large proportion of CYPwCF are able to benefit from HEMT. The difference in health status is likely to become wider in the population of CYPwCF. Including participants with the full range of symptoms and disease severities, and ensuring that research is designed to offer the opportunity for CYPwCF to voice their own thoughts and perceptions of PA and exercise, is vital.

2.4 Physical activity and exercise participation interventions

There has been an international effort to improve the health and fitness of CYP, in health and disease populations, by reducing sedentary behaviours and improving levels of PA (Micheli et al., 2011). In 2010, the World Health Organisation (WHO) and the International Olympic Committee (IOC) signed a memorandum of understanding committing to work collaboratively at national and international level to promote physical and grassroots sports activities (Mountjoy et al., 2011). This political drive has been supported by a wealth of published work discussing the evidence about PA and exercise interventions.

van Sluijs et al. (2011) authored a review of reviews and updated systematic review summarising the evidence on family and community interventions on the levels of PA of CYP. They identified six family-based (involving a family member) and four community (child only, and away from school) intervention studies. The variations in intervention and use of outcomes resulted in the authors concluding that the effectiveness of these types of interventions remained unclear, however the little evidence that was assimilated was mostly from those targeted at families and set in the home. Whilst the generalisability of these findings to the CF population was limited, considering family-based intervention as the most valuable appeared sensible and in line with the identified role of parents/carers. As part of the same series of work, Kriemler et al. (2011) authored a similar paper addressing the effects of school-based interventions. A total of 20 appropriate studies were identified demonstrating a positive effect of school-based interventions on overall PA levels of

CYP. There was weaker evidence to suggest that aerobic fitness could be positively affected by the school-based interventions. Whilst these results were positive, the impact of school-based interventions on CYPwCF has not been identified. Given the additional PA and exercise advice required by CYPwCF (in relation to dietary intake and hydration, and, for some, blood glucose control and oxygen supplementation), generalised school-based interventions may or may not result in a positive effect for CYPwCF.

A Cochrane review investigating PA interventions for people with CF only identified 4 studies which met inclusion criteria, including a total of 199 participants with mean age range of 13.2-19.5years (Cox et al., 2013). All 4 studies were designed to assess the effect of a training intervention, thus effect on PA participation was a by-product rather than primary aim. One included study (Schneiderman-Walker et al., 2000) reported improvements in activity participation at 1, 2 and 3 years after starting an exercise intervention when compared to a control group receiving no intervention. The intervention consisted of a home exercise programme, carried out 3 times per week independently by the participants, with telephone support every 4-6 weeks. Levels of PA were assessed using daily activity diaries therefore self-report bias may have influenced the results. However, the study by Hebestreit et al. (2010), which also involved activity counselling and exercise advice, demonstrated greater time spent in vigorous activity state, assessed by accelerometry, at 18 and 24 months. This effect was not realised at 12 months therefore suggesting that a longer duration was necessary to achieve effect, possibly related to time taken to form PA habits. This was supported by the final 2 studies included in the systematic review, both of which delivered supervised training but resulted in no change in PA participation after the supervised interventions: one was delivered during inpatient hospital admission (Selvadurai et al., 2002), and the other for 12 weeks duration (Klijn et al., 2004).

Despite a possible positive impact on PA participation, the Schneiderman-Walker et al. (2000) study demonstrated no significant change in exercise capacity, thus questioning the effectiveness of the exercise intervention. Similar results were reported by Hommerding et al. (2015) and Rovedder et al. (2014) whereby

participants who received written and verbal guidance on physical activities self-reported an increase in levels of PA compared to the control group (Hommerding et al., 2015), and participants who carried out a home exercise programme demonstrated increased upper limb muscle strength (Rovedder et al., 2014). However, again no change in exercise capacity was demonstrated in either study. A further 3 studies (Ledger et al., 2013, Urquhart et al., 2012, Black et al., 2009), all with some element of directly supervised exercise, demonstrated improvements in exercise capacity measures, indicating more effective exercise training occurred, however impact on levels of PA was not measured. It appeared that supervised exercise may have more effect on exercise capacity in CYPwCF than independent exercise although unfortunately there was a lack of research investigating the impact that supervised exercise interventions have on levels of PA participation.

Nevertheless, supervised exercise interventions are more costly, both in terms of time and money, to implement in clinical practice, and UK CF centres have limited resources to be able to provide that level of support to their patient group. In fact, a survey conducted in 2010 demonstrated that many UK CF centres struggled to offer any patient-specific exercise training programme at all (Stevens et al., 2010). Researchers and clinicians have investigated innovative solutions to this problem (Hebestreit et al., 2018). For example, Cox et al. (2015) developed an internet-based PA promotion programme for adults with CF. This study was limited by a small sample size (n = 10) but participants rated acceptability highly with median score for perceived benefit of 4.0 on a 5-point Likert scale. Feasibility was also relatively high with median score for desire to use the programme of 3.5.

Another example of an innovative part-solution to this healthcare service limitation is the public-private collaboration between a CF unit and a UK fitness provider (Rand et al., 2012, Douglas et al., 2016a). Since 2011, CYPwCF receiving care from the Great Ormond Street Hospital (GOSH) CF unit have been able to access free gym membership and personal training (for CYP aged >5years) at a Nuffield Health and Wellbeing Centre. Between 2011 and 2016 the number of collaborating centres increased from 5 to 17, with membership increasing to more than 100 CYPwCF and more than 1850 personal training sessions attended. In 2017, this scheme was

extended to a further 4 paediatric CF units and plans put in place to expand to provide access to Nuffield Health exercise facilities to all CYPwCF in the UK (Nuffield Health, 2018).

However, supervised exercise programmes are not effective for all CYPwCF (Nixon et al., 2001, Gruber et al., 2011, Douglas et al., 2016b). The wide variations in levels of participation are likely to be a reflection of the varying exercise motivations and abilities in the population of CYPwCF. The available evidence suggested that longer-term support might aid maintenance of PA participation.

2.4.1 Maintaining physical activity and exercise participation

It has been acknowledged that the health benefits associated with PA and exercise only last as long as participation is maintained (Prasad and Cerny, 2002, van Sluijs et al., 2011). Thus it is important to understand the patterns of maintaining PA and exercise participation in CYPwCF in order to help identify the factors impacting PA maintenance in individuals in the future. Despite the increasing volume of literature examining PA and exercise interventions, less is known about patterns of PA maintenance. van Sluijs et al. (2011) were unable to draw clear conclusions about the longer-term effect of the family- and community-based CYP PA intervention studies considered in their review. Only 3 of the 10 reviewed studies included follow-up for longer than 6 months post-intervention, and only 1 of those demonstrated a significantly positive intervention effect. More specifically to the CF population, Kriemler et al. (2013) carried out 24 months of follow-up testing of the adolescent and adult participants involved in their partially supervised exercise intervention study. The intervention consisted of either 3x week strength or aerobic exercise training, either in a gym or the participant's home. Trainers were present for a minimum of 1x week gym-based sessions, and all participants received monthly telephone support for their exercise training. This was continued for 6 months, after which participants were asked to continue with the same exercise programme independently for a further 6 months during which time no support was available. The authors concluded that the positive effects of both strength and aerobic training on lung function measures, and aerobic training on aerobic capacity, were all lost by the 24-month stage. This suggested that either some

independent participation was maintained for a short duration but not longer-term, or that participation continued but effectiveness of training reduced without even partial-supervision.

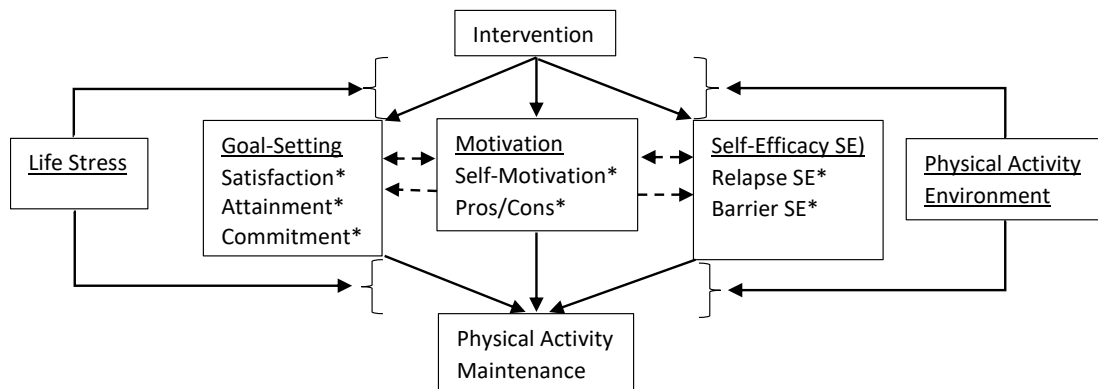
Happ et al. (2013) conducted a study exploring the perceptions of children with CF and their parents about an unsupervised, home-based exercise programme. The intervention involved static cycling 3x week for 6 months, during which time the researchers provided weekly telephone support. Participants were then encouraged to continue training for an additional 6 months without telephone support. The research team reported that participant motivation had already fallen by the end of the first 6 months of the programme, and approximately half planned to decrease or stop the training at this stage. The small sample size ($n = 11$) was common for qualitative research, but limited transferability of the findings. However, the message vocalised by the participants and parents that they did not wish to continue training must be considered. It could be that the cycle training was not engaging enough for CYPwCF to carry out alone over a longer time period, or that the lack of support did not encourage engagement. It was possible that the participants compensated for the decrease in activity associated with stopping the cycle training by introducing an alternative activity, however there was no evidence of this. Either way, it is sensible to anticipate these issues, and future research exploring the value of support for and interest in the training could help clarify the important elements of a training programme to help maintain engagement.

However, the novelty, or more importantly its short-term value, of even the most engaging of interventions is significant. Howe et al. (2016) reported on the use of an augmented reality game, *Pokemon GO*TM, which involves collecting virtual characters from real-world locations, and is played on mobile devices. The game incentivises walking by releasing more characters with walking distance covered. The authors reported that the game had a positive impact on the 560 participants in their survey. In the 4 weeks before downloading the game, participants achieved on average 4256 (SD 2697) daily steps. This increased to 5123 (SD 3371) by the end of the first week of play, but this positive effect then gradually declined so that by 6 weeks after installing the game, daily step count had returned to baseline levels.

This provided evidence that participants had not used a different form of PA in lieu of the one they had stopped, as the outcome measure (step count) used in this study enabled collection of PA data by any activity. This indicated that a novelty engagement may help with initiating a change in activity, but alone is not sufficient to maintain participation. Appropriate and relevant theoretical frameworks may assist in developing a deeper understanding of the correlates and predictors for PA maintenance.

2.4.2 Theoretical frameworks

Theorists have proposed many different theoretical frameworks during the process of trying to improve knowledge and understanding of the complexities involved with facilitating behaviour change in relation to PA and exercise (Nigg et al., 2008). Whilst a number have been more commonly discussed in the development of some interventions, such as trans-theoretical model (TTM) which includes stages of change (SOC), the health belief model (HBM), the social cognitive theory (SCT) and theory of planned behaviour (TPB) (Nigg et al., 2008, Lovell et al., 2010, Akerberg et al., 2017), and the youth physical activity promotion model (YPAP) specifically related to CYP (Welk, 1999), less consideration has been given to the maintenance of behaviour change. Nigg et al. (2008) discussed the limitations of these theoretical models in relation to the maintenance of PA behaviours. Behaviour maintenance has been defined by Kwasnicka et al. (2016) as ‘the continuous performance of a behaviour following an initial intentional change at a level that significantly differs from the baseline performance in the intended direction’. In this instance, the maintenance of adequate levels of PA in CYPwCF may involve a change in behaviour to increase levels of PA to those that result in health and well-being benefits for some CYPwCF, but for others maintaining current behaviour of already satisfactory levels of PA is required. By proposing a new model focusing solely on PA maintenance, the physical activity maintenance model (PAM), Nigg et al. (2008) integrated all relevant individual, inter-personal and community factors (see Figure 1).



* Constructs specific to maintenance of physical activity which may be correlated to each other.

Figure 1: The physical activity maintenance model (PAM), (Nigg et al., 2008)

This model identified the constructs that may be relevant for maintaining PA, and highlighted the intricate interactions that exist between them. The difficulties that have already been discussed in relation to PA and exercise participation for CYPwCF may result in an even more complex picture. The impact of their CF disease and treatment on their confidence and independence, and the additional impact of parents and clinical teams, as yet is not well understood or documented.

2.5 Summary

The literature discussed in this review has demonstrated that CYPwCF experience physical health and well-being benefits as a result of PA and exercise. PA and exercise interventions can be effective for CYPwCF who are able to engage in the intervention, thus demonstrating that appropriate PA and exercise can have positive health effects. Nevertheless, these benefits are only experienced for as long as participation is maintained. Less is known about the impact to health and well-being, as well as PA maintenance, once an exercise intervention is withdrawn.

Patterns of exercise and PA in CYPwCF appear to be relatively similar to the non-CF population. However, the known sex-based and age-related differences in maintaining PA participation, with boys taking part more than girls and levels of participation falling with age, are concerning. Furthermore, studies describing the levels of PA in CYP generally report group-level results. In these instances, the detailed and varied patterns of participation of individual CYP is hidden.

Barriers and facilitators to PA and exercise are well documented. But, approaches to tackle the concerning fall in participation need to be specific to address the complexities that exist for CYPwCF. There are a set of CF specific challenges and motivations which must be considered. For example, when studying self-efficacy in CYPwCF, the impact of treatments, symptoms, exercise capacity limitations and isolation (resulting from guidance to prevent cross-infection) must be considered. Interventions can be effective but little evidence exists of long-term effect of maintaining PA participation. And, all reviewed studies fell short of long-term PA tracking, thus questioning whether true patterns of PA of CYP have been presented.

Engaging some CYPwCF in PA and exercise, and then changing exercise behaviours to maintain participation, remains notoriously challenging. Ensuring everyone with CF is able to experience the health and emotional well-being benefits of PA and exercise, and minimise the burden of their disease, is a key priority for the CF healthcare team. Offering opportunities and facilities to take part in physical activities does not result in positive behaviour changes in every CYPwCF. Intrinsic factors, such as cognition, emotion, temperament and motivation, influence whether a specific intervention will be effective for a specific individual. It is important for CF clinicians to be able to easily identify those who need more support to be active enough to experience health and well-being benefits. In addition, establishing the factors that contribute to maintaining PA and exercise participation is a priority to make future exercise interventions and service developments effective in the long-term.

2.6 Research question and overall aim and objectives of PhD

Having considered the literature discussed in this chapter and the PA maintenance model proposed by Nigg et al (2008), it was clear that different CYPwCF have different PA and exercise barriers, facilitators, motivators and opportunities. The researcher (HD) speculated that some CYPwCF might maintain PA and exercise participation consistently without encouragement, some would require more support such as a personal trainer or have levels of PA that vary over time, and others would not engage with PA and exercise at any cost, as well as a spectrum in

between. It was hypothesised that specific PA behaviour pattern clusters would exhibit specific and distinct characteristics of:

- Exercise capacity and capability
- Self-efficacy for PA
- Reported barriers to and facilitators for PA
- Impact of parents/carers
- Self-reported levels of PA participation
- Objectively measured levels of PA participation

By conducting this PhD research, the researcher anticipated being able to identify these clusters and establish if the maintenance of PA was predictable in CYPwCF. By enabling CF clinical teams to identify distinct groups of CYPwCF with distinct PA behaviour patterns, the appropriate levels of PA support and facilitation could be provided to enable each CYPwCF to participate in and maintain a PA and exercise programme as a routine part of their CF health management.

The research questions (Table 2) were developed in response to the identified deficits in the literature, the aims of the funding grant (see section 3.3 for details) and all stakeholders involved in this work.

Table 2: Gaps in the literature, research questions, study phase and chapter location

Gap in the literature	Research question	Study phase	Chapter location
The longer-term impact that exercise interventions have on the health, well-being and PA maintenance of CYPwCF	1. What happened to the health, well-being and PA maintenance of CYPwCF after withdrawal of a supervised exercise intervention?	Phase 1 Exploratory	4, 5 & 6
The barriers to and facilitators for maintaining PA in CYPwCF	2. What affects the maintenance of PA in CYPwCF?	Phase 1 Exploratory	4, 5 & 6
	3. What are the barriers to and facilitators for maintaining PA in CYPwCF?	Phase 1 Exploratory	4, 5 & 6
The extent to which CYPwCF maintain PA participation	4. What are the patterns and maintenance of PA over time in CYPwCF?	Phase 2 Confirmatory	7, 8 & 9
Predictors for maintenance of PA in CYPwCF	5. Can the maintenance of PA in CYPwCF be predicted?	Phase 2 Confirmatory	7, 8 & 9

Key: CYPwCF children and young people with cystic fibrosis, PA physical activity

The aims were to:

1. Develop a detailed understanding of the PA maintenance behaviours, and health and well-being impact, following a two-year long supervised exercise intervention,
2. Understand the barriers to and facilitators for the participation in and maintenance of exercise and PA in CYPwCF,
3. Identify the patterns of PA maintenance in CYPwCF over time,
4. Identify the predictors for exercise and PA maintenance behaviours in CYPwCF.

3 Study development

3.1 Introduction

A number of factors were involved in the development of this research study, to ensure that it answered the research questions identified in section 2.6 in a clinically meaningful way. This chapter is structured as follows:

1. Introducing the researcher,
2. Context within a wider body of work,
3. The patient and public involvement that has shaped the methodological decisions,
4. Methodology in the context of a pragmatic philosophy,
5. Detail of the mixed methods design,
6. Sequencing and priority weighting of each phase of work,
7. General methods employed throughout the study.

3.2 Introducing the researcher

This thesis was written from the perspective of a researcher who has many years of experience working as a clinical physiotherapist with CYPwCF. A significant proportion of this clinical work involved motivating and engaging CYPwCF to exercise and be physically active as part of the management of their condition. As well as providing this routine clinical care, the researcher also acted as an exercise trainer for an exercise intervention RCT, INSPIRE-CF, which was undertaken within the GOSH CF centre between 2012 and 2015. In addition to the significant role that PA and exercise have played in the professional life of the researcher, sport and exercise have always been a large part of her personal life. The researcher has therefore experienced first-hand the physical and psychosocial benefits that PA, sport and exercise can bring. This personal perspective could be considered an influencing factor for this research, with a potential for partiality, particularly when interpreting findings. Measures were put in place to ensure that the potential inherent bias was mitigated as far as practicable, for example double coding of qualitative data, discussion and checking of interpretation and findings with the supervisory team, and scrutinising the published evidence-base to compare

findings. However, the relevant personal and professional experience that this researcher has may also have enabled greater insight, and therefore facilitated a greater understanding of the participants, and their behaviours and attitudes.

3.3 Context

Despite the evidence identifying the value of PA and exercise for CYPwCF, it was apparent from the literature discussed in Chapter 2 that the levels of PA of many CYPwCF fell below recommendations. Therefore, it was likely that many CYPwCF were missing out on the potential health and well-being benefits associated with being physically fit and active. Whilst the impact of many exercise behaviour change interventions have been investigated (Cox et al., 2013), less was known about how best to support individuals to maintain effective participation over the lifespan. This has been identified as a point of research relevance by the CF community. In 2016, the James Lind Alliance initiative established a Priority Setting Partnership with the CF community, including people with CF, family and carers of people with CF, clinicians and researchers, in order to identify and prioritise the gaps in the evidence-base of managing CF. Two of the top ten research priorities identified by the James Lind Alliance Cystic Fibrosis research priority setting programme were:

- what are the effective ways of simplifying the treatment burden of people with CF;
- what effective ways of motivation, support and technologies help people with CF improve and sustain adherence to treatment (Rowbotham et al., 2017).

The concept of treatment burden was investigated further, and the Question CF research group identified that exercise and PA were rated amongst the top five most important treatments by people with CF and their families (Davies et al., 2019). Despite this, many CYPwCF remained unable to maintain participation.

As part of the CF Trust's research strategy, a number of Strategic Research Centres (SRC) were created with the aim of developing networks of researchers to work together to tackle particular aspects of CF (Cystic Fibrosis Trust, 2017c). The Youth Activity Unlimited SRC: PA, exercise, sport and recreation promotion for

adolescents with CF (<http://sshs.exeter.ac.uk/youthactivityunlimited/>) was developed to address the difficulties that CYPwCF have in maintaining PA and exercise participation. Specific aims were to:

- Understand patterns of PA in CYPwCF,
- Understand psychosocial and physiological barriers to exercise participation,
- Develop resources for CYPwCF, their parents and clinicians to help support PA and exercise participation (University of Exeter, 2016).

The researcher (HD) was funded by the Youth Activity Unlimited SRC, and therefore this study, and resultant thesis, were designed to contribute to the work of this SRC.

3.4 Patient and public involvement and engagement

CYPwCF and their families, and stakeholders (including the CF Trust, clinicians and the wider CF community) were involved from the outset of this research, with the aim of improving the relevance and applicability of the findings (Beresford, 2007, INVOLVE, 2012). They helped to:

1. Identify the value of predicting the maintenance of PA and exercise behaviours in CYPwCF,
2. Select the measurement tools used,
3. Develop the semi-structured interview schedules,
4. Review the participant and parent information sheets.

They were involved with all aspects of the project, and dissemination of findings (Cystic Fibrosis Trust, 2019). In addition, the opinions of practicing CF clinicians informed the aims and resultant design of the project. For example, CF clinicians discussed the importance of being able to identify whether someone was likely to maintain PA and exercise participation or not, and therefore the type and level of support that they require, at one of the annual UK CF Exercise Network meetings (Tomlinson et al., 2018).

3.5 Methodology

3.5.1 Research paradigms

Researchers should be aware of their own attitudes and system of beliefs to scientific investigation, and therefore to which research paradigm they most align. This will impact how a researcher asks research questions, and also how those questions should be answered. There are study design, sampling, data collection and analysis preferences associated with each research paradigm. The history of research philosophy and resultant paradigms will be discussed in the context of the current research study, focusing on three of the most commonly acknowledged paradigms: (post) positivism, constructivism and pragmatism (Teddlie and Tashakkori, 2009).

Historically, the positivist paradigm, later replaced by post-positivism, dominated the research field. Positivism was defined by Bowling (2004) as assuming 'that there is a single objective reality which can be ascertained by the senses, and tested subject to the laws of the scientific method'. Post-positivism addressed some of the criticisms of positivism by acknowledging the important role that value systems can play in how a researcher conducts research and interprets data. However, post-positivists believe that the impact of a researcher's value system on their research can be controlled (Teddlie and Tashakkori, 2009). These paradigms are linked to quantitative methodologies, and use the hypothetico-deductive model as their basis (Teddlie and Tashakkori, 2009). The hypothetico-deductive model describes a method of investigation whereby a hypothesis is derived from a theory or conceptual framework, and numerical data and statistical analyses are used to test the hypothesis. Positivists, and more recently post-positivists, have limited ability to investigate the meaning of phenomena because the methodologies can only measure objectively, i.e. they are confirmatory in nature. Thus, for this research focus, human behaviour would occur as a result of an extrinsic cause, a hypothesis could be constructed identifying this cause, and this could be tested to confirm or refute this as fact. Criticism of this deductive approach in the 1950s and 1960s led to the development of an alternative paradigm: constructivism (Teddlie and Tashakkori, 2009, Morgan, 2007).

Teddlie and Tashakkori (2009) described constructivism as ‘the view that researchers individually and collectively construct the meaning of the phenomena under investigation’. This paradigm is linked to qualitative methodologies. Constructivists believe that the values of both researcher and participant impact observations, and that research methodologies must incorporate an understanding of those being studied. Because reality is multiple and constructed, it is not possible to identify cause from effect, and only individual, rather than general, statements are possible (Teddlie and Tashakkori, 2009). Qualitative research, aligned with constructivism, is exploratory and inductive in nature. This offers limited insight for the focus of this research, and may lead to a process of exploration without confirmation.

It is clear that the philosophies of (post) positivism and constructivism are fundamentally opposed, thus limiting researchers to one or the other. This caused some disagreement amongst scientific philosophers and thus a third paradigm was presented to dispel the either/or debate (Teddlie and Tashakkori, 2009, Greene et al., 1989, Morgan, 2007, Creswell, 2010). Teddlie and Tashakkori (2009) described pragmatism as embracing ‘superordinate ideas gleaned through consideration of perspectives from both sides of the paradigms debate in interaction with the research question and real-world circumstance’. It is with this philosophy in mind that the stated research questions, and therefore study design and approach, have been developed.

3.5.2 Pragmatic approach

The fundamental philosophy of pragmatism is that the subject matter should be viewed in terms of its practicality and use, and that the research question is at the centre of all decisions. The researcher is then able to choose to use inductive and deductive reasoning, and that both may be considered in different phases of the research process. The pragmatist will use quantitative or qualitative methodologies, or both together, to address the research question with action rather than philosophising taking priority (Teddlie and Tashakkori, 2009). They believe in, and occupy, the middle ground of the previous either/or paradigm debate, and have

adopted the practical approach of ‘what works’, using all quantitative and qualitative methodologies (Morgan, 2007, Morgan, 2014, Biesta, 2010).

3.5.2.1 Epistemology and ontology

The nature of this research required an interactive relationship between researcher and participants to answer the research questions. This was important for the early stages in order to explore the barriers to and facilitators for maintaining PA participation. However, other parts of this research, such as identifying clusters of PA maintenance behaviours with quantitative data, did not require interaction. This is in line with pragmatic philosophy (Teddlie and Tashakkori, 2009).

Whilst (post) positivists believe in realism, or the existence of one true reality which is value-free, and constructivists believe in multiple constructed realities, pragmatists consider that there is an external reality, but that there may be multiple explanations of reality and that best explanations involve personal value systems. This, along with the practical ‘what works’ approach to tackling research questions, means that pragmatism is associated with mixed method study designs (Morgan, 2007, Denscombe, 2008, Tashakkori and Teddlie, 2010). This study was exploratory and confirmatory, first exploring the factors that affect the maintenance of PA in CYPwCF (addressing research questions 1-3) and then confirming the theories developed from phase 1 by investigating the predictability of maintenance of PA in CYPwCF in phase 2 (addressing research questions 4 and 5). Thus, the study design was most aligned with the pragmatic approach using mixed methods (Teddlie and Tashakkori, 2009). This has facilitated methodological opportunities and enabled decisions to be made in response to each research question.

3.5.3 Mixed methods study design

Tashakkori and Creswell (2007) defined mixed methods research as ‘research in which the investigator collects and analyses data, integrates the findings, and draws inferences using both qualitative and quantitative approaches or methods in a single study or program of inquiry’. This approach is advantageous as the combination of data from contrasting methods and findings from multiple data sources can produce a more complete picture of the phenomena. In addition,

biases inherent to particular single-method approaches can be avoided thus improving data accuracy (Denscombe, 2008, Tashakkori and Teddlie, 2010, Morgan, 2014). For this project, neither qualitative nor quantitative methods alone would have been able to generate the rich, thorough and rigorous data required for a full investigation into the maintenance of PA behaviours in CYPwCF. Therefore, a mixed methods approach was required to combine and integrate the strengths of both qualitative and quantitative data and analyses, and enable a detailed and thorough exploration.

A number of different mixed method study designs have been described, identifying the study structure by considering the sequencing of the phases of work, the level of priority given to the quantitative and qualitative elements, and the stage at which different data or findings are integrated (Teddlie and Tashakkori, 2009, Creswell and Plano Clark, 2011). This study used an exploratory sequential mixed methods approach to facilitate a comprehensive investigation into the maintenance of PA behaviours in CYPwCF (Creswell and Plano Clark, 2011). There were 2 phases of work. The first phase explored the maintenance of PA, impact on health and well-being and the perceptions of barriers to and facilitators for the maintenance of PA in CYPwCF who had experienced the withdrawal of a supervised exercise intervention. The second phase set out to confirm ideas developed from the Phase 1 work by identifying objectively measured patterns of PA maintenance in CYPwCF and then establishing if those patterns could be predicted.

3.5.3.1 Study sequencing

The sequencing of this study can be seen in Figure 2. One difficulty with mixed method research is the time and resources required to conduct a thorough study where each phase of work informs the next. However, the pragmatic philosophy with which this study was carried out enabled some strands of work (3 parts in phase 1) to be carried out in parallel, to limit burden to participants (detailed in section 4.1), and then some sequentially (phase 1, followed by phase 2). This was conducted with the assumption of mutual relevance, therefore findings of phase 1 informed phase 2, but both phases contributed to the key findings of the whole research project.

The first phase of work used an inductive approach, and addressed research questions 1-3, with main findings presented in chapter 5 and discussed in chapter 6. It began with observations, and built ideas and a testable hypothesis. This informed the second phase during which the hypothesis was tested and research questions 4 and 5 were addressed. The main findings of the second phase of work are presented in chapter 8 and discussed in chapter 9. The integrated interpretation, or triangulation, of the findings is discussed in chapter 10. Chapter 10 also provides a conclusion to the study, summarises implications and suggests further research. Comprehensive explanation of the methods used in each phase and element of work is presented in chapters 4 and 7.

3.5.3.2 Priority

The level of priority given to each phase of quantitative and qualitative data collection and analysis can vary with different mixed method approaches (Creswell and Plano Clark, 2011). This project attributed equal weighting to the 3 studies of phase 1 in informing phase 2. Phase 1 investigated what happened to a group of CYPwCF who had previously taken part in an exercise intervention study, particularly considering their exercise maintenance, and explored the barriers and facilitators to exercise in the same group of CYPwCF and their parents. The 3 studies within phase 1 investigated different aspects of exercise maintenance, all of which contributed to the theory being tested in phase 2. There was no evidence from previous literature that 1 aspect had a higher level of importance, thus equal weighting was attributed. Phase 2 then tested the developed theories in a new and larger sample, identifying objectively measured patterns of PA maintenance and establishing if patterns could be predicted by 3 simple clinical outcome measures.

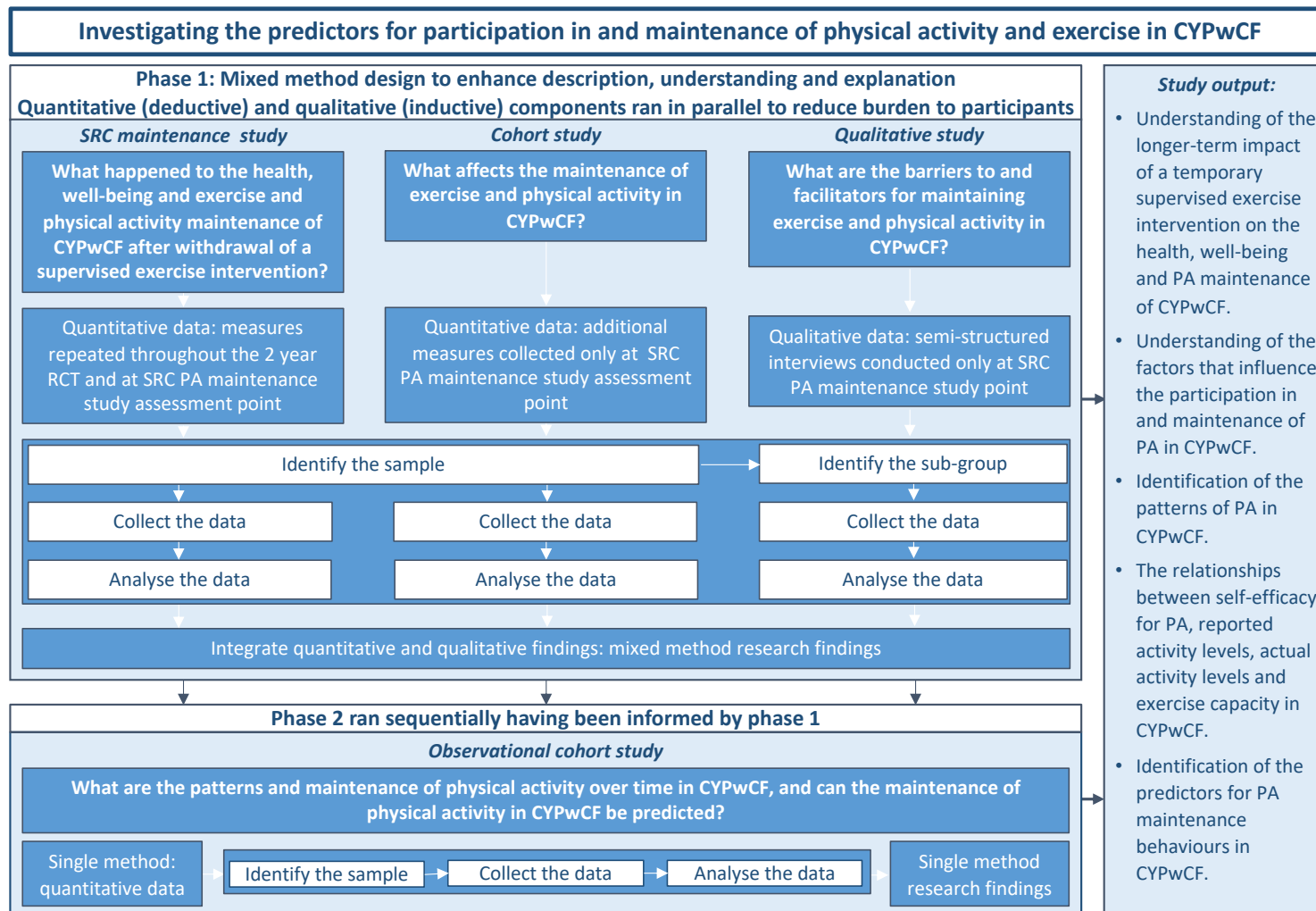


Figure 2: Diagrammatic representation of study sequencing

3.6 General methods

Some general and common methods were used throughout this study. Detail of the specific methods employed for individual study phases is provided in the relevant chapters (chapters 4 and 7).

3.6.1 Study design

The overall exploratory sequential mixed methods approach to the research addressed in this thesis was conducted in 2 phases. Phase 1 consisted of 3 parts.

- a) The SRC PA maintenance study: this longitudinal study investigated the impact that the withdrawal of a supervised exercise intervention had on the health, well-being and PA maintenance in CYPwCF,
- b) This cohort study investigated what affected the maintenance of exercise and PA in CYPwCF who had previously experienced a supervised exercise intervention,
- c) This qualitative study explored the exercise and PA experiences of CYPwCF who had experienced a supervised exercise intervention, and their perceptions of barriers to and facilitators for maintaining PA.

Participants were recruited to phase 1 from 1 London CF centre.

Phase 2 was a single observational cohort study which identified patterns of PA maintenance in CYPwCF and whether those patterns were predictable by 3 simple clinical outcome measures. Participants were recruited to phase 2 from 3 London CF centres thus reducing the risk of bias that a particular clinical team or CF management approach might introduce.

3.6.2 Study population

This research focused on CYPwCF. CF clinicians working at specialist CF centres identified participants using the following inclusion criteria:

- Diagnosis of CF based on clinical features and supported by an abnormal sweat test, and where possible, the identification of CF-causing genotype,
- Parent/guardian able and willing to give informed consent,

The following exclusion criteria were applied to both phases of work:

- CYPwCF who had undergone lung transplantation,
- Presence of a clinically significant medical condition other than CF,
- CYPwCF or parent/guardian unwilling or unable to sign consent/assent to participate in the study,
- CYPwCF unable to understand or answer questionnaires in English with verbal support.

3.6.3 Ethical considerations

3.6.3.1 *Risks and burdens to participants*

There were no anticipated intrusive risks or excessive burdens to taking part in any part of this research. Participation, however, may have been demanding of each participant's time. Each participant only attended the hospital on one occasion for phase 1 of this study. Every effort was made to ensure this was during a routine admission or a clinical visit, however if a participant and his or her parent/carer requested an appointment at a different time from planned clinic visits then the researcher accommodated this. Participation in phase 2 was offered as either a face-to-face appointment at the relevant hospital, timed with a routine admission or clinical visit, or as a telephone call, arranged at a convenient time for the participant and a parent/carer.

For phase 1, participation took 30-60 minutes, and involved completing three questionnaires and an exercise capacity test. The results of the exercise capacity tests were also used for routine clinical monitoring thus reducing participant burden further by completing additional repeated tests. A sub-sample also completed a semi-structured interview as part of phase 1, ranging from 10-40 minutes duration. For phase 2, participation involved completing two questionnaires taking 15-30 minutes to complete. Burden was minimised by utilising activity tracker and exercise capacity test data collected in conjunction with another research study.

Provisions were made that if a participant reported health or psychological concerns whilst participating in any part of the study they would have been advised by the researcher to contact the CF clinical team. The researcher would have also

referred the participant to the relevant member of the CF clinical team and the participant made aware of this action. However, no such health or psychological concerns were reported.

3.6.3.2 Potential benefits to participants

There were no direct benefits to participants for taking part in this study. Participants may have gained an increased understanding of their own PA and exercise patterns, behaviours and participation, or a more general awareness of the importance of PA and exercise in CF. It was possible that this may have had positive health consequences either immediately or in the future. Participants may have found it rewarding to participate in research that aimed to benefit other individuals with CF.

3.6.3.3 Confidentiality and GDPR compliance

All data were de-identified for storage and analysis. Any information given to the research team was not discussed outside of the research team, or between group members unless necessary. However, if there was any indication that a participant was a risk to themselves or to others then confidentiality would have been broken, and participants made aware of this. In this event, after informing the participant, the researcher would have discussed the issue with the relevant body (i.e. member of the healthcare team). However, no such concerns occurred.

No record of participants' names were kept with any data generated. Each participant was assigned a phase-specific code, and the records of codes and names were kept separately. This allowed the data to remain anonymous but enabled the identification of participants if necessary. Direct but anonymised quotations from the participants in the semi-structured interviews have been included in this thesis. Any data published were not personally identifiable.

3.6.4 Study procedure

3.6.4.1 Participant recruitment

CYPwCF who met inclusion and exclusion criteria were invited to participate in the specific study phase by a clinical physiotherapist from the relevant CF centre.

Approved age appropriate information sheets and parent/guardian information

sheet (Appendix 1 for phase 1 and Appendix 2 for phase 2) were sent, along with an invitation letter. The researcher then contacted the potential participant and parent/guardian to explain the project purpose and procedures in more detail, why they were being asked to consider participation in the project, and the associated risks, burdens and benefits. They were then given an opportunity to ask any questions. The potential participant and the parent/guardian were given at least 48 hours to discuss and make a decision as to whether to participate or not. If consent was agreed a consent form was completed and a copy offered for the parent/guardian to keep (Appendix 3 for phase 2, N.B. consent for phase 1 was already granted as part of the original consent to participate in INSPIRE-CF therefore no consent form was required for this PA maintenance assessment work).

Most participants were unable to give their own consent to participate due to their age. Therefore, a parent/guardian provided consent, and participants provided assent in concordance with the legal requirements in England as set out in the Children Act 1989 and Medical Research Council (2004) MRC Ethics Guide, medical research involving children (Appendix 4 for phase 2, N.B. consent for phase 1 was already granted as part of the original consent to participate in INSPIRE-CF therefore no assent form was required for this PA maintenance assessment work).

3.6.4.2 Data collection

All data were collected in line with the relevant policy or standard operating procedure for each outcome measure. Standardised instructions were used for implementing questionnaires and functional tests. All testers received training on the use of each outcome measure prior to collecting any data. This ensured appropriate and optimal use of each outcome measure to facilitate collection of reliable data.

3.6.4.2.1 Participant information

General demographic information was gathered about each participant from his or her medical records. This included date of birth, sex, genotype and lung function (measured by spirometry). These data were collected to demonstrate how the study samples compared to the wider CF population. In addition, spirometry data were used as an indication of disease severity.

3.6.4.2.1.1 Age

Decimal age was calculated (to the nearest 0.1 year) between date of testing and date of birth.

3.6.4.2.1.2 Anthropometric measurements

Height in centimetres (cm) and weight in kilograms (kg) were routinely recorded at all CF clinic visits and during hospital admission as part of the spirometry test procedure. These were measured in line with the CF centre lung function laboratory protocols, and used to calculate body mass index (BMI) using the following equation:

$$BMI = \frac{weight (kg)}{height (m^2)}$$

3.6.4.2.1.3 Genotype

It is well recognised that F508del is the most commonly identified mutation in the UK CF population, with 49.3% carrying 2 copies (UK Cystic Fibrosis Registry, 2019). Of the remaining 50.7% of the UK CF population, 40.5% carry 1 copy of F508del and another mutation, and 10.2% have two other mutations. Whilst it was important to demonstrate how representative the study samples were of the general UK CF population, the implications of specific genotype were not examined. There was concern that further identification of genotype could risk compromise to anonymity of participants, therefore 3 categories were used for classing genotype: homozygous for F508del, heterozygous for F508del, or no copy of F508del.

3.6.4.2.1.4 Lung function

Spirometry, conducted as part of routine CF clinic visits or during hospital admissions, was used to describe the samples throughout both phases of this study, and as an outcome in phase 1. Spirometry was performed according to the CF centre lung function laboratory protocols, in line with European Respiratory Society (ERS) and American Thoracic Society (ATS) standards (Miller et al., 2005). Predicted values and z-scores for FEV₁ were calculated using the Global Lung Initiative reference equations (ERS Task Force Report, 2012). The percentage of predicted FEV₁ (ppFEV₁) was used to classify disease severity: >70% indicated mild disease,

≥40-70% indicated moderate disease, and <40% indicated severe disease. FEV₁ z score was used as an outcome measure for phase 1.

3.6.4.3 *Practical considerations*

Due to the significant risk of cross-infection of respiratory pathogens between people with CF, the routine strict clinical infection control practises were followed to minimise risk to study participants. These included:

- Research appointments being scheduled with enough time between to avoid contact between participants,
- Rooms used for data collection, including all contents, equipment and furniture, were cleaned with wipes designated for use in clinical areas,
- Rooms were left vacant and open to ventilate for at least an hour between use.

3.6.5 *Data analysis*

Various statistical techniques have been employed throughout this thesis, detailed in the phase specific methods chapters (4 and 7). All analyses were conducted using IBM SPSS Statistics 24 (IBM Corp., Armonk, NY, USA), with the exception of 1 component of analysis in the SRC PA maintenance study (Part A) of phase 1 and 2 components of analysis in phase 2 which were conducted in R (R Foundation for Statistical Computing, Vienna, Austria). Normality of data were assessed using Kolmogorov-Smirnov normality test (with Lilliefors Significance correction). Normally distributed data were described using mean (M) and standard deviation (SD), whilst non-normally distributed data were described using median and inter-quartile range (IQR). Non-normally distributed data were either analysed using an appropriate non-parametric test, or, when appropriate, data were transformed to achieve normality.

The initial *p*-value indicating statistical significance was set at 0.05. However, post-hoc corrections were required for some elements, therefore the specific *p*-value threshold for each element was adjusted accordingly.

Effect sizes were calculated using the following equations:

- For paired samples comparisons (paired samples t-test):

$$Eta\ squared = \frac{t^2}{t^2 + (N-1)}$$

- For independent samples comparisons (independent samples t-test):

$$Eta\ squared = \frac{t^2}{t^2 + (N1+N2-2)}$$

- For independent sample comparisons (Mann-Whitney U test): $r = \frac{z}{\sqrt{N}}$

Where t = t value, N = number, z = z score

Criteria proposed by Cohen (1988) were used to interpret effect size values and correlation coefficients (Table 3).

Table 3: Effect size criteria (Cohen, 1988)

	Effect size		Correlation coefficients
	<i>Eta squared</i>	<i>r</i>	<i>r</i>
Small	0.01	0.1	0.10 – 0.29
Medium	0.06	0.3	0.30 – 0.49
Large	0.14	0.5	0.50 – 1.0

3.6.5.1 Comparison by age, sex and disease severity

Comparisons by age, sex and disease severity were considered throughout this research. CF lung disease is progressive, with expected deterioration in lung function through life. It is well documented that life expectancy is reduced in females compared to males (UK Cystic Fibrosis Registry, 2019). Therefore, CF health status is related to age and sex, and may impact exercise capacity and PA participation and maintenance. However, health status is known to vary between individuals, even with similar age, sex and genotype characteristics. Therefore, it was important to identify health status using percent predicted of FEV₁ (ppFEV₁) to explore impact on outcomes. In addition, it has been recognised that PA participation differs between males and females, and declines in both sexes (as discussed in section 2.3), thus it was important to consider impact of age and sex during both phases of this study.

3.7 Summary

This chapter presented the context of the study, including the researcher, and the philosophy and rationale for the selected methodology. It identified why the mixed methods approach was deemed by the researcher to be the most appropriate. It described that this study design facilitated the detailed exploration enabled by the qualitative elements, and then further generalised understanding with the quantitative components of work (Creswell and Plano Clark, 2011, Miles and Huberman, 1994, Ivankova et al., 2006, Greene et al., 1989, Morse and Niehaus, 2016, Tashakkori and Creswell, 2007, Teddlie and Tashakkori, 2009).

Methodological processes common to both phases of the study were presented, including the study population, ethical considerations, participant recruitment, data collection and data analyses. The methodological overview presented in this chapter will form the foundation for the discussion of the specific data collection, organisation and analysis procedures relevant to each phase of work that follows.

4 Phase 1 Methods

As discussed in chapter 2, there was clear evidence that supervised exercise programmes could have a positive effect on health, well-being and PA maintenance for CYPwCF. However, there remained limited evidence about how long those benefits are sustained once an intervention is withdrawn, as well as the positive and negative factors affecting the maintenance of PA. Phase 1 of this programme of research aimed to investigate the health, well-being and PA maintenance of CYPwCF 13-38 months after withdrawal of a 2-year long, weekly, supervised exercise intervention, INSPIRE-CF. It aimed to assess whether this unique population managed to maintain levels of PA independently, and therefore any associated health and well-being effects, once the exercise training was withdrawn. The experience of participation in and subsequent withdrawal of the supervised exercise intervention enabled the participants to offer a deeper insight into the factors affecting the maintenance of PA than CYPwCF without this experience. In order to put the first phase of this research into context, the methods of the INSPIRE-CF study are briefly summarised:

- INSPIRE-CF was a two-arm, single centre RCT investigating the effects of a weekly-supervised exercise intervention on lung function, exercise capacity and quality of life for CYPwCF.
- All CYPwCF aged 6-14 years, with a wide range of lung disease severity, receiving care from the CF service at GOSH were invited to participate between late 2012 and early 2014 (n = 84).
- A total of 71 CYPwCF were recruited. Participants who were randomised to the exercise training group (n = 37) received a weekly supervised and individually prescribed 45-60 minutes exercise training session at a gym facility near to the participant's home, in addition to standard CF care.
- Participants in the control group (n = 34) continued to receive standard CF care, but not the additional supervised exercise training. In addition, 5 CYPwCF who had been part of a previous quality improvement initiative (the Frequent Flyer Programme (Ledger et al., 2013)) received the same exercise

training as the intervention group, and continued for the duration of INSPIRE-CF.

- Exercise capacity, lung function and quality of life were measured prior to randomisation at baseline, and then repeated at 1 and 2 years.
- By the end of INSPIRE-CF, 4 participants had withdrawn, therefore 67 INSPIRE-CF participants completed the testing at 2 years. The weekly training sessions were withdrawn after the 2 years assessment point, and standard CF care continued for all participants.
- Participants completed their two-year long involvement in INSPIRE-CF 13-38 months before this research.

By studying this population in detail at this point, the researcher was able to investigate whether any health, well-being and PA maintenance effects were sustained or lost after the exercise training was withdrawn, and any differences between the individual health, exercise and quality of life trajectories of this population, during and after a supervised exercise intervention. If trajectories varied then it would be valuable to be able to predict those variations in CYPwCF in the future. In addition, this population was able to offer a unique insight into the barriers to and facilitators for maintaining exercise and PA participation, and the factors affecting the maintenance of participation.

It should be noted that, since 2011, including the research period, all CYPwCF receiving CF care at GOSH also had access to free gym membership and weekly personal training as part of the GOSH-Nuffield programme. Discussed in chapter 2, this innovative exercise service was available to all CYPwCF cared for by GOSH, and was independent from participation in INSPIRE-CF. A total of 24 INSPIRE-CF participants had a GOSH-Nuffield programme membership (exercise training n = 13, control n = 11), however levels of participation in training were not known.

4.1 Study design

There were 3 components to phase 1 of this research (Figure 3) aiming to address research questions 1-3:

1. What happened to the health, well-being and PA maintenance of CYPwCF after withdrawal of a supervised exercise intervention?
2. What affects the maintenance of exercise and PA in CYPwCF?
3. What are the barriers to and facilitators for maintaining exercise and PA in CYPwCF?

The overall design was mixed methods with 2 quantitative studies and 1 qualitative study.

Part A (SRC PA maintenance study, a quantitative study) aimed to assess the impact that the withdrawal of the supervised exercise intervention had on measurable outcomes: exercise capacity, lung function, HRQoL and PA participation.

Part B (Factors affecting the maintenance of PA, a quantitative study) aimed to investigate the factors affecting the maintenance of PA including self-efficacy for PA, self-reported levels of PA and parent/carer reported barriers to PA.

Part C (Barriers to and facilitators for the maintenance of PA, a qualitative study) aimed to explore the exercise experiences of CYPwCF and their perceptions of the factors that helped or hindered the maintenance of PA.

The 3 studies were run in parallel to reduce the time and burden involved for participants in this clinical research, the participant journey is presented in Figure 4. This mixed methods approach enabled rigour in assessing the impact that withdrawal of the supervised exercise training had on measurable outcomes as well as investigating the factors affecting the maintenance of PA and exploring the barriers to and facilitators for the maintenance of PA. The 3 parts of phase 1 contributed to the integrated findings, answered research questions 1-3, and informed the second phase of work.

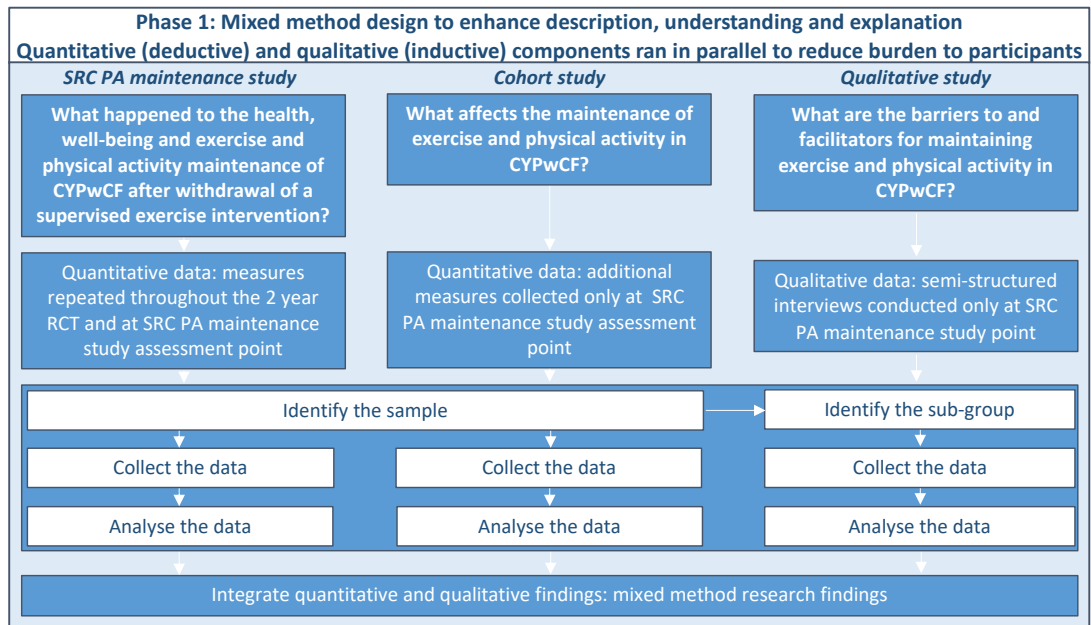


Figure 3: Diagrammatic representation of the 3 studies contributing to phase 1 of this research

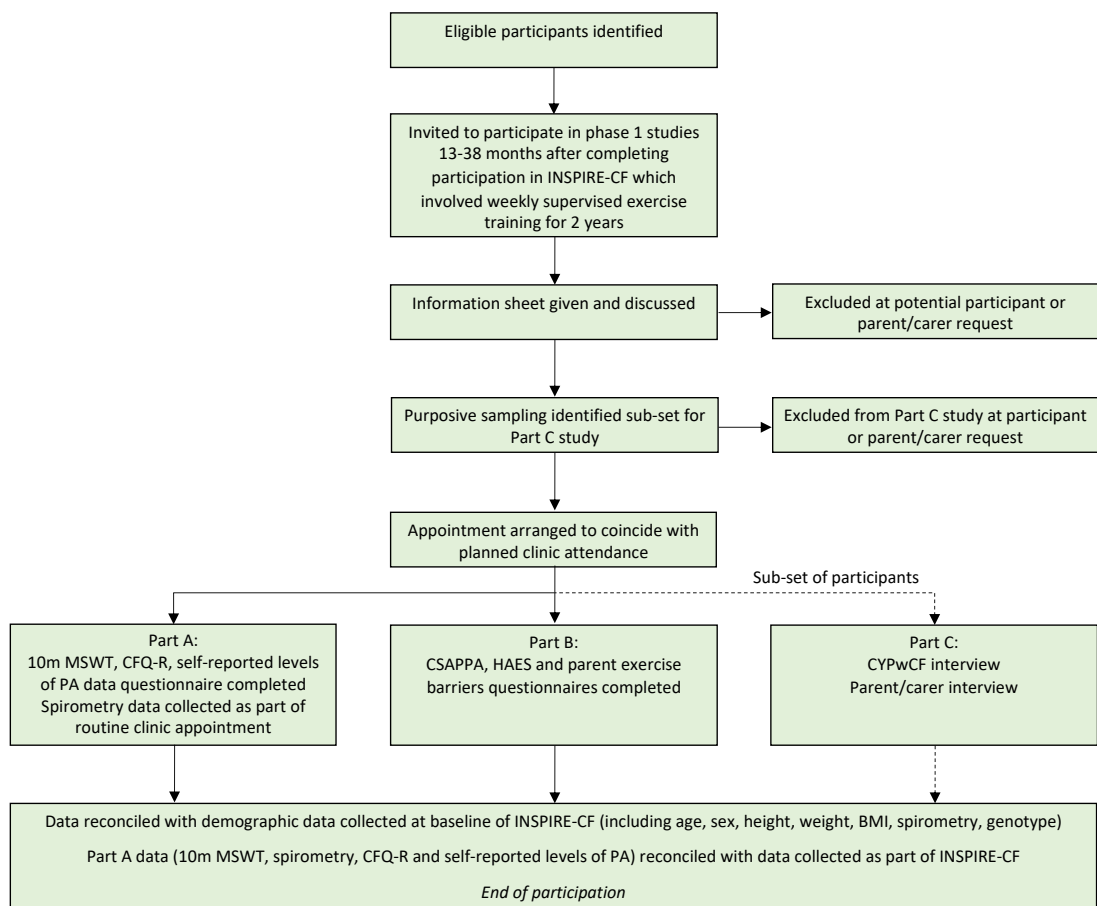


Figure 4: Flowchart detailing participation process for phase 1 of this project

4.1.1 Part A: SRC PA maintenance study

This section of work used a quantitative approach to investigate the health, well-being and exercise and PA maintenance of CYPwCF who had previously participated in INSPIRE-CF (research question 1). It was not known if the participants maintained PA and exercise participation following the end of the intervention. The researcher anticipated that some participants would have maintained PA and exercise participation after INSPIRE-CF ended, and that they would have continued to experience benefits associated with maintained participation, whilst others would have stopped exercising and benefits may, to some extent, have been lost. Part A aimed to examine the individual effects of the maintenance of PA, following the withdrawal from a weekly, supervised exercise intervention (INSPIRE-CF), on:

- functional exercise capacity, measured by an incremental walk/run exercise test, the 10m Modified Shuttle Walk Test (10m-MSWT),
- lung function, measured by spirometry, namely FEV₁,
- HRQoL, measured by Cystic Fibrosis Questionnaire-Revised (CFQ-R),
- self-reported activity levels, measured by a simple questionnaire.

These outcome measures were used throughout the INSPIRE-CF study, with assessment points at baseline, 1-year and end of study at 2-years. An additional 10m-MSWT was also conducted at 6-months into INSPIRE-CF. Therefore, the data collected from individual participants at each INSPIRE-CF assessment point were aligned with those collected as part of this PA maintenance study, and enabled the construction of health, well-being and exercise and PA maintenance trajectories for individual CYPwCF during and after INSPIRE-CF.

4.1.2 Part B: Factors affecting the maintenance of physical activity

It has been suggested that self-efficacy for PA may be an important indicator for PA and exercise participation and maintenance (Sallis et al., 2000, Spink et al., 2006, Moola et al., 2012, Patterson et al., 2016), thus it was important to investigate the self-efficacy for PA in CYPwCF. As discussed in section 2.3.1.2, the significant influence that parents have on the activity levels of their child has also been demonstrated, and therefore parents perception of exercise and PA for themselves

was important to consider in this population. The researcher expected that self-perceptions of adequacy and predilection for PA (self-efficacy), self-reported levels of PA, and parent/carer barriers to PA and exercise participation would all have an impact on the attitude to PA and exercise, and maintenance of PA in CYPwCF. The population of CYPwCF who had experienced the withdrawal of a supervised exercise intervention also participated in this Part B study. This cohort of CYPwCF could offer greater clarity about maintenance of PA status than a population of CYPwCF whose levels of PA, and therefore maintenance status, were unknown. This section of work used a cohort design to investigate the relationships between the self-efficacy for PA of CYPwCF, their self-reported levels of PA, barriers to their parents/carers own PA and exercise participation, and PA maintenance in CYPwCF (research question 2). The method of collecting self-reported levels of PA data used throughout INSPIRE-CF was a simple yet non-validated questionnaire. This method was repeated as part of the SRC PA maintenance study for consistency, but it was important to also collect self-report data using an appropriately validated tool. The Part B study aimed to:

- Investigate self-perceptions and parent-perceptions of adequacy and predilection for PA amongst CYPwCF (self-efficacy), measured by the Children's Self-perceptions of Adequacy and Predilection for Physical Activity (CSAPPA) questionnaire (Hay, 1992);
- Identify barriers to exercise amongst parents of CYPwCF, measured by an exercise barriers questionnaire (US Department of Health and Human Services, 1999);
- Examine the self-reported levels of PA in CYPwCF, measured by the Habitual Activity Estimation Score questionnaire (HAES) (Hay and Cairney, 2006).
- Explore the relationships between self-efficacy for PA (CSAPPA score), self-reported levels of PA (HAES score) and parent/carer barriers to PA and exercise (exercise barriers questionnaire score, and the maintenance of PA in CYPwCF.

4.1.3 Part C: Barriers to and facilitators for the maintenance of physical activity

This section of work used a qualitative approach to explore the psychosocial impact that participation in INSPIRE-CF had on the maintenance of PA in CYPwCF, and their barriers to and facilitators for the maintenance of PA. Average attendance to INSPIRE-CF exercise training sessions was $62\pm 14\%$ (mean \pm SD). However, patterns of attendance varied widely with individual ranges varying from 16% to 93%.

Therefore, this population were likely to be able to give an interesting and unique insight into the psychosocial limitations or barriers to, and facilitators for, PA and exercise participation and maintenance in CYPwCF (research question 3). This study aimed to:

- Explore the PA and exercise experiences of CYPwCF, particularly in relation to supervised exercise;
- Identify attitudes towards PA and exercise amongst CYPwCF and their parents;
- Explore barriers and facilitators to exercise and PA maintenance;
- Identify why some CYPwCF maintain participation but others do not.

Due to the significant impact that parents have on the levels of PA participation of their CYPwCF, separate interviews were conducted with CYPwCF and a parent/carer in order to explore the experiences, attitudes and perceived barriers and facilitators to PA maintenance from both perspectives. The researcher anticipated that trends may be identified between the exercise attitudes and experiences of CYPwCF and parents, and the barriers and facilitators to exercise and PA maintenance that they reported.

4.2 Study population

Of the 71 participants who were recruited to INSPIRE-CF, 4 did not complete the initial two years (1 control, 3 exercise training). Reasons for withdrawing from INSPIRE-CF were: re-locating and therefore change of CF care centre (n = 1), no longer wanted to exercise (n = 2), and other health problems (n = 1). Another participant completed INSPIRE-CF but received a lung transplant prior to this PA maintenance study and was therefore not eligible to participate. A total of 17

INSPIRE-CF participants were no longer receiving CF care from the GOSH CF service at the point of PA maintenance assessment. The majority (n = 16) had transitioned to adult care, and 1 had relocated so transferred to a different paediatric CF service. In addition, 3 of the 5 CYPwCF who completed the INSPIRE-CF exercise training as an extension to the Frequent Flyer Programme had also transitioned to adult services.

The remaining 51 participants were eligible for recruitment (49 INSPIRE-CF and 2 Frequent Flyer), and their parents/carers, were informed about phase 1 (Parts A, B and C) of this research by letter, and then contact made by telephone to invite them to participate. Appointments were made to coincide with a time that the CYPwCF and parent/carer were attending GOSH for an appointment. Consent and assent was covered by the original INSPIRE-CF trial, however all participants were given an information sheet (Appendix 1) for this study, and any questions raised were answered by the research team.

4.3 Funding

The CF Trust Youth Activity Unlimited strategic research centre funded the researcher. INSPIRE-CF, and the extension for this PA maintenance work, were funded by the GOSH charity.

4.4 Ethical approval and considerations

Approval for this work was granted with an amendment to the original application made for the exercise intervention RCT, INSPIRE-CF (Appendix 5). Ethics approval was granted by South East Kent research ethics committee (REC reference: 12/LO/1135, IRAS ID: 107522).

4.5 Part A: SRC PA maintenance study procedures

4.5.1 Sample

The 51 participants who had completed INSPIRE-CF and were still under the care of the GOSH CF unit were eligible and invited to participate in this SRC PA maintenance study (Part A). The recruitment process is detailed in section 4.2.

4.5.2 Data collected

The measurement tools used to collect data during INSPIRE-CF were repeated for this PA maintenance study, thus enabling direct comparison of the individual trajectories during and after INSPIRE-CF. These included:

- functional exercise capacity, measured by 10m-MSWT,
- lung function, measured by spirometry, namely FEV₁,
- HRQoL, measured by CFQ-R,
- self-reported activity levels, measured by a simple questionnaire.

4.5.2.1 Exercise capacity

Exercise capacity was measured as an indicator of fitness of the participants to help identify whether participants managed to maintain PA participation independently after the supervised exercise intervention was withdrawn. If exercise capacity was maintained or gained between the end of the INSPIRE-CF exercise training and the SRC PA maintenance study assessment point then it suggested that enough PA had been maintained to benefit physical health. However, if exercise capacity fell between the end of the INSPIRE-CF training and the SRC PA maintenance study assessment point then it was considered that PA had not been maintained.

The 10m-MSWT is an externally paced, incremental, field-based exercise test (Singh et al., 1992, Selvadurai et al., 2003). The 25-level version has been shown to be reliable and repeatable for people with CF (Elkins et al., 2009), and without ceiling effect, therefore it is useful for measuring near maximal functional exercise capacity. To date, there has been no evidence of the minimal clinically important difference (MCID) or minimal detectable change (MDC) in 25-level 10m-MSWT. However, del Corral et al. (2019) evaluated the MCID and MDC in the 15-level version of the 10m-MSWT in CYPwCF. As the 25-level 10m-MSWT is the 15-level version but with an additional 10-level extension, to eradicate any ceiling effect, it was appropriate to consider the results of this work. del Corral et al. (2019) identified an MCID of 60m in a small sample, however the MDC with 90% confidence intervals, detected in a larger study sample within the same programme

of work, was 97.08m. Therefore, it was safest to consider a change of 97.08m or more to be important (del Corral et al., 2019).

The 25-level 10m-MSWT was used as a measure of functional exercise capacity during INSPIRE-CF and the SRC PA maintenance study. As per test protocol, 2 cones were placed 9m apart on flat, even ground, with 50cm at each end for participants to pass around the cone. The standardised audio instructions were played to all participants before starting the test. All participants were familiar with the test having completed it as part of INSPIRE-CF testing previously, and during routine clinical care. Measurements included:

- distance covered (metres) and level achieved (Appendix 6),
- heart rate (HR) and oxygen saturation at baseline, end of test and 3-minute recovery (Nonin model 2500 pulse oximeter; Nonin Medical Inc., Plymouth, Minnesota, USA),
- rated perceived exertion (RPE) using OMNI scale at baseline, end of test and 3-minute recovery (Appendix 7).

The test was ended when the participant failed to complete 2 consecutive shuttles in time with the audio recording, or stopped voluntarily. Reasons for stopping were recorded. Peak HR and RPE were used as indicators of effort. The distance achieved during the test was used as the value of exercise capacity for analysis. With permission of individual participants, all 10m-MSWT test results were shared with the clinical CF team for use as part of ongoing clinical monitoring.

4.5.2.2 Lung function

Lung function data, measured by spirometry, were collected at each INSPIRE-CF assessment point and the SRC PA maintenance study. Details can be seen in section 3.6.4.2.1.4. FEV₁ is a key indicator of health status for CYPwCF. Therefore, FEV₁ z score was used as the indicator of lung function for analysis to understand the impact that maintaining PA participation had on the physical health of CYPwCF. To date, no MCID for FEV₁ z score has been agreed for CYPwCF, therefore analysis was limited to the discussion of any change, without a threshold of clinical importance.

4.5.2.3 Health-related quality of life

The CFQ-R is a validated disease-specific health-related quality of life measurement tool widely used as a clinical and research outcome measure with people with CF, to measure perceived impact on health, well-being and daily life (Henry et al., 1997, Quittner et al., 2000). There are three questionnaires: child (6-13 years), adolescent/adult (14+) and parent (<https://cfqr.github.io/>). The CFQ-R addresses a number of different domains, 7 of which are common across all questionnaires: physical, emotion, eating, body image, treatment burden, respiratory and digestion. Questions are answered using a 4-point Likert scale and generate scores for each HRQoL domain. The range is 0 to 100, with a higher score indicating better HRQoL. Only the respiratory domain has evidence of an MCID, where a change of 4.0 points is meaningful during a period of stable health (Quittner et al., 2009).

For the SRC PA maintenance study, each CYPwCF completed the age-appropriate questionnaire. There are significant and important discrepancies between CYP and parent perceptions of a CYP's HRQoL (Hegarty et al., 2008, Havermans et al., 2006, Tluczek et al., 2013, Groeneveld et al., 2012, Douglas et al., 2017). Only CYPwCF perception was considered for this study, as this was considered to be the most relevant for understanding what affects the maintenance of PA and exercise participation in CYPwCF. The maintenance of PA was considered to potentially impact physical, body image and respiratory domains, thus scores for these domains were considered relevant and analysed for this study. In addition, the presence and then removal of the supervised exercise intervention may have impacted on perception of treatment burden, therefore scores for this domain were also included in analysis for this study. It was hypothesised that if CYPwCF considered the supervised exercise intervention to be part of CF treatment and therefore was a burden then independent maintenance was less likely than if CYPwCF did not perceive the exercise intervention to be a burden or part of CF treatment.

4.5.2.4 Self-reported physical activity

At each test stage of INSPIRE-CF, participants were asked to record type, duration and frequency of regular weekly exercise and physical activities that they

participated in, thus this self-report method was continued in the SRC PA maintenance study to allow direct comparison (Appendix 8). Total weekly activity time in minutes was calculated for each participant, and used for analysis. This revealed the perceptions that CYPwCF had of their own maintenance of PA.

4.5.3 Data analysis

Almost all statistical analyses were conducted using IBM SPSS Statistics 24 (IBM Corp., Armonk, NY, USA). The generalised estimating equations (GEE) and associated analyses of covariance (ANCOVA) were run in R (R Foundation for Statistical Computing, Vienna, Austria) using the 'gee' package in R (Carey et al., 2019). Independent *t*-tests (for normally distributed continuous variables), Mann-Whitney U tests (for non-normally distributed continuous variables) and Chi-square tests (for categorical variables) were used to identify demographic characteristic differences between INSPIRE-CF participants who participated in the SRC PA maintenance study and those who did not, and also differences between control and exercise training groups amongst those who participated in the SRC PA maintenance study.

In order to examine the impact of PA maintenance on the health and well-being trajectories of CYPwCF, mixed between-within subjects analyses of variance (ANOVA) were conducted. These assessed the impact of the 2-year-long supervised exercise intervention on exercise capacity, lung function, HRQoL and self-reported PA level, and compared the impact of control and exercise training groups. The use of multiple ANOVAs increases risk of a Type I error, therefore a stricter α level of 0.01 was applied (Pallant, 2007, Tabachnick and Fidell, 2014). The mixed between-within subjects ANOVAs were limited to considering time as assessment point only. Further understanding of the impact of time considered continuously was required. Therefore GEE were run to enable comparison of the trajectories of control and exercise training groups for each variable, both during and after INSPIRE-CF. GEE takes account of the repeated measures over time, and incorporates the within individual variations (Ballinger, 2004). An independent covariance structure was selected because the participants were independent of each other. One-way between groups analyses of covariance (ANCOVA) were then conducted to

compare the change in trajectory for each variable and control/exercise training group combination from during INSPIRE-CF to after INSPIRE-CF. This also enabled the identification of those who maintained PA participation after the withdrawal of the supervised exercise intervention and those who did not.

4.6 Part B: Factors affecting the maintenance of physical activity study procedures

4.6.1 Sample

The 51 participants who had completed INSPIRE-CF and were still under the care of the GOSH CF unit, and at least 1 parent/carer per CYPwCF, were eligible and invited to participate in this Factors affecting then maintenance of PA study (Part B). The recruitment process is detailed in section 4.2.

4.6.2 Data collected

Three measurement tools were used to collect data for the Part B: Factors affecting the maintenance of PA study. These were completed at the same assessment appointment as the SRC PA maintenance study.

4.6.2.1 *Self-efficacy for physical activity*

The CSAPPA is a reliable and valid tool used to measure generalised self-efficacy for PA in children (Hay, 1992). Hay (1992) investigated test-retest reliability with 606 children aged 9-14years recruited from 3 schools in Ontario, Canada, tests were repeated after 2 weeks. The CSAPPA demonstrated good test-retest reliability, with correlation coefficients of $r = 0.84-0.90$ ($p < 0.001$) (difference by school year group). Internal consistency was also moderate to strong. Correlations between each item and the subtotal for each of the 3 factors (adequacy, predilection and enjoyment) ranged from 0.65 to 0.85 for appropriate factors and 0.27 to 0.59 for inappropriate factors. Hay (1992) also compared the CSAPPA scores to self-reported PA participation, teacher-reported PA participation and a motor competence score. Correlations were moderate to good and varied by school year group: self-reported PA participation $r = 0.45-0.73$, teacher-reported PA participation $r = 0.50-0.67$, motor competence score $r = 0.70-0.82$ ($p < 0.01$). These results suggested that the CSAPPA demonstrated moderate to good construct validity. Predictive validity was

investigated in 543 children aged 9-13years recruited from 2 schools in Ontario, Canada. Each participant completed the CSAPPA and a simple activity questionnaire which identified organised sports and free-play activity participation. Multiple stepwise regressions were used to predict organised sports and free-play participation from the 3 CSAPPA factors. Adequacy was the strongest factor for predicting organised sports participation: $r = 0.3008-0.5982$ ($p < 0.001$). Predilection was the strongest factor for predicting free-play participation: $0.6030-0.7788$ ($p < 0.001$).

Although the reliability and validity data were generated from CYP without identified health or developmental problems, and the CSAPPA has been predominantly used to-date as a screening instrument for Developmental Coordination Disorder (Hay et al., 2004, Grant-Beuttler et al., 2017), this measure was useful for this Part B study of CYPwCF as it generated a generalised self-efficacy score, as well as individual scores for each of the embedded factors: adequacy, predilection and enjoyment (Appendix 9). Questions are answered using a 4-point scale. Higher scores indicated greater self-efficacy for PA. Each participant in the Part B study completed the CSAPPA.

In the paediatric clinical setting, many conversations occur between parent/carer and clinician. Considering the known discrepancies between CYPwCF and parent/carer reported HRQoL (Douglas et al., 2017), it was important to understand both CYPwCF and parent/carer perception of the CYPwCF's self-efficacy for PA in order to assess whether similar discrepancies existed with this tool. Therefore, 1 parent/carer per CYPwCF also completed a parent version of the CSAPPA (Appendix 10). This reported the parent/carer's perception of the CYPwCF's self-efficacy for PA. Analysis was conducted on overall self-efficacy for PA scores, and for each domain, for both CYPwCF and parent/carer reported questionnaires.

4.6.2.2 Self-reported levels of activity

The HAES is a self-report questionnaire which generates an estimation of time spent in four different activity states (inactive, somewhat inactive, somewhat active, very active) for a typical weekday and a typical weekend day during the previous 2 weeks (Hay and Cairney, 2006). It therefore provides a summary of self-

perceived intensity and duration of activity (somewhat active + very active) per day for all waking hours (Appendix 11). There is evidence of reliability and validity in the CF population (Boucher et al., 1997, Schneiderman-Walker et al., 2005, Wells et al., 2008, Ruf et al., 2012, Paranjape et al., 2012, Schneiderman et al., 2013, Bradley et al., 2015). Wells et al. (2008) investigated the reliability of the HAES. A total of 14 children, young people and adults with CF completed the HAES on 2 occasions, 1 week apart. The authors reported statistically significant intraclass correlation coefficients (ICC) for time spent somewhat active (ICC = 0.55, $p = 0.0004$) and time spent active (ICC = 0.68, $p = 0.0001$) indicating moderate reliability. Schneiderman-Walker et al. (2005) and Wells et al. (2008) reported on convergent validity by comparing data generated by the HAES with data generated by activity diaries. Schneiderman-Walker et al. (2005) reported moderate agreement between data collected in summer ($r = 0.62$, $p < 0.002$, mixed model regression) but no statistically significant agreement for other seasons in 109 CYPwCF. Wells et al. (2008) also reported low to moderate agreement between HAES and activity diaries (ICC = 0.22-0.64, $p < 0.0001$) for time spent in different activity levels. When compared to accelerometer collected data, the HAES demonstrated relatively poor convergent validity: -2.3 to 2.9hours (limits of agreement) (Wells et al., 2008) and Pearson's product correlation of $r = 0.326$ ($p = 0.037$) for time spent in MVPA (Ruf et al., 2012). The study conducted by Ruf et al. (2012) reported non-significance for ICC from 41 CYP and adults with CF. Paranjape et al. (2012) compared time spent in MVPA for responders ($n = 30$) and non-responders ($n = 26$) to a 2-month long exercise regimen. The authors reported no significant difference in time spent in MVPA between responders and non-responders for weekdays, but a statistically significant difference for weekend days ($p = 0.03$, Wilcoxon signed-rank test) indicating limited discriminate validity. Data generated by the HAES have been found to correlate to other CF-related outcomes. Boucher et al. (1997) demonstrated moderate correlation between time spent somewhat active and active with body mass percentage (BMP) in 21 female CYPwCF (Pearson's product correlation: $r = 0.466$, $p = 0.033$), and this improved to $r = 0.675$ ($p = 0.023$) when just CYPwCF with severe airflow obstruction were included. Schneiderman-Walker et al. (2005) demonstrated a statistically significant but weak association between

weekday total activity time and peak rate of oxygen consumption (VO_2 peak) using mixed model regression ($r = 0.24$, $p = 0.02$). They also reported an association with FEV_1 decline for their female participants ($p = 0.02$) but not their male participants. In a later study, Schneiderman et al. (2013) identified a weak association between rate of change in total activity time (hours per day) and decline in FEV_1 in 212 CYPwCF over 9 years ($r = 0.19$, $p = 0.007$). Paranjape et al. (2012) demonstrated responsiveness of the HAES by comparing results before and after the 2-month exercise regimen in 59 CYPwCF. Using Wilcoxon signed-rank test, the authors reported statistical significance for both weekdays and weekend days ($p = 0.040$ weekdays, $p = 0.017$ weekend days). Despite the mixed reports of reliability and validity of the HAES, Bradley et al. (2015) reported in a position statement on PA assessment in CF that the HAES had the most conclusive reliability and validity data in the CF population compared to other self-report outcome measures, therefore this tool was used to measure reported activity levels in CYPwCF in this cohort study. Each CYPwCF completed the HAES with the assistance of a parent/carer and the researcher as required. Time identified as 'very active', defined by the HAES as requiring 'lots of movement and makes you breathe/sweat' was considered the most appropriate indicator of moderate-to-vigorous physical activity (MVPA). Each participant generated a value of time spent in MVPA in minutes for both a weekday and a weekend day. As with the CSAPPA, there was no published evidence of normative values for the HAES, but comparisons could be made within the study sample.

4.6.2.3 Parent PA and exercise barrier questionnaire

Naturally, parents or carers have a significant impact on the PA and exercise opportunities that CYP encounter (Trost et al., 1998, Davison et al., 2003, Edwardson and Gorely, 2010, Hennessy et al., 2010). As discussed in section 2.3.1.2, the evidence of the relationship between child and parent levels of PA was not conclusive, and there was a dearth of evidence investigating the link between parental attitudes to PA and the levels of PA in CYPwCF. Therefore, it was considered important to measure barriers to parent/carer exercise participation to further understand the impact of parent/carer PA and exercise attitudes on

CYPwCF, and whether there was a relationship between parental PA and exercise attitudes and the maintenance of PA in CYPwCF. In view of the lack of validated measures, a number of possible tools were reviewed. This included discussion with the parents of 2 CYPwCF who were not eligible to participate in this study, but were involved in the development of the project as part of the patient and public involvement and engagement (PPIE) process. Ease of completion was deemed to be the most important factor and therefore the Barriers to Being Active Quiz was used (US Department of Health and Human Services, 1999) (Appendix 12). As with the CSAPPA, this tool generated an overall score, and a score for each individual domain: lack of time, social influence, lack of energy, lack of willpower, fear of injury, lack of skill and lack of resources. Each parent/carer who attended with his/her CYPwCF for the phase 1 assessment appointment completed this questionnaire. However, the questionnaire was also offered to any other parent/carer in the household in order to capture the different views and attitudes that may impact the individual CYPwCF. Parents/carers who were not present at the appointment were asked to return the questionnaire to the researcher by email.

4.6.3 Data analysis

All statistical analyses were conducted using IBM SPSS Statistics 24 (IBM Corp., Armonk, NY, USA). In order to understand the factors that affect the maintenance of PA, independent *t*-tests (for normally distributed data) and Mann-Whitney U tests (for non-normally distributed data) were used to identify differences in the CSAPPA overall and domain scores (self-efficacy), self-reported levels of PA, and parent/carer PA and exercise barriers between control and exercise training groups. Paired-samples *t*-tests and Pearson product-moment correlation coefficients were carried out to compare and explain CYPwCF-reported and parent/carer-reported CSAPPA overall and domain scores. They were also used to examine self-reported levels of PA for weekdays and weekend days. Spearman's rank order correlation was used to investigate the relationship between the self-reported levels of PA measured by the 2 different methods: HAES as part of the cohort study, and simple questionnaire as part of the Part A: SRC PA maintenance study. A Friedman test was

carried out to investigate the differences between domains of the parent/carer exercise barriers questionnaire. This contributed to the understanding of the impact of the different parent/carer exercise barriers on the maintenance of PA in CYPwCF. Post-hoc analyses were conducted using Wilcoxon Signed Rank Tests.

4.7 Part C: Barriers to and facilitators for the maintenance of physical activity study procedures

4.7.1 Sample and recruitment

Purposive sampling was used to identify more than 30 participants from the Parts A and B studies' sample (the 51 participants who had completed INSPIRE-CF and were still receiving CF care from the GOSH CF unit) who were characteristically representative of the whole cohort of CYPwCF eligible to participate in phase 1 of this research. This included a range of age, sex and disease severity, as well as incorporating CF clinicians' perceptions of levels of PA. A sample fulfilling this range of characteristics was expected to be able to provide the depth and richness of data required for this qualitative element (Rees, 2007, Carter and Henderson, 2005, Bowling, 2004). Recruitment continued until data saturation was reached.

4.7.2 Data collected

Semi-structured interviews were the most appropriate method of data collection for this qualitative study. They enabled exploration of the different exercise attitudes and experiences, and perceptions of barriers to and facilitators for maintenance of PA, and whether these related to why some CYPwCF managed to maintain PA and exercise participation and others did not. Using this approach offered the opportunity to investigate the experiences of the participants, and thus to present the findings as real descriptions in their own words, ensuring that the true results were captured (Rees, 2007, Bowling, 2004). As previously identified, parents/carers have a significant impact on the PA and exercise participation of their CYPwCF, thus it was important that the PA and exercise attitudes and experiences, and perceptions of barriers to and facilitators for maintenance of PA, of both parents/carers and CYPwCF were heard in this study.

Following training in in-depth interviewing, the researcher (HD) developed interview schedules including a topic guide of key areas to cover during the interviews, and specific questions to help stimulate conversation when needed (CYP- and parent/carer-specific- see Appendix 13). The development of the interview schedules was guided by expert opinion from the supervisory team, and gaps in current knowledge. They were then refined following consultation with CYPwCF who were not eligible to participate in the study. This involved conversations with two independent parents, an 8 year old child and a 15 year old young person. All were given a brief explanation of the topic areas and information that the researcher (HD) wanted to gain from the interviews, and were then asked to comment on the schedule wording and content. Priority was given to questions exploring topics such as CYPwCF and parent/carer PA and exercise attitudes and experiences including interventions, barriers and facilitators to maintaining PA, role of family and advice to others. The interview schedules were structured so that participants were initially eased into the subject matter by first being asked to identify their favourite activities. They were then guided into deeper thought about their PA experiences, attitudes and behaviours. The researcher sought to explore individual comments in order to reveal the beliefs of each participant. Conversation continued until everything on the topic guide had been discussed, and the participant did not wish to say anything more.

All interviews were conducted one-to-one between the researcher (HD) and CYPwCF or parent/carer at GOSH. All CYPwCF were offered the opportunity to have a parent/carer in the room with them for the duration of the interview if they wished. The questions were asked in an open manner to try and stimulate conversation and explore the participants own thoughts rather than be directed by the researcher (HD). Emerging concepts were explored further. All interviews were recorded using an Olympus VN-731PC digital voice recorder. Recordings were labelled by [INSPIRE-CF participant number]-CYP or -parent, downloaded, and stored as Windows Media Audio files in a password protected UCL storage folder. Interviews were transcribed verbatim into text documents by the researcher (HD),

stored by participant number, and entered into QSR NVivo 11 (QSR International, Warrington, UK) for analysis.

4.7.3 Data analysis

Data were analysed using a thematic content analysis approach. This was first developed for applied policy research (Ritchie and Spencer, 1994), and has since been used widely in health research (Gale et al., 2013). This work used the seven stages of analysis described by Gale et al. (2013), whilst incorporating the approaches of Corbin and Strauss (2008), Miles and Huberman (1994) and Strauss (1987):

1. Transcription: Interviews were transcribed verbatim into text documents by the researcher.
2. Familiarisation with the interview: Interview transcripts were read and re-read.
3. Coding: This study used an inductive coding approach whereby data were reviewed line by line, and labelled. Labels, or themes, of a similar nature were grouped together into categories.
4. Developing a working analytical framework: The categories and themes were then organised into a working framework.
5. Applying the analytical framework: The coding from further interviews were then reconsidered in line with the working framework, and the framework amended until all themes were included, related to each other and categorised.
6. Charting data into the framework matrix: Transcripts were re-read and codes checked for their alignment with the allocated themes and categories, and revised as necessary.
7. Interpreting the data: Each category was considered in turn. The themes that it contained were identified, supported by direct quotes from the transcripts, and related back to the aims of the study.

Two researchers (HD+SD) thoroughly read, re-read and coded the transcripts independently. Coding was then compared and discussed until consensus was reached, and the early framework was developed using these codes. The framework was then applied to the qualitative data to allow further themes to be identified. The framework was refined throughout the process until the hierarchy of

categories developed which contained, organised and summarised all themes with identified representative quotes. This approach enabled categories and themes, and thus the framework, to develop inductively from the voiced experiences of the participants.

4.8 Integration of findings

The value of mixed methods research is in the thoroughness of findings generated by using both quantitative and qualitative approaches. However, the biggest challenge lies in the process of integrating the findings (Teddlie and Tashakkori, 2009, Creswell and Plano Clark, 2011). Phase 1 of this project comprised of 2 quantitative studies (Parts A and B) and 1 qualitative study (Part C). The data from each study were analysed and reported individually. The findings of all 3 studies were then integrated at the interpretation stage. This enabled full and thorough analysis of each dataset and the identification of key results, and then enhancement of the findings with the comparison, analysis and assimilation of quantitative and qualitative data at the final stage of analysis.

5 Phase 1 Results

Of the 51 participants who had completed the 2-year INSPIRE-CF exercise intervention study and were still receiving their CF care from the GOSH CF unit, 2 CYPwCF did not wish to participate in phase 1 of this research (Parts A, B and C), because:

1. Did not want to complete an exercise capacity test,
2. Anxiety about currently unexplained symptoms.

The remaining 49 CYPwCF all participated in the 2 quantitative studies contributing to phase 1 of this research (Parts A and B), 20 from the control group, 29 who had received the exercise training. The participants who took part in this phase of research were representative of the whole INSPIRE-CF cohort, with the age at baseline demonstrating the only statistically significant difference (Table 4). This was to be expected because the majority of those who did not take part in the SRC PA maintenance study had transitioned to adult CF centres and were therefore older. However, as no significant differences were detected in any other characteristics or baseline measurements, this sample was considered to be representative of the whole INSPIRE-CF cohort.

Table 4: Demographic information for INSPIRE-CF participants, and comparison between those who took part in the SRC PA maintenance (Part A) study and those who did not

		Total	Participated	Did not participate	p
n = (%)	Total	69 (100%)	49 (71%)	20 (29%)	0.119
	Control	33 (48%)	20 (41%)	13 (65%)	
	Exercise training	36 (52%)	29 (59%)	7 (35%)	
Age in years at recruitment to INSPIRE-CF (mean ± SD)		9.89 ± 2.97	8.69 ± 2.00	12.84 ± 2.92	< 0.0005 ¹ *
Sex (%)	Male	35 (51%)	28 (57%)	7 (35%)	0.160
	Female	34 (49%)	21 (43%)	13 (65%)	
Genotype (%)	F508del / F508del	44 (64%)	29 (59%)	15 (75%)	0.454
	F508del / Other	19 (27%)	15 (31%)	4 (20%)	
	Other / Other	6 (9%)	5 (10%)	1 (5%)	
FEV₁ z score (mean ± SD)		-1.09 ± 1.26	-1.00 ± 1.30	-1.31 ± 1.17	0.357 ¹
Distance in metres achieved during 10m- MSWT: median (IQR)		900 (765-1075)	860 (750-1030)	995 (810-1242)	0.055 ²
CFQ-R score: Median (IQR)	Physical	92.6 (81.5-100)	92.6 (85.2-100)	94.4 (75.9-100)	0.861 ²
	Body image	88.9 (55.6-100)	88.9 (66.7-100)	77.8 (55.6-88.9)	0.108 ²
	Treatment burden	55.6 (44.4-77.8)	55.6 (44.4-77.8)	66.7 (47.2-77.8)	0.433 ²
	Respiratory	83.3 (77.8-94.4)	83.3 (77.8-94.4)	86.1 (73.6-94.4)	0.963 ²
Self-reported levels of physical activity (minutes per week): Median (IQR)		270 (150-445)	285 (160-450)	225 (68-424)	0.341 ²

Key: FEV₁ forced expiratory volume in the first second, IQR interquartile range, n number, SD standard deviation, 10m-MSWT 10metre modified shuttle walk test

¹ t test for independent samples for continuous variable with normal distribution,

² Mann-Whitney U test for continuous variable with non-normal distribution, Chi-square test for all categorical variables.

* reached level of significance α 0.05

Staggered recruitment to INSPIRE-CF meant that the time between the end of that study and participation in the Part A SRC PA maintenance assessments for individuals ranged from 13-38 months, with a predominance towards a longer time gap (median 31months). Only 4 participants attended for Part A SRC PA maintenance assessment less than 24 months after their end of INSPIRE-CF

assessment date. Demographic data of the phase 1 participants are presented in Table 5. There were no significant differences in characteristics between control and exercise training groups. All participants completed the 2 quantitative studies (Part A: SRC PA maintenance and Part B: Factors affecting the maintenance of PA) included in phase 1 of this programme of research, and a subset also took part in the qualitative study (Part C: Barriers to and facilitators for the maintenance of PA). This phase of work was designed to answer the first 3 research questions:

1. What happened to the health, well-being and PA maintenance of CYPwCF after withdrawal of a supervised exercise intervention? (Part A: SRC PA maintenance study)
2. What affects the maintenance of exercise and PA in CYPwCF? (Part B: Factors affecting the maintenance of PA study)
3. What are the barriers to and facilitators for maintaining exercise and PA in CYPwCF? (Part C: Barriers to and facilitators for the maintenance of PA qualitative study).

Table 5: Demographic information for phase 1 participants

		Control group	Exercise training group	<i>p</i>
n = (%)		20 (41%)	29 (59%)	
Age in years at recruitment to PA maintenance study (mean ± SD)		13.3 ± 2.2	13.3 ± 2.2	0.981 ¹
Age group (%)	9-11 years	7 (35%)	11 (38%)	0.797
	12-14 years	8 (40%)	9 (31%)	
	15+ years	5 (25%)	9 (31%)	
Sex (%)	Male	12 (60%)	16 (55%)	0.967
	Female	8 (40%)	13 (45%)	
Genotype (%)	F508del / F508del	13 (65%)	16 (55%)	0.333
	F508del / Other	4 (20%)	11 (38%)	
	Other / Other	3 (15%)	2 (7%)	
Time between end of 2 years of exercise training and PA maintenance assessment in days (median/IQR)*		964 (907-1000)	966 (894-1023)	0.745 ²
Disease severity (%)	Mild ppFEV₁ ≥70%	14 (70%)	24 (83%)	0.293
	Moderate ppFEV₁ 40-69%	6 (30%)	5 (17%)	
	Severe ppFEV₁ <40%	0	0	
Interviewed (%)	Yes	6 (30%)	14 (48%)	0.325
	No	14 (70%)	15 (52%)	

Key: IQR interquartile range, n number, ppFEV₁ percent of predicted forced expiratory volume in the first second (using GLI reference equation (Quanjer et al., 2012)), SD standard deviation

¹ *t* test for independent samples for continuous variable with normal distribution,

² Mann-Whitney U test for continuous variable with non-normal distribution, Chi-square test for all categorical variables.

Nil reached level of significance α 0.05

5.1 Part A: SRC PA maintenance study

The key measures collected throughout INSPIRE-CF (at baseline, 6months (exercise capacity only), 1year and end of INSPIRE-CF at 2years assessment points) were repeated at this PA maintenance assessment point, and data from all assessment points were included to track trajectory of:

- exercise capacity (measured by distance achieved during 10m-MSWT),
- lung function (measured by FEV₁ z score),
- physical, treatment burden, body image and respiratory quality of life domains (measured by CFQ-R),
- Self-reported levels of PA (measured by INSPIRE-CF survey).

These data were analysed to address research question 1: ‘what happened to the health, well-being and PA maintenance of CYPwCF after withdrawal of a supervised exercise intervention?’. Of the 49 CYPwCF who participated in this Part A SRC PA maintenance study, 1 CYPwCF (exercise training group) chose not to complete the 10m-MSWT or self-reported levels of PA at PA maintenance assessment point, therefore there were 48 complete sets of data for these outcomes. CFQ-R data were missing for 1 participant at the 1-year time point of INSPIRE-CF so there were also 48 complete sets of data for this outcome. There were complete sets of spirometry data for all 49 participants.

5.1.1 Comparing the results from control and exercise training groups across time points

The data were first analysed at group level for each outcome measure, comparing results for control and exercise training groups in order to understand the impact that the exercise intervention had on the health, well-being and PA maintenance of CYPwCF. Where a between-group difference was identified, the impact of age, sex and disease severity was also analysed. Initial analyses were performed using assessment time points as an ordinal variable to enable group comparisons by using mixed between-within subjects ANOVA.

5.1.1.1 Exercise capacity

The distance achieved during 10m-MSWT increased for both control and exercise training groups over the duration of INSPIRE-CF (Table 6). The rate of increase appeared to vary between control and exercise training groups, with a greater rate of increase, represented by the steeper gradient, for the exercise training group who received the exercise training (Figure 5). At the conclusion of INSPIRE-CF, when the training intervention stopped, this increase appeared to continue for the Part A SRC PA maintenance study participants who had been in the control group, but not for those who had received the exercise training.

Table 6: Distance achieved during 10m-MSWT at each time point by group for phase 1 participants

Time point	Control			Exercise training		
	n	M (metres)	SD	n	M (metres)	SD
Baseline	20	920	214	28	862	183
6 months	20	960	238	28	927	185
One Year	20	988	218	28	996	187
Two years	20	1037	278	28	1152	138
PA maintenance assessment	20	1140	356	28	1106	231

Key: M mean, n number, SD standard deviation

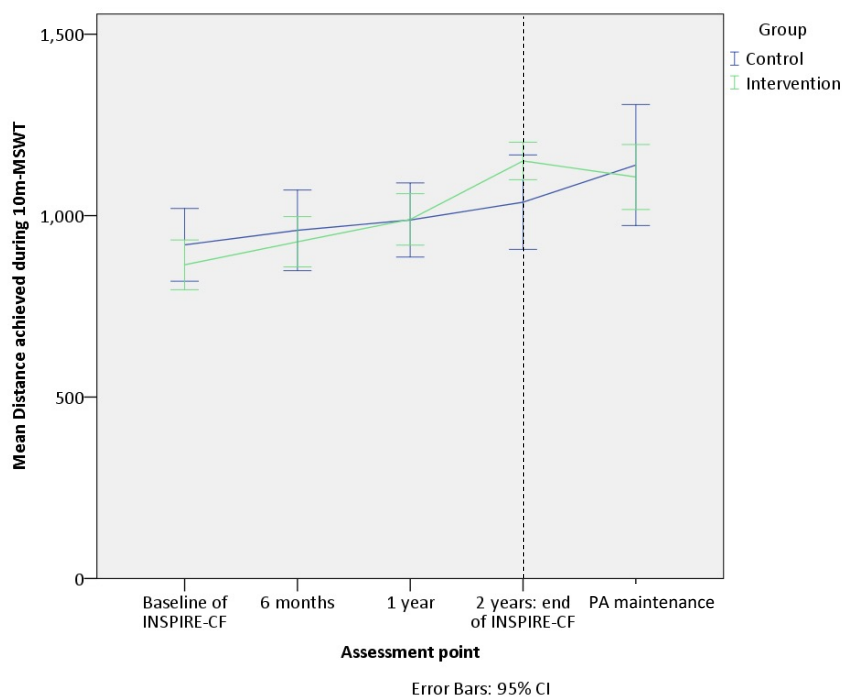


Figure 5: Mean distance achieved during 10m-MSWT at each time point by group for phase 1 participants

A mixed between-within subjects ANOVA was conducted to assess the impact of the 2-year-long supervised exercise intervention on the distance achieved during 10m-MSWT, across the 5 time points (pre-intervention, 6 months, 12 months, 24 months end of study, and PA maintenance assessment 13-38 months later). This revealed whether participants who had received the exercise training were able to maintain PA independently or not after the exercise training had been withdrawn. Preliminary analyses were performed to ensure no violation of the assumptions of normality, homogeneity of variance and homogeneity of inter-correlations. In this instance, the assumption of normality was violated ($p = 0.004$), therefore the data were transformed using square root to achieve normality ($p = 0.060$). The assumption of homogeneity of variances was also violated for the end of 2 year time point (Levene's Test of Equality of Error Variances $p = 0.001$). However, the 2 groups were similar in size (largest/smallest = 1.4) and ANOVA is reasonably robust to violations of this assumption in this situation (Pallant, 2007). To further minimise the risk of a Type I error, a more stringent α level was set to 0.01 (Tabachnick and Fidell, 2014). There was a significant interaction between exercise training/control group and time point with very large effect size, Wilks' Lambda = 0.60, $F(4, 43) = 7.26$, $p = <0.0005$, partial eta squared = 0.403. This signified that there was a difference in change in distance achieved during 10m-MSWT over time points between control and exercise training groups. Because of this significant interaction, further assessment of main effects for each independent variable was not appropriate. Bonferroni corrected post hoc tests showed a significant improvement in distance achieved during 10m-MSWT between all test points that occurred during INSPIRE-CF where the time gap was greater than 6 months ($p = <0.0005$ for all). However, this improvement was not sustained between the end of INSPIRE-CF at 2 years and the PA maintenance assessment ($p = 1.0$). This suggested that the benefits gained to distance achieved during 10m-MSWT by the exercise training group during the course of INSPIRE-CF were lost by the PA maintenance assessment point. Participants in the control group demonstrated a consistent pattern with a steady increase in distance achieved during 10m-MSWT throughout INSPIRE-CF and to the PA maintenance assessment point.

5.1.1.1.1 Impact of age, sex and disease severity

There was no clear impact of age group on the pattern of change in distance achieved during 10m-MSWT for either control or exercise training group (Figure 6), with the only statistically significant difference between age groups occurring at baseline for the control group when the oldest age group (15-16year olds) achieved a statistically significantly greater distance during 10m-MSWT than the youngest age group (9-11year olds) (Kruskal Wallis test, $p = 0.022$). This suggested that the fall in distance achieved during 10m-MSWT experienced by the exercise training group between the end of the 2-year-long exercise intervention and the PA maintenance assessment affected all age groups similarly.

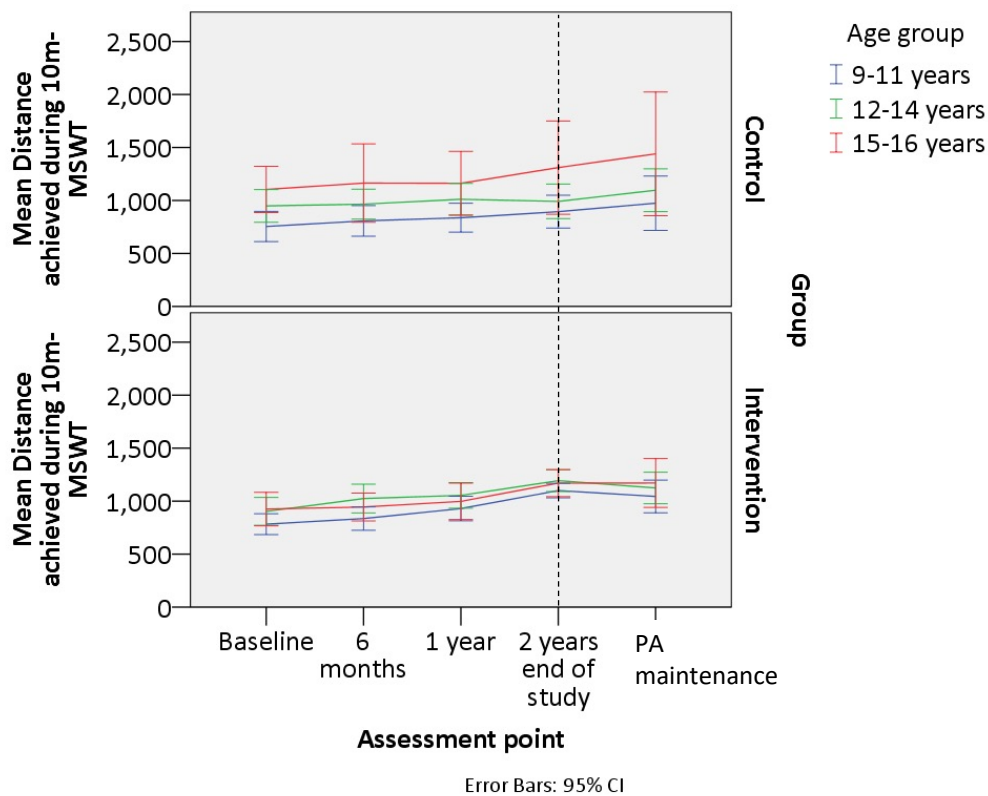


Figure 6: Mean distance achieved during 10m-MSWT at each time point by age group for phase 1 participants. Top: control group, bottom: exercise training group

Males appeared to have a greater rate of increase in distance achieved in 10m-MSWT, than females across both control and exercise training groups (Figure 7). However, there were no statistically significant differences between males and females across all time points for both control and exercise training groups, with the exception of the exercise training group at the PA maintenance assessment

time point (Mann-Whitney U test, $p = 0.047$). This suggested that the fall in distance achieved during 10m-MSWT experienced by the exercise training group between the end of the 2 year-long exercise intervention and the PA maintenance assessment was greater for females than males, perhaps indicating that males maintained more PA than females after withdrawal of the exercise training.

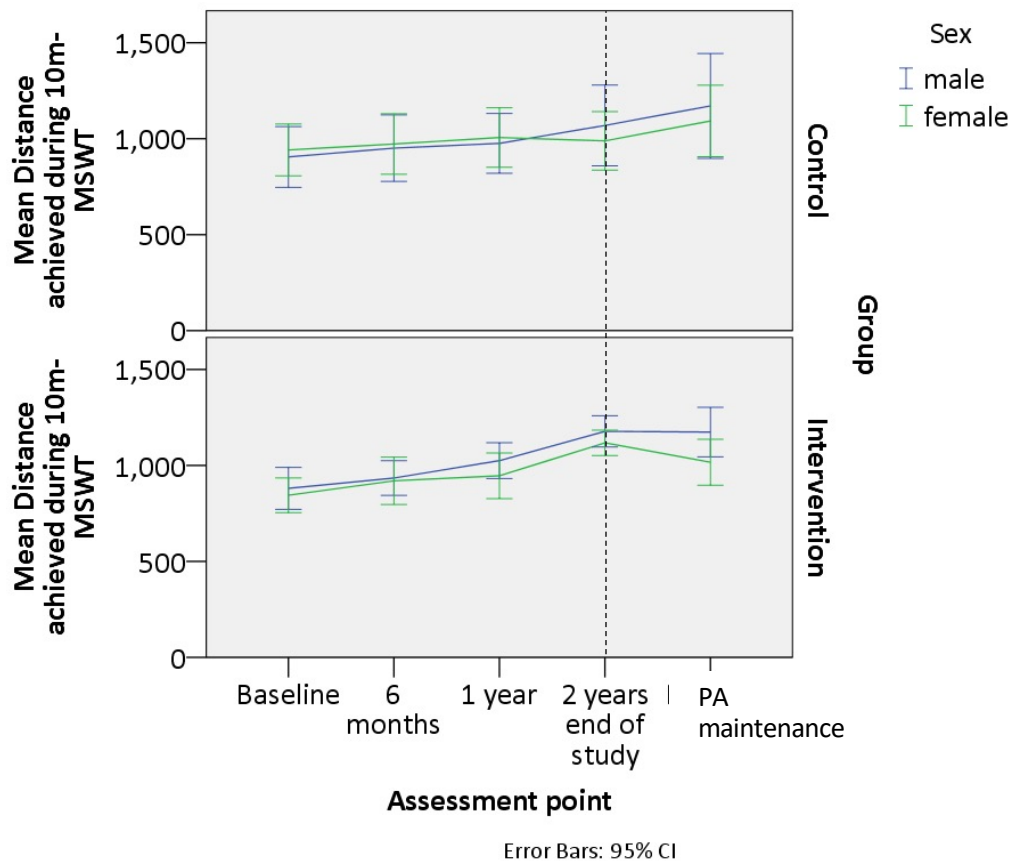


Figure 7: Mean distance achieved during 10m-MSWT at each time point by sex for phase 1 participants. Top: control group, bottom: exercise training group

There were minimal differences between distance achieved during 10m-MSWT by those with mild disease severity and those with moderate disease severity in both control and exercise training groups (Figure 8). The only statistically significant difference occurred in the exercise training group at the one year assessment point where those with milder disease had a slight improvement in distance achieved during 10m-MSWT compared to the 6-month assessment time point, but those with moderate disease had a slight decline (Kruskal Wallis test, $p = 0.022$). However, this between-group difference had resolved by the end of the 2 year exercise intervention and remained absent at the PA maintenance assessment point,

indicating that the fall in distance achieved during 10m-MSWT experienced by the exercise training group after withdrawal of the supervised training affected those with both mild and moderate disease. This perhaps suggested that the maintenance of PA was independent of disease severity. The participants with mild disease in the control group demonstrated a notable increase in distance achieved during 10m-MSWT, whereas those with moderate disease did not and remained fairly stable. However, this did not meet the level of significance, perhaps because of the small group size (control group: mild disease n = 14, moderate disease n = 6) and varied distances achieved resulting in wide confidence intervals.

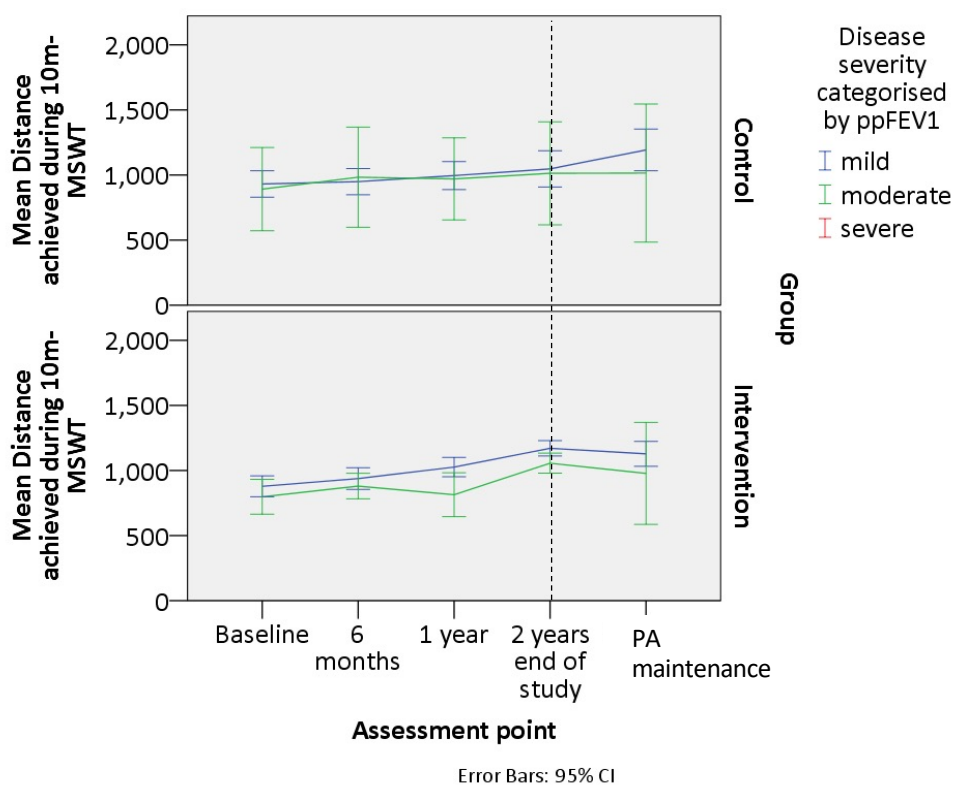


Figure 8: Mean distance achieved during 10m-MSWT at each time point by disease severity for phase 1 participants.
Top: control group, bottom: exercise training group

5.1.1.2 Lung function

There was a steady fall in FEV₁ z score in the exercise training group which was not observed in the control group (Table 7). There was a wide distribution amongst both groups at each time point, with substantial overlap of 95% confidence intervals (Figure 9).

Table 7: FEV₁ z score at each time point by group for phase 1 participants

Time point	Control			Exercise training		
	n	M	SD	n	M	SD
Baseline	20	-1.33	1.28	29	-0.78	1.29
One Year	20	-1.43	1.15	29	-0.94	1.21
Two years	20	-1.32	1.08	29	-1.22	1.25
PA maintenance assessment	20	-1.36	1.64	29	-1.32	1.37

Key: M mean, n number, SD standard deviation

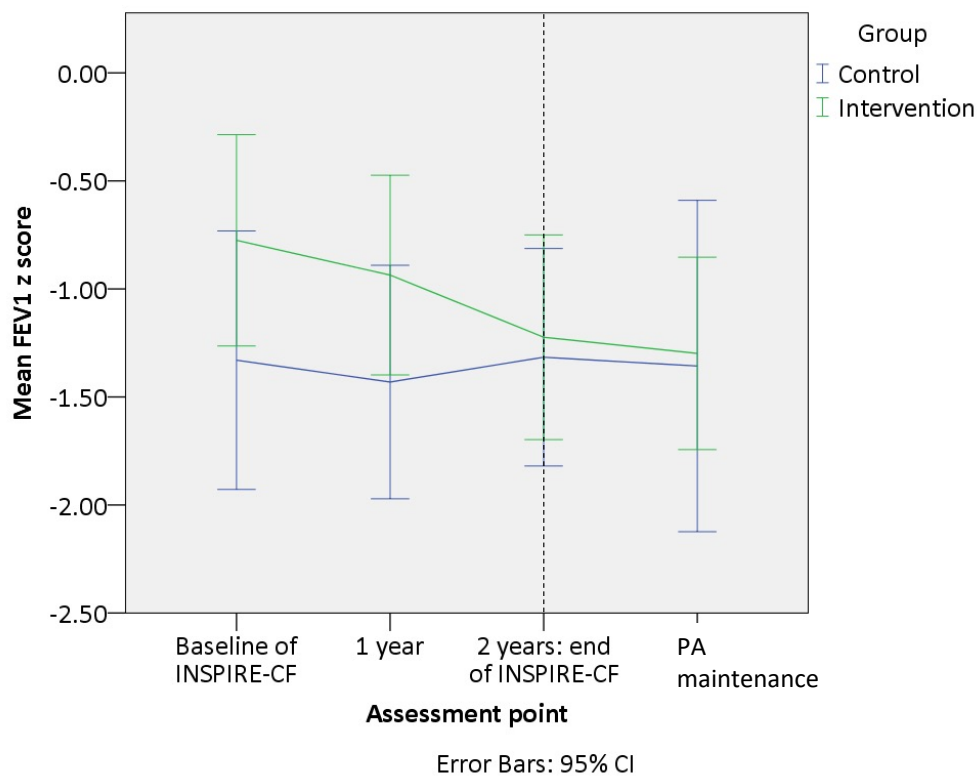


Figure 9: Mean FEV₁ z score at each time point by group for phase 1 participants

A mixed between-within subjects ANOVA was conducted to assess the impact of the 2-year-long supervised exercise intervention and then subsequent withdrawal on lung function (measured by spirometry generating an FEV₁ z score), across the 4 time points (pre-intervention, 12 months, 24 months end of exercise training, and PA maintenance assessment 13-38 months later). Preliminary analyses were performed to ensure no violation of the assumptions of normality, homogeneity of variance and homogeneity of inter-correlations. As with the exercise capacity ANOVA, the assumption of homogeneity of variances was violated, this time for the

baseline time point (Levene's Test of Equality of Error Variances $p = 0.010$). However, the 2 groups continued to be similar in size (largest/smallest = 1.4), and the stricter α level of 0.01 was employed thus reducing the risk of a Type I error. There was no significant interaction between exercise training/control group and time point, Wilks' Lambda = 0.88, $F(3, 45) = 2.04$, $p = 0.121$, partial eta squared = 0.120. The main effect for time point was not significant, $F(2, 5) = 1.36$, $p = 0.260$, with the FEV₁ of both groups fluctuating across time points. The main effect for control/exercise training group was also not significant, $F(1, 47) = 0.88$, $p = 0.354$, partial eta squared = 0.18. These results suggested that the exercise intervention had no significant impact on FEV₁ z score, either during the exercise intervention or after it was withdrawn.

5.1.1.3 Quality of life

Health-related quality of life data were collected (CFQ-R reported by CYPwCF) at each assessment point. Four domains of the measure were considered to be of relevance for the maintenance of PA in CYPwCF: physical, body image, treatment burden and respiratory. Scores fluctuated for both control and exercise training groups across the assessment time points (Figure 10), but were generally very high (higher score indicates better quality of life) for all domains (Table 8).

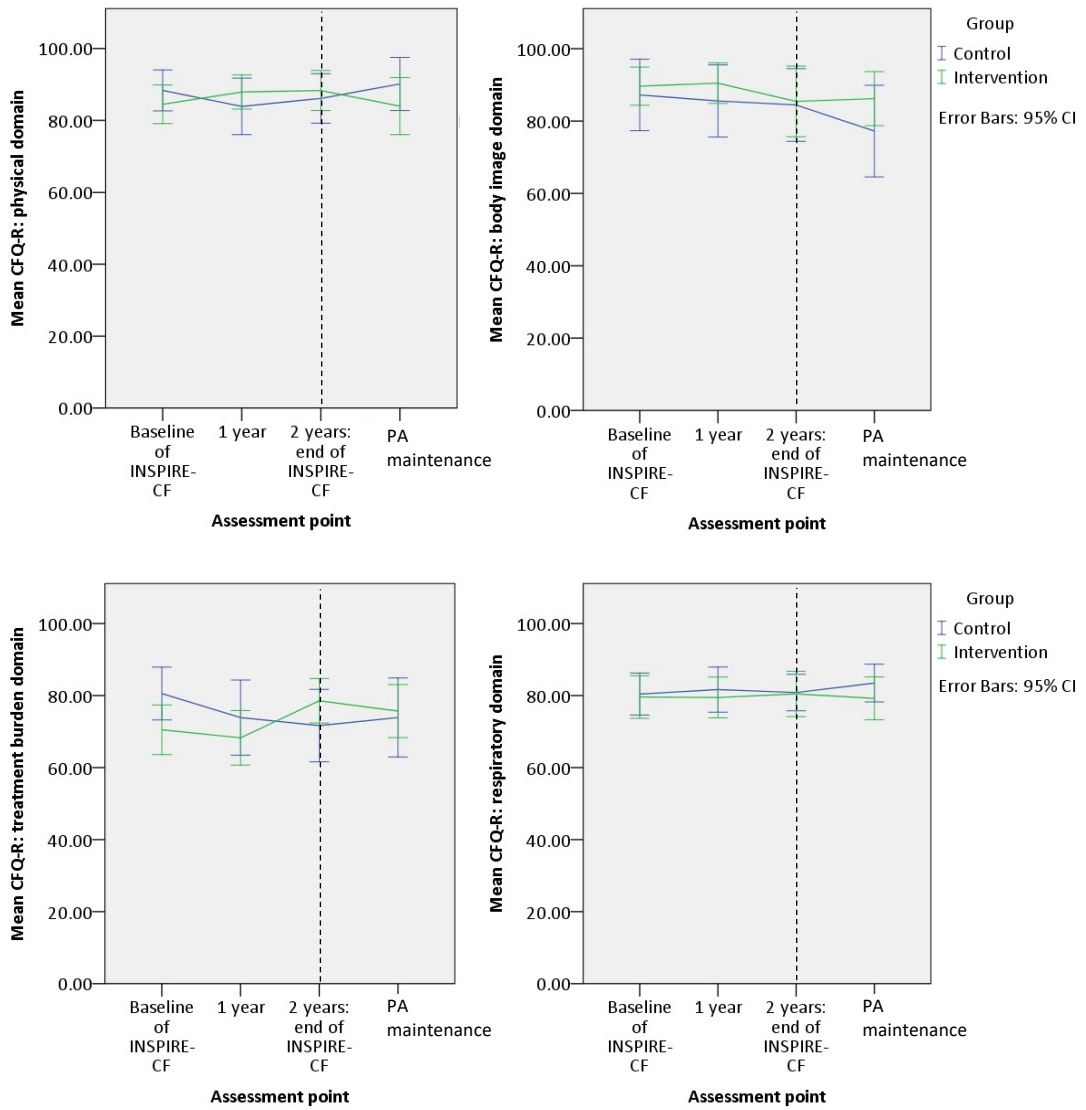


Figure 10: Mean CFQ-R score at each time point by group and domain for phase 1 participants

Table 8: CFQ-R score at each time point by domain and group for phase 1 participants

Domain	Time point	Control			Exercise training		
		n	Median	IQR	n	Median	IQR
Physical	Baseline	20	94.4	83.3-98.6	29	88.9	75.0-97.2
	One Year	20	88.9	77.8-98.6	29	91.7	77.8-100
	Two years	20	86.1	79.2-100	29	94.4	77.8-100
	PA maintenance assessment	20	94.4	91.7-100	29	94.4	80.5-97.9
Body image	Baseline	20	100.0	77.8-100	29	100.0	83.3-100
	One Year	20	88.9	80.6-100	29	94.4	88.9-100
	Two years	20	88.9	77.8-100	29	100.0	88.9-100
	PA maintenance assessment	20	88.9	55.6-100	29	88.9	77.8-100
Treatment burden	Baseline	20	83.3	77.8-88.9	29	66.7	55.6-88.9
	One Year	20	72.2	55.6-100	29	77.8	55.6-77.8
	Two years	20	77.8	58.3-88.9	29	77.8	66.7-88.9
	PA maintenance assessment	20	77.8	66.7-88.9	29	77.8	66.7-88.9
Respiratory	Baseline	20	83.3	75.0-91.7	29	83.3	70.9-91.7
	One Year	20	83.3	75.0-91.7	29	83.3	66.7-91.7
	Two years	20	83.3	75.0-91.7	29	83.3	75.0-91.7
	PA maintenance assessment	20	83.3	75.0-91.7	29	83.3	75.0-91.7

Key: IQR interquartile range, n number

Mixed between-within subjects ANOVAs were conducted to assess the impact of the 2-year-long supervised exercise intervention and then subsequent withdrawal on the 4 quality of life domains across the 4 time points (pre-intervention, 12 months, 24 months end of exercise training, and PA maintenance assessment 13-38

months later). Preliminary analyses were performed to ensure no violation of the assumptions of normality, homogeneity of variance and homogeneity of inter-correlations. The assumption of normality was violated for each of the 4 domains. However, in this instance it was not appropriate to transform the data to try to achieve normality. The difference between the mean and 5% trimmed mean did not exceed 3 points (below MCID of 6) for any domain at any time point, thus the skew was likely to be related to the generally high scores and transformation would have limited the value of interpretation. Homogeneity of variance was only violated by the body image domain, therefore the stricter α level of 0.01 was again applied. The body image domain also just violated the homogeneity of inter-correlation ($p = 0.001$, with a more conservative α level set at 0.001 because of the sensitivity of this statistic), therefore had a statistically significant interaction been detected for this domain then this would need to have been interpreted with caution. There were no main effects for control/exercise training group or time for any of the considered domains (Table 9). There were also no significant interactions between exercise training/control group and time point for any domain, suggesting that CFQ-R did not detect any impact of the exercise intervention on the health-related quality of life of the participants. There appeared to be some difference in trajectories for the treatment burden domain where the exercise training group reported less burden (higher score) than the control group at the 2 years end of INSPIRE-CF assessment point (Figure 10). This did not reach the level of significance (Table 9), possibly as a result of the notable overlap of confidence intervals and the tendency towards high scores.

Table 9: Mixed between-within subjects ANOVAs for each relevant CFQ-R domain for phase 1 Part A study

Domain	Effect of time	Effect of control/exercise training group	Interaction between control/exercise training group and time
Physical	$F(3, 44) = 0.10$ $p = 0.959$	$F(1, 46) = 0.09$ $p = 0.760$	$F(3, 44) = 1.29$ $p = 0.290$
Body image	$F(3, 44) = 1.73$ $p = 0.174$	$F(1, 46) = 0.78$ $p = 0.381$	$F(3, 44) = 0.70$ $p = 0.599$
Treatment burden	$F(3, 44) = 0.85$ $p = 0.474$	$F(1, 46) = 0.29$ $p = 0.592$	$F(3, 44) = 2.28$ $p = 0.092$
Respiratory	$F(3, 44) = 0.10$ $p = 0.960$	$F(1, 46) = 0.57$ $p = 0.453$	$F(3, 44) = 0.18$ $p = 0.911$

5.1.1.4 Self-reported physical activity

The self-reported levels of PA increased across the duration of assessments for both groups (Table 10), although the rate appeared to vary by group between each assessment point (Figure 11).

Table 10: Self-reported levels of PA per week at each time point by group for phase 1 participants

Time period	Control			Exercise training		
	n	Median (minutes)	IQR	n	Median (minutes)	IQR
Baseline	20	297	169-473	28	240	150-450
One Year	20	260	180-487	28	350	240-445
Two years	20	333	184-532	28	389	300-520
PA maintenance assessment	20	372	185-623	28	433	233-604

Key: IQR interquartile range, n number

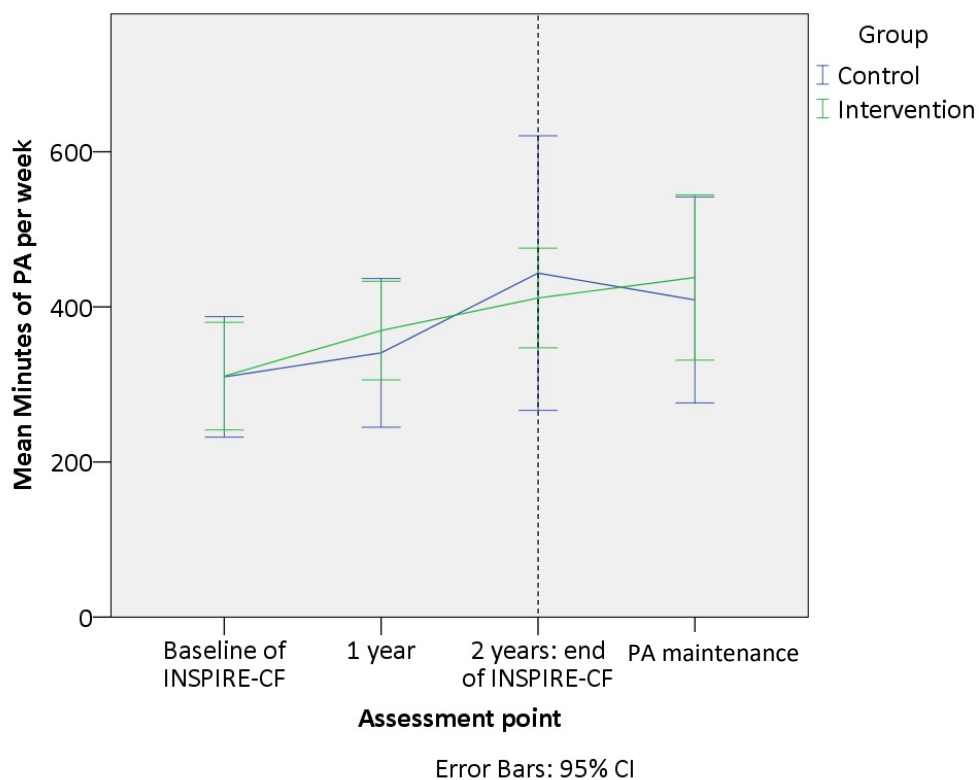


Figure 11: Mean levels of self-reported PA per week by group for phase 1 participants

A mixed between-within subjects ANOVA was conducted to assess the impact of the 2-year-long supervised exercise intervention on the self-reported levels of PA of the participants, across 4 time periods (pre-intervention, 12 months, 24 months end of exercise training, and PA maintenance assessment point 13-38 months

later). Preliminary analyses identified non-normal distribution of the data, therefore they were transformed (square root of minutes of PA per week) to achieve normality. Homogeneity of variance was violated at the 2 years end of INSPIRE-CF assessment point, therefore the stricter α level of 0.01 was again applied to minimise a Type I error occurring. Homogeneity of inter-correlation was also violated ($p = 0.001$, with α level set at 0.001), therefore had a statistically significant interaction been detected then this would need to have been interpreted with caution. The main effect of control/exercise training group was not significant, $F(1, 46) = 0.40$, $p = 0.530$. There was a large main effect for time point, $F(3, 44) = 4.02$, $p = 0.013$, partial eta squared = 0.215, with the levels of PA per week increasing for both groups from baseline to PA maintenance assessment. However, the stricter α level meant this did not quite reach significance. There was no significant interaction between exercise training/control group and time point, $F(3, 44) = 0.31$, $p = 0.820$. These results suggested that the exercise intervention did not have an impact on the self-reported levels of PA per week.

5.1.2 Comparing results from the control and exercise training groups across continuous time

Analysis to this point had considered time point only. However, the duration of time was variable between assessment points and between participants. This was particularly notable for the PA maintenance assessment when participants were all tested over the course of a 6-month period. Participants were recruited to INSPIRE-CF over 19 months, with their initial participation lasting 2 years. This resulted in the PA maintenance assessment point being conducted at 13 months after INSPIRE-CF for some participants and up to 38 months after for others. It was, therefore, important to explore the data by considering time as a continuous variable, to understand if the findings remained true. The signal from the CFQ-R data was limited, perhaps due to the tendency towards higher scores at all assessment points which limited the potential for positive change. Therefore the CFQ-R data were not included in further analysis.

The end of INSPIRE-CF assessment point (at 2 years) was identified as ‘day 0’ to enable standardisation. Days prior to day 0 were during the INSPIRE-CF study when the control group continued with standard CF care and the exercise training group received standard CF care and the exercise intervention. Both groups received standard CF care during the time after day 0. The trajectories of control and exercise training groups for each variable were established using GEE. Comparisons were then made between trajectories of control and exercise training groups for both during and after INSPIRE-CF (Table 11). There were statistically significant differences between the trajectories of control and exercise training groups for distance achieved during 10m-MSWT during INSPIRE-CF: the exercise training group increased significantly more than the control group. This remained statistically significant for the after INSPIRE-CF time period, but the direction of difference reversed: the control group increased significantly more than the exercise training group.

Table 11: Comparison of the trajectories (generated by generalised estimating equations) of control and exercise training groups for each variable, during and after INSPIRE-CF for phase 1 Part A study

Variable	Time period	β coefficient	<i>p</i>
10m-MSWT	During INSPIRE-CF	0.21	< 0.0005*
	After INSPIRE-CF	-0.17	< 0.0005*
FEV₁ z score	During INSPIRE-CF	-0.001	0.17
	After INSPIRE-CF	-0.0002	0.44
Self-reported levels of physical activity	During INSPIRE-CF	0.0004	0.882
	After INSPIRE-CF	0.001	0.84

Key: FEV₁ forced expiratory volume in the first second, 10m-MSWT 10metre modified shuttle walk test

The GEE results were used to generate a visual indication of the trajectories (Figure 12). On visual inspection, the trajectories did not appear to differ from those generated using assessment point as an ordinal variable (section 5.1.1). It must be noted that the results for self-reported levels of PA for GEE were transformed using square root to establish normal distribution, thus accounting for the difference in profile for this variable. Further analysis using a one-way between-groups ANCOVA was conducted to investigate the change in trajectory of each variable and group

combination from during to after INSPIRE-CF. The independent variable was during or after INSPIRE-CF, and the dependent variables were distance achieved during 10m-MSWT, lung function (FEV₁ z score) and self-reported levels of PA. The effect of time was then controlled as the covariate.

For distance achieved during 10m-MSWT, after adjusting for time, there was a significant difference between the slopes during and after INSPIRE-CF for the exercise training group ($F = 31.05, p < 0.0005^*$), but not for the control group ($F = 0.19, p = 0.662$). However, similarly to the ANOVAs conducted above, for both FEV₁ z score and self-reported levels of PA, there were no statistically significant differences between the slopes during and after INSPIRE-CF for control or exercise training groups (lung function control: $F = 0.01, p = 0.93$, exercise training: $F = 0.33, p = 0.566$; levels of PA control: $F = 1.17, p = 0.28$, exercise training: $F = 3.11, p = 0.080$). This indicated that considering time continuously rather than assessment points did not affect the findings of this study. The exercise intervention did not appear to impact the lung function or self-reported levels of PA of the CYPwCF who took part. There was a detectable impact on distance achieved during 10m-MSWT during INSPIRE-CF, but that benefit was lost by the point of PA maintenance assessment suggesting that PA was not maintained to the level of the exercise intervention.

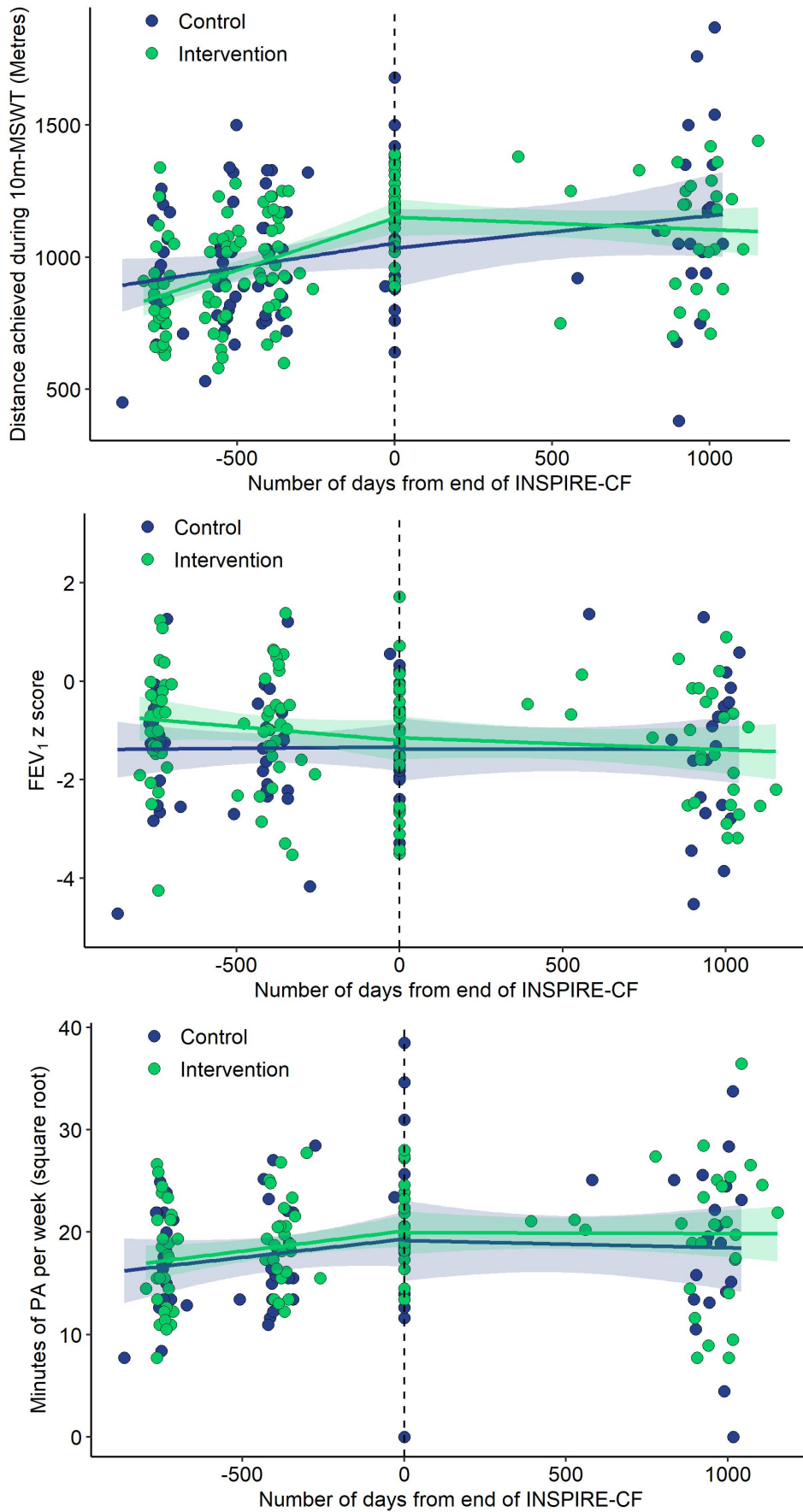


Figure 12: Exercise capacity (top), lung function (middle) and activity levels (bottom) over time by group, with line calculated using GEE for phase 1 participants
 Shaded areas represent 95% CI of lines
 NB The data for minutes of PA per week were transformed using square root to establish normal distribution

5.1.3 Variation in the trajectories of individuals

Having investigated the impact of the exercise intervention at group level, it was important to examine the trajectories of individual participants in terms of exercise capacity, lung function and self-reported levels of PA. This would help to identify if the trends of maintenance of PA and exercise behaviours varied between participants within the groups. When analysed at group level, the mean distance achieved during 10m-MSWT increased over time in both control and exercise training groups, with a significantly greater increase experienced by the exercise training group during the 2-year study. However, when individual trajectories were examined it became apparent that there were notable variations in the trajectories of individual participants (Figure 13). There were participants in both control and exercise training groups whose exercise capacity increased at each assessment point, and others whose trajectories fluctuated with some positive change and some negative change between assessment points.

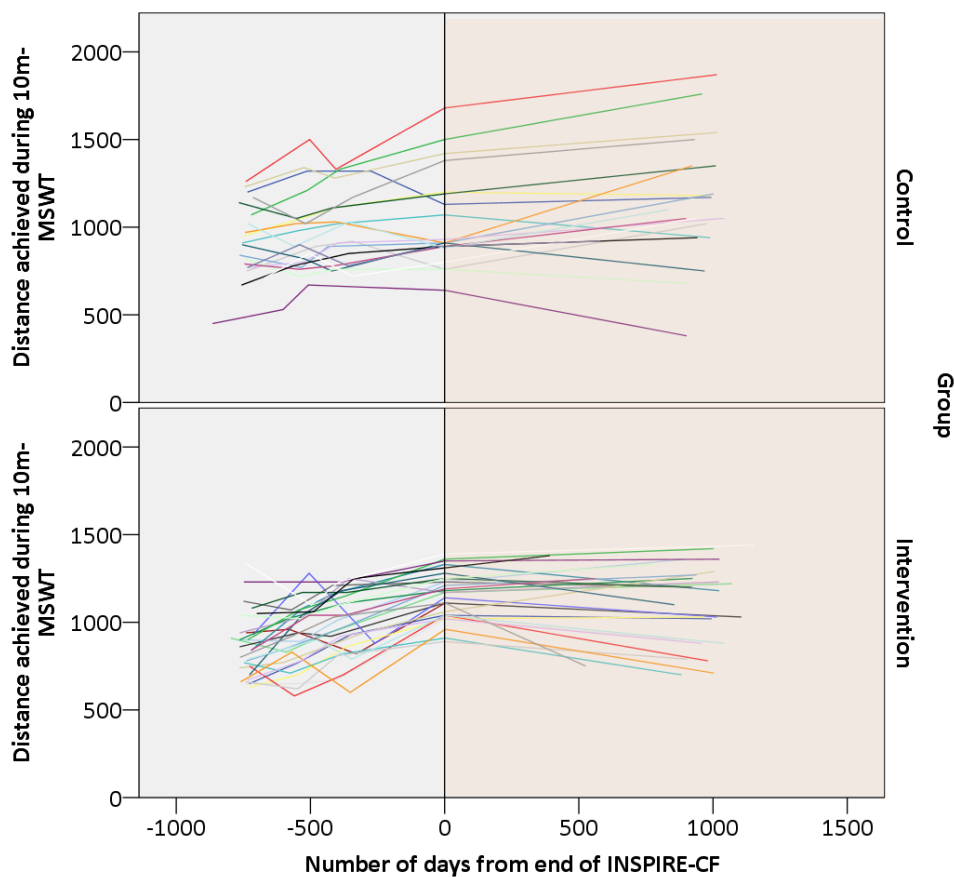


Figure 13: Exercise capacity trajectories of individual participants over time, during (grey shading) and after INSPIRE-CF (orange shading), for control (top) and exercise training (bottom) groups as part of phase 1.

These variations in trajectories were also apparent in FEV₁ z-score (Figure 14) and self-reported levels of PA (Figure 15). Some of the self-reported minutes of PA appeared to be extremely high, for example 1 participant reported doing nearly 1500minutes of PA per week (over 3.5hours every day). Whilst this is unlikely to be an accurate report of actual levels of PA, the notable variations suggested that individuals within the study followed many different trajectories both during and after INSPIRE-CF. Furthermore, on visual examination of Figure 13, Figure 14 and Figure 15, it appeared that the trajectory of each variable differed substantially within individuals (each coloured line was allocated to the same participant in each figure).

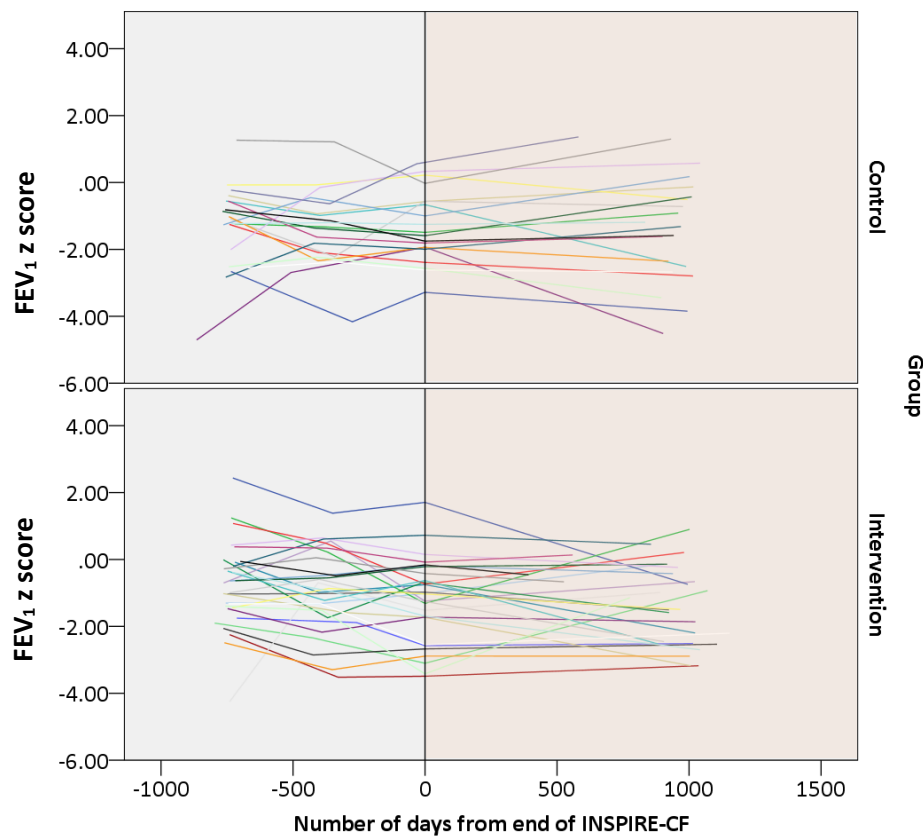


Figure 14: Lung function trajectories of individual participants over time, during (grey shading) and after INSPIRE-CF (orange shading), for control (top) and exercise training (bottom) groups as part of phase 1

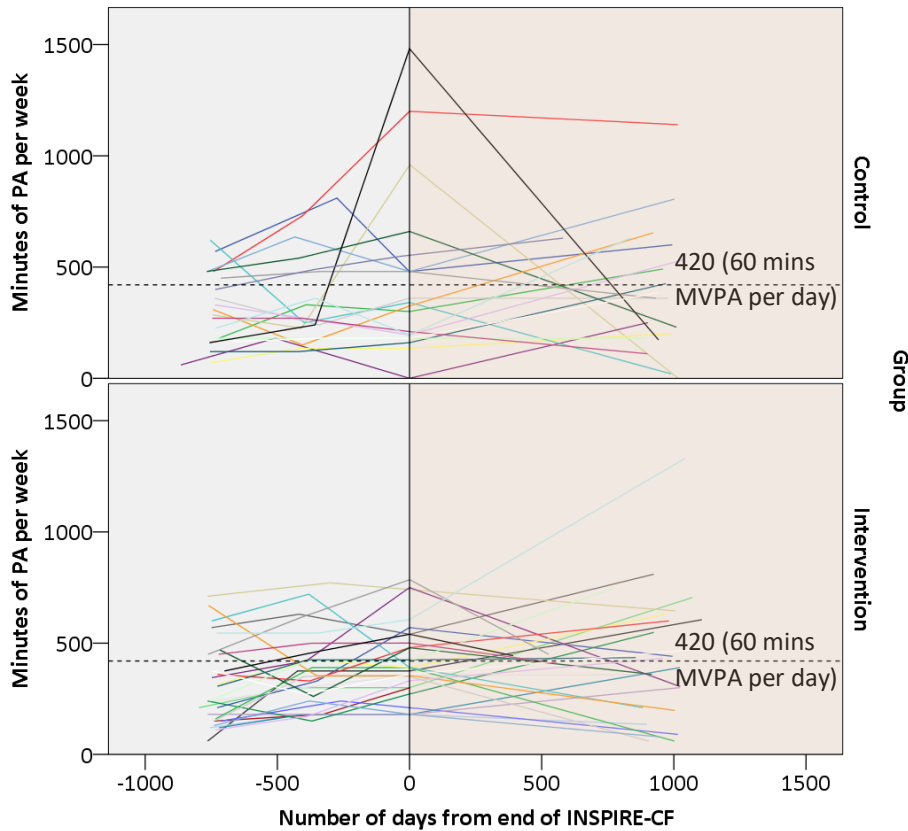


Figure 15: Trajectories of self-reported activity levels of individual participants over time, during (grey shading) and after INSPIRE-CF (orange shading), for control (top) and exercise training (bottom) groups as part of phase 1

The direction and degree of change in exercise and PA participation for each participant during and after INSPIRE-CF were compared (Figure 16). Self-reported participation in PA was limited. There was a risk of recall bias, reporting bias and it also involved the individual's perception of effort and when activity occurred which may differ substantially to physiologically measured PA. Due to the limitations of self-report, and the significant impact that the exercise intervention had on distance achieved during 10m-MSWT, the distance achieved during 10m-MSWT was considered as an indicator of exercise and PA participation. All participants in the exercise training group demonstrated a positive change during the 2-year study, with distance achieved during 10m-MSWT increasing by more than the MDC (97.08m) in 27 of the 28 participants (96%). This included 23 (82%) who experienced an extreme increase by more than 200m (more than twice the MDC).

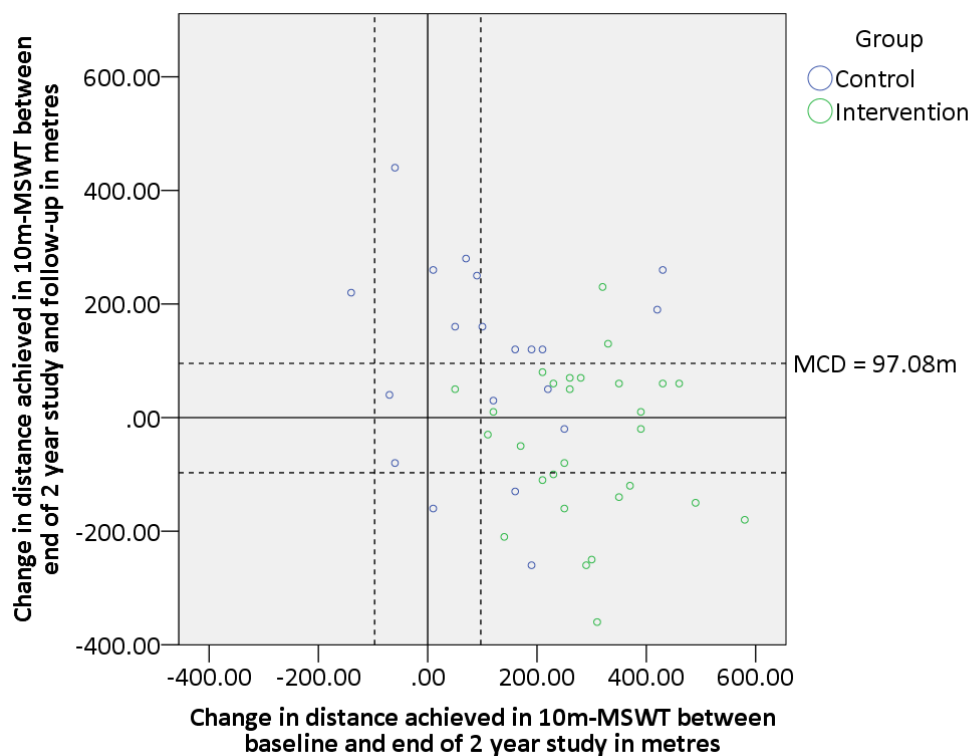


Figure 16: Scatterplot presenting the change in exercise capacity during and after participation in INSPIRE-CF by group as part of phase 1

The maintenance of distance achieved during 10m-MSWT in the exercise training group following the withdrawal of the exercise intervention followed a different trajectory. A total of 15 participants (54%) in the exercise training group demonstrated a negative change between the end of INSPIRE-CF and the PA maintenance assessment point. This decrease was extreme (more than 200m) in 4 cases (14%), and indicated that many of the participants were unable to maintain the benefits to exercise capacity resulting from the exercise intervention.

Whilst some participants were not able to maintain exercise capacity after the intervention was withdrawn, Figure 16 also demonstrated that 13 participants in the exercise training group (46%) did manage to maintain and, in some cases, even improve their distance achieved during 10m-MSWT further. Most notably, 1 participant increased by more than 200m both during and after INSPIRE-CF, indicating maintenance of PA and exercise behaviours. However, when these results were considered in line with the change in FEV₁ z score (Figure 17), it appeared that there was little link between maintenance of PA and exercise, and impact on lung function. This was perhaps not surprising given the lack of change detected in FEV₁ z score described in section 5.1.1.2.

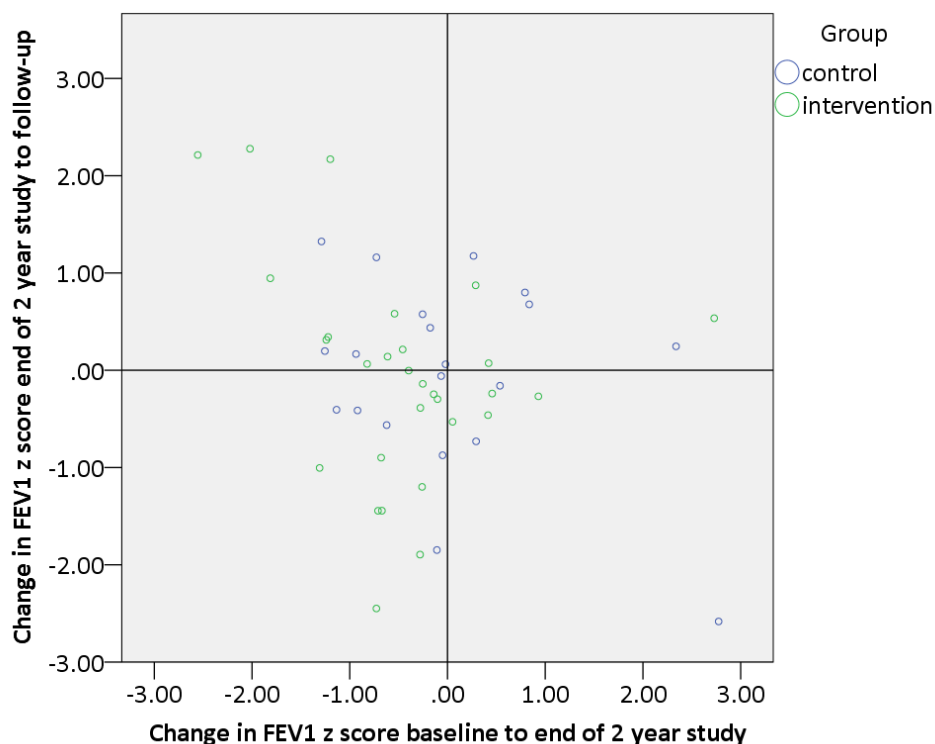


Figure 17: Scatterplot presenting the change in lung function during and after participation in INSPIRE-CF by group as part of phase 1

In contrast, only 16 of the 20 participants in the control group (80%) demonstrated an increase in distance achieved during 10m-MSWT during the course of INSPIRE-CF, with 11 (55%) over the MDC, and only 5 (25%) achieving an extremely positive change of more than 200m. This supports the previous findings that those in the exercise training group experienced greater improvements in distance achieved during 10m-MSWT as a result of the exercise intervention than those in the control group who were not supported to maintain or increase PA. Furthermore, 4 participants in the control group (25%) were unable to maintain the distance achieved during 10m-MSWT during the course of INSPIRE-CF.

The change in distance achieved during 10m-MSWT between end of INSPIRE-CF and PA maintenance assessment point was different for the control group compared to the exercise training group, with only 5 (25%) demonstrating a negative change between the end of study and PA maintenance assessment points, and only 1 with a fall greater than 200m. This must be considered in context. The control group did not demonstrate any extreme positive changes during the course of INSPIRE-CF, and therefore the maintenance of distance achieved during 10m-MSWT during the

period of time between end of INSPIRE-CF assessment and PA maintenance assessment represented a continued steady increase (as observed in Figure 12).

5.1.4 Summary of the Part A: SRC PA maintenance study

This first study (Part A) aimed to answer research question 1: what happened to the health, well-being and PA maintenance of CYPwCF after withdrawal of a supervised exercise intervention. When examined at a group level, it was clear that the increase in PA with the INSPIRE-CF exercise intervention resulted in a positive benefit to exercise capacity. However, this benefit was lost by the time of the PA maintenance assessment point suggesting PA was generally not maintained. The benefit to exercise capacity did not lead to a gain in FEV₁ z score, suggesting that lung function was independent of exercise capacity, or possibly more simply that FEV₁ z score is not a sensitive enough measure of health for this sample of CYPwCF.

The trajectories of individual participants varied substantially. Some participants were able to maintain PA and exercise participation independently after the supervised intervention was withdrawn, and thus continued to experience the benefits to exercise capacity. However, for other participants, the withdrawal of the supervised exercise intervention led to a decline in distance achieved during 10m-MSWT, possibly as a result of decline in PA participation. Further work was conducted to try to understand why some CYPwCF were able to maintain, whilst others were not.

5.2 Part B: Factors affecting the maintenance of physical activity

In addition to the repeated measures, 3 new outcome measures were also collected from each participant at the PA maintenance assessment time point to try and explore factors that might affect the maintenance of PA and exercise. The new outcome measures were:

- The CSAPPA questionnaire that quantifies self-efficacy for PA. It consists of 3 domains: adequacy, predilection and enjoyment. The CYPwCF and a parent/carer completed a copy of this questionnaire separately. Both were reporting their perception of the CYPwCF's self-efficacy for PA.
- The HAES, which is a validated questionnaire for collecting self-reported levels of PA. CYPwCF, with the assistance of a parent/carer, completed this questionnaire for 1 weekday and 1 weekend day in the previous 2 weeks thus generating data for 2 days.
- A parent/carer PA and exercise barriers questionnaire. This was completed by parents/carers and was the only component that focused on the PA and exercise behaviours of parents/carers rather than those of CYPwCF. More than 1 parent/carer completed this questionnaire in some family groups resulting in data from 68 questionnaires being collected. Details of participants can be seen in section 5.2.3.

All participants completed each outcome measure therefore there were 49 datasets for this study. The data from each outcome measure were analysed individually, comparing control and exercise training group results, and for CSAPPA, both CYPwCF- and parent-reported results. Given the small sub-group size, further analysis by age, sex and disease severity was not appropriate.

5.2.1 Self-efficacy for physical activity

Generalised self-efficacy for PA ranged from 28 to 76 for CYPwCF and 24 to 76 for parents (minimum possible score is 19 and maximum possible score is 76, with higher scores indicating greater self-efficacy for PA). Both CYPwCF and parents reported higher overall self-efficacy scores in the control group than the exercise

training group (Figure 18), although the between-group differences did not reach statistical significance and only had a small effect size (Table 12).

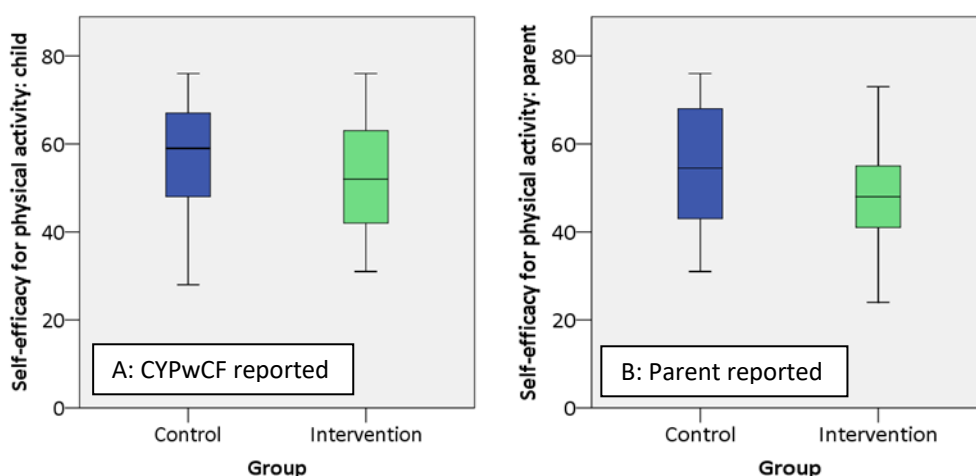


Figure 18: Box plots presenting overall self-efficacy for physical activity scores by group for phase 1 participants, CYPwCF reported (A) and parent reported (B)

Table 12: Independent-samples t-tests comparing control and exercise training group results for CYPwCF and parent reported overall self-efficacy for physical activity scores for phase 1 participants

		Mean (\pm SD)	t value (df)	p value	Mean difference (95% CI)	Effect size
CYPwCF reported	Control	57.7 (\pm 12.9)	1.25 (47)	0.219	4.68 (-2.9 to 12.3)	0.032
	Exercise training	53.0 (\pm 13.0)				
Parent reported	Control	55.1 (\pm 13.9)	1.47 (47)	0.149	5.74 (-2.1 to 13.6)	0.044
	Exercise training	49.3 (\pm 13.1)				

Key: df degrees of freedom, SD standard deviation

5.2.1.1 Self-efficacy for physical activity domains

Results for each of the 3 component domains were analysed. The adequacy domain ranged from 8 to 28 for CYPwCF reported, and 7 to 28 for parent/carer reported (minimum possible score is 7, maximum possible score is 28). The predilection domain ranged from 10 to 36 for CYPwCF reported, and 11 to 36 for parent/carer reported (minimum possible score is 9, maximum possible score is 36). And, the enjoyment domain ranged from 3 to 12 for both CYPwCF and parent reported (minimum possible score is 3, maximum possible score is 12). Again, the control group scored higher than the exercise training group for all domains, and when

reported by both CYPwCF and parents/carers (Figure 19). Almost all between-group differences were not statistically significant (Table 13 and Table 14). The exception to this was that of the enjoyment domain reported by both CYPwCF and parents/carers, where the exercise training group were reported to enjoy PA less than the control group, with a medium effect size. These results suggested that self-efficacy for PA was similar for control and exercise training groups, but that the control group reported greater enjoyment than the exercise training group. This remained true for both CYPwCF and parent reporting.

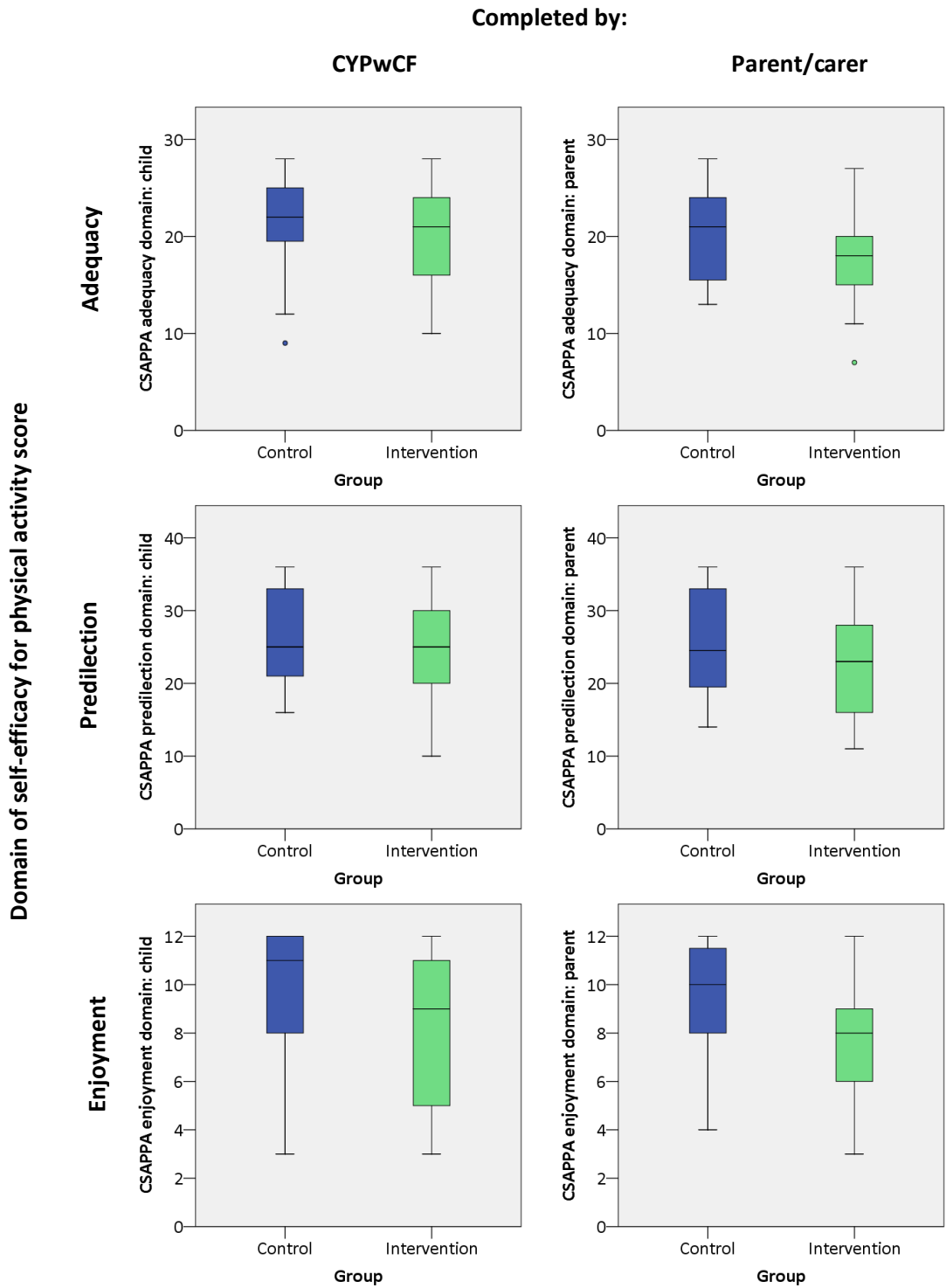


Figure 19: Box plots presenting scores for specific domains of self-efficacy for physical activity by group for phase 1 participants, and completed by CYPwCF and parent/carer

Table 13: Independent-samples t-tests comparing control and exercise training group results for normally distributed self-efficacy for physical activity domain scores reported by CYPwCF and parents/carers in phase 1

Domain	CYPwCF or parent	Mean (±SD)	Mean difference (95% CI)	t value (df)	p value	Effect size: eta squared	
Adequacy	CYPwCF	Control	21.3 (±5.3)	1.40 (-1.7 to 4.5)	0.90 (47)	0.373	0.02 (small)
		Exercise training	19.9 (±5.4)				
	Parent	Control	20.2 (±4.8)	1.41 (-0.8 to 4.9)	1.47 (47)		
		Exercise training	18.1 (±4.9)				
Predilection	CYPwCF	Control	26.5 (±6.5)	1.50 (-2.4 to 5.4)	0.77 (47)	0.445	0.01 (small)
		Exercise training	25.0 (±6.8)				
	Parent	Control	25.5 (±7.3)	2.0 (-2.2 to 6.3)	0.95 (47)		
		Exercise training	23.5 (±7.3)				

Table 14: Mann-Whitney U test comparing control and exercise training group results for non-normally distributed self-efficacy for physical activity domain scores reported by CYPwCF and parents/carers in phase 1

Domain	CYPwCF or parent	Median (IQR)	U value	Z value	p value	Effect size	
Enjoyment	CYPwCF	Control	11.0 (8-12)	192	-2.023	0.043*	0.3 (medium)
		Exercise training	9.0 (5-11)				
	Parent	Control	10.0 (8-12)	182	-2.214		
		Exercise training	8.0 (6-10)				

Key: IQR interquartile range

5.2.1.2 Comparison of CYPwCF and parent/carer reported self-efficacy for physical activity

The relationship between CYPwCF and parent/carer perceptions of the CYPwCF's self-efficacy for PA (as measured by CYPwCF and parent/carer reported CSAPPA) was investigated. Paired-samples t-tests were performed on overall self-efficacy scores, and for each domain (Table 15). CYPwCF scored statistically significantly higher than parents/carers for the overall score and adequacy domain, with moderate and large effect size respectively.

Table 15: Paired-samples *t*-tests and Pearson product-moment correlation coefficients explaining the relationships between CYPwCF and parent reported overall and domain-specific self-efficacy for physical activity scores in phase 1

Domain	CYPwCF or parent	Mean (±SD)	Mean difference (95% CI)	<i>t</i> value (df)	Effect size: eta squared	Correlation (<i>r</i>)
Overall self-efficacy	CYPwCF	54.9 (±13.0)	3.2 (0.8 to 5.7)	2.6 (48) <i>p</i> = 0.011*	0.13 (moderate)	0.794 <i>p</i> < 0.0005*
	Parent	51.7 (± 13.6)				
Adequacy	CYPwCF	20.5 (±5.4)	1.6 (0.4 to 2.7)	2.7 (48) <i>p</i> = 0.009*	0.14 (large)	0.706 <i>p</i> < 0.0005*
	Parent	18.9 (±4.9)				
Predilection	CYPwCF	25.6 (±6.7)	1.3 (-0.2 to 2.8)	1.7 (48) <i>p</i> = 0.090	0.06 (moderate)	0.716 <i>p</i> < 0.0005*
	Parent	24.3 (±7.3)				
Enjoyment	CYPwCF	8.8 (±3.1)	0.3 (-0.3 to 0.9)	1.0 (48) <i>p</i> = 0.327	0.02 (small)	0.719 <i>p</i> < 0.0005*
	Parent	8.5 (±2.6)				

Key: CI confidence interval, df degrees of freedom, SD standard deviation

This statistical test was limited to only demonstrating the degree of difference between CYPwCF and parent/carer reported self-efficacy for PA. Further understanding of the direction of relationship between CYPwCF and parent/carer reported outcomes was required, thus Pearson product-moment correlation coefficients were calculated for the overall score and for each domain. Preliminary analyses were performed to ensure no violation of the assumptions of normality, linearity and homoscedasticity. There were strong, positive correlations between all CYPwCF and parent paired variables (Table 15), with high levels of CYPwCF-perceived self-efficacy for PA associated with high levels of parent-perceived self-efficacy for PA. However, a Bland and Altman analysis identified wide limits of agreement (-13.6 to 20.0) (Figure 20). This suggested a large variation in differences, with some CYPwCF-parent dyads scoring similarly, and others with large and likely meaningful discrepancies. As this research has focussed on the maintenance of exercise and PA behaviours of CYPwCF, the CYPwCF perception of self-efficacy for PA should be considered as the priority for further analysis, but this finding should be considered valuable to inform clinical practice: CYPwCF must be

involved in conversations about their own view of PA because there is not always agreement with parent/carer perception.

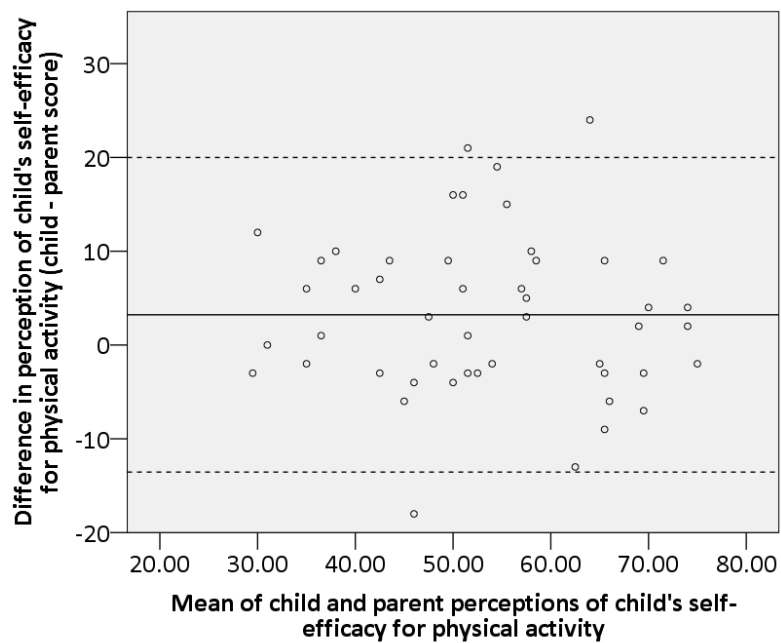


Figure 20: Bland and Altman plot for CYPwCF and parent perception of CYPwCF's self-efficacy for physical activity for phase 1 participants, with the representation of limits of agreement (dotted lines) from $-1.96SD$ to $1.96SD$

5.2.2 Self-reported activity levels

Self-reported time spent in MVPA ranged from 0 to 482 minutes (0-8hours) for weekdays and 0 to 525 minutes (0-8.5hours) for weekend days. The reported levels of PA were similar between control and exercise training groups for both weekday and weekend days (Figure 21), with no statistically significant differences noted (Table 16). This suggested that there was no latent effect of the exercise intervention on the maintenance of PA.

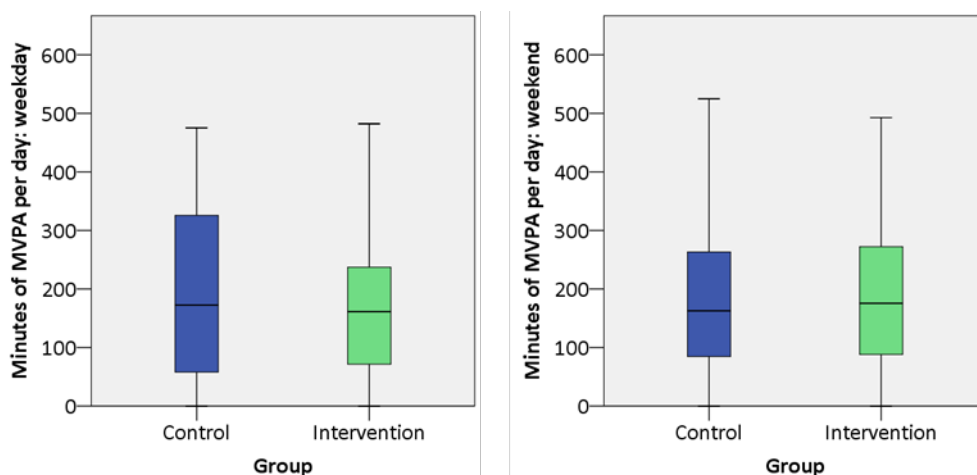


Figure 21: Box plots presenting self-reported physical activity levels for CYPwCF for weekday and weekend day for phase 1 participants

Table 16: Independent-samples t-tests comparing control and exercise training group results for self-reported physical activity levels in phase 1

		Mean (±SD)	t value (df)	p value	Mean difference (95% CI)	Effect size
Weekday	Control	188 (±158)	0.34 (47)	0.738	14 (-70 to 99)	0.002 (small)
	Exercise training	174 (±135)				
Weekend day	Control	188 (±155)	0.48 (47)	0.976	1 (-81 to 84)	0.000019 (very small)
	Exercise training	187 (±131)				

Key: CI confidence interval, df degrees of freedom, SD standard deviation

5.2.2.1 Comparison of weekday and weekend day self-reported physical activity levels

The relationship between weekday and weekend day self-reported PA levels (both measured by HAES) was investigated. Since there was no difference in self-reported PA levels between control and exercise training groups, data were analysed together. Paired-samples t-tests were performed on self-reported minutes spent in MVPA for weekdays and weekend days. There was no statistically significant difference between self-reported minutes spent in MVPA during weekdays and weekend days (Table 17).

Table 17: Paired-samples t-test and Pearson product-moment correlation coefficient explaining the relationship between self-reported time spent in MVPA during weekdays and weekend days for phase 1 participants

Domain	Mean (±SD)	Mean difference (95% CI)	t value (df)	Effect size: eta squared	Correlation (r)
Weekday	179 (±143)	-8 (-48 to 32)	-0.42 (48)	0.004 (very small)	0.520 $p < 0.0005^*$
Weekend day	188 (±140)		$p = 0.678$		

Key: df degrees of freedom, SD standard deviation

This statistical test was limited to only demonstrating the degree of similarity between self-reported time spent in MVPA for weekdays and weekend days. Further understanding of the degree of the relationship was required, thus a Pearson product-moment correlation coefficient was calculated. Preliminary analyses were performed to ensure no violation of the assumptions of normality, linearity and homoscedasticity. There was a strong, positive correlation between self-reported time spent in MVPA during weekdays and weekend days (Table 17), with high levels of self-reported PA for weekdays being associated with high levels of self-reported PA for weekend days.

5.2.2.2 Comparison of self-reported physical activity levels at PA maintenance assessment point as collected by HAES and INSPIRE-CF method

The relationship between the self-reported levels of PA collected by the 2 different methods was investigated. The HAES is a validated tool and recorded time spent in different activity states for a weekday and weekend day in the previous 2 weeks. The INSPIRE-CF method was unvalidated and recorded frequency and duration of structured physical activities in a typical week. If there was a significant correlation between the data generated by the 2 different methods then an opportunity would have existed to draw further conclusions about PA participation throughout INSPIRE-CF when self-reported PA was only measured by the INSPIRE-CF method. Minutes of PA per day for both weekday and weekend day (collected by HAES) were compared with minutes of PA per week (collected by INSPIRE-CF survey method) (Figure 22). Given the clear violation of homoscedasticity with wide distribution of points on the scatterplots, Spearman's rank order correlations were conducted. There was a statistically significant medium, positive correlation

between HAES reported minutes of PA per day for weekend days and self-reported minutes of PA per week, $\rho = 0.317$, $n = 48$, $p = 0.028$. However, the correlation between HAES reported minutes of PA per day for weekdays and self-reported minutes of PA per week was small, and did not reach statistical significance, $\rho = 0.202$, $n = 48$, $p = 0.169$. This suggested that 1 method was potentially superior at measuring self-reported PA to the other. Or it may have simply been that the 2 methods were measuring different constructs, for example, the INSPIRE-CF method measured frequency and duration of structured physical activities, whereas the HAES measured time in different activity states which involves unstructured activities and also an individual's perception of different activity states.

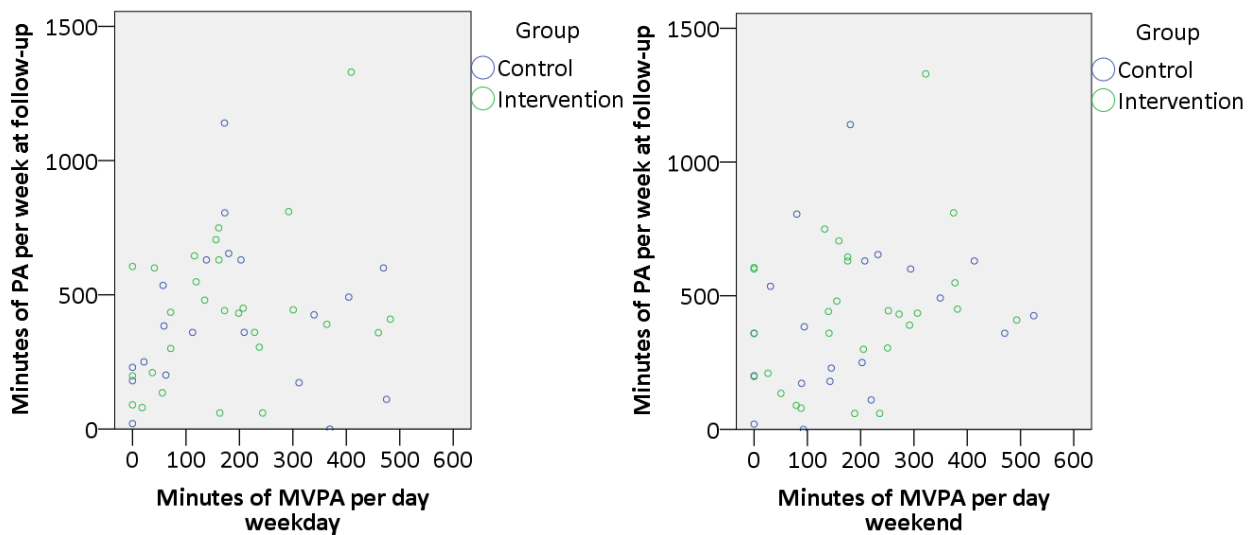


Figure 22: Scatterplots of self-reported physical activity levels collected by HAES and INSPIRE-CF survey method for phase 1 participants.
Left: HAES weekday, right: HAES weekend day.

5.2.3 Parents/carers own barriers to PA and exercise participation

The barriers experienced by parents/carers to their own PA and exercise participation were investigated using a questionnaire. A total of 68 parents/carers completed the questionnaire and were included in this part of analysis (Table 18).

Table 18: Details of the parent/carer sample for phase 1

		Group (n)		Total
		Control	Exercise training	
Participating parent	Mother	16	27	43
	Father	12	12	24
	Other	0	1	1
	Total	28	40	
Number of participating parents per family	1	12	18	30
	2	8	11	19

Key: n number

The total barriers maximum possible score was 63, and a lower score indicated fewer barriers to PA and exercise. Results for total barriers score ranged from 0 to 44. The parents/carers of CYPwCF in the exercise training group appeared to report, on average, more barriers to PA and exercise than those of CYPwCF in the control group (Figure 23). However, this did not reach statistical significance when an independent-sample t-test was conducted, mean difference -4.56 (95% CI: -10.42 to 1.31), $t(66) = -1.55$, $p = 0.126$ (two-tailed).

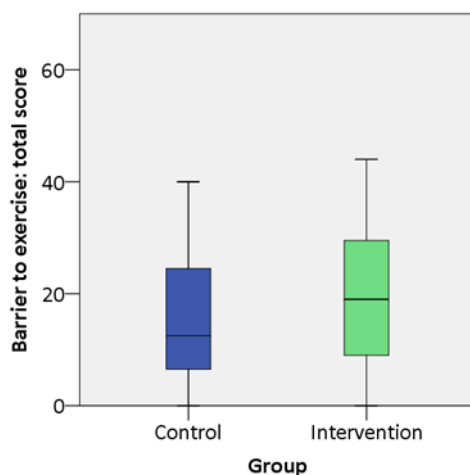


Figure 23: Box plot presenting overall barriers to parent/carer exercise participation scores by group for phase 1 participants

5.2.3.1 Parent/carer barriers to PA and exercise participation domains

Results for each of the 7 component domains (as defined by the questionnaire), and synergies between domains, were analysed. Parent/carer scores for the lack of time, social influence, fear of injury and lack of skill domains all ranged from 0 to 8

(maximum possible score for all domains was 9). Lack of energy, lack of willpower and lack of resources all ranged from 0 to 9. Median score ranged from 3 for lack of time to 0 for fear of injury (Figure 24). The results of the Friedman Test indicated that there was a statistically significant difference in the scoring across the domains, $\chi^2(6, n = 68) = 151, p < 0.005$. Post-hoc analysis was conducted with individual Wilcoxon Signed Rank Tests, using a Bonferroni adjusted alpha value of 0.002 (Table 19). There were statistically significant differences between individual pairings of lack of time, social influence, lack of energy and lack of willpower, and fear of injury, lack of skill and lack of resources. The only exception to this was the relationship between social influence and lack of resources, which did not reach significance. Results suggested that lack of time, energy and willpower, and social influence presented greater barriers to parent/carer PA and exercise than lack of skill and resources, and fear of injury. Identifying what created barriers to parent/carer PA and exercise was important to then understand any resultant impact on the maintenance of PA of CYPwCF.

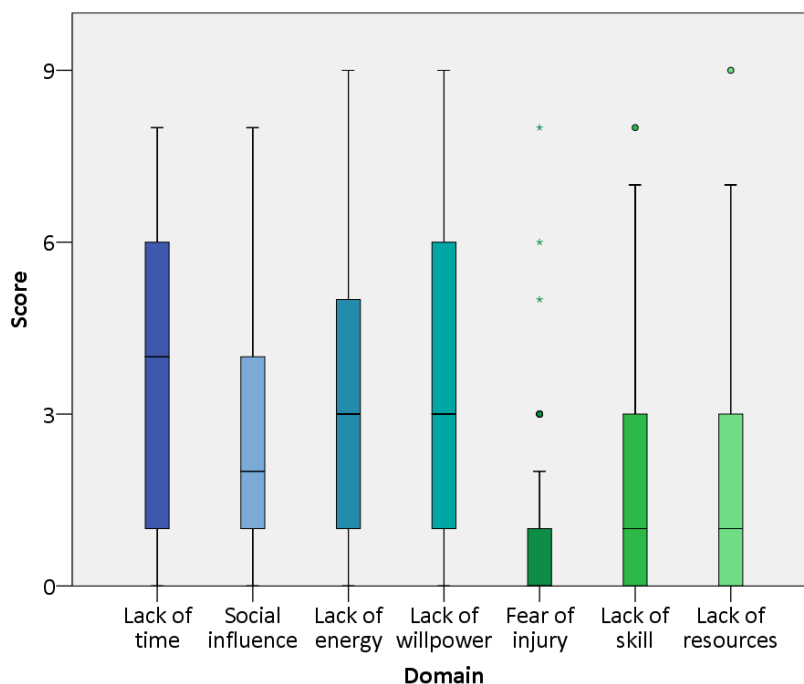


Figure 24: Box plots presenting barriers to parent/carer exercise participation scores by domain for phase 1 participants

Table 19: Individual Wilcoxon Signed Rank Tests explaining the differences between the domain scores for the parent/carer barriers to exercise participation for phase 1 participants

	Lack of time	Social influence	Lack of energy	Lack of willpower	Fear of injury	Lack of skill	Lack of resources
Lack of time		$z = -2.43$ $p = 0.015$ $r = -0.29$	$z = -1.11$ $p = 0.267$ $r = -0.13$	$z = -0.02$ $p = 0.986$ $r = -0.002$	$z = -6.71$ $p < 0.0005^*$ $r = -0.81$	$z = -5.11$ $p < 0.0005^*$ $r = -0.62$	$z = -4.58$ $p < 0.0005^*$ $r = -0.56$
Social influence			$z = -1.41$ $p = 0.159$ $r = -0.17$	$z = -2.11$ $p = 0.035$ $r = -2.56$	$z = -5.03$ $p < 0.0005^*$ $r = -0.61$	$z = -3.22$ $p = 0.001^*$ $r = -0.39$	$z = -2.32$ $p = 0.020$ $r = -0.28$
Lack of energy				$z = -0.93$ $p = 0.350$ $r = -0.11$	$z = -6.22$ $p < 0.0005^*$ $r = -0.75$	$z = -4.43$ $p < 0.0005^*$ $r = 0.54$	$z = -3.73$ $p < 0.0005^*$ $r = -0.45$
Lack of willpower					$z = -6.17$ $p < 0.0005^*$ $r = -0.75$	$z = -4.70$ $p < 0.0005^*$ $r = -0.57$	$z = -4.06$ $p < 0.0005^*$ $r = -0.49$
Fear of injury						$z = -1.49$ $p = 0.136$ $r = -0.18$	$z = -2.74$ $p = 0.006$ $r = -0.33$
Lack of skill							$z = -1.01$ $p = 0.313$ $r = -0.12$
Lack of resources							

* Statistically different

5.2.4 Was there a difference in self-efficacy for physical activity, self-reported levels of physical activity, and parent/carer physical activity and exercise barriers between control and exercise training groups?

Having analysed the components of each variable in detail individually, it was important to analyse them together in order to understand the characteristics of the 2 groups and any potential longer-term impact of the intervention. It was possible that the exercise training intervention would have facilitated greater PA maintenance in the participants who received the training than those who received standard CF care only. Therefore, a one-way between-groups multivariate analysis of variance (MANOVA) was performed to investigate group differences in self-efficacy for PA, self-reported levels of PA and parent barriers to PA and exercise. Four dependent variables were used: child-reported self-efficacy for PA, self-reported levels of PA for a weekday and a weekend day, and parent barriers to PA and exercise. It should be noted that it was only possible to include 1 parent/carer

response to the barriers questionnaire per CYPwCF participant. Therefore, the parent/carer who attended the assessment with their CYPwCF was included in the MANOVA. A Mann-Whitney U test revealed no significant difference in the parent/carer PA and exercise barrier scores for those included in the MANOVA (median = 18, n = 49) and those that were not (median = 11, n = 19), $U = 360$, $z = -1.44$, $p = 0.149$. The independent variable for the MANOVA was INSPIRE-CF group allocation (control/exercise training). Preliminary assumption testing was conducted to check for normality, linearity, univariate and multivariate outliers and homogeneity of variance-covariance matrices, with no serious violations noted. The assumption of multicollinearity required that variables were only moderately correlated ($r < 0.8$). CYPwCF and parent/carer reported self-efficacy scores (measured by CSAPPA) were strongly correlated ($r = 0.8$) therefore only CYPwCF self-efficacy for PA scores were included in the MANOVA. Self-reported levels of PA for weekdays and weekend days (measured by HAES) were strongly correlated but only to $r < 0.6$, and considering the wide 95% confidence interval of the mean difference (-48 to 32) it was appropriate to include both variables in the MANOVA. There was no statistically significant difference between control or exercise training groups on the combined dependent variables, $F(4, 44) = 0.63$, $p = 0.645$, thus further analysis exploring the maintenance of PA could be conducted with the data from both groups combined.

5.2.5 Relationships between self-efficacy for physical activity, self-reported levels of physical activity, parent/carer physical activity and exercise barriers, and exercise capacity, and the maintenance of physical activity and exercise

Having established that there were no significant differences in outcomes between the control and exercise training groups, the data were explored further with both groups together. The purpose of this was to understand the relationship between variables, and the resultant impact on exercise capacity in the first instance. The relationships between variables including exercise capacity at PA maintenance assessment point (measured by 10m-MSWT) were investigated using Pearson product-moment correlation coefficient (Table 20). Preliminary analyses had already been performed on this dataset, and no violation of the assumptions of

normality, linearity and homoscedasticity were noted. CYPwCF perception of their own self-efficacy for PA (measured by CSAPPA) was the only variable that correlated with exercise capacity at PA maintenance assessment point, albeit a medium correlation. There were no other correlations between variables, other than, perhaps unsurprisingly, weekday and weekend self-reported levels of PA.

Table 20: Pearson product-moment correlation coefficients explaining the relationships between CYPwCF self-efficacy for physical activity, self-reported activity levels for both weekday and weekend, parent/carer exercise barriers and maintenance of physical activity and exercise in phase 1

	Self-efficacy for physical activity	Self-reported activity level-weekday	Self-reported activity level-weekend	Parent/carer exercise barriers	Exercise capacity
Self-efficacy for physical activity		$r = 0.27$ $p = 0.061$	$r = 0.27$ $p = 0.063$	$r = -0.21$ $p = 0.149$	$r = 0.46^*$ $p = 0.001$
Self-reported activity level-weekday			$r = 0.52^{**}$ $p < 0.0005$	$r = 0.01$ $p = 0.98$	$r = 0.21$ $p = 0.146$
Self-reported activity level-weekend				$r = 0.07$ $p = 0.642$	$r = 0.17$ $p = 0.247$
Parent/carer exercise barriers					$r = -0.16$ $p = 0.265$
Exercise capacity					

* Medium positive correlation, ** Large positive correlation

To investigate the maintenance of PA and exercise was more complex. As exercise capacity was the only objectively measured variable with detectable change as a result of the exercise intervention during the INSPIRE-CF study, it was considered to be appropriate to use change in distance achieved during 10m-MSWT as an indicator of maintenance of PA. Therefore, analysis of the group of participants who were known to have achieved a positive change in distance achieved during 10m-MSWT during INSPIRE-CF was conducted. If a positive trajectory continued during the period of time between the end of INSPIRE-CF and the PA maintenance assessment then CYPwCF were considered to have successfully maintained PA participation (indicated by the green shaded area in Figure 25). However, if exercise capacity fell during this period of time then CYPwCF were considered to have not

managed to maintain PA participation (indicated by the red shaded area in Figure 25).

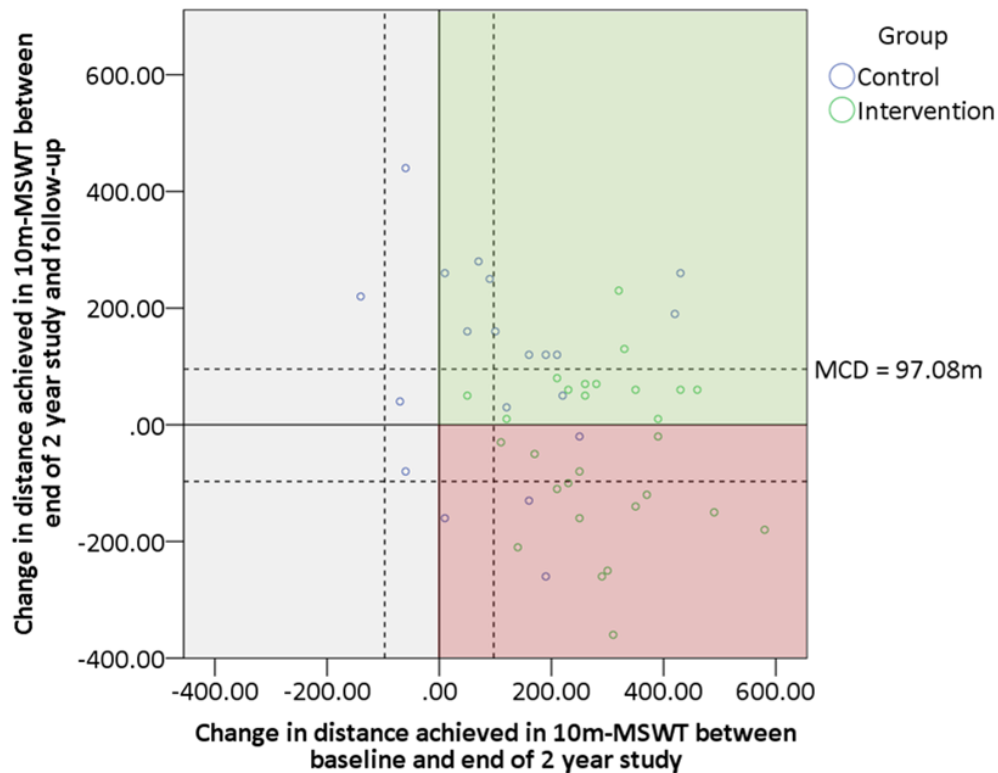


Figure 25: Scatterplot presenting the change in exercise capacity during and after participation in INSPIRE-CF by group for phase 1 participants, with indication of maintained activity (green shading) or not maintained activity (red shading)

There were 44 participants identified as having an increase in distance achieved during 10m-MSWT during the INSPIRE-CF study period. Of those, 25 managed to maintain PA participation (as indicated by further increase in distance achieved during 10m-MSWT to PA maintenance assessment point), and 19 did not (decline in distance achieved during 10m-MSWT to PA maintenance assessment point).

Interestingly, only 29% of female participants (n = 5) maintained distance achieved during 10m-MSWT compared to 74% of male participants (n = 20) suggesting there were differences in PA maintenance behaviours between females and males.

Mann-Whitney U tests were conducted to explore the differences in self-efficacy for PA (measured by CYPwCF-reported CSAPPA), self-reported levels of PA (measured by HAES) and parent/carer PA and exercise barriers (measured by questionnaire) between those who were identified as maintainers and those who were not (Table 21). Again, self-efficacy for PA was the only variable which

demonstrated a significant difference between those who maintained and those who did not. These findings suggested that the barriers to PA and exercise experienced by parents/carers, and self-reported levels of PA did not impact on the ability of a CYPwCF to maintain PA participation, and thus exercise capacity. However, the self-efficacy for PA of a CYPwCF appeared to be an important factor.

Table 21: Mann-Whitney U tests comparing self-efficacy for physical activity, self-reported activity levels and parent/carer exercise barriers for maintainers and non-maintainers in phase 1

Variable	Maintained activity	Median (IQR)	U value	Z value	p value	Effect size
Self-efficacy for physical activity	Yes	63.0 (52-70)	100	-3.27	0.001*	0.5 (large)
	No	46.0 (37-60)				
Minutes of MVPA: weekday	Yes	161 (92-269)	212	-0.61	0.545	-0.1 (small)
	No	172 (21-292)				
Minutes of MVPA: weekend	Yes	176 (91-243)	209	-0.68	0.499	-0.1 (small)
	No	141 (0-307)				
Parent/carer barriers to PA and exercise	Yes	19.0 (7-28)	214	-0.56	0.577	-0.1 (small)
	No	21.0 (14-27)				

Key: IQR interquartile range, MVPA moderate-vigorous physical activity

5.2.6 Summary of the factors affecting the maintenance of physical activity study

This second study (Part B) aimed to answer research question 2: what affects the maintenance of PA in CYPwCF. Self-efficacy for PA, self-reported levels of PA and parent PA and exercise barriers were measured by questionnaires. Both CYPwCF and parents reported their perception of the child or young person's self-efficacy. Results were varied with some CYPwCF and parents reporting higher self-efficacy for PA than others. There were varied discrepancies between child/young person-reported and parent-reported self-efficacy for PA. This indicates how important it is for clinicians to direct focus to CYPwCF in conversations about PA rather than their parents.

Self-reported levels of PA were generally high (mean ~3hours per day for both weekdays and weekend days). These high values raised questions about the

accuracy of these reports. Self-report is liable to report and recall biases, and also involves an individual's perception of PA. Further work was required to understand self-reported levels of PA in relation to more objectively measured PA.

Parents reported experiencing barriers to their own PA and exercise participation. Lack of time, lack of energy, lack of willpower and social influence were the most notable barriers. However, these did not seem to be linked to the maintenance of PA in their child/young person. In fact, self-efficacy for PA (CYPwCF-reported) had the strongest, and only statistically significant association with the maintenance of PA in CYPwCF.

5.3 Part C: Barriers to and facilitators for the maintenance of physical activity

Semi-structured interviews were used to explore the PA and exercise maintenance experiences, attitudes and behaviours, and perceptions of barriers to and facilitators for PA maintenance, of a sub-group of CYPwCF and their parents. Purposive sampling identified 35 participants from the Parts A and B studies cohort who were deemed by a GOSH CF physiotherapist and the researcher (HD) to be likely to fulfil a range of characteristics (age, sex, control/exercise training group, and PA and exercise participation levels). Data saturation was reached after 40 interviews were conducted (20 CYPwCF and 20 parent interviews). The interview sub-group was generally characteristically representative of the whole cohort, although proportionately more females were interviewed than males (Table 22). The results from the SRC PA maintenance study identified that male participants were much more likely to maintain distance achieved during 10m-MSWT than female participants (section 5.2.5). In order to reduce burden, participants were invited for interview on the same day as they participated in the SRC PA maintenance study. This design meant that the difference in maintenance of distance achieved during 10m-MSWT between males and females was not identified until all data had been collected, thus it was not possible to rectify the skew of male to female interview participants. However, recruitment continued until data saturation was reached and no new themes were identified. This design also meant that it was inevitable that the interview sub-group had a shorter time between end of INSPIRE-CF study and PA maintenance assessment compared to the non-interview sub-group. This was considered to have minimal impact on the findings from this qualitative work.

Table 22: Demographic information of the interview sub-group compared to the non-interview sub-group of phase 1

		Interviewed	Not interviewed	<i>p</i>
n =		20	29	
	Control group	6	14	0.325
	Exercise training group	14	15	
Age in years (mean ± SD)		13.3 ± 2.1	13.3 ± 2.3	0.925 ¹
Sex	Male	6	22	0.004*
	Female	14	7	
Genotype	F508del / F508del	11	18	0.054
	F508del / Other	9	6	
	Other / Other	0	5	
Disease severity (%)	Mild ppFEV₁ ≥70%	17	21	0.299
	Moderate ppFEV₁ 40-69%	3	8	
	Severe ppFEV₁ <40%	0	0	
Percentage of weeks trained throughout study (mean ± SD)		65 ± 11	62 ± 13	0.489 ¹
Time between end of 2-year study and PA maintenance assessment in days (median/IQR)		920 (891-964)	1002 (935-1023)	0.005 ^{1*}
Self-efficacy for physical activity (CSAPPA score)	Child reported	53 ± 11	56 ± 14	0.395 ¹
	Parent reported	49 ± 11	54 ± 15	0.181 ¹
Self-reported minutes of MVPA	Weekday	212 ± 166	157 ± 123	0.183 ¹
	Weekend day	196 ± 128	182 ± 150	0.723 ¹
Parent barriers to exercise (questionnaire score)		n = 30 19.0 ± 12.5	n = 38 16.5 ± 11.7	0.390

Key: CSAPPA children's self-perception of adequacy in and predilection for physical activity, IQR interquartile range, MVPA moderate-vigorous physical activity, n number, ppFEV₁ percent of predicted FEV₁, SD standard deviation

t test for independent samples for all continuous variables with normal distribution, Chi-square test for all categorical variables

¹ Mann-Whitney U test for continuous variables with non-normal distribution,

* reached level of significance α 0.05

The interview sub-group included participants from both control and exercise training groups of INSPIRE-CF, detailed in Table 23. This enabled the exploration of different perspectives of maintenance of PA as those who experienced the exercise training had received different additional support which may have influenced the maintenance of PA in those participants. All CYPwCF chose to be interviewed without a parent present. Almost all parent interviews were conducted with 1 parent, with the exception of 1 parent pair (control) who requested to be interviewed together.

Table 23: Demographic information for the interview sub-group comparing control and exercise training groups of phase 1

		Control group	Exercise training group	<i>p</i>
n =		6	14	
Age in years (mean ± SD)		14.1 ± 1.8	13.0 ± 2.2	0.836
Sex	Male	2	4	1.000
	Female	4	10	
Genotype	F508del / F508del	4	7	0.642
	F508del / Other	2	7	
	Other / Other	0	0	
Time between end of 2 year study and PA maintenance assessment in days (median/IQR)		911 (895-959)	921 (890-966)	0.805
Parent interviewed	Mother	5	12	0.574
	Father	2	2	

Key: IQR interquartile range, n number, SD standard deviation
Mann-Whitney U test for all continuous variables,
Fisher's exact test for all categorical variables.
Nil reached level of significance α 0.05

Due to the semi-structured design, the duration of interviews varied. The shortest was a CYPwCF interview that lasted 5 minutes, and the longest was a parent interview lasting 39 minutes. The majority were 12-30 minutes long. The semi-structured approach meant that some interviews were more conversational in nature and all aspects of the topic guide (Appendix 13) were addressed without specific questions, whereas other interviews required more direction from the interviewer and specific questions were used to cover everything in the topic guide.

The data were analysed using thematic content analysis to identify categories and themes discussed by the CYPwCF and parent participants (Figure 26), details of this method can be found in section 4.7.3. The developed framework consisted of 4 main categories, which contained sub-categories, group themes and individual themes. Direct quotes have been used to provide evidence of the coding process and support the findings. Quotes are denoted in blue italic text, and followed by category and theme level coding. More than 1 meaning was derived from some phrases therefore some phrases have been coded into 2 or more different themes. All thematic coding has been included for each quote for transparency.

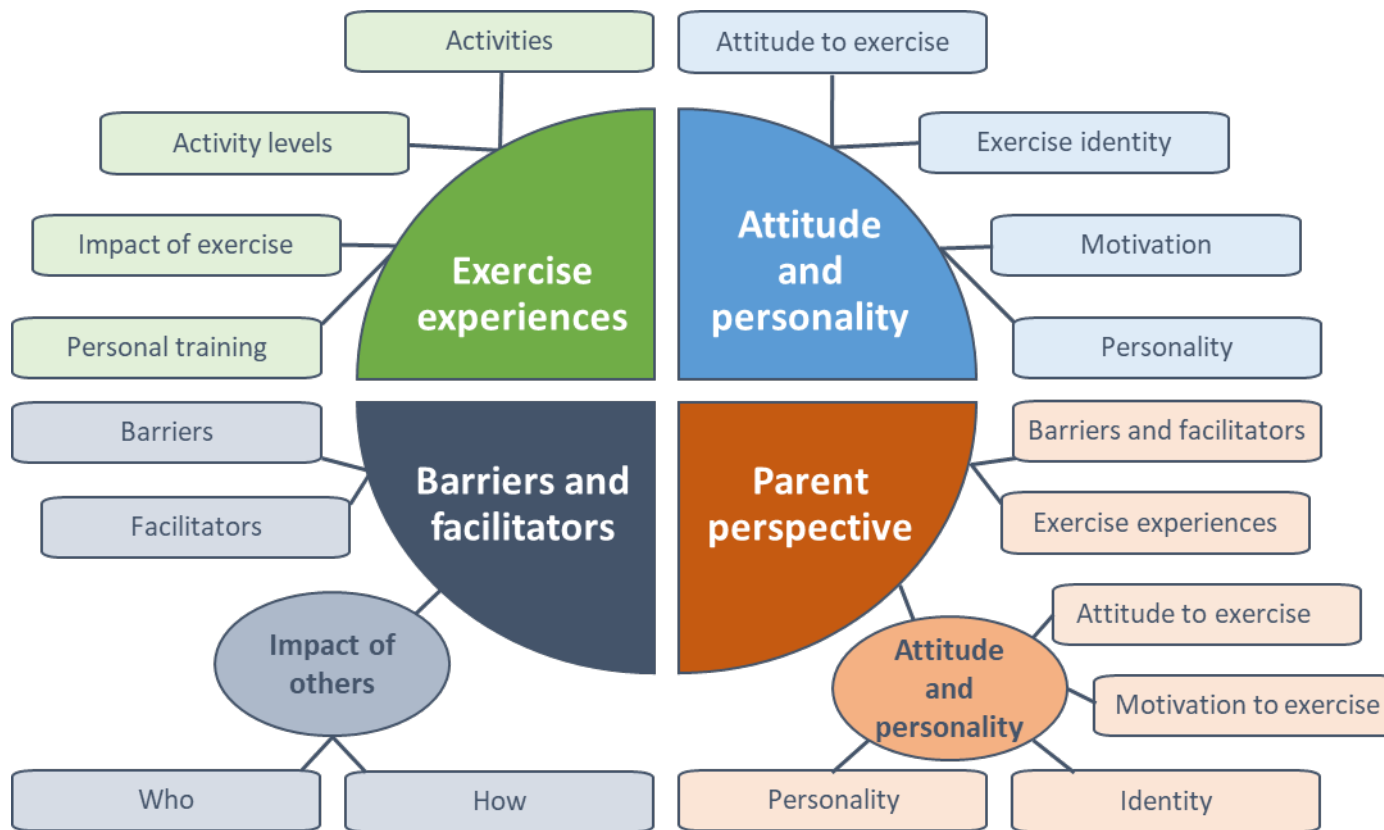


Figure 26: The framework of categories identified from the semi-structured interviews with CYPwCF and parents as part of phase 1

5.3.1 Experience of exercise

Interview participants were asked about their experience of exercise, and 4 main group themes were identified (Figure 27).

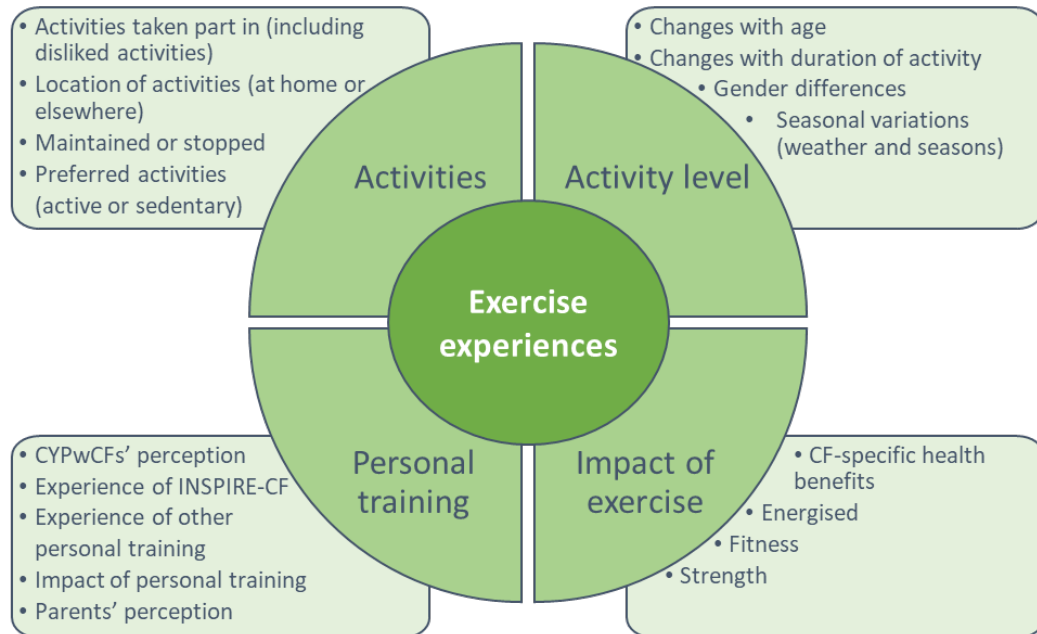


Figure 27: Themes identified in the exercise experiences category as part of phase 1

5.3.1.1 Activities and activity level

Some CYPwCF were wholly positive about physical activities, and others preferred sedentary pastimes. All participants reported taking part in some form of PA regularly, although 2 CYPwCF reported that their only regular activity was physical education at school. Another 2 CYPwCF reported participating in as many as 6 different PA, sport or exercise sessions each week.

Despite varied levels of participation, all participants identified physical activities that they found enjoyable. Twelve CYPwCF reported preferring informal physical activities, such as scootering and cycling, and 8 CYPwCF reported enjoying structured sport and exercise, such as gym training, dance and team sports. Ten CYPwCF took part in regular structured exercise, including 4 who reported not enjoying formal sports. These 4 were attending weekly gym-based personal training and were positive about maintaining these sessions. Many CYPwCF and parents talked about activities that they had given up.

'He just gets bored and loses interest... We've been through the karate stage with him and he went twice and lost interest. After me buying everything for him. We've been through all sorts of different things and he'll get bored and 'no, I'm not going there anymore.'

Parent participant

Exercise experiences: Activity level: Changes with duration of activity

Exercise experiences: Activities: Maintained or stopped

One parent participant reported that she felt finding supervised and structured activities (such as team sports) for girls was more difficult than for boys, although this was not mentioned by any CYPwCF or other parents. However, 13 parents and CYPwCF voiced the impact that weather and seasons had on activity levels:

'In summer there's more going on in terms of going for a bike ride, or swimming. We do much more activities or walking, stuff like that in the summer. But winter time we are kind of home-bound.'

Parent participant

Exercise experiences: Activity level: Seasonal variations (weather and seasons)

Levels of participation varied within individuals as well, and 8 parents and 1 CYPwCF discussed changes in levels of participation in relation to age.

'I feel I've just become lazier.'

CYPwCF participant

Exercise experiences: Activity level: Changes with age

'She was always the sort of girl that would love to go down the park, loved climbing, loved everything. Now she's very much into social media.'

Parent participant

Exercise experience: Activity level: Changes with age

Parent perspective: Attitude and personality: Identity: CYPwCF: Sporty or not sporty

5.3.1.2 *Impact of exercise*

All participants recognised benefits of PA, sport and exercise including CF-specific health benefits. In addition, participants also reported a noticeable impact on fitness and strength as a result of their exercise participation. One participant discussed that exercise made her feel more energised and happy, and this also became a motivator for undertaking more exercise.

'It makes me feel more energised and happy, because I know I've done a good work out and I know that it's good.'

CYPwCF participant

Exercise experiences: Impact of exercise: Energised
Attitude and personality: Attitude to exercise: Positive or negative

5.3.1.3 Personal training

A total of 18 CYPwCF participants had experience of personal training. The majority (n = 14) had received training as part of the 2-year long exercise intervention study INSPIRE-CF. The additional 4 who were in the control group of INSPIRE-CF had accessed an optional personal training service offered as a result of a collaboration between the GOSH CF physiotherapy service and Nuffield Health, a UK fitness provider. The views that participants had of personal training were varied. Some loved it from the beginning, some did not enjoy it, and the attitude of others changed as the training continued.

'Once I started doing it more I was like I don't really like it.'

CYPwCF participant

Exercise experiences: Personal training: CYPwCFs' perception

'The first weeks I was like urgh this time of the week again, I've got to go, and then by the end of it I was really looking forward to it because it was a time that I didn't have to sit at home. I'm actually going out and doing something different.'

CYPwCF participant

Exercise experiences: Personal training: CYPwCFs' perception
Exercise experiences: Activity level: Changes with duration of activity

'He was terrible at the beginning, and even the trainers, I felt so sorry for them ... because he doesn't want to put the effort in. But he came on such a long way that I didn't want it to end.'

Parent participant

Exercise experiences: Personal training: Parents' perception
Exercise experiences: Personal training: Impact of personal training

Some CYPwCF and parent participants noted the impact that personal training had made. Five CYPwCF reported that regular personal training had resulted in a change of exercise identity, i.e. they became more 'sporty'.

'I think it had such an impact ... It didn't just have an impact on CF, it was having an impact everywhere ... It's changed our lives definitely.'

Parent participant

Exercise experiences: Personal training: Impact of personal training

'I didn't really think I was going to be very good because I didn't really like exercise and I didn't do any sports. Now it's really fun, and I've started all the groups and sports.'

CYPwCF participant

Exercise experiences: Personal training: Impact of personal training

Exercise experiences: Personal training: Experience of INSPIRE-CF

Exercise experiences: Personal training: CYPwCFs' perception

Attitude and personality: Exercise identity: Sporty or not sporty

'He can now strive for whatever he wants ... I think if you talked to him about exercise now he's got a 'yes I can do it I'm really good'.'

Parent participant

Exercise experiences: Personal training: Impact of personal training

One CYPwCF described how she felt that personal training had affected her other sport and exercise activities as it had resulted in increased stamina and fitness.

In summary, the findings from the 'exercise experiences' category were that CYPwCF had varied exercise experiences and held differing attitudes towards PA. All CYPwCF recognised the benefits of being physically active and were able to identify at least 1 PA that they enjoyed but many reported struggling to maintain participation and had given up some activities, suggesting that enjoyment alone is not enough to keep CYPwCF engaged in PA. Personal training worked for some but not all CYPwCF, even resulting in a positive change in exercise identity for a few. The different experiences and attitudes would likely result in different maintenance of PA patterns. The findings also suggested that there may have been a fall in level of PA associated with age for at least 1 CYPwCF, this was worthy of further investigation in phase 2 of this research.

5.3.2 Attitude and personality

The semi-structured interview schedule did not specifically address attitude and personality, however themes within this category were raised by all interview participants. There were 4 main themes identified (Figure 28).

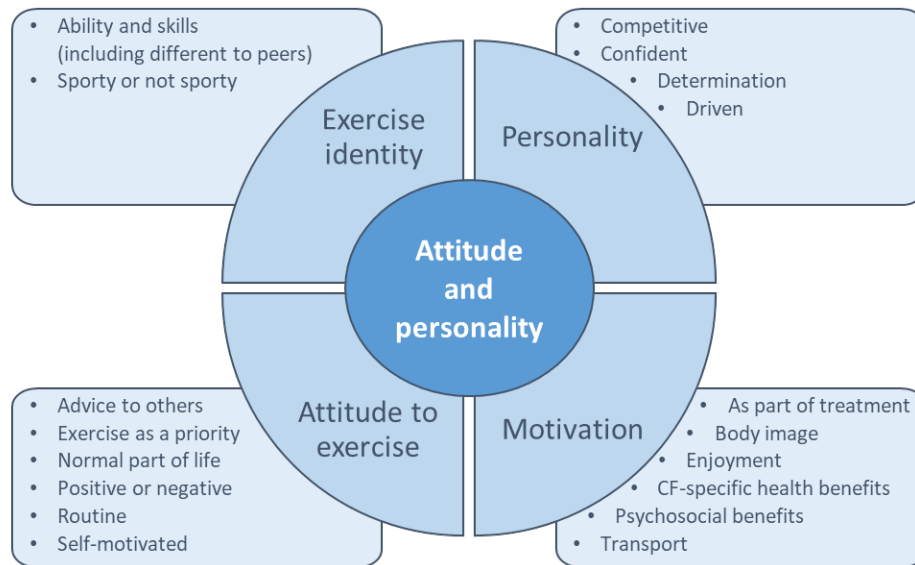


Figure 28: Themes identified in the attitude and personality category as part of phase 1

5.3.2.1 Exercise identity

Even though participants were not directly asked, 17 CYPwCF and parents discussed exercise identity during the interviews: 4 identified the CYPwCF as 'sporty', 8 as 'not sporty', and 5 as 'becoming sporty'.

'She's always said she's bad at sport'

Parent participant

Attitude and personality: Exercise identity: Sporty or not sporty

'She was very nervous because she's not very sporty and hadn't done much exercise up to that point ... but now her confidence is completely different.'

Parent participant

Attitude and personality: Exercise identity: Sporty or not sporty
 Exercise experiences: Personal training: Impact of personal training
 Exercise experiences: Personal training: Parents' perception

'I didn't get into exercise until about year 6, but say if I'd got into it earlier then I may have been a little bit more sporty and then my lung function may have improved a little bit earlier. Not that that's a bad thing but I just would start exercising a little bit earlier because it does make a difference.'

CYPwCF participant

Attitude and personality: Exercise identity: Sporty or not sporty
 Attitude and personality: Attitude to exercise: Advice to others

Both parent and CYPwCF participants commented on the exercise ability differences between the CYPwCF and his/her peers.

'He's eons away from the other kids with his exercise capabilities ... Somebody commented just the other day about how toned [CYPwCF] is and how his physique is totally different from the other kids, and how fit he actually is.'

Parent participant

Attitude and personality: Exercise identity: Ability and skills (including different to peers)

Parent perspective: Attitude and personality: Identity: CYPwCF: Abilities and skills

'There's this one where we have to push with my legs, I can usually do 3 or 4kg, quite strong. That's something my friends can't necessarily do.'

CYPwCF participant

Attitude and personality: Exercise identity: Ability and skills (including different to peers)

Attitude and personality: Personality: Confident

5.3.2.2 Personality

Both CYPwCF and parents raised various aspects under the group theme of personality. 'Competitive' was raised most frequently, by 7 CYPwCF and 8 parents.

'She loved looking where the older kids were and, actually, she was top.'

Parent participant

Attitude and personality: Personality: Competitive

Attitude and personality: Exercise identity: Ability and skills (including different to peers)

Barriers and facilitators: Facilitators: Intrinsic: Competition

'From a competitive point of view ... swimming is hilarious, she does back stroke and she will nearly kill herself to beat everybody.'

Parent participant

Attitude and personality: Personality: Competitive

Barriers and facilitators: Facilitators: Intrinsic: Competition

'I'm not very competitive and I always feel pathetic. I feel like I'm rubbish, all the time.'

CYPwCF participant

Attitude and personality: Personality: Competitive

Attitude and personality: Personality: Confident

Attitude and personality: Exercise identity: Sporty or not sporty

'I like doing stuff that you can win at.'

CYPwCF participant

Attitude and personality: Personality: Competitive

Barriers and facilitators: Facilitators: Intrinsic: Competitive

Both parents and CYPwCF also discussed confidence, and how some CYPwCF gained confidence with exercise as a result of their personal training.

'She's definitely come on in confidence, and she knows that she can do it now. Before she was 'well oh exercise I know I can do my dancing but I don't do anything else'.'

Parent participant
Attitude and personality: Personality: Confident
Attitude and personality: Personality: Determination
Exercise experience: Personal training: Impact of personal training

Almost exclusively, parents raised the themes of 'determination' and 'driven'. Only 1 quote from a CYPwCF was coded as driven. These aspects of personality had both positive and negative impacts on exercise participation.

'She can be very stubborn, anybody that might be a little bit critical or she thinks is making fun of her then she completely sort of goes away from it.'

Parent participant
Attitude and personality: Personality: Determination

'She surprises me all the time with how hard she works.'

Parent participant
Attitude and personality: Personality: Driven

'She's quite intrepid ... in terms of going out and having fun and doing something active, she's always up for it.'

Parent participant
Attitude and personality: Personality: Driven

5.3.2.3 Attitude to exercise

Attitudes towards PA, sport and exercise were varied. Some reported that PA, sport and exercise were just a normal part of life and with some CYPwCF clearly identifying their weekly activity schedule. One CYPwCF stated that exercise was a priority in his life:

'For me personally around 8 or 9 [out of 10], it's very important.'

CYPwCF participant
Attitude and personality: Attitude to exercise: Exercise as a priority

Other CYPwCF had a more negative attitude to exercise.

'There's sometimes that I can't be arsed and I just can't be bothered.'

CYPwCF participant
Attitude and personality: Attitude to exercise: Positive or negative
Barriers and facilitators: Intrinsic: Attitude to exercise (including boring and considered a treatment)

'Sporty things, like football, especially football, I just really see no point in it, it's pointless.'

CYPwCF participant

Attitude and personality: Attitude to exercise: Positive or negative
Exercise experiences: Activities: Preferred activities

Some CYPwCF expressed a mixed attitude to exercise, enjoying it but struggling with self-motivation at times:

'I suppose it was fun but then having to go there every Sunday, sometimes I just wanted to have to lie in in bed, rather than having to get up and do exercise.'

CYPwCF participant

Attitude and personality: Attitude to exercise: Positive or negative
Attitude and personality: Attitude to exercise: Self-motivated
Exercise experiences: Personal training: CYPwCFs' perception

CYPwCF participants were asked directly what advice they would offer to other CYPwCF about exercise. Finding fun and enjoyable activities were frequently mentioned, as well as 'just do it' and 'give it a try'. Six CYPwCF responded with motivational statements such as:

'Always believe in yourself, because no matter how you think you won't do it, you'll be able to, gradually in time. Learn over time, no matter what, you'll be able to do it, might just take a little bit of time.'

CYPwCF participant

Attitude and personality: Attitude to exercise: Advice to others

One CYPwCF discussed maintenance of exercise when considering advice he would offer to other CYPwCF:

'Just don't stop, because if you stop you're most likely not going to continue, which is why I'm trying to do it now. I've learnt I shouldn't have stopped because as soon as I stopped, I stopped completely. And I need to stop stopping and start again.'

CYPwCF participant

Attitude and personality: Attitude to exercise: Advice to others

5.3.2.4 Motivation

Whilst all CYPwCF acknowledged the CF-specific health benefits of PA and exercise, fun and enjoyment were the most frequently cited reasons for undertaking PA and exercise.

'I know it's good for me, but that's not why I do it, I do it because I enjoy it.'

CYPwCF participant

Attitude and personality: Motivation: Enjoyment
Attitude and personality: Motivation: CF-specific health benefits

Two CYPwCF reported considering PA and exercise as part of their physiotherapy treatment, and 3 mentioned using physical activities such as skate boarding and cycling as a form of transport. The mental health and well-being benefits of exercise were also raised by 2 CYPwCF and 1 parent participant.

In summary, the 'attitudes and personality' category contained themes that indicated that attitudes to PA were varied amongst the CYPwCF who were interviewed. Some reported PA as a normal part of life and something that they prioritised, whereas others were less positive and noted that it required effort. Most CYPwCF who were interviewed labelled themselves with a positive or negative exercise identity, and expressed that activities being fun and sociable made them more enjoyable and thus maintenance more likely. Some CYPwCF reported being motivated by the health and well-being benefits of PA. The personality traits that were discussed in relation to the maintenance of PA were a competitive nature, confidence in one's own abilities, and determination. Identifying these in CYPwCF may help to identify who is likely to maintain PA and who is not.

5.3.3 Barriers and facilitators to maintenance of participation

The barriers and facilitators to maintenance of PA, sport and exercise participation were explored in detail during the semi-structured interviews. This category also identified the importance of the impact of other people (Figure 29). There was some overlap of this theme to the others. For example, weather was coded as an extrinsic barrier, but was also identified for inclusion as part of the seasonal variations within the exercise experiences category. Weather was identified as a barrier but also as having an impact on the activity levels of individual participants, therefore was coded in both themes.

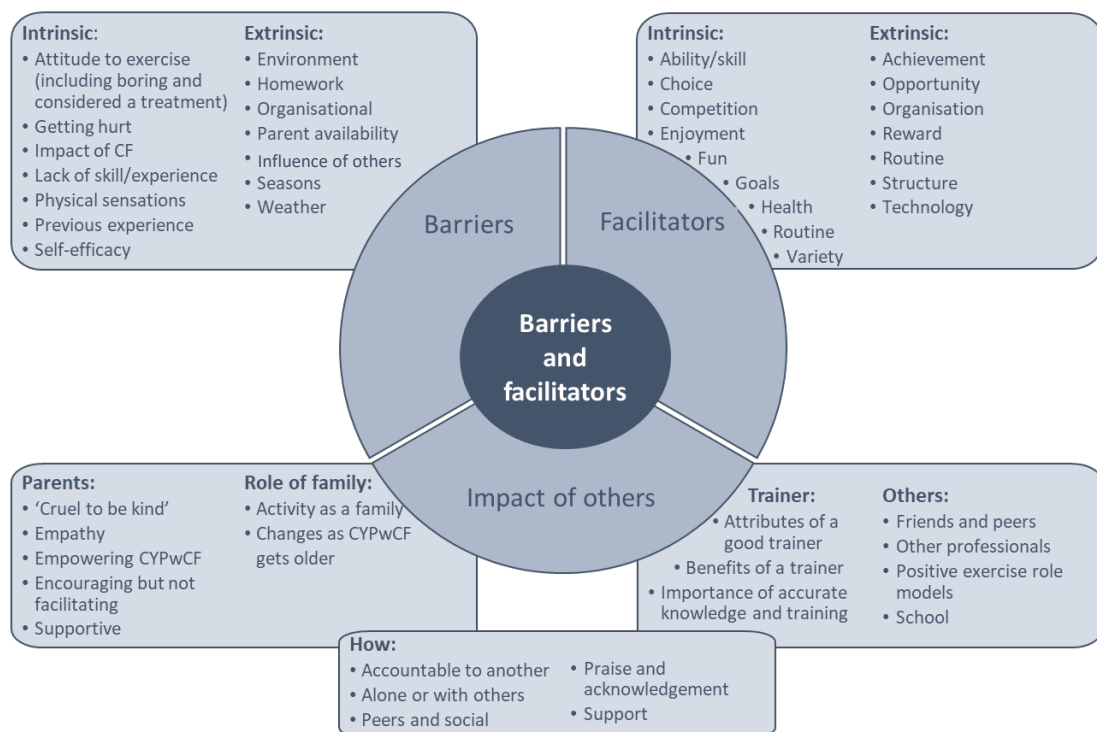


Figure 29: Themes identified in the barriers and facilitators category as part of phase 1

5.3.3.1 Barriers and facilitators

Barriers and facilitators were categorised into intrinsic and extrinsic factors. CYPwCF reported intrinsic factors in greater frequency than extrinsic factors for both barriers and facilitators (Table 24). However, parents cited extrinsic barriers more frequently than intrinsic, but intrinsic facilitators more frequently than extrinsic. Interestingly, competition was cited as a barrier by some CYPwCF, but a

facilitator by others. Habit has previously been identified as key to maintaining many health behaviours (Phillips et al., 2016, Hoo et al., 2019), however it was only mentioned by 3 participants in this study.

Table 24: Most frequently reported barriers and facilitators to maintenance of physical activity, sport and exercise participation in CYPwCF with number of references from phase 1 Part C study

	CYPwCF reported	Parent reported
Barriers	58 references:	43 references:
	Intrinsic	
	<ul style="list-style-type: none"> • Physical sensations • Impact of CF • Self-efficacy • Lack of skill/experience 	<ul style="list-style-type: none"> • Self-efficacy • Impact of CF • Physical sensations • Attitude to exercise
	Extrinsic	
	29 references:	51 references:
	<ul style="list-style-type: none"> • Influence of others • Homework • Weather 	<ul style="list-style-type: none"> • Influence of others • Homework • Parent availability
Facilitators	47 references:	34 references:
	Intrinsic	
	<ul style="list-style-type: none"> • Fun • Ability/skill • Variety 	<ul style="list-style-type: none"> • Fun • Variety • Ability/skill
	Extrinsic	
18 references:	28 references:	
<ul style="list-style-type: none"> • Technology • Achievement 	<ul style="list-style-type: none"> • Technology • Routine 	

Key: CYPwCF child or young person/children and young people with cystic fibrosis

There was agreement in the most frequently cited intrinsic and extrinsic barriers cited by CYPwCF and parents. Physical sensations, such as pain or fatigue, the impact of CF and self-efficacy were the key intrinsic barriers identified by both CYPwCF and parents, and influence of others and amount of homework referred to most often as extrinsic barriers.

'She can sometimes completely withdraw because she thinks she's failing'

Parent participant
Barrier and facilitators: Barrier: Intrinsic: Self-efficacy
Attitude and personality: Personality: Confident
Parent perspective: Identity: CYPwCF: Abilities and skills

Even though they were asked directly about barriers to the maintenance of PA and exercise participation, 5 CYPwCF were unable to identify any barriers.

Barriers were reported at greater frequency than facilitators by both CYPwCF and parents. Both groups identified that PA, sport and exercise must be fun to keep a CYPwCF engaged, but that developing skills, a variety of activities and technology also contributed to maintaining participation.

'I think it's just because it's not very fun, just running, so it can be fun, because earlier me and my dad had a race to get here, we were running late, and that was fun because we were having a competition.'

CYPwCF participant
Barriers and facilitators: Facilitators: Fun
Attitude and personality: Personality: Competitive

5.3.3.2 *Impact of others*

The impact of other people was frequently identified in this category, thus was coded in further detail. Many parents reported actively encouraging and facilitating their CYPwCF to be active. This took different forms with some exercising with their CYPwCF and others facilitating independent activity. Nine parents actively facilitated their CYPwCF's participation in sport or exercise.

'I don't care, I put a costume on and I go swim with him because that's what he likes.'

Parent participant
Barriers and facilitators: Impact of others: Parents: Supportive

'I do hide remote controls for the playstation ... I won't allow him to be a bedroom slob.'

Barriers and facilitators: Impact of others: Parents: 'Cruel to be kind'
Parent perspective: Attitude and personality: Attitude to exercise: CYPwCF: Exercise as a priority

The role of the wider family was also discussed with some families trying to be active together, although this appeared to change as CYPwCF get older:

'When they were younger, I must admit, we were very much more active.'

Parent participant

Barriers and facilitators: Impact of others: Role of family: Changes as CYPwCF gets older

Beyond the family, friends, school, other professionals, such as scout group leaders, and positive PA and exercise role models all had an impact on the activity levels reported by CYPwCF and their parents.

'I had this really nice PE teacher who really thought it was a good thing for me to do, and she really pushed me to try and get involved. I got signed up for the 800m which I really really really didn't want to do, but she was telling me that I can do it so I did it. She was encouraging me to try it and give it a go. It was really hard because it was really hot. But I'm pretty proud of what I got, I got fourth.'

CYPwCF participant

Barriers and facilitators: Impact of others: Others: School
Barriers and facilitators: Impact of others: How: Support

Both CYPwCF and parents reported that PA, sport and exercise participation facilitation by an adult was important. The role of a personal trainer was highly valued by the 18 families who had experience of regular training. All CYPwCF who had this experience reported themes of 'fun', 'variety' and 'ability/skill'.

'She was just really fun, but also I got on with her really well, and I did the things because she made it really fun.'

CYPwCF participant

Barriers and facilitators: Impact of others: Trainer: Attributes of a good trainer

CYPwCF and parents expressed the benefits of an established relationship with a skilled trainer clearly:

'To know he had that one on one made a huge difference because I didn't feel like I could do it, or else was I taking on too much by actually taking on that as well. To have somebody paying attention to him and his needs and seeing what he could do and actually pushing him in that direction, instead of me maybe doing damage to him because I don't know how far or hard to actually push him.'

Parent participant

Barriers and facilitators: Impact of others: Trainer: Benefits of a trainer
Barriers and facilitators: Impact of others: Trainer: Importance of accurate knowledge and training

Parent perspective: Attitude and personality: Attitude to exercise: CYPwCF: Want help and support

'I kind of was happy that it stopped, but I was also sad because I lost having [personal trainer].'

CYPwCF participant

Barriers and facilitators: Impact of others: Trainer: Benefits of a trainer
Exercise experiences: Personal training: CYPwCFs' perception

Some CYPwCF and parents identified the sociable aspects of PA, sport and exercise, and reported that the support of other people, and receiving praise and acknowledgement helped maintain participation. Being accountable to another person was identified as a strong facilitator for taking part in some exercise at a particular time, and also the amount of effort put into the session:

'For us it's about knowing that that's the time we've got to be there and that's the time that we're there.'

Parent participant

Barriers and facilitators: Impact of others: How: Accountability to another
Barriers and facilitators: Impact of others: Trainer: Benefits of a trainer

'I suppose when she was doing it with you she wanted to show you she could do it well, whereas I'm mum and it doesn't matter.'

Parent participant

Barriers and facilitators: Impact of others: How: Accountability to another
Barriers and facilitators: Impact of others: Trainer: Benefits of a trainer
Parent perspective: Attitude and personality: Attitude to exercise: CYPwCF: Want help and support

In summary, many different intrinsic and extrinsic barriers and facilitators were identified, some of which were relevant to some CYPwCF and some to others. This further supported the finding that different CYPwCF experience PA differently, and therefore their ability to maintain participation will also be different. However, all CYPwCF appeared to be influenced by other people, thus enhancing the role of an appropriate facilitator may well help CYPwCF to maintain PA participation. Habit did not feature highly in the discussions of CYPwCF or their parents. Habit may not be so relevant for CYPwCF compared to adult with CF, or it may be that it continues to be important in helping maintain participation but is not recognised by CYPwCF themselves or their parents.

5.3.4 Parent perspective

The semi-structured interviews with parents generated additional themes, thus a separate category was created to contain themes specific to the parent perspective (Figure 30).

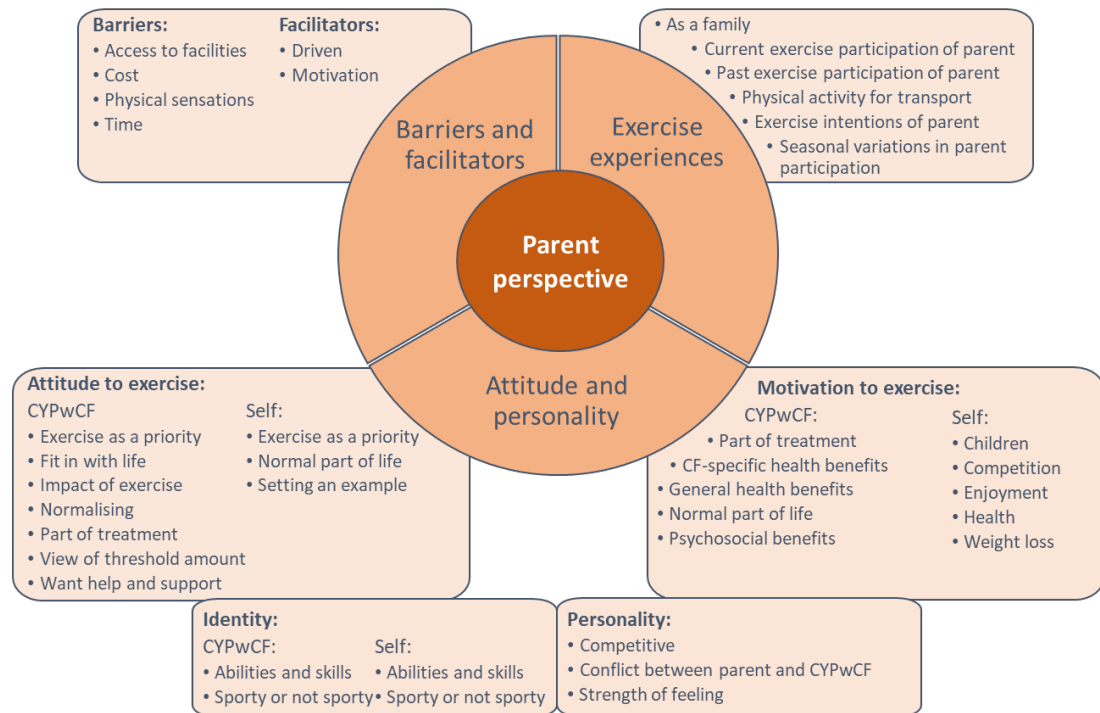


Figure 30: Themes identified in the parent perspective category as part of phase 1

5.3.4.1 Barriers and facilitators

Although not asked directly, some parents discussed barriers and facilitators to their own PA and exercise. The reported barriers were different to those for their CYPwCF's PA and exercise, and included lack of time, financial cost, and access to facilities.

'The problem is the expense.'

Parent participant

Parent perspective: Barriers and facilitators: Barriers: Cost

The key facilitators identified by parents for their own PA and exercise participation were intrinsic.

'It's only just now where [CYPwCF's] 14 so she can be left alone in the house that I'm able to get to the gym a lot more. And I drag my sister with me, but I'm happy to go on my own, it doesn't bother me.'

Parent participant

Parent perspective: Barriers and facilitators: Facilitators: Driven

Parent perspective: Attitude and personality: Identity: Self: Sporty or not sporty

5.3.4.2 *Exercise experiences*

Parents also had varied PA and exercise experiences. Most discussed experiences involving family group activities, although 3 parents reported this varied dependent on the season. In addition, 10 parents talked about their own current independent exercise participation as well. The majority referred to exercise classes, gym attendance or solo sports such as golf and cycling, with only 2 parents mentioning participation in team sports.

'I go to the gym, I always do Zumba classes on Tuesday and Thursday, I absolutely love it.'

Parent participant

Parent perspective: Exercise experiences: Current exercise participation of parent

Eight parents reported enjoying PA, sport or exercise themselves and regularly participated, and others were completely avoidant. Most parents, bar 4, expressed that they were less active currently than they had been. Many reported that they associated having children with a fall in activity levels.

I did netball and long distance running at school but when I left school and went to work for the bank I joined a netball team and only finished playing when [first child] was 5. And then I swam a mile a day for 6 years, so really I would say everything stopped when I had [CYPwCF].

Parent participant

Parent perspective: Exercise experiences: Past exercise participation of parent

Four parents discussed their plan to increase their own exercise and PA participation, and 3 reported walking or cycling regularly for transport.

5.3.4.3 *Attitude and personality*

Parents were unanimously positive in their attitude towards PA, sport and exercise for their CYPwCF, however attitudes towards their own participation were varied. Parents cited 'exercise as a priority' and 'want help and support' most frequently

when discussing attitudes to exercise for their CYPwCF, with 35 and 28 references respectively.

'It helps taking her somewhere else so there's more enthusiasm. If I take her into the gym at home, she's kind of dopey. But if she's in the gym she's being worked properly, you know, so there's that difference between parent and, not a stranger obviously because [trainer] is certainly not a stranger now, but a different role.'

Parent participant

Parent perspective: Attitude and personality: Attitude to exercise: CYPwCF: Want help and support

Barriers and facilitators: Impact of others: Trainer: Benefits of a trainer

'If we didn't do INSPIRE, I would have needed help. I mean INSPIRE was the first time I'd ever walked into a gym ever, so I really didn't know, I mean I've no idea what to do. But then that's a certain element of training the parents.'

Parent participant

Parent perspective: Attitude and personality: Attitude to exercise: CYPwCF: Want help and support

Exercise experiences: Personal training: Experience of INSPIRE-CF

Parents also discussed the important impact that exercise can have. PA was considered a normal part of life and treatment, and therefore parents reported trying to fit it in to everyday life as much as possible.

'My opinion is that it's the exercise that she does that helps her to function at a higher level than her lung function would suggest.'

Parent participant

Parent perspective: Attitude and personality: Attitude to exercise: CYPwCF: Impact of exercise

Parent perspective: Attitude and personality: Attitude to exercise: CYPwCF: Exercise as a priority

Parent perspective: Attitude and personality: Motivation to exercise: CYPwCF: CF-specific health benefits

Seven parents were clear that they had a view of a threshold amount of daily activity for their CYPwCF:

'For me it's the right kind of exercise, because I don't doubt that she does enough steps ... but it's that high intensity stuff.'

Parent participant

Parent perspective: Attitude and personality: Attitude to exercise: CYPwCF: View of threshold amount

Only 4 parents identified exercise for themselves as a priority, compared to 13 identifying it as a priority for their CYPwCF. However, 6 exercised regularly to set an example to their CYPwCF.

'The thing is, if you're asking someone to do it and you're not willing to do it yourself, then how do you expect the child to be compliant?'

Parent participant

Parent perspective: Attitude and personality: Attitude to exercise: Self: Setting an example

The reasons parents cited as motivation for their CYPwCF to exercise were similar to their attitudes to PA and exercise for their CYPwCF: it was considered a part of treatment as well as a part of normal life, and also resulted in CF-specific and general health and well-being benefits. However, motivation for parents own PA and exercise participation was different. Weight management or loss was the most frequently cited motivation to exercise for parents:

'I'm not very good at the dieting side of things because of having to have the food in the house for [CYPwCF], so I try to exercise to combat that.'

Parent perspective

Attitude and personality: Motivation to exercise: Self: Weight loss

Other health and well-being benefits, enjoyment and a competitive nature were also reported as motivators for parents own PA and exercise participation. One parent acknowledged that her CYPwCF was her biggest motivator to be active and exercise:

'I want to be able to do everything with her, and enjoy it ... I think it does play quite a role privately in my head. It does motivate you, it makes you realise as not having CF just how much more effort she puts into things. So there's no excuse not to do it yourself.'

Parent participant

Parent perspective: Attitude and personality: Motivation to exercise: Self: Children

As with the interviews with CYPwCF, some parents identified their own exercise identity of their CYPwCF and that of themselves. There was agreement between CYPwCF and parent reported CYPwCF exercise identity. Additionally, 6 parents identified themselves as 'sporty' and 7 as 'not sporty'. Not all 'sporty' parents were currently regularly active, and not all active parents facilitated exercise for their CYPwCF.

Conflict between CYPwCF and parent was reported by 2 parents, both of whom exercised regularly but their CYPwCF were reluctant to engage in structured sport and exercise.

'I love it. I don't know why she's so adamant, it's such a shame.'

Parent participant

Parent perspective: Attitude and personality: Personality: Conflict between parent and CYPwCF

Some aspects of the parent interviews were expressed with a strong sense of feeling. The end of INSPIRE-CF, and therefore the end of the personal training, was most notable:

'He come on such a long way that I didn't want it to end. It had to end, but I was gutted, I was hoping they would extend it.'

Parent participant

Parent perspective: Attitude and personality: Personality: Strength of feeling
Exercise experiences: Personal training: Impact of personal training
Exercise experiences: Personal training: Parents' perception

In summary, the parents of CYPwCF who were interviewed also had varied attitudes to and experiences of PA, both for themselves and their child. Active parents did not necessarily result in active CYPwCF, in fact for some parent/CYPwCF dyads, conflict occurred between an active parent and a reluctant child which seemed to have a further negative impact on the PA participation of the child. This is particularly important for clinicians to be aware of and not assume that an active parent is able to act as an appropriate PA facilitator for their child.

5.3.5 Summary of barriers to and facilitators for the maintenance of physical activity study

This Part C study used a qualitative design to address research question 3: what are the barriers to and facilitators for maintaining PA in CYPwCF. A total of 40 semi-structured interviews (20 with CYPwCF and 20 with parents) were analysed using thematic content analysis to understand the PA and exercise maintenance experiences, attitudes and behaviours of CYPwCF, as well as barriers and facilitators. The detailed exploration of the data enabled the development of a comprehensive framework. This resulted in some key findings being identified:

- CYPwCF and their parents valued PA, sport and exercise, and agreed with CF guidelines that it is essential for health outcomes. But exercise experiences were varied and CYPwCF held differing attitudes towards PA. The different experiences and attitudes would likely result in different maintenance of PA patterns. This was important to consider for the integration of qualitative and quantitative findings at the end of this phase of the project.
- A sense of exercise identity appeared to be important for most participants, with 17 voluntarily discussing their own identity. This may have been related to the ability of individual CYPwCF to maintain PA participation thus was also considered for the integration stage of analysis.
- All CYPwCF recognised the health and well-being benefits of being physically active and were able to identify at least 1 PA that they enjoyed, but many reported struggling to maintain participation and had given up some activities. This demonstrated that the maintenance of PA, sport and exercise is challenging and enjoyment of an activity alone is not enough to keep CYPwCF engaged in PA.
- The findings suggested that there may have been a fall in level of PA associated with age for at least 1 CYPwCF. This would require further investigation in the second phase of this research.
- Maintenance of PA can be facilitated by: sociability, fun and 'normality'; developing skills, achieving goals and receiving praise and acknowledgement; and the inclusion of an adult, either a trainer or supporter. Personal training worked for some but not all CYPwCF, and even resulted in a positive change of exercise identity for a few.
- Many different facilitators were discussed by different CYPwCF. This further supported the finding that different CYPwCF experience PA differently, and therefore their ability to maintain participation will also be different. However, accountability to another, most notably a trainer, was thought to be the most significant facilitator of maintained participation. People are important and the relationships built between adult facilitators and CYPwCF appeared to be supportive of the maintenance of PA.

- Habit may not be so relevant for CYPwCF compared to adults with CF, or it may be that it continues to be important in helping maintain participation but is not recognised by CYPwCF themselves or their parents.
- The personality traits that were discussed in relation to the maintenance of PA were a competitive nature, confidence in one's own abilities (or self-efficacy for PA), and determination. This was in agreement with the results of the factors affecting the maintenance of PA study which demonstrated that the self-efficacy for PA (measured by CSAPPA) scores were significantly different for those who maintained PA compared to those who did not. Identifying this in CYPwCF in the clinical setting may help to identify who is likely to maintain PA and who is not.
- Many different barriers were identified, some of which were relevant to some CYPwCF and some to others. Intrinsic barriers to PA participation appeared to be greater in number and significance for CYPwCF than extrinsic barriers, but appropriate support and PA facilitation appeared to counteract all barriers to participation.
- Parent exercise identity did not necessarily relate to the exercise identity or level of participation of the CYPwCF. In other words, active parents did not necessarily facilitate PA participation for their child.

5.4 Integration of qualitative and quantitative results

The quantitative results of the interview participants were explored in relation to the qualitative findings in order to develop a thorough understanding of the factors that appeared to indicate maintenance of PA.

5.4.1 Exercise identity, self-efficacy for physical activity and maintaining participation

In total, 17 of the CYPwCF who were interviewed raised exercise identity. Self-efficacy for PA, as defined in section 2.3.1.1, refers to an individual's perception of their own skills and competence in physical activities. For the purposes of this research it was considered to encompass self-perceived confidence in abilities and enjoyment of physical activities. Exercise identity is different to self-efficacy, and in this research related to an individual's self-identified characteristics, or self-image. Whilst both terms relate to an individual's psychological identity, the constructs are different and the relationship between self-efficacy for PA and exercise identity, and resultant impact on maintaining PA participation, were explored.

Those who identified as 'sporty' before personal training ($n = 4$) had higher self-efficacy scores ($>63/76$) than those who identified as 'not sporty' ($n = 8$) ($<52/76$) (Figure 31). However, having a positive exercise identity, either as a result of personal training or not, did not appear to indicate that an individual was more likely to maintain participation (Figure 32). Half ($n = 4$) of those who had a positive exercise identity maintained and half ($n = 4$) did not. However, there was a clearer relationship between a negative exercise identity and maintenance: only 1 participant who identified as 'not sporty' still managed to maintain but 5 did not.

The 6 CYPwCF who were interviewed and managed to maintain PA participation (i.e. those in the green shaded area of Figure 32; participants 9, 10, 14, 16, 17 and 20 in Figure 31) had self-efficacy scores of $\geq 50/76$, suggesting that self-efficacy for PA was perhaps a stronger indicator of maintaining PA than exercise identity. This relationship was inconsistent as participants who scored highest for self-efficacy for PA did not manage to maintain. However, this relationship was in agreement with

the quantitative results from the whole cohort (section 5.2.5) thus warranted further investigation in phase 2 of this research.

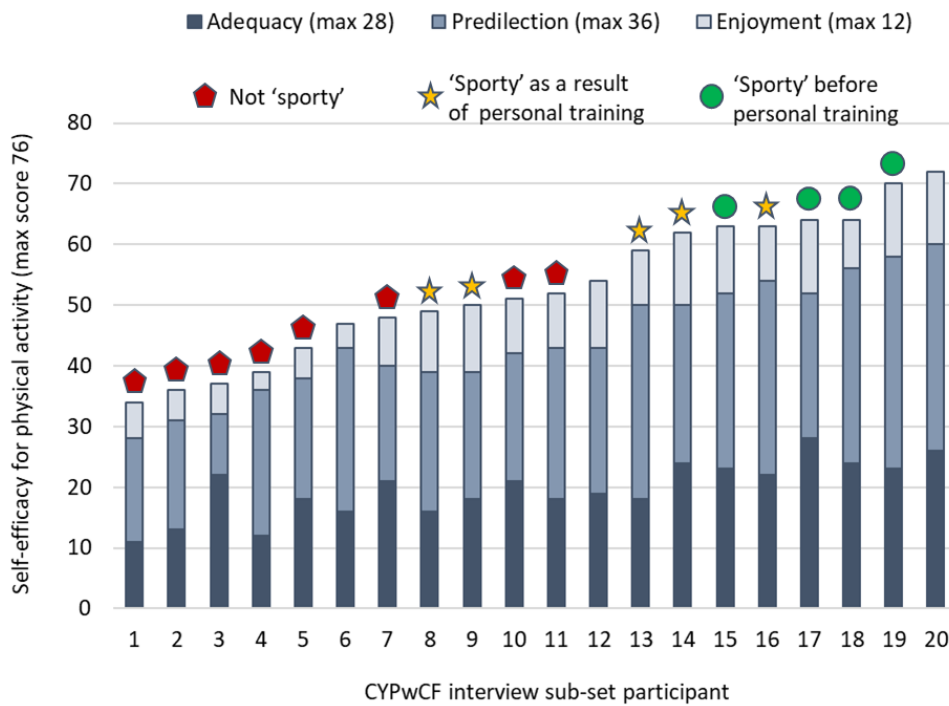


Figure 31: Individual CYPwCF interview participant self-efficacy scores and exercise identity for phase 1 Part C participants

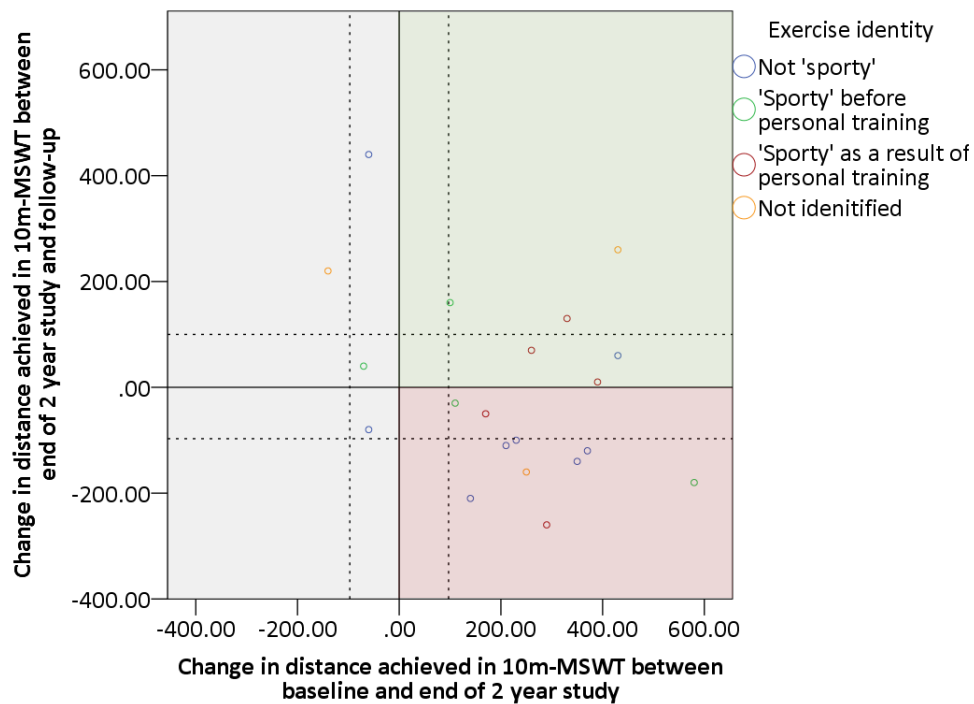


Figure 32: Scatterplot presenting the change in exercise capacity during and after participation in INSPIRE-CF for the phase 1 Part C interviewed sub-set by exercise identity, with indication of maintained activity (green shading) or not maintained activity (red shading)

5.4.2 The barriers to and facilitators for physical activity identified by maintainers

Considering the number and frequency of reported barriers to and facilitators for the maintenance of PA, further analysis was undertaken to explore whether maintainers reported common barriers or facilitators. At least 1 of the 6 CYPwCF interviewees who maintained PA identified all of the most frequently cited barriers to PA (Table 24). Of note, 4/6 identified 'lack of skill/experience', and 3/6 identified 'self-efficacy'. 'Self-efficacy' was not identified by any non-maintainers. Again, this highlighted the potential link between self-efficacy for PA and maintaining participation, but also the lack of clear indicators of maintenance from barriers and facilitators alone. It was clear that simply asking CYPwCF what their barriers to and facilitators for the maintenance of PA are would not generate enough information to be able to identify who was likely to maintain PA and who was not.

A total of 5 CYPwCF were unable to identify any barriers to their maintenance of PA. Paradoxically, they all tended to have reported lower self-efficacy for PA (scored the sample mean or less in all CSAPPA domains). Importantly, 2/5 were maintainers, further demonstrating that identifying the maintenance of PA was more complex than simple questioning alone.

'Achievement' was cited as a facilitator by 5 CYPwCF, all of whom had lower self-efficacy scores (≤ 54), and identified as being not sporty or having become sporty as a result of personal training. This suggested that some CYPwCF who were low in self-efficacy for PA considered that achieving goals would be helpful for maintaining participation. However, these participants were not currently able to maintain participation, perhaps because they were not being supported to achieve goals.

The CYPwCF who were managing to maintain PA participation reported a variety of barriers to and facilitators for PA. There did not appear to be a pattern of reporting that might have pointed to an indicator of maintenance of PA. However, self-efficacy was noted to be the only barrier reported solely by maintainers, supporting the findings throughout this phase of work that self-efficacy was a potential indicator for the maintenance of PA and worthy of further research in phase 2.

5.5 Summary of phase 1 results

Phase 1 of this research investigated the health, well-being and PA maintenance of CYPwCF who had previously participated in a supervised exercise intervention RCT. In addition, the barriers to and facilitators for PA maintenance were explored, and the relationship between self-efficacy for PA, self-reported levels of PA, and parent/carer PA and exercise barriers, and maintenance of PA were investigated. The results from the group level analysis demonstrated that the supervised exercise intervention resulted in a positive effect on functional exercise capacity, but that this effect was lost after the intervention was removed. There did not appear to be a benefit to lung function, quality of life or self-reported levels of PA.

On further investigation of the trajectories of individual CYPwCF, it became apparent that some participants maintained PA participation following the removal of the exercise intervention, and others did not. Parent PA and exercise barriers and self-reported levels of PA did not appear to be indicators of maintained participation. Furthermore, the self-identified exercise identity or CYPwCF reported PA barriers and facilitators did not seem to be indicators of maintenance.

Results suggested that self-efficacy for PA was potentially related to maintainer status, and that those with higher self-efficacy for PA were more likely to be maintaining PA, independent of exercise identity. Parent/carer PA and exercise barriers did not seem to impact on the self-efficacy for PA for the related CYPwCF. Moreover, self-efficacy appeared to be modifiable in some CYPwCF as a result of the INSPIRE-CF supervised exercise intervention: having a trainer helped by overcoming modifiable intrinsic barriers such as building skills and confidence (self-efficacy).

6 Phase 1 Discussion

6.1 Introduction

Phase 1 of this research investigated an exclusive and interesting population of CYPwCF who had all been participants in a 2-year-long supervised exercise RCT, INSPIRE-CF. This enabled the comprehensive investigation of their unique insight into the factors affecting the maintenance of PA. Phase 1 consisted of 3 studies designed to address the first 3 research questions:

1. What happened to the health, well-being and PA maintenance of CYPwCF after withdrawal of a supervised exercise intervention? (Part A: SRC PA maintenance study, a quantitative study)
2. What affects the maintenance of PA in CYPwCF? (Part B: Factors affecting the maintenance of PA, a quantitative study)
3. What are the barriers to and facilitators for maintaining PA in CYPwCF? (Part C: Barriers to and facilitators for the maintenance of PA, a qualitative study)

The anticipated outputs from this phase of the research are identified in Figure 33.

- Understanding of the longer-term impact of a temporary supervised exercise intervention on the health, well-being and PA maintenance of CYPwCF.
- Understanding of the factors that influence the participation in and maintenance of exercise and physical activity in CYPwCF.

Figure 33: Research outputs anticipated from phase 1 studies

The key findings identified in chapter 5 are discussed in line with the literature and the strengths and limitations of this research. Conclusions are then drawn with implications for phase 2 of this research programme and recommendations for clinical practice identified.

6.2 What happened to the health, well-being and physical activity maintenance of CYPwCF after withdrawal of a supervised exercise intervention?

To date, most research investigating the effects of exercise interventions on people with CF have only measured outcomes up to the end of the intervention, enabling conclusions to be drawn on the effects of exercise training, but not what happens

after the intervention is withdrawn. Radtke et al. (2017) conducted a systematic review designed to assess the effects of exercise training on exercise capacity (measured by peak oxygen consumption), lung function (measured by FEV₁) and HRQoL in people with CF. Follow-up assessments off-training were carried out in 7 of the 15 studies that met the inclusion criteria, but the interventions in 2 of those studies were short-term and conducted during hospital admissions (Michel et al., 1989, Selvadurai et al., 2002). In these instances, it was difficult to distinguish the effects of the training programme and those of recovery from exacerbation, thus value of the results was limited. The remaining 5 studies, involved exercise training that was similar to the intervention used in the INSPIRE-CF study, and were at least partially supervised and delivered during health stability (Klijn et al., 2004, Hebestreit et al., 2010, Santana-Sosa et al., 2012, Kriemler et al., 2013, Santana-Sosa et al., 2014). These studies will be discussed in line with the findings of the current study.

6.2.1 Health trajectories

There were 2 aspects of physical health measured as part of the SRC PA maintenance study: functional exercise capacity and lung function.

6.2.1.1 Functional exercise capacity

The group-level analysis results of the SRC PA maintenance study demonstrated that the exercise intervention had a positive impact on functional exercise capacity, with a statistically significantly greater improvement in distance achieved during 10m-MSWT in the exercise training group than the control group during the course of INSPIRE-CF. However, this benefit was lost by the PA maintenance assessment point indicating that the positive impact was dependent on the intervention continuing and maintaining PA independently did not appear possible for many of the participants. This was in contrast to the findings of other studies investigating the effect of withdrawal of an exercise intervention. Klijn et al. (2004) conducted an RCT investigating the effects of anaerobic training on anaerobic and aerobic performance, lung function, body composition, peripheral muscle strength, and HRQoL in 20 CYPwCF, aged 9-18years. The 11 participants in the training group undertook 30-45minutes of supervised exercise training (in bouts of 20-30seconds

of anaerobic work) twice a week for 12 weeks. This training regimen resulted in detectable changes at the end of 12 weeks of training in aerobic and anaerobic performance, and the physical functioning domain of the HRQoL measure. The positive effect on anaerobic performance and HRQoL remained at follow-up re-assessment 12 weeks after the end of the study. This was a shorter time to follow-up than the current study, thus might explain the sustained impact of the training. However, the benefits to aerobic performance were lost by follow-up, in line with the findings of the current study.

Hebestreit et al. (2010) investigated the long-term effects of a home-based, partially supervised conditioning programme in young people and adults with CF. Participants, aged 12 to 40 years old, were recruited from 3 CF centres in Germany. Participants randomised to the intervention group (n = 23) were asked to take part in 3 additional hours of sport per week for the first 6 months of the study, and then to maintain or increase PA for the second 6 months. Those in the intervention group received activity counselling at baseline and repeat assessments visits at 3- and 6-months. They also had the opportunity to access logistic and/or financial support to implement their PA plan. The 15 participants randomised to the control group were asked to maintain their usual physical activities for the same 12 months. After 12 months of participating, participants in both groups were advised that they were free to change their PA behaviours. The investigators collected data on maximal exercise capacity (primary outcome), fitness, levels of PA, lung function and HRQoL. Measures were taken at baseline and repeated at 3-, 6-, 12-, 18- and 24-months. The results identified a positive effect on maximal exercise capacity as a result of the intervention, which was sustained at 12-months (the partial supervision and support was withdrawn at 6 months) and even at the repeat assessments at 18- and 24-months suggesting that the intervention had a positive effect on levels of effective exercise, and therefore exercise capacity, and that this change was maintained. There was a statistically significant difference in levels of PA in the second 12 months of the study, when the intervention group participated in more vigorous PA than the control group. This suggested that PA behaviour had changed and was maintained as a result of the intervention in this study. The

difference between the Hebestreit et al. (2010) and INSPIRE-CF interventions may explain at least some of the difference in results. Hebestreit et al. (2010) utilised activity counselling to support the participants in their study to increase levels of PA. Participants identified which physical activities they wanted to use and when to fit that into their weekly schedules. INSPIRE-CF delivered a fully supervised and facilitated gym-based exercise intervention. The partial supervision and activity counselling may have empowered participants to maintain participation beyond the supervised period more than a fully supervised and facilitated exercise intervention. Furthermore, adult participants were involved in the Hebestreit et al. (2010) study. Whilst there was no difference in trajectories of distance achieved during 10m-MSWT between the age groups in the SRC PA maintenance study (i.e. all age groups demonstrated an increase in distance achieved during 10m-MSWT as a result of the exercise intervention, and that was not maintained by PA assessment point), adults with CF may demonstrate different maintenance patterns than CYPwCF as a result of greater independence and autonomy, and more experience of managing more severe CF disease.

Santana-Sosa et al. (2012) investigated the effects of 8 weeks of combined aerobic and resistance training in CYPwCF by RCT. The investigators also collected data 4 weeks after the intervention was withdrawn to study the detraining effects. There were 11 CYPwCF in both control and intervention groups. The control group continued to receive standard CF care including education about the benefits of PA. The intervention group also received supervised exercise training, consisting of 20-40minutes of aerobic exercise (cycle ergometry) and a circuit of 11 resistance exercises repeated 3 times, on 3 days each week. Exercise capacity (peak oxygen consumption measured during ramped treadmill test) increased with training and then reduced again during the detraining period for those in the intervention group, but remained stable across all assessment points for those in the control group. The muscle strength outcomes demonstrated the same trajectories, suggesting that the exercise intervention was effective at increasing exercise capacity and muscle strength, but the gains were lost once training ceased. It was interesting to note that whilst there were no statistically significant differences in

age, height, weight or BMI between the 2 groups at baseline, there were substantially more participants who were pancreatic insufficient in the control group than the intervention group (81.8% and 45.5% respectively). Furthermore, the participants in the control group had notably more bacterial growths recorded than those in the intervention group. This may suggest that the participants in the intervention group may have had more functioning CFTR and therefore less significant CF disease than the control group. This may have had an impact on the health-related outcome measures evaluated as part of this study.

In a second RCT, Santana-Sosa et al. (2014) assessed the effects of 8 weeks of inspiratory muscle training (IMT), and combined aerobic and resistance training on lung volumes, inspiratory muscle strength and exercise capacity in CYPwCF. Again, the investigators included re-assessment at 4 weeks after the interventions were withdrawn to establish the detraining effects. There were 10 CYPwCF in control and intervention groups. In this study, the participants in the control group received standard CF care and IMT twice per day but at only 10% of baseline peak inspiratory pressure, thus sham IMT. The intervention group received standard CF care and 8 weeks of the exercise intervention (on 3 days a week, similar to that described in Santana-Sosa et al. (2012)) and IMT twice per day. The trajectories for exercise capacity (measured by peak oxygen consumption) were the same as those identified by the group's 2012 study (Santana-Sosa et al., 2012): the intervention had a positive effect on exercise capacity but the benefits were lost after the training was withdrawn. The between-group differences in pancreatic sufficiency and bacterial growth that were noted in the earlier study were not present in the later study raising confidence that the intervention was the cause for the effect on exercise capacity. The muscle strength measures conducted in this later study demonstrated a positive effect of training, with benefits only to leg press retained at 4 week follow-up.

The effect of the INSPIRE-CF exercise intervention, and subsequent withdrawal, appeared to be consistent for all age groups and across disease severity, however there were sex-based differences. Female participants appeared to experience a greater decline in functional exercise capacity after withdrawal of the exercise

intervention than male participants. Male participants who had received the exercise intervention demonstrated more stability in functional exercise capacity than female participants, but there was still a notable difference in comparison to the males in the control group. The benefits gained to functional exercise capacity by male and female participants as a result of the exercise training were lost after withdrawal of the intervention, and this loss was greater for females than males. This is of particular importance given the sex-based differences in health status in CF, where females already experience reduced life expectancy compared to males (UK Cystic Fibrosis Registry, 2019). Furthermore, it has been well-recognised that the levels of PA fall earlier and more significantly for females than males (Farooq et al., 2017). This may have been a contributing factor to the cause of the more significant fall in functional exercise capacity post-intervention for the female participants. However, it highlights the importance of the discrepancy, and that clinicians working with CYPwCF must be aware of and address the specific needs of female patients. Unfortunately, this level of analysis was not presented in any of the identified literature.

6.2.1.2 Lung function

There was no detectable benefit to lung function, measured by FEV₁ z score, as a result of the change in PA associated with the INSPIRE-CF exercise intervention. This finding was in line with the literature previously discussed (Klijn et al., 2004, Hebestreit et al., 2010, Santana-Sosa et al., 2012). Santana-Sosa et al. (2014) also identified that the intervention in their RCT (combined aerobic and resistance training and IMT) had no impact on FEV₁, but did demonstrate a positive and sustained impact on peak inspiratory pressure. The clinical importance of this was unclear.

Kriemler et al. (2013) reported a different finding. The investigators aimed to determine the effects on FEV₁ of 6 months of partially supervised aerobic training or supervised strength training on 39 adults with CF. A total of 29 participants undertook the training programmes (17 aerobic training and 12 strength training). However, the participants recruited to the control group (n = 10) experienced a significant deterioration in FEV₁ during the study period, therefore the investigators

included data from adults with CF recruited to the control group of a different trial as well as age-matched CF registry data from Switzerland and Germany. Participants were assessed (or registry data sought) at baseline, 3 and 6 months when the intervention was withdrawn. Follow-up assessments were repeated at 12 months and 24 months. The authors reported a positive impact on ppFEV₁. Both aerobic and strength training groups demonstrated a positive change (aerobic: +5.8 ± 0.95, strength: +7.4 ± 2.5), whilst the Swiss and German control groups (and registry data) demonstrated a negative change by the end of study at 6 months. However, this impact was no longer detectable by the re-assessment at 24 months (18 months off training). This study involved adults with CF which may contribute to the difference in impact in FEV₁ when compared to the current study. Many adults with CF have more significant CF lung disease than most CYPwCF. Lung function that is below the expected value for an individual may be more likely to be impacted by an exercise intervention, whereas lung function within the 'normal' range may not be so prone to a positive change. Furthermore, this research was conducted a number of years ago. The health of people with CF is improving year on year (UK Cystic Fibrosis Registry, 2020), thus the impact of the exercise interventions on FEV₁ may have been more detectable in the past when lung function of people with CF was more frequently below the normal range. However, the loss of detectable benefit by the follow-up assessment is supportive of the results from the current study which identified that the benefits of a successful intervention are only experienced for as long as participation is maintained. Withdrawing an intervention from an individual with CF may result in a negative impact on their health.

The group-level analysis of the SRC PA maintenance study data established that the exercise intervention had a short-term positive impact on functional exercise capacity (distance achieved during 10m-MSWT), but not on lung function (FEV₁ z score). Even this benefit was lost by the PA maintenance assessment point. However, when the individual trajectories of the physical health outcomes (exercise capacity and lung function) were examined, it became clear that the impact of the intervention on individual CYPwCF was more significant, and maintained, for some

but not for others. Clinical practice should be based on sound evidence, however the findings of this SRC PA maintenance study highlight that the PA advice and support given to CYPwCF and their families should be individualised.

6.2.2 Well-being trajectories

HRQoL was measured by CFQ-R at each assessment point during INSPIRE-CF and as part of the SRC PA maintenance study. The results demonstrated that the exercise intervention did not have a statistically significant impact on the 4 relevant HRQoL domains (physical, body image, treatment burden and respiratory), however it should be noted that the CFQ-R data collected at baseline were all relatively high (indicating better HRQoL). It is difficult for an intervention to demonstrate a positive impact if the perception of HRQoL was already good. There was an interesting trend in the treatment burden domain, where there was an improvement in results for the exercise training group between 1year and end of INSPIRE-CF assessment points. Whilst this change was not statistically significant, it must be considered in the context of an increase in treatment demand (a weekly supervised exercise intervention). This positive trend only occurred after 1year of training. This may indicate that exercise was considered to be a normal part of life by CYPwCF, rather than an additional element of treatment, and therefore enjoyable and not perceived as a burden.

The evidence-base was also found to be inconclusive. Hebestreit et al. (2010) reported that the only detectable impact of their intervention on HRQoL was in subjective health perception, where the intervention group demonstrated a statistically significant increase compared to the control group. This improvement in HRQoL was maintained throughout the post-intervention study period, in line with the exercise capacity results reported in this study. This suggested that health perception was associated with physical fitness. Klijn et al. (2004) also reported a statistically significant improvement in a different HRQoL domain: physical functioning. However, this study was conducted a number of years ago. There have been year-on-year substantial and important improvements in the health of CYPwCF (UK Cystic Fibrosis Registry, 2019). It was possible that the participants in the Klijn et al. (2004) study were more unwell as a result of more severe CF disease

and therefore experienced worse HRQoL. The HRQoL outcome measure results were generally high at each assessment point of the INSPIRE-CF and the SRC PA maintenance studies. This may explain the differences in the findings between the Klijn et al. (2004) and SRC PA maintenance studies.

More recently, Santana-Sosa et al. (2012) also reported that HRQoL remained unchanged despite the exercise intervention implemented in this RCT. However, the authors only reported analysing data as a total CFQ-R score rather than the individual domains. Analysis of individual relevant domains, such as physical functioning, may have resulted in different conclusions. In the later study conducted by the same group, Santana-Sosa et al. (2014) identified a trend towards significance indicating an improvement in HRQoL ($p = 0.071$). Yet again this was a report of total CFQ-R score rather than analysis and reporting of specific domains as the tool has been designed. A stronger, and potentially significant, signal may have been detected by analysing the scores for individual domains.

The impact of exercise interventions on HRQoL was varied across the evidence-base, thus remained inconclusive. This may have been a limitation of the sensitivity of the outcome measures used, particularly as the health of people with CF continues to improve year-on-year.

6.2.3 Physical activity maintenance

Data on levels of PA maintenance throughout INSPIRE-CF were only collected by an unvalidated, simple questionnaire. This method was repeated as part of the SRC PA maintenance study to enable direct comparison of the trajectories of control and exercise training groups during INSPIRE-CF and after the study ended. The results demonstrated that the levels of self-reported PA increased in both groups over the course of the INSPIRE-CF study. There was some indication that the rate of increase was greater for the control group than the exercise training group between the 1year and 2years assessment point, although the 95% confidence intervals were wide suggesting that the self-reported levels of PA for participants within the control group were more varied at this point. This was more evident when the PA trajectories of individual participants were examined. Three participants appeared to increase self-reported levels of PA to over 900minutes per week (15hours) which

was not observed in the exercise training group. There was then a fall in self-reported levels of PA for the control group between the end of INSPIRE-CF and the SRC PA maintenance assessment point. This was not observed in the exercise training group who demonstrated a continuous positive trajectory both during INSPIRE-CF and for the PA maintenance period. It should also be noted that the INSPIRE-CF intervention was an additional 45-60minutes of structured exercise each week for participants in the exercise training group. Whilst there was an increase in self-reported levels of PA in the exercise training group during INSPIRE-CF, this was not different from the control group suggesting that the exercise intervention did not fully explain the change in self-reported levels of PA. Furthermore, the self-reported levels of PA continued to increase in the exercise training group during the PA maintenance period, after the exercise intervention was withdrawn. Participants either replaced the INSPIRE-CF exercise session with other physical activities and additional PA as well, or this unvalidated questionnaire did not measure actual levels of PA. Even validated methods of collecting data on self-reported levels of PA are known to be limited by risk of recall and report biases, and the individual's perception of activity. There was poor correlation between the self-reported levels of PA data collected by the simple INSPIRE-CF questionnaire and those collected by HAES (a validated tool) as part of the Part B study. This added to the misgivings about the validity and reliability of the INSPIRE-CF method and thus findings should be interpreted with caution.

However, there were some similarities with the available literature. Hebestreit et al. (2010) measured self-reported PA as part of their exercise intervention RCT, although there were no details of the method used for this. The authors reported that self-reported levels of PA increased in the intervention group by just over 2hours per week during the first 12 months of the study (6months supported, 6months requested to maintain). PA measured by accelerometry corroborated the increase in PA in the intervention group during the same time, but only by 1hour per week and this increase was not statistically significant when compared to the PA levels of the control group.

The trajectories of self-reported levels of PA measured by INSPIRE-CF method for individual CYPwCF were varied with extremes (both high and low) observed in both groups. Whilst it was not possible to draw conclusions on the levels of PA in the participants, it was clear that the PA behaviour patterns were different between participants, in line with the results from the other measures discussed above.

6.2.4 Summary

In summary, at a group-level, the INSPIRE-CF exercise intervention had a positive impact on functional exercise capacity, but not FEV₁ z score, HRQoL or self-reported levels of PA. In line with most of the evidence-base, the benefit to functional exercise capacity was lost by SRC PA maintenance assessment point indicating that the benefit only lasted as long as the intervention continued, and that PA was not maintained independently. This was greater for females than males. However, the trajectories of functional exercise capacity, FEV₁ z score, HRQoL and self-reported levels of PA for individual CYPwCF were widely varied. Some participants demonstrated a positive trajectory even after the intervention ceased, and others did not. This suggested differences in the PA behaviours between different CYPwCF with some managing to maintain PA participation and others not. It also highlighted the limitation of group analysis, where the signals of some individual CYPwCF were lost. In the clinical setting, the individual child or young people must be considered, therefore understanding the differences between individuals is vital in order to develop appropriate assessment and support of PA maintenance behaviours. In the clinical setting, it would be extremely useful to be able to predict who is likely to maintain PA participation without additional support and who will not, and therefore needs appropriate and targeted interventions. If prediction is not possible then it is of paramount importance that appropriate assessment occurs in order to enable all CYPwCF to receive the appropriate support to maintain adequate PA to experience the associated health and well-being benefits.

6.3 What affects the maintenance of physical activity in children and young people with CF?

The results from the SRC PA maintenance study demonstrated that the levels of PA amongst CYPwCF were varied, as was individual capacity for maintaining PA

independently. This cohort of CYPwCF had a unique insight into the maintenance of PA, having participated in the exercise intervention RCT, thus the factors affecting the maintenance of PA were explored in the same sample. For this clinical research, 3 simple outcome measures were used to establish if self-efficacy for PA, self-reported levels of PA and barriers to parents PA were related to the maintenance of PA in CYPwCF. These factors were all identified from the literature as being important to the levels of PA in CYPwCF and the outcome measures were easy to use in a clinical setting.

6.3.1 Self-efficacy for physical activity

Self-efficacy for PA, measured by CSAPPA, was varied but generally high amongst the CYPwCF who took part in this study, reported by both CYPwCF and their parents. Those participants who were identified as PA 'maintainers' had significantly greater self-efficacy for PA than those identified as 'non-maintainers', and with a large effect size. This was in line with some of the literature discussed in section 2.3.1.1. Patterson et al. (2016) identified a significant correlation between self-efficacy for PA and levels of PA in CYP who had received a liver transplant. Furthermore, self-efficacy for PA was identified as a correlate of PA participation in CYP in a literature review conducted by Sallis et al. (2000). Furthermore, Kwasnicka et al. (2016) discussed the importance of 'maintenance motives' including 'enjoyment of behaviour and satisfaction with outcome', 'self-determination' and 'identity' as a key theme in relation to behaviour maintenance from their systematic review of behaviour theories to explain behaviour change maintenance. More specifically in the CF population, Street et al. (2016) explored the experiences of PA for adults with CF using a qualitative approach, and highlighted the relevance of self-efficacy for PA. The investigators interviewed 12 adults with CF, analysing the transcripts with interpretative phenomenological analysis to understand how the participants made sense of and derived meaning from their PA experiences. They reported that the participants who were regularly active tended to demonstrate greater self-efficacy for PA, and adjustment to and acceptance of their PA abilities. Those who were less active appeared less able to adjust or view themselves positively if their PA abilities were lower than they had been previously,

or low in comparison to healthy peers. The authors concluded that ‘working on building confidence in exercising in social situations may be key in building self-efficacy and reaching acceptance. In addition, it may enhance exercise adherence by increasing the benefits of socially enriched environments’. The study by Street et al. (2016) did not involve any participants under the age of 18 years, therefore an older and likely sicker population than those involved in the current study.

However, the findings were also in line with literature involving non-CF populations, as discussed above, so it seemed likely that the finding of the current study, that self-efficacy for PA was a potential indicator for levels of PA, was a true finding.

Interestingly, there were significant but inconsistent differences between CYPwCF- and parent-reported self-efficacy for PA. Discrepancies such as this have been identified in reporting of HRQoL in CF (Havermans et al., 2006, Hegarty et al., 2008, Groeneveld et al., 2012, Tluczek et al., 2013, Douglas et al., 2017). In the paediatric clinical setting, parents or carers are present for almost all interactions between healthcare professionals and CYPwCF. It is not uncommon that the parent or carer leads the conversation with the healthcare professional with the child or young person present, possibly contributing to the discussion or possibly distracted with another activity. Due to the known discrepancies between CYPwCF- and parent-reported self-efficacy for PA and HRQoL, it is of paramount importance that CYPwCF are at the centre of discussions about PA in CF clinical settings.

6.3.2 Self-reported levels of physical activity

Data were collected on self-reported time spent in PA, measured by the HAES. Results demonstrated that the CYPwCF involved in this study reported varied but generally high levels of PA. Activity levels were similar for weekdays and weekend days, mean \pm SD 179 \pm 143 minutes and 188 \pm 140 minutes respectively. These values equate to 3 hours of MVPA per day for both weekdays and weekend days which were extremely high and perhaps not an accurate representation of actual levels of PA. Savi et al. (2013) compared HAES reported PA with accelerometer recorded PA in adults with CF. A total of 20 adults with CF (recruited from 1 CF clinic in Rome, Italy) and 11 age-matched controls contributed 4 days of accelerometer data (2 weekdays and 2 weekend days, collected by arm-worn accelerometer) and HAES

data (self-reported PA for a weekday and a weekend day). The authors reported that the HAES questionnaire over-estimated levels of PA. This study was conducted in adults with CF, but the findings of the current study suggested that this may also be the case in CYPwCF as well. Self-report measures are vulnerable to recall and report biases where participants either consciously or sub-consciously remember and report more PA than actually took place. Furthermore, reporting PA involves an individual's perception of activity. It was possible that the more effort an individual made, for higher intensity PA, the more significant it appeared to be to them and therefore was reported as taking up a greater proportion of time than low intensity PA or inactivity. Self-report is widely used in clinical practice, either using validated measures such as the HAES, or simple questioning such as the INSPIRE-CF method. This study demonstrated a significant difference between these 2 methods of self-reported levels of PA. Therefore, it was apparent that further investigation into the relationship between self-reported levels of PA and objectively measured levels of PA in CYPwCF was needed in phase 2 of this research.

6.3.3 Barriers to parent physical activity and exercise participation

The barriers to parent/carer PA and exercise participation were measured by questionnaire in order to investigate the impact that parental attitude to PA had on the maintenance of PA in CYPwCF. The greatest barriers were lack of time, lack of will-power, lack of energy and social influence. Lack of skill, lack of resources and fear of injury posed less of a barrier to parent/carer PA participation. However, in this cohort of CYPwCF, there was no link between parent/carer barriers to PA and exercise participation and CYPwCF PA participation, as demonstrated by Mann Whitney U test investigating the relationship between PA maintainer status and parent/carer barriers to exercise questionnaire score. There has been some evidence that parent/carer PA and exercise participation has an influence on the PA participation of their child. Rodrigues et al. (2017) investigated the association between parent PA levels and child sport participation using a cross-sectional study design. This study was discussed in more detail in section 2.3.1.2. The authors reported a positive association, and that both a mother's and father's own PA participation had an influence on the child's participation in sport. Emirza et al.

(2018) evaluated the levels of PA in CYPwCF and those of their parents. PA data were collected from a small sample of 13 child-parent pairs using self-report questionnaires. The authors concluded that the levels of PA of CYPwCF and their parents were similar. However, this study was published as a conference abstract, therefore only limited information about the sample, data collection and analysis methods were available. Furthermore, the PA data were collected using self-report questionnaire which is vulnerable to recall and report biases. The small sample size also limited the transferability of the findings. Both of the studies discussed here suggested a positive link between parent PA participation and CYP PA participation. However, neither study discussed the relationship between barriers to parent PA and exercise participation, and the levels of PA amongst CYP as assessed in the current study. The current study identified that there was no link between reported barriers to parent PA and exercise participation, and levels of PA of CYPwCF, but did not involve the measurement of parent PA participation. Whilst it is perhaps logical to consider that reported barriers to parent PA and exercise participation may have an impact on parent levels of PA, this link has not been proven thus the discrepancies between findings of the current study and those published may be as a result of the different elements being investigated.

6.3.4 Summary

In summary, the only factor that correlated with functional exercise capacity at the PA maintenance assessment point was self-efficacy for PA. Self-efficacy for PA was the only factor associated with maintainer status and this was supportive of the evidence-base. This warranted further investigation in phase 2 of this research to establish if it was a predictor of PA maintenance. Self-reported levels of PA and parent barriers to PA and exercise participation were not statistically significantly different between PA maintainers and non-maintainers. However, self-reported levels of PA are frequently collected in the clinical setting, thus it was important to develop an understanding of the relationship between self-reported levels of PA and objectively measured maintenance of PA in CYPwCF in phase 2 of this research.

6.4 What are the barriers to and facilitators for maintaining physical activity in children and young people with CF?

Semi-structured interviews were conducted with CYPwCF and a parent/carer to investigate the PA experiences, attitudes, barriers and facilitators.

6.4.1 Experiences of and attitudes towards physical activity

Through thematic analysis, the findings suggested that all CYPwCF and their parents valued PA, but experiences, and therefore levels of participation, were varied. Most CYPwCF reported preferring informal activities to structured exercise, although half took part in regular, formal exercise. This finding was in agreement with the evidence-base (Fereday et al., 2009, Moola et al., 2012, Shelley et al., 2018).

Fereday et al. (2009) used focus groups incorporating multiple techniques (including maps, photographs and 'traffic light posters') to collect qualitative data from children with chronic diseases and their parents about their experiences and perceptions of PA. The sample of 25 children and parents included 5 CYPwCF, 6 with asthma and 14 with type 1 diabetes, all resident in South Australia. The participants reported having a range of PA experiences and took part in a wide variety of different activities. Whilst only a small proportion of the sample were CYPwCF, the findings were in line with other CF-specific research. Moola et al. (2012) explored the perceptions towards PA in 14 CYPwCF aged 11-17years, based in Canada. The investigators used semi-structured interviews and grounded theory analysis. The authors also reported that the participants in their sample had different attitudes towards and experiences of PA. Shelley et al. (2018) investigated CYPwCF's perceptions of PA in a UK-based sample. The 9 participants were aged 8-16years and recruited from a single CF centre. This small and geographically limited sample may have limited transferability, but the author reported similar findings to those of other studies thus increasing confidence: participants took part in a wide variety of activities.

All 20 of the CYPwCF interviewed in the current study recognised the health and well-being benefits of being physically active, again this was in agreement with other literature (Swisher and Erickson, 2008, Moola et al., 2011, Happ et al., 2013, Moola and Faulkner, 2014, Shelley et al., 2018, Denford et al., 2019). Swisher and

Erickson (2008) used semi-structured interviews and constant comparative analysis to explore perceptions of PA participation in CYPwCF from a single CF centre in the US. Participants were aged 13-17years and each undertook 2 interviews 3-4weeks apart. The first interview elicited overall attitudes to PA and the factors that influenced participation, and the second interview was designed to verify and elaborate on the responses. The participants represented a range of disease severity with ppFEV₁ ranging from 27 to 102. The current study did not have any participants with severe lung disease (ppFEV₁ <40), perhaps due to the improved health of CYPwCF since the Swisher and Erickson (2008) study was conducted, however the consistency of findings suggested that CYPwCF recognise the health and well-being benefits of PA regardless of disease severity.

A sense of PA identity appeared to be important to many participants in the current study, with 17 of the 20 interviewees voluntarily discussing their own identity. There was limited evidence of this in literature (Street et al., 2016). Denford et al. (2019) explored the motives, barriers and enablers of PA in CYPwCF through photo-elicitation and semi-structured interviews. The 12 participants, aged 12-18years, identified themselves as active (9 participants) or inactive (3 participants), although this was directly asked by the researchers thus it was not possible to conclude that this sense of identity was important to the participants. Happ et al. (2013) identified that child personality traits were an important indicator of participation suggesting that there is something about an individual child or young person that means they are likely to remain physically active or not. The investigators conducted serial semi-structured interviews to describe the exercise experiences of CYPwCF and their parents during participation in a 6-month programme of self-regulated home-based exercise as part of an RCT. Similar to the design of the current study, a subgroup of 11 purposively selected participants of the RCT were interviewed, although Happ et al. (2013) conducted the interviews during the RCT, at 2- and 6-months.

PA was considered by participants to be a normal part of life and this appeared to motivate CYPwCF to take part. Normalcy has been discussed in the literature as being important for CYPwCF, and PA, sport and exercise can facilitate environments

where CYPwCF are able to participate alongside their non-CF peers and forget about their CF (Moola et al., 2011, Moola et al., 2012, Street et al., 2016, Shelley et al., 2018, Denford et al., 2019).

6.4.2 Barriers to physical activity

Many different barriers were identified by the CYPwCF who were interviewed in this current study, some were relevant to some CYPwCF but not others. Intrinsic barriers to PA participation appeared to be greater in number and significance for CYPwCF than extrinsic barriers. This was similar to barriers to PA identified in the literature. The Denford et al. (2019) study reported that their health, time required for homework, a low value of PA, previous negative experience of sport and environmental factors (including weather) all acted as barriers to PA participation. The study was vulnerable to bias as participants had to contact the research team to be involved, thus those with an interest in PA were perhaps more likely to volunteer. However, the barriers that were identified were similar to those identified in the current study and other international literature. The key intrinsic barriers cited by both CYPwCF and parents in the current study, and supported by literature, were: unpleasant physical sensations (Swisher and Erickson, 2008, Moola et al., 2011, Happ et al., 2013, Shelley et al., 2018), impact of CF (Swisher and Erickson, 2008, Fereday et al., 2009, Moola et al., 2012, Happ et al., 2013, Moola and Faulkner, 2014, Shelley et al., 2018, Denford et al., 2019) and self-efficacy for PA (Moola and Faulkner, 2014). Lack of skills/experiences was also cited by CYPwCF, but attitude towards PA was cited by parents. Neither of these barriers were found to have been reported in other literature. Influence of others (Fereday et al., 2009, Moola et al., 2011) and homework (Happ et al., 2013, Denford et al., 2019) were both cited as extrinsic barriers by CYPwCF and parents. Weather (Denford et al., 2019) and boredom/disinterest (Swisher and Erickson, 2008, Moola et al., 2012, Denford et al., 2019) were cited by CYPwCF and parent availability (Happ et al., 2013) by parents. Interestingly, a number of other barriers were identified in the literature but not from the current study: lack of time (Moola et al., 2011, Moola et al., 2012, Happ et al., 2013, Denford et al., 2019), low mood/depression (Moola et al., 2012, Moola and Faulkner, 2014), a negative experience of sport (Denford et al.,

2019) and availability of facilities (Happ et al., 2013, Shelley et al., 2018). All of these studies investigating the barriers to PA in CYPwCF were of a qualitative design. The nature of qualitative research results in small sample sizes but richness of data. The differences in the identified barriers may be as a result of the small sample sizes generating slightly different barriers. It may be that some barriers are particularly pertinent to a geographical area, for example lack of facilities may affect one area more than another. However, there was notable agreement between the findings of many of the identified barriers from the current study and literature, particularly the dominance of intrinsic over extrinsic barriers. Nevertheless, the findings of the current study suggested that appropriate support and PA facilitation appeared to counteract all barriers to participation.

6.4.3 Facilitators of physical activity

CYPwCF and parents reported that variety, fun and enjoyment of physical activities helped the maintenance of participation, supported by the evidence-base (Swisher and Erickson, 2008, Moola et al., 2012, Shelley et al., 2018, Denford et al., 2019). All participants were able to identify at least 1 PA that they enjoyed, but many reported struggling to maintain participation and had given up some activities. This demonstrated that the maintenance of PA, sport and exercise was challenging and enjoyment of an activity alone was not enough to keep CYPwCF engaged in PA. The findings suggested that maintenance of PA could be facilitated by developing skills, achieving goals and receiving praise and acknowledgement (Moola et al., 2012, Denford et al., 2019).

The personality traits that were discussed in relation to the maintenance of PA were a competitive nature, confidence in one's own abilities (or self-efficacy for PA), and determination (Happ et al., 2013). This was in agreement with the results of the Part B: Factors affecting the maintenance of PA study which demonstrated that the self-efficacy for PA (measured by CSAPPA) scores were significantly higher for those who maintained PA compared to those who did not. Identifying this in CYPwCF in the clinical setting may help to identify who is likely to maintain PA and who is not.

Technology, such as activity trackers, was identified as a facilitator for the maintenance of PA by both CYPwCF and parents. However, this was not mentioned in any of the available literature. This could be a reflection of the limitations of small sample sizes involved in qualitative literature, or it could be that technology has had an increased role in PA and the lives of CYPwCF in more recent years, hence previously published literature did not identify technology as a facilitator.

Habit-formation has been discussed as a key facilitator for the maintenance of treatment behaviours for adults with CF (Phillips et al., 2016, Hoo et al., 2019). However, habit was only mentioned briefly by 3 of the interview participants and did not appear in the literature pertaining to CYPwCF reviewed for this discussion chapter. Therefore, either habit-formation was less relevant for CYPwCF compared to adults with CF, less relevant to PA than other aspects of treatment, or it may be that it continued to be important in helping maintain PA participation but was not recognised by CYPwCF or their parents.

Accountability to another, most notably a trainer for many of the participants in this study, was thought to be a significant facilitator of maintained PA participation. People were important and the relationships built between adult facilitators and CYPwCF appeared to be supportive of the maintenance of PA. Moola et al. (2011) explored the experiences that parents of children with CF and congenital heart disease had with regards to their own child's PA. A total of 29 parents (16 to CYPwCF aged 10-18years) were interviewed. Interviews were analysed using thematic analysis and identified the importance of positive role models as facilitators for PA for their child. The current study highlighted the importance of other people in facilitating PA for CYPwCF, in agreement with other literature. This could be friends providing sociability (Moola et al., 2012, Moola and Faulkner, 2014, Shelley et al., 2018), practical support or facilitation by parents (Fereday et al., 2009, Shelley et al., 2018) or parents acting as a PA role model for their CYPwCF (Moola et al., 2012, Happ et al., 2013). The role of personal trainers worked for some but not all of the CYPwCF interviewees in the current study, and even resulted in a positive change of exercise identity for a few. However, other

professionals, such as Scout leaders, were also identified as effective adult facilitators.

6.4.4 The role of parents

Like the CYPwCF, the parents interviewed as part of this study had different PA attitudes and experiences. All parents were positive about PA for their CYPwCF, but attitudes towards PA for themselves were more varied. The parent participants acknowledged that PA was less of a priority for themselves than for their CYPwCF, although some reported that they wanted to set an example for their child. However, parent exercise identity was not necessarily indicative of self-reported level of PA, and self-reported level of PA was not necessarily indicative of facilitating PA for their CYPwCF. In other words, active parents did not necessarily facilitate PA participation for their child. In fact, conflict was noted between 2 active parents and their children who happened to be reluctant to participate in PA. This has also been reported in the evidence-base (Shelley et al., 2018). Conversely, some parents who were not active identified as effective facilitators of PA for their CYPwCF. This was in contrast to the findings of Moola et al. (2011), Moola et al. (2012) and Happ et al. (2013) who all reported that sedentary parents had a detrimental effect on the PA of their CYPwCF.

6.4.5 Summary

In summary, the participants who were interviewed as part of the Part C: Barriers to and facilitators for the maintenance of PA study reported that they had varied PA experiences. Furthermore, those who had the same experience, personal training in this instance, experienced that differently. Some loved it from the beginning, some hated it all the way through, whilst others were transformed as a result of the training. This supported the findings of the other 2 components of phase 1 of this research: that CYPwCF are different to each other and therefore have different requirements to help their own maintenance of PA.

Having considered the findings of this study in line with the evidence-base, the concept of an individual's exercise identity appeared to be important, and was modifiable in some CYPwCF with appropriate support. Personal training seemed to

be helpful for some CYPwCF who were not keen on formal exercise, and it helped to change attitude, build confidence and sense of exercise identity.

Intrinsic barriers were greater in number and significance than extrinsic barriers, but all appeared to be surmountable with appropriate support and facilitation.

Enjoyment of physical activities was important for CYPwCF participation, but maintenance was more complex and enjoyment alone did not mean that all CYPwCF would continue to participate. The impact of other people was significant, but could be a barrier or facilitator to the maintenance of PA by CYPwCF.

Appropriate adult facilitators appeared to be important. For some CYPwCF a parent could take on this role. However, for other CYPwCF another adult proved to be more beneficial. In fact, the conflict between CYPwCF and parents could be detrimental to the maintenance of PA for some. Clinicians must be aware that active parents do not always have active children, and inactive parents sometimes manage to facilitate high levels of PA for their child.

6.5 Methodological strengths and limitations

This research was the first to investigate, in detail, the long-term impact of a supervised exercise intervention on the health, well-being and PA maintenance of CYPwCF, and to understand their perspectives on what affects the maintenance of PA. This study had a number of methodological strengths. The researcher had access to a rare population who had had the experience of a supervised exercise intervention as part of the INSPIRE-CF RCT. The participants were able to share their unique experiences and insights of PA maintenance both during and after the supervised exercise intervention period. The mixed methods design enabled the researcher to gain a well-rounded but also in-depth view of the PA experiences of the participants as well as the impact of the exercise intervention on the health, well-being and PA maintenance. The researcher was able to recruit almost all CYPwCF (96%) who were eligible to participate increasing confidence in the results. Furthermore, the sample size for the qualitative element (20 CYPwCF and parent pairs resulting in 40 interviews) was large for such work. Data saturation was reached with these interviews, increasing the trustworthiness of the findings.

The parallel design was practical in this clinical research, and reduced the time and burden involved for participants, although this may have resulted in reduced relevance of some of the interview topics. The parallel design also facilitated the immediate integration of findings thus maximising the strengths and minimising the limitations of each individual study.

These studies also had a number of limitations. It was not possible to conduct a power calculation for the first 2 studies in phase 1 of this research (Part A: SRC PA maintenance study and Part B: Factors affecting the maintenance of PA study) because the potential sample was limited to those who had taken part in INSPIRE-CF and remained eligible to participate. Only 2 eligible CYPwCF (4%) did not participate in this research, therefore the sample was as large as possible. Nonetheless, the signal detected in some outcome measures, such as self-efficacy for PA, contributed to the plan for investigation in phase 2 of this research.

The sample for phase 1 of this research was limited to the younger participants from the original INSPIRE-CF study. Older INSPIRE-CF participants were not eligible to participate in phase 1 of this research because they no longer received their CF care from the GOSH CF service. They may have had different PA experiences and generated additional findings which were missed by their exclusion, especially given the known transitions in PA behaviours during adolescence.

Participants were recruited from a single CF centre. As part of their standard CF care, all participants would have received the same approach to PA support and facilitation, although the exercise training group also received a weekly supervised exercise training session. It was possible that the lack of statistically significant differences between the control and exercise training groups was as a result of the nature of the physiotherapy and PA support and recommendations made by the clinical CF team. However, the findings were in line with the literature discussed in chapter 2 thus were likely to be a true finding.

The sample for the qualitative study investigating the barriers to and facilitators for the maintenance of PA included more females than males. It was noted in the SRC PA maintenance study that the distance achieved during 10m-MSWT fell more

significantly for the female participants in the exercise training group than the male participants. There was potential that this reflected a difference in the maintenance of PA between females and males which may have resulted in different barriers to and facilitators for PA. The findings from the interviews may have been biased towards female-reported barriers and facilitators rather than male-reported. However, recruitment continued until data saturation was reached so the impact of this should have been minimised.

The lead researcher for this work (HD) was immersed in the research having been involved with testing and exercise training throughout INSPIRE-CF, and within a clinical role at the GOSH CF unit. Therefore she was known to the participants. This could have had mixed effects. Participants may have felt more at ease during the testing and interviews because the setting and researcher were familiar. However this may also have resulted in some reporting bias as participants may have responded in a way they thought the researcher wanted (Bowling, 2004). This has been considered and every attempt made to reduce this element of bias by removing a direct link between the participant and researcher. For example, interview participants were asked what advice they might give to others ('what advice would you give to other CYP about carrying on with exercise and activity?'), and to consider the views of others ('can you think of other children and what it might be that would make it difficult for them to be active or do exercise?'). To ensure that the analysis of the qualitative data was not influenced by the lead researcher's involvement in the work, the second coder (SD) was independent, had no previous involvement with the research and had not met, and did not meet, any of the participants. Despite this difference, the early coding frameworks independently developed were very similar, and consensus easily reached between the two coders. This contributed to the credibility of the findings.

Another limitation of this work was the way in which self-reported PA participation data were collected throughout INSPIRE-CF. This was not considered to be an important outcome of the original INSPIRE-CF study thus was not collected using a validated tool. However, this was a relevant and important element of the Part A: SRC PA maintenance study, therefore the same approach was employed to enable

direct comparison across assessment points. The HAES was also used as part of the Part B: Factors affecting the maintenance of PA study. Using a validated measure of self-reported levels of PA at this point enabled direct comparison of the data collected by the INSPIRE-CF method thus developing understanding of the value of this measure.

Exercise capacity testing during the INSPIRE-CF study included 10m-MSWT and also a cycle ergometer cardiopulmonary exercise test (CPET) using the Godfrey protocol (Godfrey and Mearns, 1971). However, due to the high time and effort burden to participants, and significant financial cost and limited value over and above that of using 10m-MSWT alone, CPET was not used for the Part A: SRC PA maintenance study. The SRC PA maintenance study identified detectable differences between the trajectories of distance achieved during 10m-MSWT of control and exercise training groups, and during and after INSPIRE-CF. Therefore, the exclusion of CPET as part of the SRC PA maintenance study did not appear to limit the value of the study.

Maintenance of PA was not directly measured in this first phase of the project, therefore a positive change in distance achieved during 10m-MSWT was used as an indicator of PA maintainer or non-maintainer status. There was risk associated with this assumption as growth could also account for some positive change. However, there was a clear signal that the INSPIRE-CF intervention affected the distance achieved during 10m-MSWT and therefore gave some clue as to maintenance of PA or not. It was clear that the withdrawal of the exercise training resulted in a negative impact and the gains achieved during the exercise intervention were lost by PA maintenance assessment point. Self-efficacy for PA had the strongest association with change in distance achieved during 10m-MSWT.

Finally, a lack of validated parent PA and exercise barriers questionnaires limited the value that this element was able to contribute. However, barriers to parent PA participation was considered important to investigate as a potential factor affecting the maintenance of PA in CYPwCF so a simple tool was selected in consultation with the parent advisors.

6.6 Summary of phase 1

Phase 1 of this research aimed to answer the first 3 research questions:

1. What happened to the health, well-being and PA maintenance of CYPwCF after withdrawal of a supervised exercise intervention?
2. What affects the maintenance of PA in CYPwCF?
3. What are the barriers to and facilitators for maintaining PA in CYPwCF?

Quantitative and qualitative data were collected and integrated and the key findings were considered in line with the evidence-base. The supervised exercise intervention, as part of INSPIRE-CF, resulted in an increase in functional exercise capacity, but this increase was not sustained beyond the end of the intervention indicating that PA was not maintained independently. Furthermore, the fall in functional exercise capacity after the withdrawal of the supervised exercise intervention was greater for females than males. PA counselling, rather than supervised exercise, may result in a longer-term benefit (Hebestreit et al., 2010). The supervised exercise intervention did not have an impact on FEV₁ z score. This may have been due to the lack of sensitivity of FEV₁ as an outcome measure. The impact that the exercise intervention had on HRQoL was inconclusive. The CFQ-R may not be sensitive enough to change in CYPwCF who generally experience good HRQoL. Assessment of the trajectories of PA participation was limited by the data collection method, but it appeared to vary between CYPwCF.

Individual participants demonstrated different trajectories with some exhibiting positive changes between each assessment point, some experiencing negative trajectories, and others fluctuating between positive and negative at each assessment point. This highlights the importance that PA advice and support is individualised in the clinical setting, and how valuable it would be to clinicians to be able to identify who needed support and what that should be.

Self-efficacy for PA was significantly higher for participants identified as PA maintainers than those identified as PA non-maintainers. There were significant discrepancies between CYPwCF- and parent-reported self-efficacy for PA.

Therefore, CYPwCF must be central to all conversations about PA to ensure that the

factors actually affecting levels of PA of CYPwCF are heard rather than the factors perceived by a parent or carer. Self-reported levels of PA were extremely high, and potentially exaggerated. Work to determine the relationship between self-reported PA and objectively measured PA in CYPwCF was required. There was no detectable link between self-reported levels of PA or parent barriers to PA and the maintenance of PA in CYPwCF.

CYPwCF had varied PA experiences, and even those who had received the same intervention experienced it differently. This added to the argument that personalisation of advice and support is paramount. The findings suggested that there may have been a fall in level of PA associated with age for at least 1 CYPwCF. This would require further investigation in the second phase of this research. All CYPwCF and their parents recognised the health benefits of being physically fit and active. This was a motivator for some CYPwCF, but not all. A sense of exercise identity was important. CYPwCF viewed themselves as 'sporty' or 'not sporty'. The most frequently cited barriers were intrinsic and included: impact of CF, unpleasant physical sensations, low self-efficacy for PA, lack of skills and experiences, attitude to PA. The negative impact of other people, competing demands including homework, weather and boredom/disinterest were also cited as barriers to PA participation. Some CYPwCF were unable to identify barriers to PA. Interestingly, they tended to score lower for self-efficacy for PA suggesting that CYPwCF may first need to experience and understand supported exercise, such as personal training, in order to identify barriers to maintaining participation.

PA being fun and enjoyable was important for maintaining participation, but the maintenance of PA is complex and enjoyment alone is not enough to ensure participation continues. Other people, most notably adult facilitators, were the most significant facilitator of maintained PA participation. A parent was not always appropriate for this role. In fact, this was detrimental to the PA participation of some CYPwCF. Parent exercise identity and PA status were not linked to the maintenance of PA in CYPwCF. This was in line with the lack of link between parent barriers to PA and maintenance of PA in CYPwCF. Therefore, the measurement of parent factors was not required for phase 2 of this research.

The findings of this phase of research were congruent with much of the literature, extending the knowledge-base and informed the work planned for phase 2.

6.7 Implications for phase 2

Having conducted the work in phase 1 of this project, the researcher (HD) started to understand more about the complexities of the maintenance of PA in CYPwCF. It was important to note that there were differences in behaviours in both control and exercise training groups of the SRC PA maintenance study, thus maintenance of PA could not be predicted by this intervention alone. Some participants in the exercise training group did not maintain PA and some participants in the control group did, and vice versa. Furthermore, self-identified exercise identity, and cited barriers to and facilitators for the maintenance of PA did not identify those who maintained PA participation and those who did not. It was established that personalising the PA advice and support for CYPwCF was important, however being able to easily identify who needed support and with what approach would be beneficial to CF clinicians.

Self-reported levels of PA were limited, therefore tracking PA objectively was key to developing further understanding of the patterns of PA maintenance in CYPwCF in phase 2 of this project. But self-reported levels of PA are frequently collected in the clinical setting, therefore understanding the relationship between objectively measured patterns of PA and self-reported levels of PA (measured by HAES) was important for phase 2.

Self-efficacy for PA provided the strongest signal of a link to the maintenance of PA therefore was important to include in phase 2. However, there were discrepancies between CYPwCF- and parent-reported CSAPPA scores. Whilst these were significant differences, there was some correlation thus it was not necessary to measure both. Measuring the perception of CYPwCF provided a useful insight into the child's relationship with exercise and PA, and had the potential to predict who would maintain PA and who would not. Therefore, CYPwCF-reported CSAPPA was prioritised to investigate the relationship between self-efficacy for PA and objectively measured patterns of PA for phase 2 of this project.

The impact of the INSPIRE-CF exercise intervention on HRQoL was inconclusive, thus the CFQ-R was not appropriate to include in phase 2. However, there were detectable differences in functional exercise capacity data (measured as distance achieved during 10m-MSWT) collected as part of phase 1 of this project. The 10m-MSWT is another frequently used clinical outcome measure. This was prioritised for inclusion in phase 2 of this work to develop greater understanding of the relationships between objectively measured patterns of PA and functional exercise capacity, self-efficacy for PA and self-reported levels of PA.

7 Phase 2 Methods

Phase 2 of this project involved a quantitative approach to investigate the relationships between exercise capacity, self-efficacy for PA, self-reported levels of PA and objectively measured levels of PA in CYPwCF. The findings from phase 1 of this programme of research identified that supervised exercise training can have a positive impact on exercise capacity, measured by 10m-MSWT, but that for many CYPwC, this benefit only lasted as long as the training continued. For those CYPwCF who were unable to maintain PA independently, the benefits to distance achieved during 10m-MSWT gained as a result of the exercise training were lost once the intervention was withdrawn. This supported the message that the maintenance of PA is of paramount importance for the health and well-being of CYPwCF. It would, therefore, be valuable for CF clinical teams to be able to identify, or predict, which of their patients maintain adequate levels of PA to experience the health and well-being benefits, and those who do not. This would ensure that CF clinical teams can direct the limited resources to support adequate PA to those who require assistance to experience the health and well-being benefits, and leave those who are able to maintain independently to do so.

Exercise capacity has been identified as an indicator of morbidity and mortality in CYPwCF (Nixon et al., 1992, Pianosi et al., 2005, Hebestreit et al., 2019). From a clinical perspective, a key aim for maintaining PA is to also maintain exercise capacity, and therefore health and well-being. Exercise capacity is frequently measured in the clinical setting and is a part of routine assessment for most CYPwCF in the UK (Cystic Fibrosis Trust, 2017b). However, an exercise capacity test alone does not identify an individual who is not maintaining adequate levels of PA and is therefore at risk of losing the associated health and well-being benefits. Identifying the PA maintenance behaviour patterns of CYPwCF is more complex. Self-report measures are relatively quick and simple, and frequently used in the clinical setting (Bradley et al., 2015). However, the results from phase 1 of this research suggested that simply asking CYPwCF about their regular physical activities may not give an accurate measure of actual levels of PA and therefore maintenance of PA behaviours. As discussed in section 2.3.2, evidence existed identifying

correlates for PA and exercise participation such as gender (Sallis et al., 2000, Farooq et al., 2017), age (Sallis et al., 2000, Farooq et al., 2017), self-perception of skills and abilities (Sallis et al., 2000, Spink et al., 2006, Moola et al., 2012, Patterson et al., 2016) and enjoying physical activities (Spink et al., 2006, Moola et al., 2012, Poobalan et al., 2012). There are additional complexities that exist for CYPwCF, such as burden of disease and treatment regimen, impact of parents and CF clinicians, and social stigma (Prasad and Cerny, 2002, Wilkes et al., 2009). Therefore, greater understanding of PA attitudes and behaviours, and the resulting impact on maintaining participation, was required to identify PA maintenance trends and, predictability of those trends, amongst CYPwCF. Phase 1 of this project investigated this, and developed the theory that the maintenance of PA behaviours in CYPwCF might be closely related to the individual's self-efficacy for PA. Phase 2 of this research aimed to identify PA maintenance behaviours and patterns amongst CYPwCF, and to assess whether PA maintenance could be predicted by 3 clinical outcome measures, including self-efficacy for PA. The researcher (HD) anticipated that PA behaviours and patterns would vary amongst CYPwCF, and that there would be discrepancies between reported levels of PA and actual levels of PA. The researcher (HD) also expected trends to be detectable which could help to identify the important correlates for maintaining exercise participation. The aims of this second phase of work were to quantify relationships between:

- exercise capacity measured by 10m-MSWT,
- self-efficacy for PA measured by CSAPPA,
- self-reported levels of PA measured by HAES,
- objectively measured levels of PA assessed by activity tracker data.

The researcher (HD) considered that PA tracking would result in the most reliable assessment of levels and maintenance patterns of PA in CYPwCF. PA tracking would, therefore, generate data giving the closest insight into the day-to-day PA behaviours of CYPwCF. However, as identified in Chapter 2, regular and routine assessment of maintenance of PA by PA tracking is not easy. This could be particularly challenging for resource-limited clinical CF services. This Phase 2 study was designed to develop an understanding of how the other outcome measures

related to PA tracking, and whether daily PA in CYPwCF could be predicted by the other outcome measures without direct measurement.

7.1 Study design

Phase 2 of this project consisted of a single longitudinal observational cohort study (Figure 34). Quantitative data were collected, using exercise capacity testing, questionnaires and activity trackers, to investigate the interactions between exercise capacity, self-efficacy for PA, self-reported levels of PA and objectively measured levels of PA, and therefore potentially answer research questions 4 and 5:

4. What are the patterns and maintenance of PA over time in CYPwCF?
5. Can the maintenance of PA in CYPwCF be predicted?

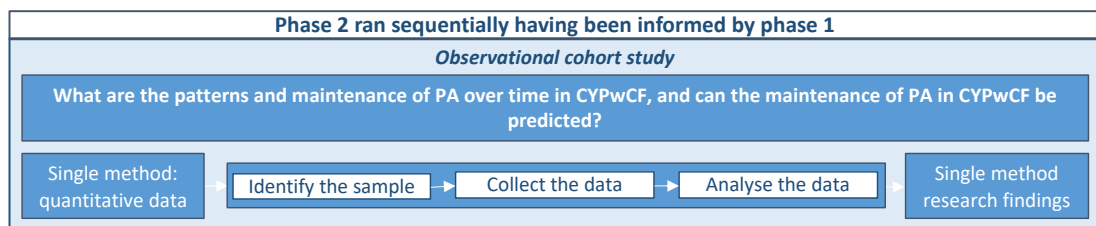


Figure 34: Diagrammatic representation of the single study of phase 2 of this research

This observational approach enabled collection of data on the normal exercise and PA routines of CYPwCF for at least 2 months. This length and detail of PA tracking had not been reported in the CF literature before. The PA tracking data collection element of the study needed to be of a long enough duration to ensure that ‘normal’ habitual PA patterns were detected rather than a novelty effect related to the introduction of a new activity tracker, and that enough data were contributed by each participant taking into consideration the need to regularly re-charge the tracker battery and ensure a balance of weekdays and weekend days (Rich et al., 2013). A previous study suggested that the moderate increase in activity associated with an activity tracking intervention (which included a motivational element) was no longer observed at 6 weeks (Howe et al., 2016). Therefore, a minimum of 2 months of PA tracking was considered appropriate to ensure that ‘normal’ habitual PA patterns were detectable and to capture a balance of weekdays and weekend days to assess differences in PA.

7.2 Population

Phase 2 of this research involved CYPwCF who received CF care from 3 London paediatric CF centres: GOSH, Royal London Hospital (RLH) and Royal Brompton Hospital (RBH). This study was run synchronously with Project Fizzyo, a 16-month longitudinal observational study investigating the physiotherapy behaviours (airway clearance and PA) of CYPwCF (Raywood et al., 2020). The researcher (HD) was a grant holder for Project Fizzyo and an active member of the research team, involved in designing and conducting the project including recruitment, data collection and data analysis. CYPwCF were able to participate in both studies concurrently as the data that were collected contributed to both studies, thereby reducing participation burden to the CYPwCF. All participants in this Phase 2 study and Project Fizzyo were issued with a commercially available activity tracker (Fitbit Alta HR™), to track continuous step count and HR data, and a tablet to sync their daily data to the research team. The researcher (HD) was able to analyse daily PA data, as well as the exercise capacity and demographic data collected at baseline for both this Phase 2 project and Project Fizzyo (including age, sex, height, weight, BMI, genotype and spirometry). Two additional questionnaires were collected specifically for this Phase 2 project. Participants were thus able to contribute to 2 research projects concurrently. Participants were invited to participate in Phase 2 of this research sequentially until the recruitment target had been reached.

7.3 Funding

The CF Trust Youth Activity Unlimited strategic research centre funded the researcher. The equipment and infrastructure used for Project Fizzyo were funded by:

- Office of Life Science Award (academic Health Science Networks and UCLP),
- UCL Rosetrees Stoneygate Prize,
- CF Trust: Clinical Excellence and Innovation Award,
- UCL Knowledge Exchange and Innovation Fund.

7.4 Ethical approval and considerations

Ethics approval was granted for Phase 2 of this research by the Newcastle and North Tyneside 1 NHS Research Ethics Service Committee (REC reference: 18/NE/0324, IRAS ID: 246187, Appendix 14), and registered with GOSH-UCL Research and Development Service as study sponsors (reference: 15IA25). Ethics approval was granted for Project Fizzyo by the London-Brighton and Sussex NHS Research Ethics Service Committee (REC reference: 18/LO/1038, IRAS ID: 228625, Appendix 15), and registered with GOSH-UCL Research and Development Service as study sponsors (reference: 17IA06).

7.5 Study procedures

7.5.1 Sample

This study aimed to recruit at least 74 CYPwCF. This was set as the minimum sample size to ensure that enough participants were recruited to enable multiple regression analyses with 3 independent variables. Despite a number of guidelines suggesting sample size calculations for this statistical technique, the more conservative formula suggested by Tabachnick and Fidell (2014) was selected:

$$N > 50 + 8m \text{ (where } m = \text{number of independent variables)}$$

CYPwCF recruited to Phase 2 of this study and Project Fizzyo were eligible to take part if they met the inclusion/exclusion criteria detailed in section 3.6.2.

7.5.2 Data collected

Eligible potential participants were identified by the clinical physiotherapist at each of the 3 CF centres acting as study sites and were sent a letter and information sheet (Appendix 2) inviting the CYPwCF to participate in phase 2 of this research. These potential participants were then contacted by telephone or email by the researcher (HD) at least 2 months after being recruited to Project Fizzyo. This ensured that the minimum period of activity tracker data had already been collected. Any questions raised about participation were answered and then an appointment was arranged if the CYPwCF and parent/carer were willing to participate. Appointments were made to coincide with a time that the CYPwCF and

parent/carer were already attending their CF clinic for an appointment, or a telephone appointment was arranged if preferred.

At the appointment, the Phase 2 study was discussed and any further questions were answered by the research team (HD and ER). Consent and assent forms were discussed and signed by a parent/carer, participant and member of the study team (Appendices 3 and 4). For those participants who took part via telephone appointment, the consent and assent forms were discussed during the telephone call and verbal agreement was taken. The paper forms were sent out to the family's home address and were signed and returned using a provided stamped-addressed envelope. The 2 questionnaires were then completed:

- Self-efficacy for PA (CSAPPA),
- Self-reported levels of PA (HAES).

Participation in phase 2 of this research was then complete. The participation process can be seen in Figure 35 and timeline of outcome measures in Figure 36.

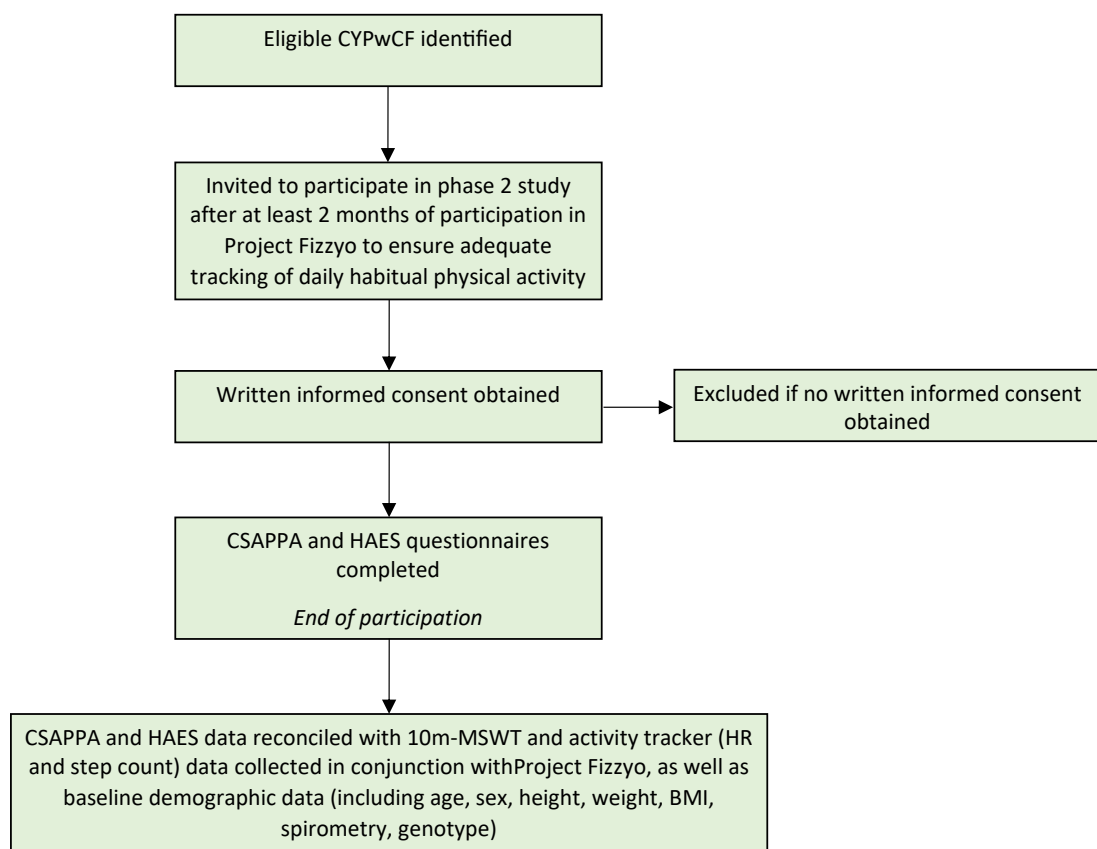


Figure 35: Flowchart detailing participation process for phase 2 of this project

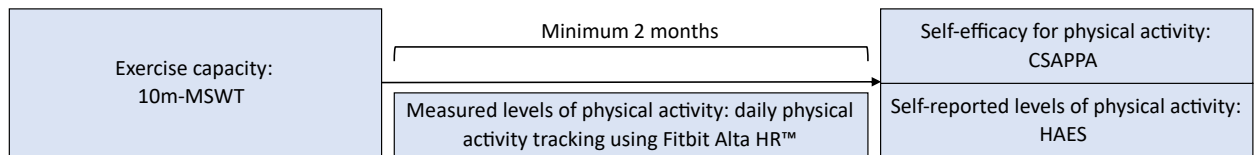


Figure 36: Timeline of outcome measures for phase 2 of this project

7.5.2.1 Exercise capacity

Exercise capacity data were collected using the 25-level 10m-MSWT as detailed in section 4.5.2.1. The 10m-MSWT was carried out in conjunction with Project Fizzyo as part of baseline testing (by ER and HD), and therefore at the start of the PA tracking for participants in phase 2 of this project.

7.5.2.2 Self-efficacy for physical activity

Self-efficacy for PA data were collected using the CSAPPA as detailed in section 4.6.2.1. For phase 2 of this study, only child-reported self-efficacy for PA was collected. As identified in phase 1 (section 5.2.1.2), there were wide variations in the differences between child and parent/carer perceived self-efficacy for PA. Therefore, it was unnecessary to also collect both child and parent/carer perceptions of the child's self-efficacy for PA for phase 2 of this study. Child's perception was prioritised. Participants completed the CSAPPA questionnaire at their phase 2 participation visit or telephone call appointment at least 2 months after PA tracking was commenced.

7.5.2.3 Self-reported levels of physical activity

Self-reported levels of PA data were collected using the HAES as detailed in section 4.6.2.2. Participants completed this questionnaire at their phase 2 participation visit or telephone call appointment at least 2 months after PA tracking was commenced. Participants were asked, where possible, to describe days that coincided with days where PA tracker data were available.

7.5.2.4 Measured levels of physical activity

Participants were asked to wear a wrist-worn Fitbit Alta HR™ (Fitbit Inc, San Francisco, CA <https://www.fitbit.com/uk>) for the duration of their participation in Project Fizzyo. Fitbit Alta HR™ is a commercially available wrist-worn activity tracker and, after consultation with a number of CYPwCF and parents during

planning, was considered to be the most feasible PA tracker for this study because of its smaller size and affordability. Fitbit™ was rated as the second most useful app or piece of technology for CF care in a survey of people with CF and their family and friends in the UK (Cystic Fibrosis Trust, 2017a). Many studies incorporating wearable activity trackers as a data collection tool have been limited by the short amount of time the trackers were actually worn by participants (Mittaine et al., 2012, Audrey et al., 2012, Wells et al., 2013, Fairclough et al., 2016). A number of studies have identified that participants prefer wrist-worn PA trackers and these are therefore worn more during a data collection period than hip-worn trackers. They were reported to be perceived as less burdensome and more comfortable by participants (Shelley et al., 2018, Fairclough et al., 2016, Audrey et al., 2012). Shelley et al. (2018) also reported that the CYPwCF that they surveyed were more likely to wear a wrist-worn, commercially available PA tracker that gave some feedback on the wearer's level of PA rather than many research-grade trackers which do not provide any information to the wearer. This was also reported by Audrey et al. (2012) in their non-CF adolescent sample.

By using a tracker that was popular amongst the study population, and selected by a representative group of CYPwCF, it was anticipated that the Fitbit Alta HR™ would be well tolerated and therefore sufficient PA data would be available. This device also facilitated continuous real-time data capture and transfer rather than using a device that required returning to the study team to download stored data. This has been identified as a problem resulting in data loss by previous studies, either through device malfunction or failure to return to the study team (Fairclough et al., 2016, Ferguson et al., 2015, Audrey et al., 2012).

Participants were provided with appropriately sized wrist straps and advised to wear the PA tracker as much as possible during waking hours, as well as overnight if they chose to. They were advised to position the tracker 2 finger widths above the ulnar prominence and tight enough that it wouldn't move but not too tight that it pinched the skin. Participants were asked to charge the device once per week as a minimum, or whenever the low battery symbol was displayed if this was more frequent.

Participants were asked to continue with their normal exercise and PA routines and to sync (with the assistance of a parent/carer) the PA tracker to the Fitbit™ app on their study tablet daily if possible to enable timely data transfer. Continuous step count (per minute) and HR (at a sampling frequency of 1-10 per minute with higher frequency occurring during activity) data were captured. The raw step count and HR data were then transferred to a secure cloud space (Microsoft Azure Research Cloud) and accessed by the research team.

A Fitbit data cleaning and processing pipeline was developed once the data had been fully explored. This is detailed in section 8.4.1. This pipeline enabled the calculation and subsequent evaluation of daily time spent in MVPA for each participant. Therefore, it was possible to investigate and distinguish the relationships between the subjective measures (self-efficacy for PA and self-reported levels of PA) and the objective measures (exercise capacity and measured time spent in MVPA).

7.6 Data analysis

Most statistical analyses were conducted using IBM SPSS Statistics 24 or 25 (IBM Corp., Armonk, NY, USA). Standardisation of distance achieved during 10m-MSWT by age and latent class growth analysis (LCGA) were run in R (R Foundation for Statistical Computing, Vienna, Austria). The latent class mixed model package was used for LCGA (Proust-Lima et al., 2017). One-way ANOVA (for normally distributed continuous variables), Welch tests (for normally distributed continuous variables but with unequal variances), Kruskal-Wallis tests (for non-normally distributed continuous variables) and Fishers exact tests (for categorical variables) were used to identify demographic characteristic differences between participants recruited from different CF centres.

Each variable was explored in turn, and age group and sex comparisons were conducted where appropriate because these appeared to be important factors from phase 1 of this research. One-way between-groups ANOVA was conducted to identify differences between the age groups in the distance achieved during 10m-MSWT standardised by age, whilst an independent *t*-test was carried out to identify

the differences between males and females. Kruskal-Wallis tests were used to identify the differences between age groups for self-efficacy for physical activity total and individual domain scores, with Mann-Whitney U tests, with Bonferroni corrected α , conducted to compare each age group. This was also conducted for age group comparisons of weekend day self-reported time spent in MVPA because this variable was non-normally distributed. Weekday self-reported time spent in MVPA was normally distributed, therefore the age group comparisons were conducted using a Welch's one-way between groups ANOVA with post-hoc Tukey test. The difference between weekday and weekend day self-reported time spent in MVPA was examined using a Wilcoxon Signed Rank test. Spearman's Rho correlation was used to investigate the relationship between self-reported time spent in MVPA and self-identified level of PA.

The PA tracker data were analysed firstly by conducting Chi-squared tests to compare time spent in MVPA by the different age and sex groups. LCGA was then used to identify patterns of PA maintenance over time. LCGA was selected as it enabled multiple sub-groups to be classified by the longitudinal change in time spent in MVPA within sub-groups and between sub-group differences in trajectory of time spent in MVPA (Jung and Wickrama, 2008). LCGA does not take account of the between-subject heterogeneity in trajectory, as Growth Mixture Modelling (GMM) does. However, LCGA was appropriate for this analysis because a relatively high number of classes were identified and thus it captured the variations between individuals and reduced the complexity and difficulty of convergence that would have occurred with GMM. Chi-squared tests were used to compare the PA patterns (as identified by LCGA) of different age and sex groups. The difference between self-reported time spent in MVPA and that measured by PA tracker was examined using a Wilcoxon Signed Rank test. Multiple regression analysis was used to explore the predictability of time spent in MVPA (measured by PA tracker) by exercise capacity (10m-MSWT), self-efficacy for PA (CSAPPA) and self-reported time spent in MVPA (HAES). Finally, linear discriminant analysis (LDA) was conducted to investigate if PA maintenance pattern (LCGA class) could be predicted by exercise capacity (10m-MSWT), self-efficacy for PA (CSAPPA) and self-reported time spent in

MVPA (HAES). LDA facilitates the prediction of group membership (>2 categories) from a set of predictors (continuous in nature and multiple) (Tabachnick and Fidell, 2014).

8 Phase 2 Results

A total of 78 CYPwCF participated in Phase 2 of this research, 15 of whom also participated in Phase 1 (11 from the exercise training group (7 were also interviewed) and 4 from the control (1 was also interviewed)). Demographic data are presented in Table 25. The majority of participants (n = 45) were recruited from centre 1, with the remaining 33 recruited from centres 2 and 3. Despite the unequal sample sizes, there were no statistically significant differences in the demographic data between centres (Table 25).

Table 25: Demographic information for phase 2 participants

	Total	Centre 1	Centre 2	Centre 3	p	
n = (%)	78 (100%)	45 (58%)	18 (23%)	15 (19%)		
Age in years at recruitment: Median (IQR)	9.2 (7.8-11.6)	9.0 (7.8-12.2)	9.2 (7.9-11.7)	9.4 (7.5-10.1)	0.839 ¹	
Age group (%)	6-8 years	36 (46%)	22 (49%)	7 (39%)	7 (47%)	0.247
	9-11 years	24 (31%)	10 (22%)	7 (39%)	7 (47%)	
	12+ years	18 (23%)	13 (29%)	4 (22%)	1 (6%)	
BMI: Mean ± SD	16.8 ± 2.1	16.7 ± 2.5	17.1 ± 1.7	16.9 ± 1.1	0.802 ²	
Sex (%)	Male	35 (45%)	20 (44%)	7 (39%)	8 (53%)	0.704
	Female	43 (55%)	25 (56%)	11 (61%)	7 (47%)	
Genotype (%)	F508del / F508del	43 (55%)	25 (56%)	11 (61%)	7 (46%)	0.548
	F508del / Other	25 (32%)	15 (33%)	6 (33%)	4 (27%)	
	Other / Other	10 (13%)	5 (11%)	1 (6%)	4 (27%)	
FEV₁ z score: Mean ± SD	-0.92 ± 1.24	-1.02 ± 1.21	-1.13 ± 1.10	-0.33 ± 1.37	0.121 ³	
Disease severity (%)	Mild ppFEV₁ ≥70%	68 (87%)	38 (84%)	16 (89%)	14 (93%)	0.813
	Moderate ppFEV₁ 40-69%	10 (13%)	7 (16%)	2 (11%)	1 (7%)	
	Severe ppFEV₁ <40%	0 (0%)	0 (0%)	0 (0%)	0 (0%)	

Key: BMI body mass index, FEV₁ forced expiratory volume in the first second, IQR interquartile range, n number, ppFEV₁ percent of predicted FEV₁, SD standard deviation.

¹ Kruskal-Wallis Test for continuous variable with non-normal distribution,

² Welch Test for continuous variable with normal distribution but unequal variances,

³ One-way analysis of variance (ANOVA) for continuous variable with normal distribution, Fishers exact test for all categorical variables. Nothing reached level of significance α 0.05

8.1 Exercise capacity

All 78 participants completed a 10m-MSWT as a measure of exercise capacity, however 6 participants did not achieve peak HR (HR_{peak}) of greater than 180 beats per minute and thus did not reach maximal exertion. Of those 6 participants, 2 completed a maximal effort 10m-MSWT later in their participation period thus data from these tests were included in analysis. Therefore, 74 participants completed a maximal effort 10m-MSWT and were included in analysis.

The distance achieved during 10m-MSWT ranged from 460m to 1520m (mean \pm SD: 988 \pm 208m) (Figure 37). Only 9 participants (12%) did not manage to complete level 10 (750m), a further 28 (38%) did not reach the end of level 12 (1020m) and 32 (43%) reached maximal effort before completing level 14 (1330m). Of the remaining 5 (7%), 1 participant exceeded the end of level 15 (1500m) before reaching maximal effort (Figure 37).

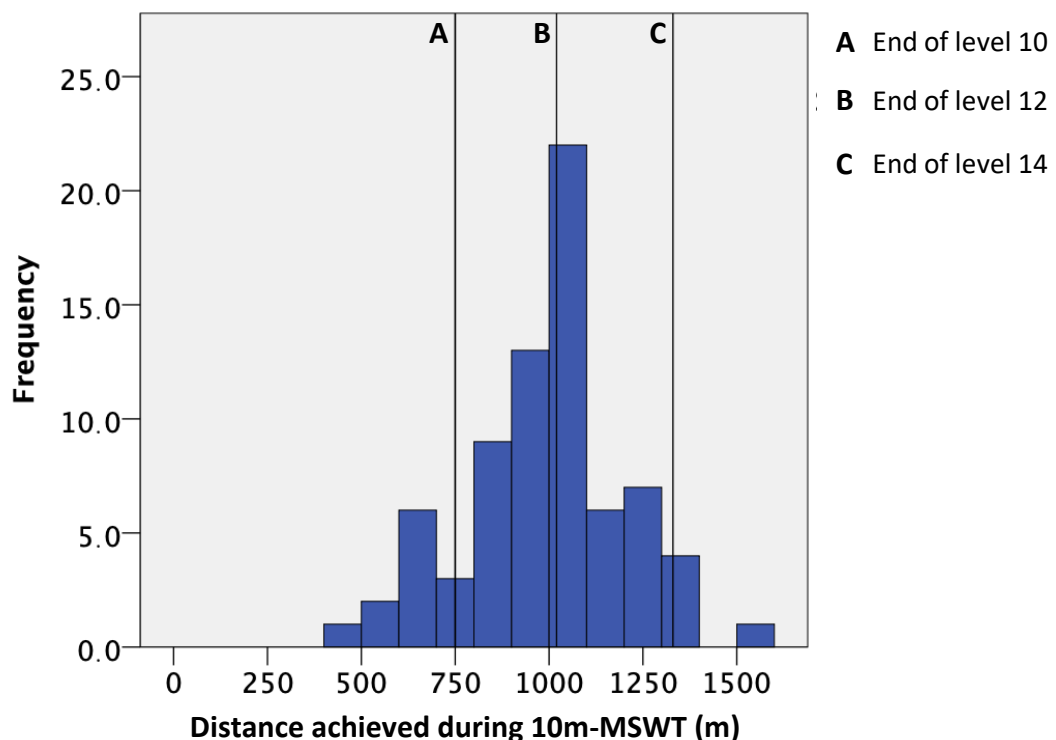


Figure 37: Histogram of distance achieved during 10m modified shuttle walk test for phase 2 participants

There appeared to be a relationship between age and distance achieved during 10m-MSWT, with older participants achieving a greater distance (Figure 38). This was unsurprising considering the increase in height, strength, leg length and

therefore stride length as a child gets older. However, as this outcome was only being considered once for each participant, rather than investigating change over time as in Phase 1, it was important to standardise the distance achieved during 10m-MSWT for age so that a fair comparison could be made.

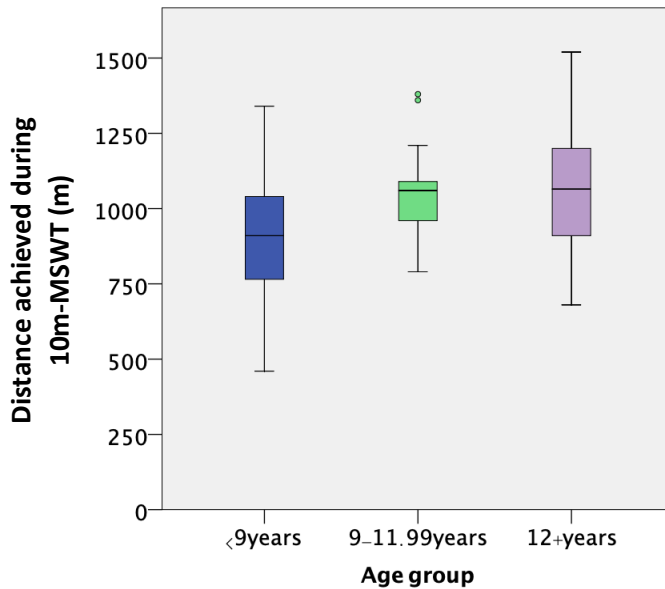


Figure 38: Box plot of distance achieved during 10m-MSWT by age group for phase 2 participants

The standardisation of distance achieved during 10m-MSWT by age was initially conducted by calculating the standardised residuals on a larger dataset of all maximal 10m-MSWT ($HR_{peak} > 180\text{bpm}$) data from Project Fizzyo participants ($n = 134$) to enable a greater number of data points to be included and thus improve the quality of the line of best fit. This involved identifying the line of best fit through distance achieved during 10m-MSWT by age (curvilinear), considering this line as the mean and setting it as 0, and then plotting the measured values by the relationship of their SD from the mean line of 0 (Figure 39) (Field, 2013).

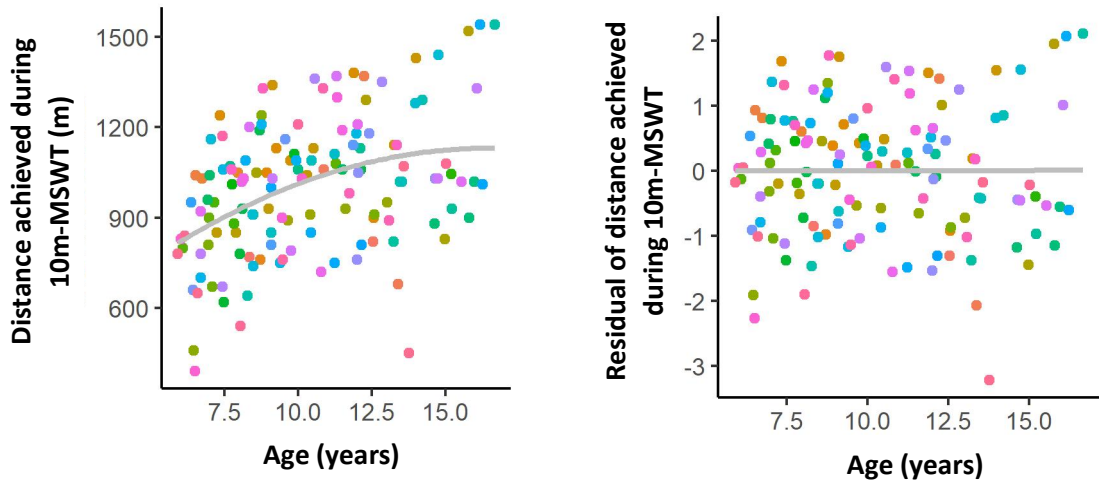


Figure 39: Standardised residuals of distance achieved during 10m-MSWT in Project Fizzyo dataset. Curvilinear line of best fit (indicated in grey) through distance achieved during 10m-MSWT by age (left) and residuals of distance achieved during 10m-MSWT by age with mean line of 0 indicated in grey (right)

The data for distance achieved during 10m-MSWT for participants who took part in this study were then plotted using the model as described above to generate the distance achieved during 10m-MSWT standardised by age (Figure 40).

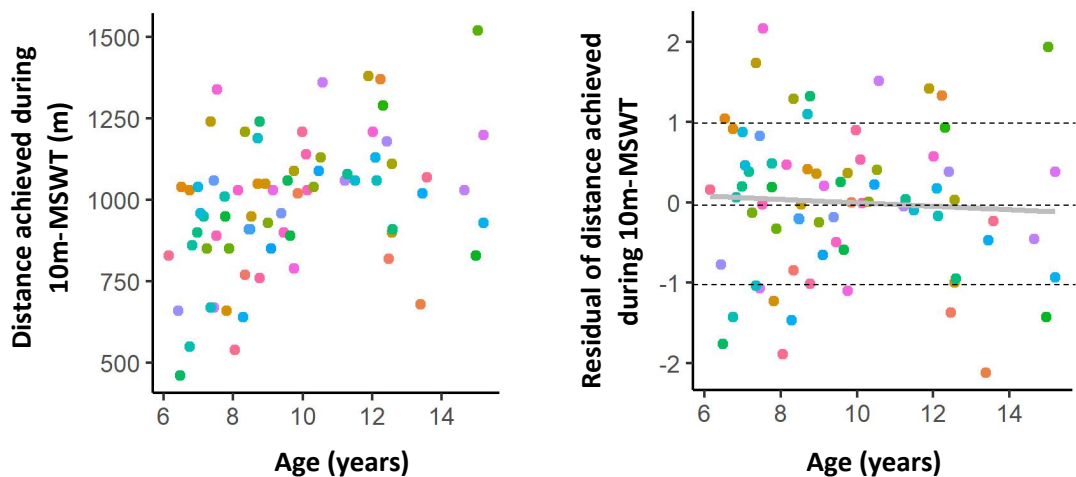


Figure 40: Standardised residuals of distance achieved during 10m-MSWT in the phase 2 dataset. Raw data values of distance achieved during 10m-MSWT by age (left) and residuals of distance achieved during 10m-MSWT by age with line of best fit indicated in grey (right)

A total of 70.2% (n = 52) achieved within 1SD of the mean for distance achieved during 10m-MSWT standardised by age, with 37.8% (n = 28) achieving between 0 and 1SD and 37.8% (n = 28) achieving between -1SD and 0. A further 12.2% (n = 9) achieved between 1 and 2SD above the mean of 0, with 1.4% (n = 1) managing to achieve a distance greater than 2SD above the mean. However, 14.9% (n = 11) achieved between 1-2SD below the mean of 0, and 1.4% (n=1) did not manage to achieve a distance within 2SD of the mean (Figure 41).

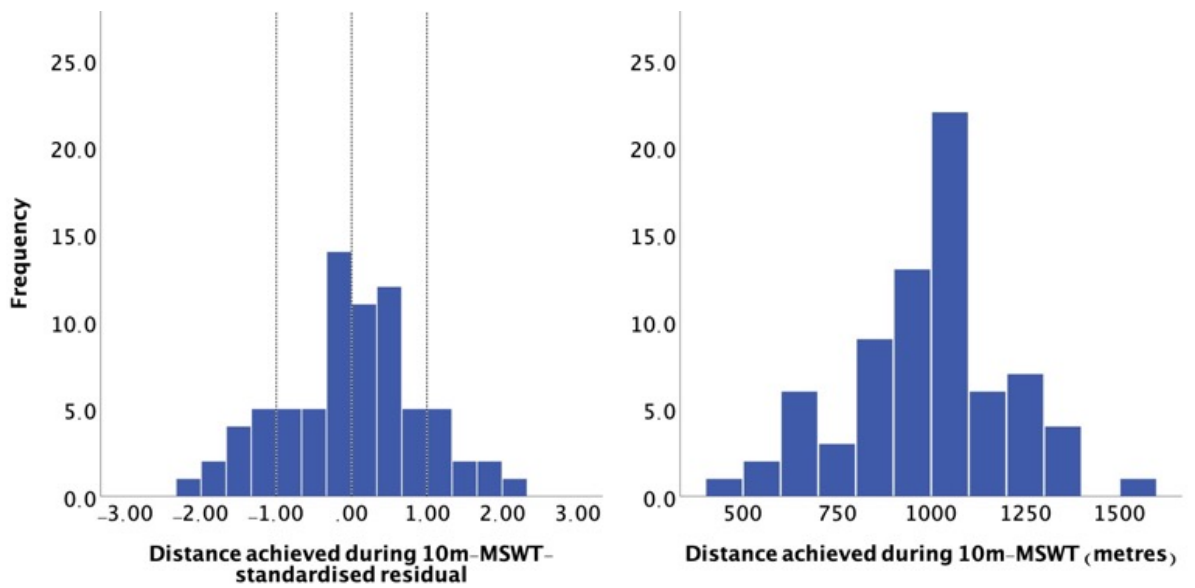


Figure 41: Histograms of distance achieved during 10m-MSWT for phase 2 participants. Left: standardised residual (by age), right: distance in metres

There were no significant differences in the distance achieved during 10m-MSWT standardised by age across the 3 age groups (ANOVA: $F(2, 71) = 0.6, p = 0.572$) (Figure 42) indicating that the participants involved in this phase of work performed similarly to those used to develop the standardised residuals.

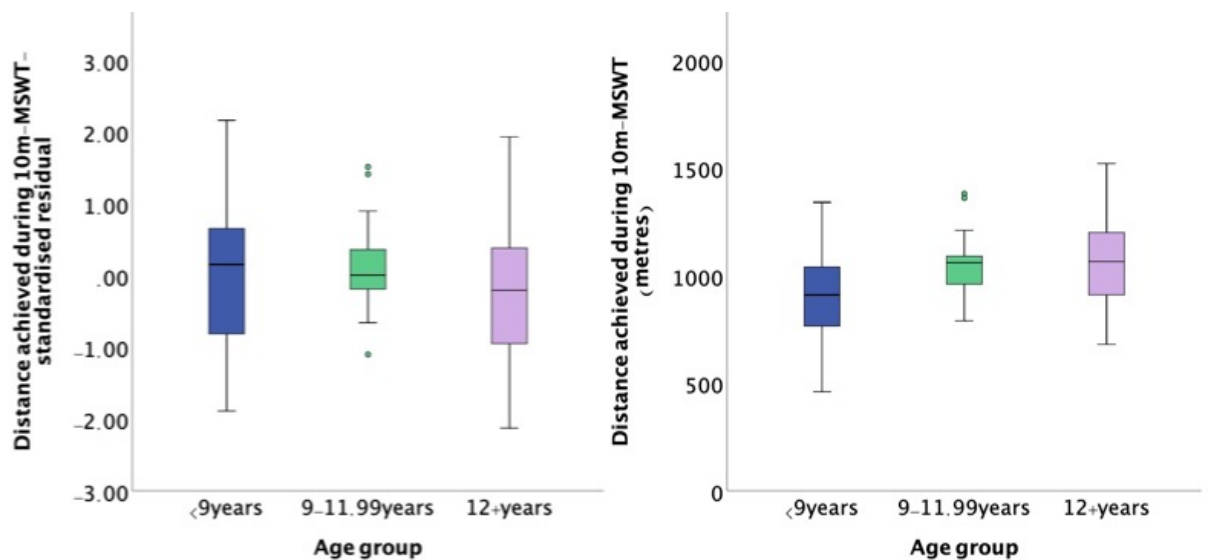


Figure 42: Box plots of age group comparisons of distance achieved during 10m-MSWT for phase 2 participants. Left: standardised residual (by age), right: distance in metres

There was also no significant difference detected when comparing distance achieved during 10m-MSWT standardised by age between males and females (independent samples t-test: $t(72) = 0.17, p = 0.865$) (Figure 43).

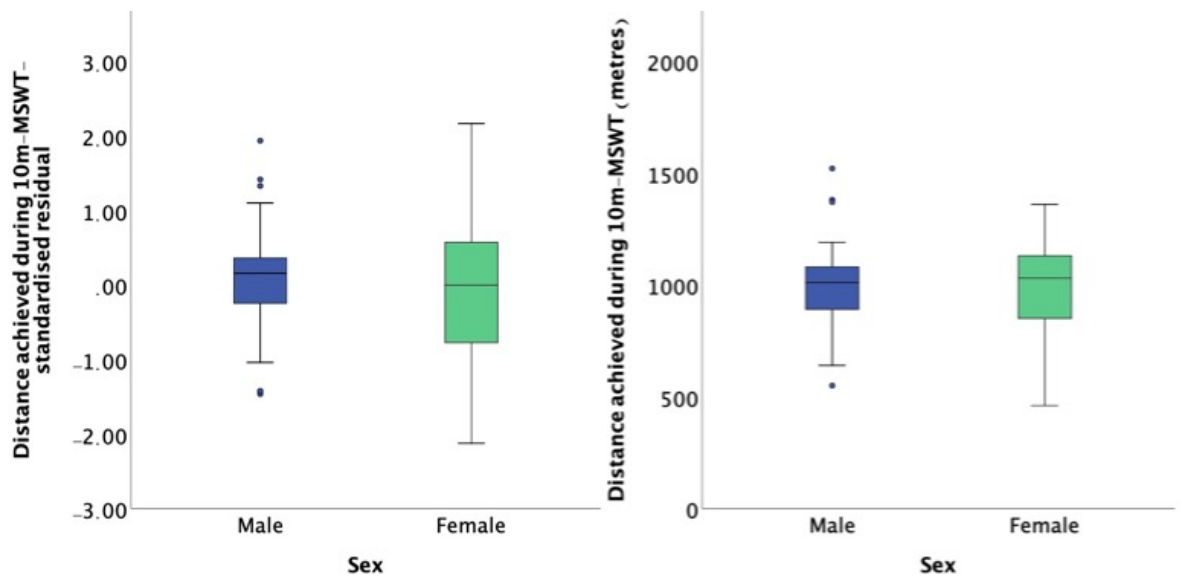


Figure 43: Box plots of male/female group comparison of distance achieved during 10m-MSWT for phase 2 participants. Left: standardised residual (by age), right: distance in metres

8.2 Self-efficacy for physical activity

All 78 participants completed the CSAPPA questionnaire to report their self-efficacy for PA. Total scores ranged from 33 to 76 (minimum possible score is 19, maximum possible score is 76, with higher score indicating greater self-efficacy) (Figure 44).

Participants generally scored highly with the median (IQR): 62.5 (53-68).

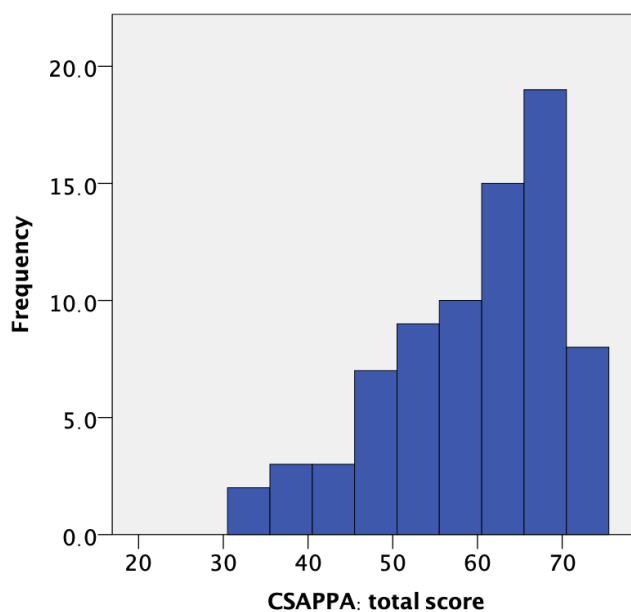


Figure 44: Histogram of CSAPPA total scores for phase 2 participants

A Kruskal-Wallis Test revealed a statistically significant difference in CSAPPA total score across the 3 different age groups (<9years: n = 36, 9-11years: n = 24, 12+years: n = 18), $\chi^2(2, n = 78) = 18.451, p < 0.0001$. The older age group (12+years) recorded a lower median score (50.5) than the 2 younger age groups (<9years: 64, 9-11years: 65) (Figure 45). Mann-Whitney U Tests revealed no statistical difference in CSAPPA total scores between the 2 younger age groups ($U = 358.5, z = -1.111, p = 0.276, r = 0.14$), however the differences between the older age group and both young groups were statistically significant with a Bonferroni adjustment applied resulting in a stricter alpha value of 0.017 (<9years compared to 12+years: $U = 132.0, z = -3.528, p < 0.0001, r = 0.48$; 9-11years compared to 12+years: $U = 57.5, z = -4.032, p < 0.0001, r = 0.62$).

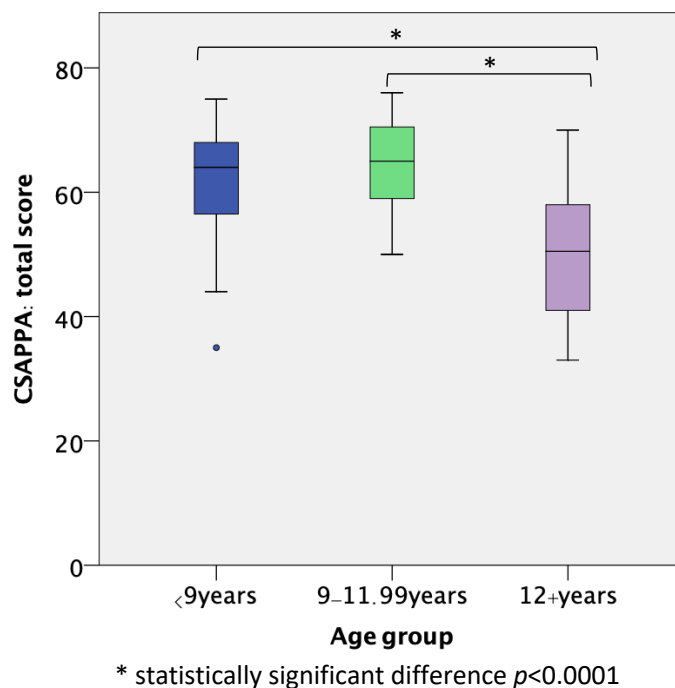


Figure 45: Box plot of CSAPPA total scores for each age group for phase 2 participants

There were no differences in the total CSAPPA scores of males and females (Figure 46). This continued across the age groups with scores for both males and females falling for the older age group (Figure 46), although the group sizes were small by this stage (<9years: 15 males/21 females, 9-11years: 13 males/11 females, 12+years: 7 males/11 females).

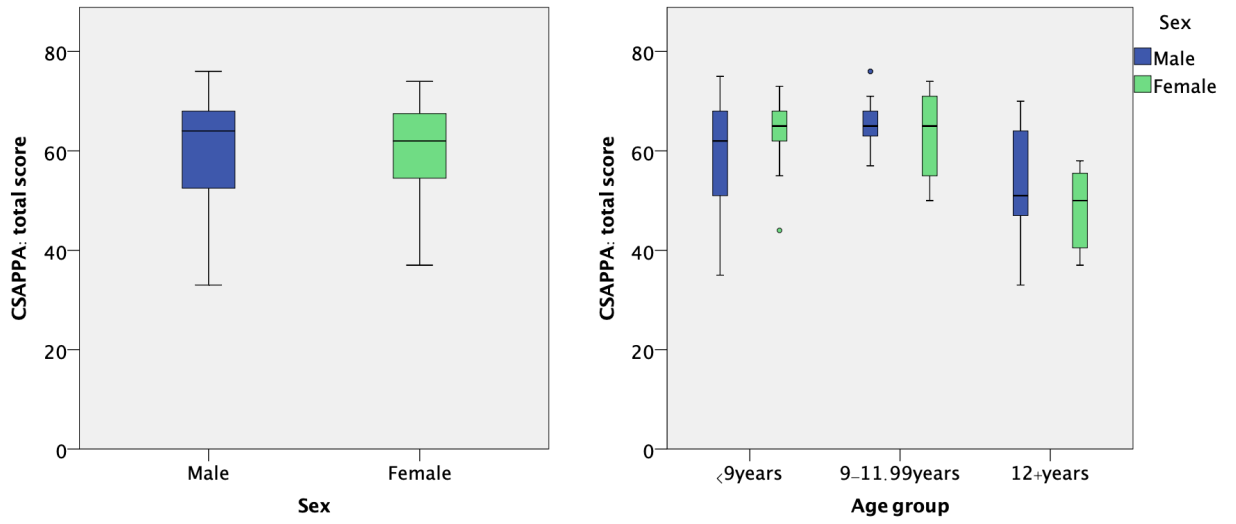
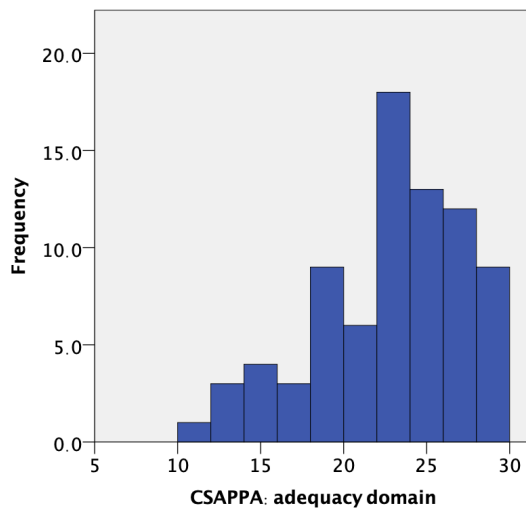


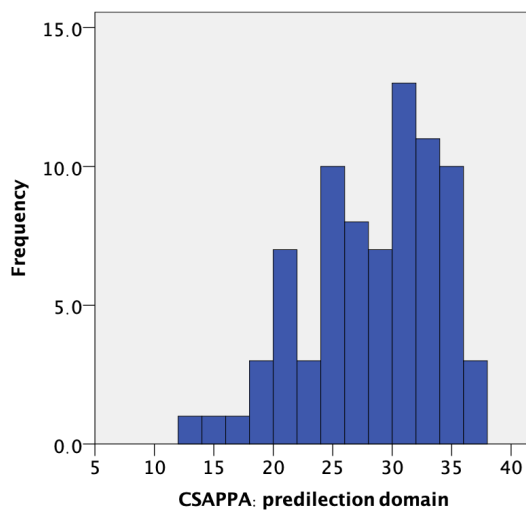
Figure 46: Boxplots of CSAPPA total scores for (L) males and females, and (R) for males and females by age group for phase 2 participants

8.2.1 Self-efficacy for physical activity individual domains

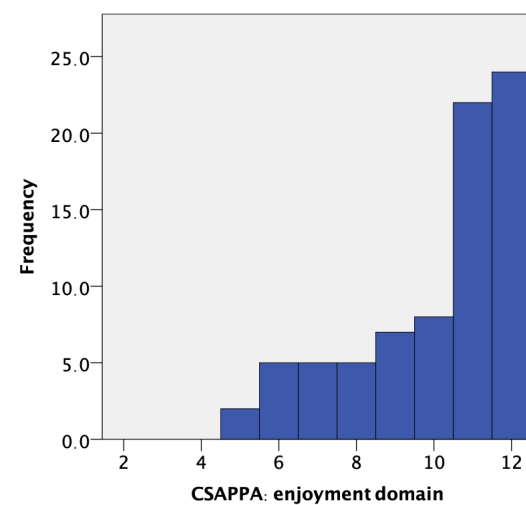
Participants scored highly for each individual CSAPPA component domain (Figure 47).



Possible score range	7-28
Median (IQR)	23 (19-26)
Range of scores	10-28



Possible score range	9-36
Median (IQR)	29 (24-33)
Range of scores	12-36



Possible score range	3-12
Median (IQR)	11 (9-12)
Range of scores	5-12

Figure 47: Histogram and summary information for CSAPPA domain scores (top: adequacy, middle: predilection, bottom: enjoyment) for phase 2 participants

Kruskal-Wallis tests were conducted to examine the impact of age group on the individual CSAPPA domain scores and revealed statistically significant differences (Table 26).

Table 26: Kruskal-Wallis Tests exploring the impact of age group on CSAPPA individual domain scores for phase 2 participants

		Age group			Kruskal-Wallis Test
		<9years n = 36	9-11years n = 24	12+years n = 18	
CSAPPA domain	Adequacy median (IQR)	22.5 (19-26)	25 (23-27)	20 (16-22)	$\chi^2 (2, 78) = 15.00$ $p = 0.001^*$
	Predilection median (IQR)	30 (25-33)	30 (27-33)	21.5 (19-27)	$\chi^2 (2, 78) = 14.22$ $p = 0.001^*$
	Enjoyment median (IQR)	11 (10-12)	11 (10-12)	8 (7-10)	$\chi^2 (2, 78) = 16.75$ $p < 0.0001^*$

Key: IQR interquartile range, n number

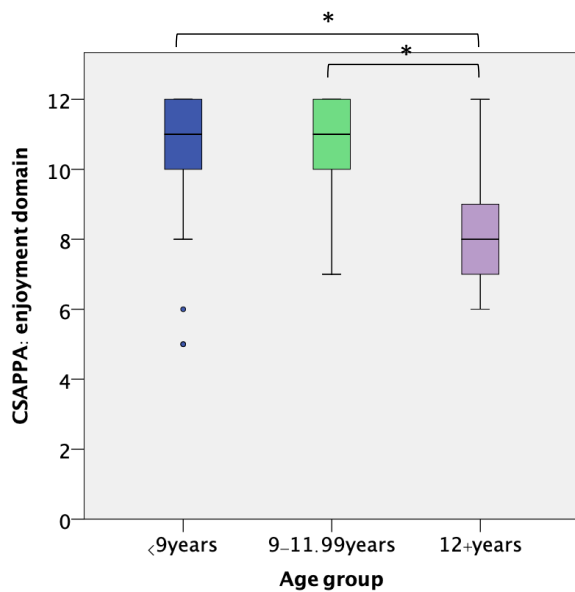
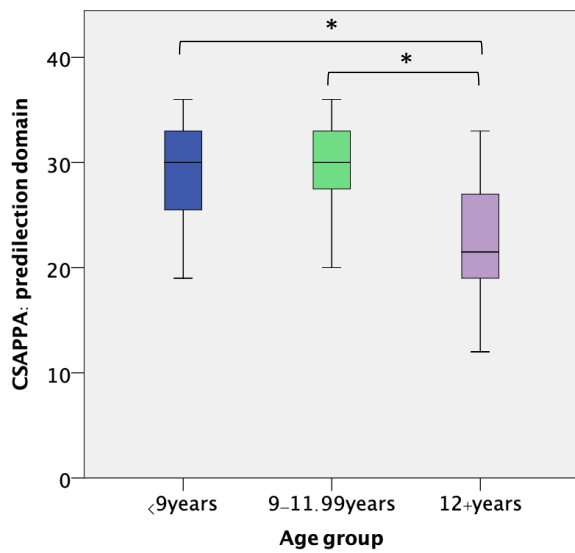
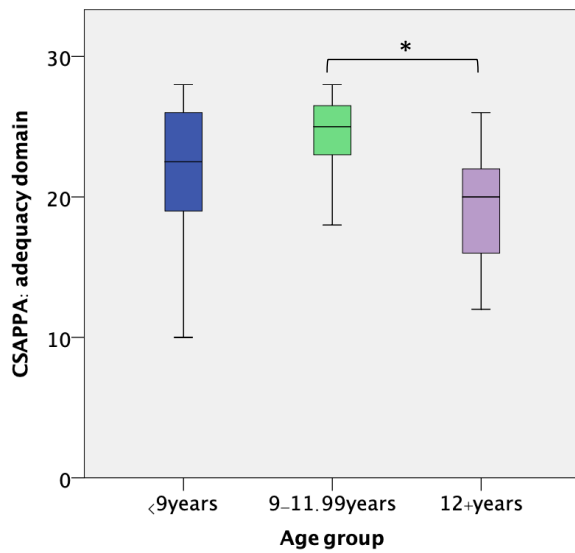
* reached level of significance α 0.05

Mann-Whitney U Tests revealed that, as with the total CSAPPA score, there were no statistically significant differences between domain scores for the 2 younger age groups. However, the older age group scored statistically significantly lower than the 2 younger age groups for all CSAPPA domains, with the exception of the adequacy domain for the youngest age group (Table 27 and Figure 48). These differences all had a medium to high effect size.

Table 27: Mann-Whitney U Tests comparing CSAPPA domain scores by age groups for phase 2 participants

Age group comparison	Domain	U value	Z value	p value	Effect size
<9years	Adequacy	300.5	-2.00	0.046	0.26
vs.	Predilection	425.0	-0.11	0.916	0.01
9-11.99years	Enjoyment	415.5	-0.26	0.794	0.03
<9years	Adequacy	201.0	-2.27	0.023	0.31
vs.	Predilection	141.0	-3.37	0.001*	0.46
12+years	Enjoyment	128.0	-3.68	<0.0001*	0.50
9-11.99years	Adequacy	62.5	-3.92	<0.0001*	0.60
vs.	Predilection	82.0	-3.41	0.001*	0.53
12+years	Enjoyment	77.0	-3.60	<0.0001*	0.56

Key: * reached level of significance Bonferroni adjusted α 0.017



* statistically significant difference $p \leq 0.001$

Figure 48: Box plots of CSAPPA domain scores (top: adequacy, middle: predilection, bottom: enjoyment) for each age group for phase 2 participants

8.3 Self-reported physical activity

All 78 participants completed the HAES questionnaire to report their levels of PA for 2 particular days (1 weekday and 1 weekend day) within the 2 weeks prior to participation. The HAES generated 2 self-reported outcomes: number of minutes of MVPA and overall activity level for the relevant day.

8.3.1 Self-reported minutes of MVPA

Self-reported time spent in MVPA ranged from 0 to 593minutes for reported weekdays (normally distributed, mean±SD: 197±129minutes) and 0 to 680minutes for reported weekend days (right-skewed, median (IQR): 152 (58-232)minutes) (Figure 49). A Wilcoxon Signed Rank Test revealed a trend towards a difference in the self-reported time spent in MVPA on weekdays compared to weekend days with weekdays tending to be more active than weekend days, however this difference did not quite reach the α level of significance, $z = -1.872$, $p = 0.061$. A Bland and Altman plot supported this finding and identified that the greatest differences occurred in pairs with higher means (>200minutes) but these differences were both negative and positive, i.e. for some participants weekdays were more active but others weekend days were more active (Figure 50). There were also some participants who reported similarly active weekdays and weekend days, and these occurred across the range of self-reported time spent in MVPA, therefore there was no clear pattern between self-reported weekday and weekend day activity levels.

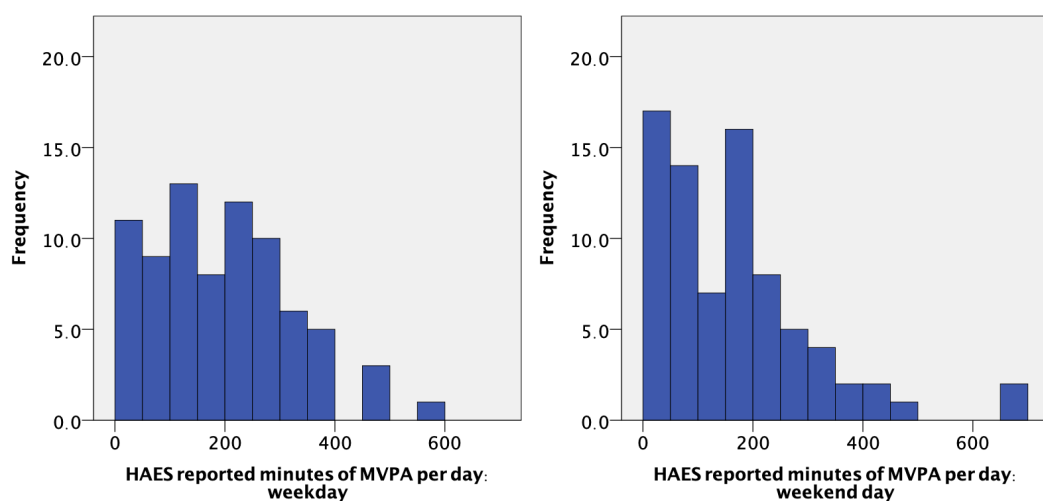


Figure 49: Histograms of HAES reported time spent in MVPA per day for weekdays (L) and weekend days (R) for phase 2 participants

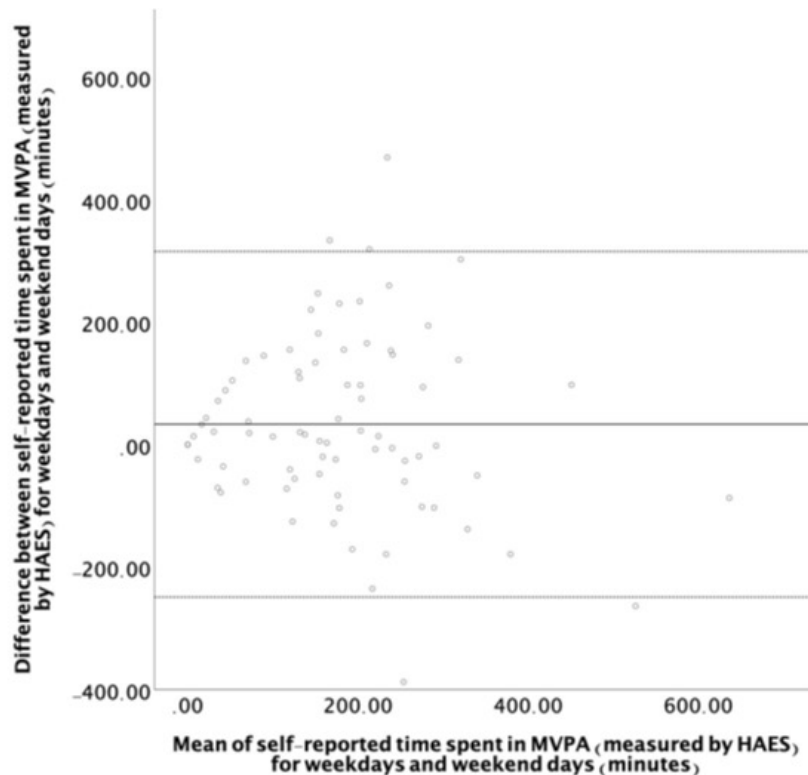


Figure 50: Bland and Altman plot for self-reported time spent in MVPA (measured by HAES) for weekdays and weekend days for phase 2 participants.
 Y axis = weekday - weekend day, therefore values >0 indicate more self-reported MVPA on weekday than weekend day, values <0 indicate more self-reported MVPA on weekend day than weekday.
 Solid line indicates mean difference of 33minutes, with limits of agreement from -1.96SD to +1.96SD represented by dotted lines

A Welch's one-way between groups ANOVA (conducted in view of violation of homogeneity of variances) revealed a statistically significant difference in self-reported minutes of MVPA for weekdays between the 3 different age groups: $p = 0.001$ (Figure 51). Post-hoc comparisons using the Tukey test indicated that the mean (\pm SD) score for 12+years (99 ± 111 minutes) was significantly lower than the mean (\pm SD) score for <9years (228 ± 121 minutes, $p = 0.001$) and 9-11years (223 ± 122 minutes, $p = 0.004$). The 2 younger age groups were not significantly different to each other.

A Kruskal-Wallis Test revealed a statistically significant difference in self-reported minutes of MVPA for weekend days across the 3 different age groups (<9years: $n = 36$, 9-11years: $n = 24$, 12+years: $n = 18$), $X^2(2, n = 78) = 13.07$, $p = 0.001$. The older age group (12+years) reported fewer minutes in MVPA (median 61minutes) than the 2 younger age groups (<9years: 182minutes, 9-11years: 135minutes) (Figure 51). Mann-Whitney U Tests revealed no statistical difference in self-reported

minutes in MVPA for weekend days between the 2 younger age groups ($U = 324.5$, $z = -1.623$, $p = 0.105$, $r = 0.21$), however the differences between the older age group and both young groups were statistically significant with a Bonferroni adjustment applied resulting in a stricter alpha value of 0.017 (<9years compared to 12+years: $U = 140.0$, $z = -3.384$, $p = 0.001$, $r = 0.46$; 9-11years compared to 12+years: $U = 121.0$, $z = -2.423$, $p = 0.015$, $r = 0.37$).

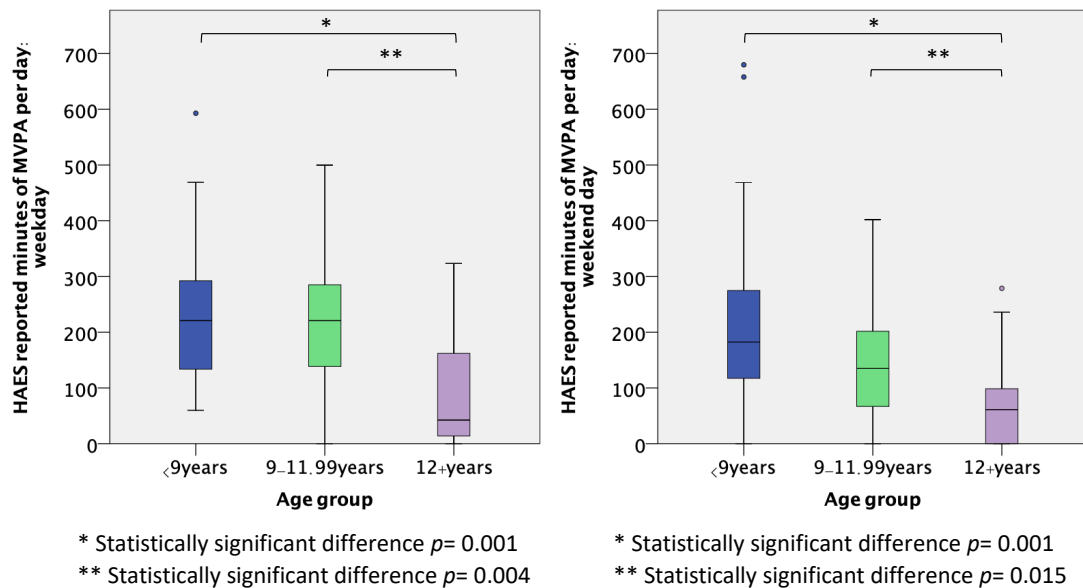


Figure 51: Box plots of self-reported minutes of MVPA by age group for phase 2 participants, left: weekdays, right: weekend days

There were no differences in the self-reported minutes in MVPA of males and females for either weekdays or weekend days (Figure 52). This continued across the age groups with little difference between male and female self-reported minutes in MVPA (Figure 53). There was perhaps a more noticeable reduction amongst the older group of females, however the group sizes were small by this stage (<9years: 15males/21females, 9-11years: 13males/11females, 12+years: 7males/11females).

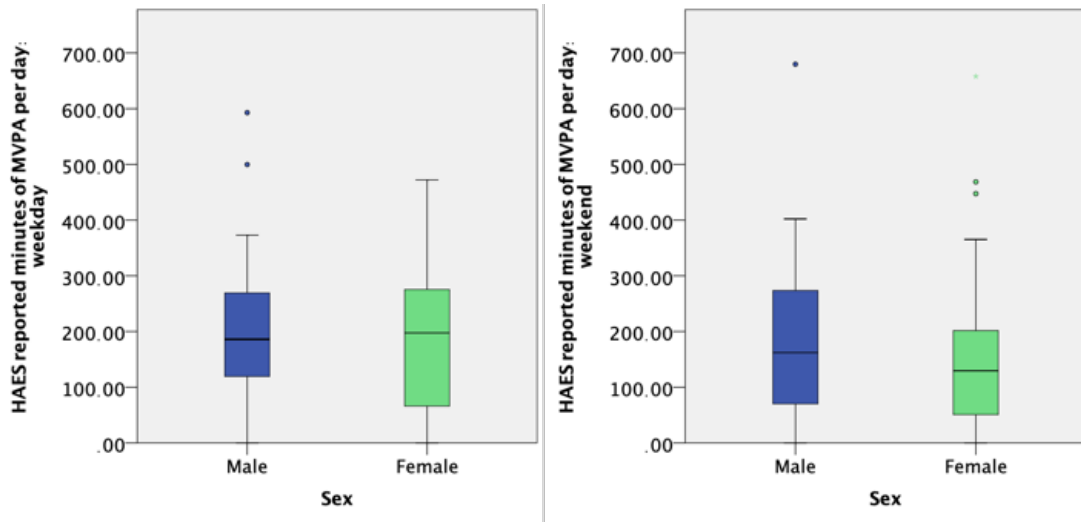


Figure 52: Box plots of self-reported minutes of MVPA for males and females for phase 2 participants, left: weekdays, right: weekend days

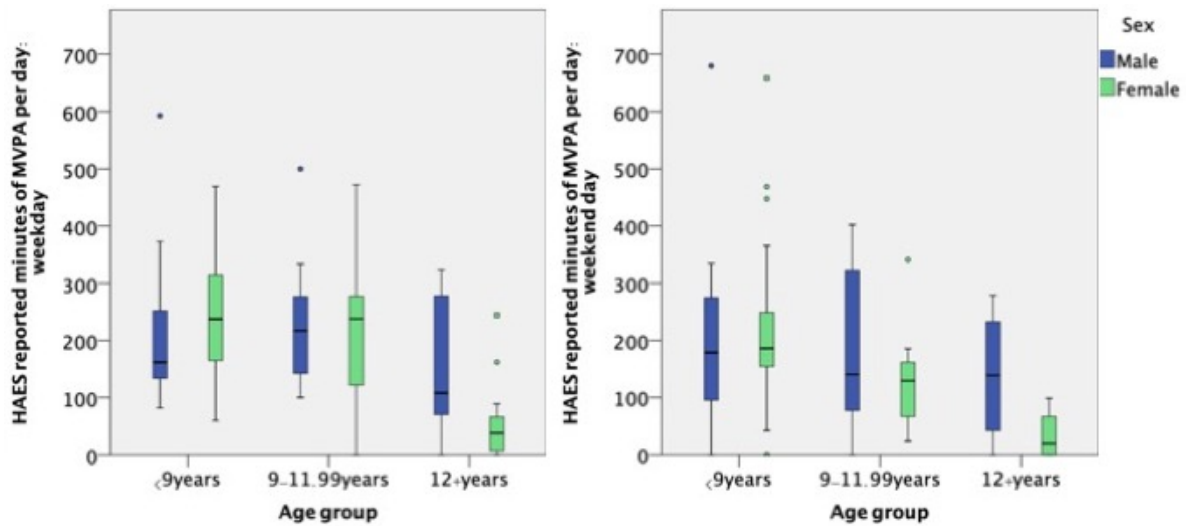


Figure 53: Box plots of self-reported minutes of MVPA for males and females by age group for phase 2 participants, left: weekdays, right: weekend days

8.3.2 Self-reported level of physical activity

As well as self-reported minutes in MVPA, the HAES also recorded self-reported level of activity for a weekday and weekend day. Each participant identified whether they perceived that they had been very inactive, inactive, somewhat inactive, somewhat active, active or very active for each of the 2 days that they described when completing the questionnaire. The majority of participants identified that they were somewhat active, active or very active on their reported weekday (n = 69, 88%) and weekend day (n = 66, 85%) (Figure 54).

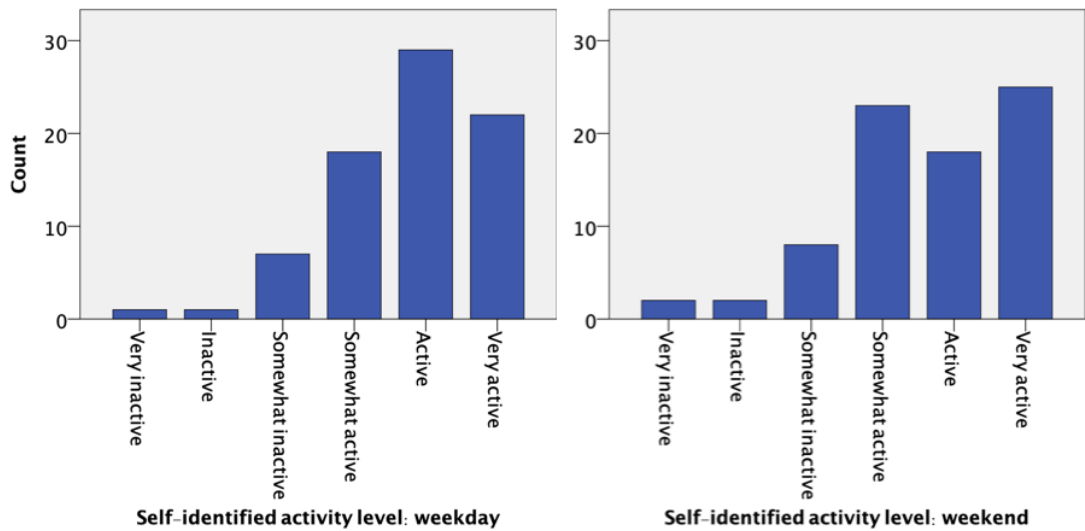


Figure 54: Frequency of self-reported activity level for phase 2 participants for weekdays (left) and weekend days (right)

The participants in the youngest age group tended to categorise themselves as more active than those in the older age groups for both weekdays and weekend days (Figure 55). Similarly, a greater proportion of participants aged 9-11 years reported that they were either active or very active for both weekdays and weekend days than those aged 12 years and older.

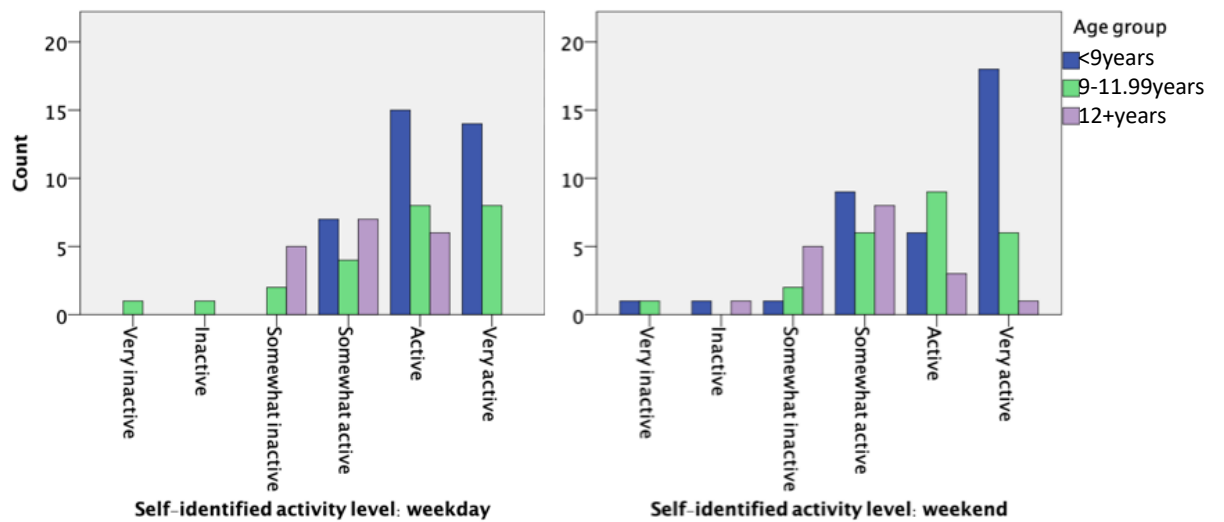


Figure 55: Frequency of self-reported activity level by age group for phase 2 participants for weekdays (left) and weekend days (right)

There was little difference in self-reported activity levels between male and female participants for weekdays or weekend days (Figure 56).

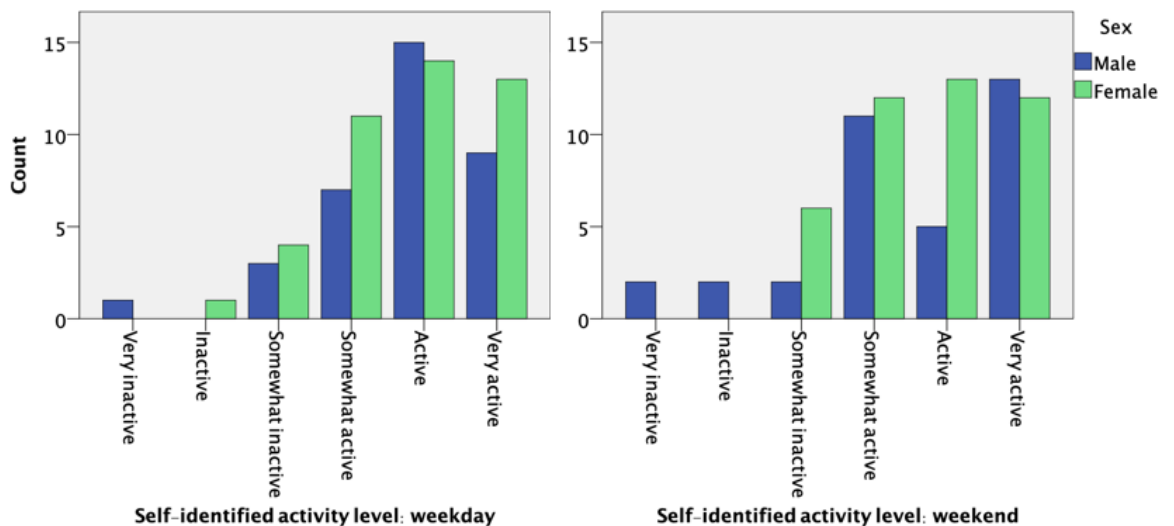


Figure 56: Frequency of self-reported activity level by males and females for phase 2 participants for weekdays (left) and weekend days (right)

8.3.3 Comparing self-reported minutes of MVPA and self-identified levels of physical activity

The relationship between self-reported minutes of MVPA and self-identified level of PA (measured by HAES) was investigated using Spearman’s rho. There was a medium correlation between the 2 variables for weekdays ($r = 0.339$, $n = 78$, $p = 0.002$) and large for weekend days ($r = 0.662$, $n = 78$, $p < 0.0001$). However, when this was explored further by age group the relationship was less consistent (Figure 57 and Table 28). Only the older age group demonstrated a statistically significant large correlation for reporting of weekdays but did not for the weekend days, whereas the 2 younger age groups did not demonstrate a statistically significant correlation for reporting of weekdays but did for weekend days.

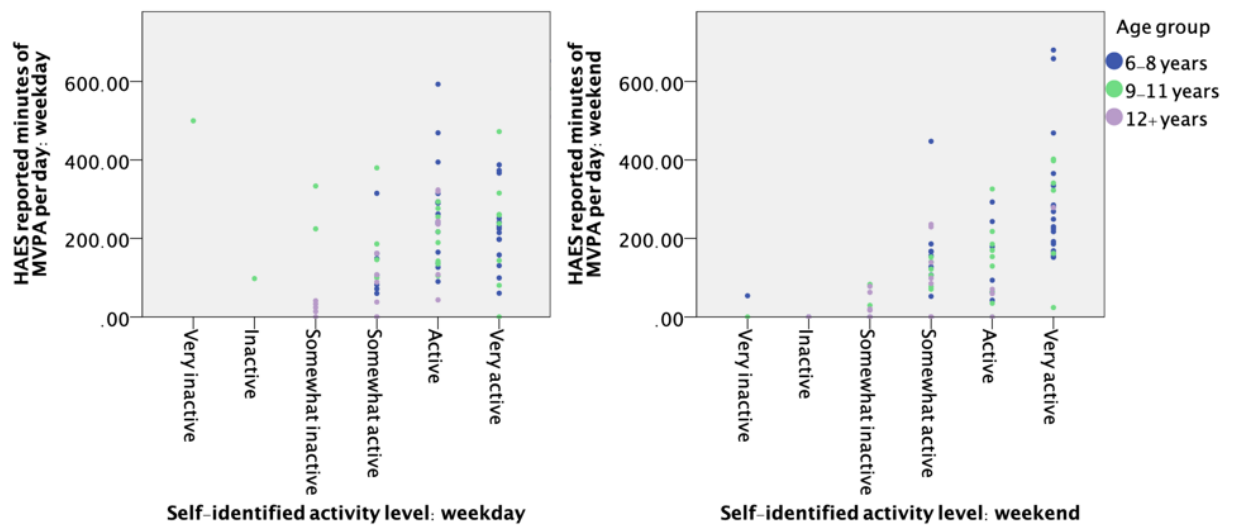


Figure 57: Scatterplots of self-reported minutes of MVPA and self-identified physical activity levels by age group for phase 2 participants for weekdays (left) and weekend days (right)

Table 28: Spearman's Rho correlations between self-reported minutes of MVPA and self-identified physical activity level by age group for phase 2 participants

		Spearman's Rho correlation	
		Weekdays	Weekend days
Age group	<9 years	$r = 0.180$ $n = 36$ $p = 0.292$	$r = 0.624^*$ $n = 36$ $p < 0.0001$
	9-11 years	$r = -0.068$ $n = 24$ $p = 0.751$	$r = 0.562^*$ $n = 24$ $p = 0.004$
	12+ years	$r = 0.697^*$ $n = 18$ $p = 0.001$	$r = 0.309$ $n = 18$ $p = 0.211$

Key: * Statistically significant large correlation at $\alpha 0.01$

8.4 Physical activity levels measured by activity tracking

Longitudinal PA data, captured by Fitbit, were collected from all 78 participants. Given the nature and duration of activity tracking, a number of data errors were identified which required resolving before the data were processed to generate the time spent in MVPA each day for each participant.

8.4.1 Activity tracking data processing

The research team (EM, ER, NF, KK, GT and HD), including trained data scientists (KK, NF and GT), developed a number of steps to clean and process the PA tracker data:

1. Step count per minute and continuous HR data entered the DRE database. A total of 57,565,677 data points were collected.
2. HR value errors were identified and removed. These errors included:
 - a. Default 70bpm value- an abnormally large number of HR values of 70bpm were identified in the dataset. It became apparent that the Fitbit defaulted to HR value of 70bpm on some occasions when it could not detect a true HR value. The first and last sequence of HR values of the day were removed if the value was 70. A total of 43,896 (<0.1%) data points were removed as a result of this process. Any other continuous sequences of default 70bpm values that occurred throughout the day were removed by the repetitions filter (b).
 - b. Repetitions- the number of consecutive value repetitions were counted in the raw HR data. The majority of repeated sequences were 2-10 values in length. Any sequence with ≥ 10 consecutive repeated HR values was considered to be physiologically unlikely and caused by a device error. Therefore, the threshold for repeating values was set and any sequence ≥ 10 consecutive repeated HR values were removed. A total of 1,865,801 (3.2%) data points were removed prior to analysis as a result of this cleaning process.
 - c. Value outlier- The percentage differences between consecutive raw HR values which occurred within 30seconds of the previous and subsequent HR values were counted. The majority of differences were between $\pm 15\%$, therefore this was selected as the threshold for detecting value outliers. Any sequence of ≤ 5 HR values that were <100bpm where there was a >15% difference between the sequence of HR values and the previous and subsequent HR values were removed if they occurred within 30seconds of the previous and subsequent HR values. A small but notable jump in HR value (≤ 5 HR values and >15% difference) during a time of relative low activity (<100bpm) was physiologically unlikely and was therefore caused by device error and required removing prior to analysis. A total of

97,980 (0.2%) data points were removed as a result of this step in the data cleaning process.

- d. Time outlier- any sequence of ≤ 20 HR values that occurred ≥ 2 minutes after the previous HR value and ≥ 2 minutes before the next HR value. These data were likely to have been caused by movement of the tracker when it was not being worn and therefore not a true HR value to be included in analysis. A total of 224,718 (0.4%) data points were removed as a result of this cleaning process.
3. The personalised MVPA threshold was then calculated for each participant for each day in the study:
 - a. The MVPA threshold (American College of Sports Medicine, 2014) was calculated as:

$$MVPA\ threshold = (0.4 * (HR_{peak} - RHR)) + RHR$$

- i. The maximal HR values (recorded from the single-lead ECG (Polar chest strap)) achieved by all participants during each 10m-MSWT that participants completed throughout the study were used to develop the age-related HR_{peak} regression line. Maximal HR values < 180 bpm were excluded to ensure that submaximal effort tests, and therefore submaximal HR values, were not included. A linear mixed effect model was then used to obtain an age-related HR_{peak} for each participant for each day of the study. As the number of 10m-MSWT performed varied between participants, the linear mixed effect model accounted for repeated measures of maximal HR. The mean intercept value was then used to create a single mean regression line for all study participants with the fixed slope obtained from the model. This ensured a unified measure for all participants and enabled HR_{peak} values to be estimated even for participants who had not achieved a maximal effort 10m-MSWT. HR_{peak} was then imputed for each participant for each day of the study using the mean

regression line and participant decimal age (participants were one day older for each day of the study, so HR_{peak} was adjusted accordingly, albeit almost imperceptibly).

- ii. A proxy resting HR (RHR) was calculated per day per participant by taking the mean HR value of the 5 lowest discrete HR minutes of HR data between 11:00-21:00. This time window was used to capture RHR during awake hours only because HR during sleep can be lower than RHR and result in a false underestimation of MVPA threshold. A linear mixed effect model was then fitted to these data to create a personalised RHR regression line for each participant based on age (decimal age for each day) and RHR measures of that participant throughout the study. This reduced the within-subject variation observed for the raw daily RHR values, whilst accounting for between-subject variation.
- b. The calculated MVPA threshold values were then rounded to the nearest integer.
- c. Occasional low MVPA threshold values were identified in the dataset therefore a lower cut-point to MVPA threshold was applied. Evidence has suggested that an HR of ≥ 120 bpm is unlikely to have been caused by anything other than activity (Rowlands and Eston, 2007). It is also recognised that the Fitbit can underestimate HR (Ismail, 2019), therefore a lower cut-point of 110bpm was applied. This resulted in any MVPA threshold calculated as < 110 bpm being capped at 110bpm.
- d. An upper cut-point was also considered necessary. A small number of daily MVPA threshold values were calculated as > 130 bpm. Whilst 120bpm may be a low MVPA threshold for CYPwCF with a higher than average RHR, an HR value of > 130 bpm was highly likely to be caused by activity physiologically (Rowlands and Eston, 2007). This was supported by examination of HR data recorded during 10m-MSWT. Fitbit HR was consistently measured at ≥ 130 bpm at level 9 of

the 10m-MSWT (speed 1.86m/s) by which all participants were running (Ismail, 2019). Therefore, any MVPA threshold HR value >130bpm was capped at that limit.

4. The time when HR was above the personalised daily MVPA threshold for each day of participation for each participant was then identified. The time that was labelled as MVPA was then validated and errors removed by the following processes:
 - a. False high HR values- any sequence of HR values above the MVPA threshold where no steps occurred for the preceding 15 minutes. Fitbit records steps even during non-stepping activities, such as cycling, therefore it was considered to be unlikely that any MVPA would occur for more than 15minutes without any step count detected. Any high HR values recorded without a step count value in the preceding 15minutes were considered to be device error and were therefore removed before analysis.
 - b. High MVPA days- the range of MVPA per day for each participant was examined and it became apparent that there were a small number of days with a large amount of MVPA (Figure 58).

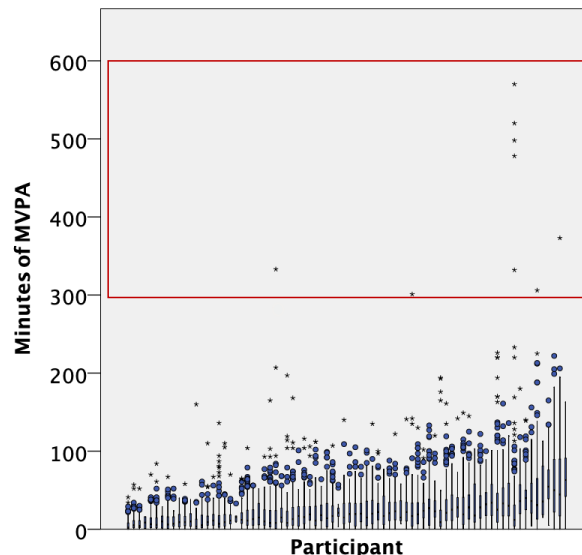


Figure 58: Boxplot of time spent in MVPA (minutes) for each participant of phase 2. Outlier days caused by device error indicated within red box

The intra-day HR and step count traces were visually inspected for a selection of these days and compared to a day with a lower amount of

MVPA. The days with ≥ 300 minutes of MVPA did not follow a physiologically feasible pattern for all activity as peaks in step count did not always tally with increased density of step count (Figure 59). However, it was clear that activity had occurred on these days indicated by density of step count and fluctuations in HR, therefore MVPA was capped at 300 minutes per day (Figure 59). A total of 9 days from 5 participants were capped at 300 minutes of MVPA.

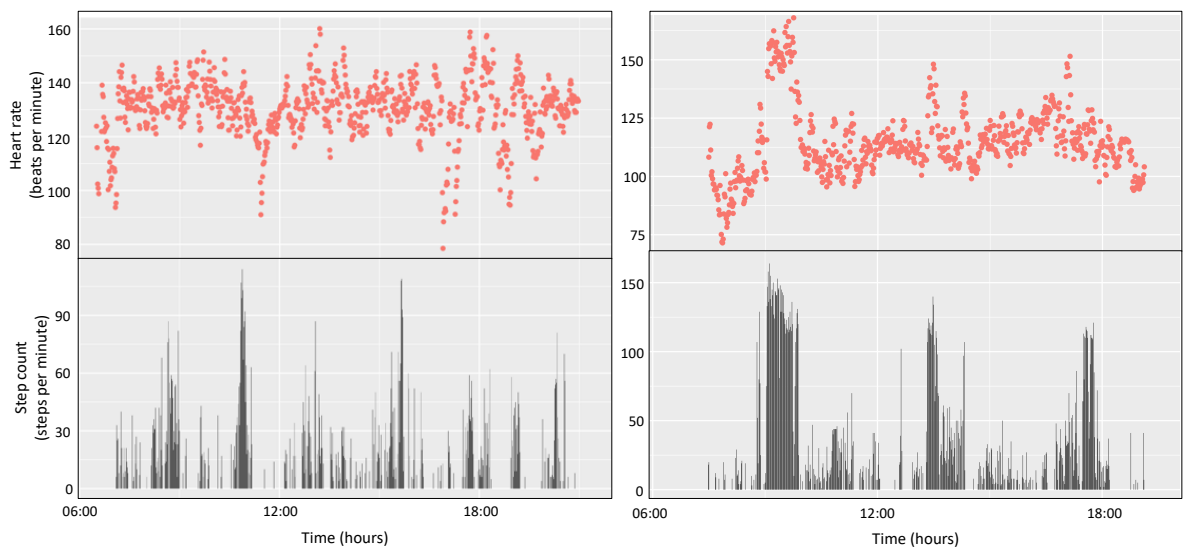


Figure 59: Left- example HR and step count trace for a day with ≥ 300 minutes of MVPA. This day was then capped at 300 minutes of MVPA because the poor correlation between HR and step count indicated device error causing a higher amount of MVPA to be identified than occurred. Right- example HR and step count trace for a day with < 300 minutes of MVPA where peaks in HR correspond to peaks in step count and therefore indicate true physical activity

8.4.2 Activity tracking data analysis

Appointments for participating in this study were timed with attendance at routine CF clinic appointments or at another time that was more convenient for individual participants. As a result, duration of participation per participant varied from 85 days to 327 days (mean 154 days). This resulted in 12,026 potential days of PA tracking data from all 78 participants. A total of 8546 days with any PA tracking data were synced with the app, processed using the cleaning and filtering pipeline described above, and retrieved from the database (minimum: 8, maximum: 223 number of days, range: 7.48-100% of days for individual participants, mean 71.27% of days).

8.4.2.1 Minimum daily wear-time considered as a valid day of physical activity data

Of the 8546 days of PA tracker data, device wear-time (i.e. the amount of time during each day when PA data were captured) varied from as low as 1 minute up to 1440 minutes (24 hours). It was important to set a threshold for minimum daily wear-time which balanced being able to include all useful data days in analysis but exclude days that did not capture sufficient data to offer confidence in the amount of MVPA that occurred during that day. This threshold was calculated by first exploring the typical wear-time patterns. Participants were asked to wear the PA tracker as much as possible during waking hours. Some participants chose to wear the PA tracker whilst sleeping but this was not stipulated in the participant information therefore there were two distinct groups of more typical daily wear-time: waking hours only and most of the day and night (Figure 60).

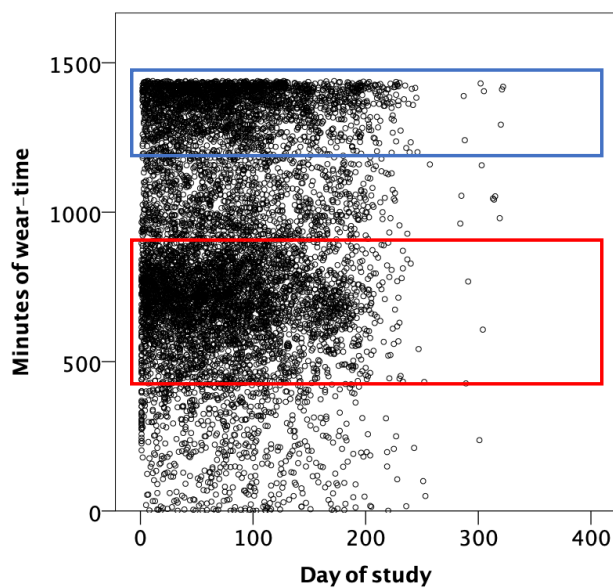


Figure 60: Scatterplot of minutes of wear-time by each day in the study for all participants in phase 2 (individual study participation varied from 85 to 327 days). The blue box (top) indicates the more densely occurring wear-time close to 24 hours. The red box (bottom) indicates the more densely occurring wear-time of waking hours only. There are fewer days that captured data for fewer than 500 minutes.

It was then important to understand the impact that wear-time had on amount of MVPA that was captured in order to be confident that daily time spent in MVPA was not being under-estimated as a result of low wear-time. This was explored by examining the relationship between time in MVPA and wear-time for each day for each participant (Figure 61). There was no clear linear relationship, however there

did appear to be a positive correlation between time in MVPA and wear-time of a low value, below 500minutes.

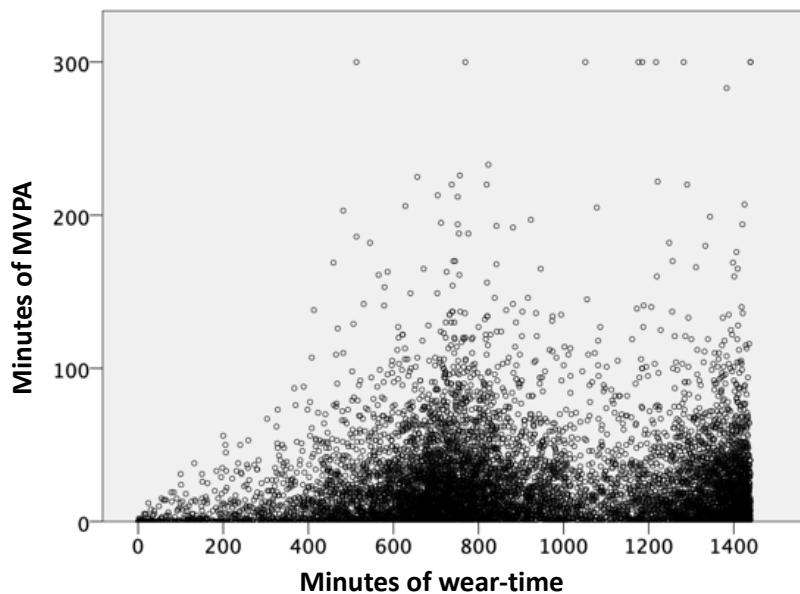


Figure 61: Scatterplot of time spent in MVPA by activity tracker wear-time for each day for each participant of phase 2

A statistically significant medium positive correlation existed between time in MVPA and minutes of wear-time for values of <500minutes of wear-time (Figure 62- left). This was true even with a more stringent α value of < 0.01 in view of the violation of assumption of independence (repeated measures in the same participants). However, there was no evidence of a correlation between time in MVPA and minutes of wear-time for values of >500minutes of wear-time (Figure 62- right). Therefore, 500minutes of activity tracker wear-time (~8 hours, 20 minutes) per day was the minimum amount of wear-time required for data to be included in analysis. This was in line with a study reported by Cooper et al. (2015) who conducted research on data from the ICAD. Cooper et al. (2015) excluded 19% of days as a result of this restriction, whereas 12.6% of days with less than 500minutes of wear-time were excluded in the current study.

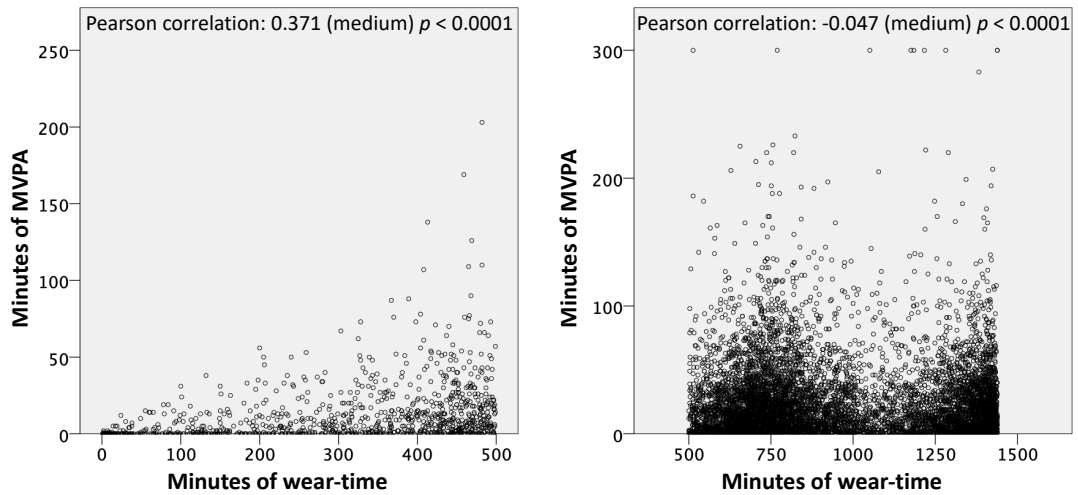


Figure 62: Scatterplots of time spent in MVPA by activity tracker wear-time for each day for each participant in phase 2 with Pearson correlations for wear-time values <500minutes (left) and wear-time values >500minutes (right)

8.4.2.2 Time spent in MVPA

A total of 7473 days had more than 500minutes of wear-time and were therefore included in analysis. Time spent in MVPA ranged from 0minutes to 300minutes (median: 17minutes, IQR: 6-35minutes) (Figure 63). Less than 20minutes of MVPA accounted for approximately half of all valid data days, with progressively smaller proportions of days as time spent in MVPA increased up to 40minutes (Table 29).

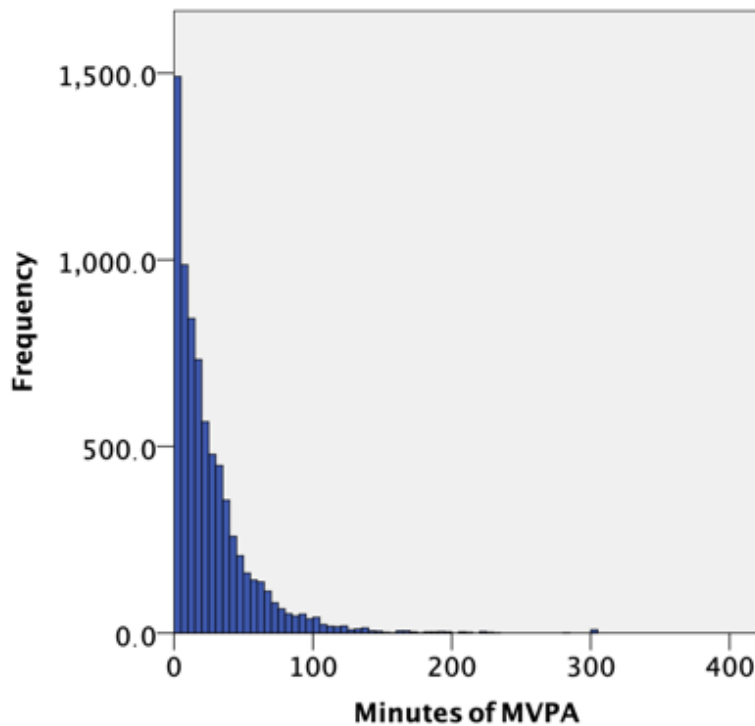


Figure 63: Histogram of time spent in MVPA for phase 2 participants

Table 29: Table of amount of days by time spent in MVPA for phase 2 participants

Time spent in MVPA per day category	Upper and lower extremes	All days % (n = 7473 days)	Weekdays % (n = 5293 days)	Weekend days % (n = 2180 days)
Low activity: <20minutes		54.2 (4054)	54.9 (2908)	52.6 (1146)
	0minutes	6.1 (455)	6.4 (341)	5.2 (114)
Moderately low activity: 20-39minutes		24.8 (1850)	24.1 (1273)	26.5 (577)
Moderately high activity: 40-59minutes		10.3 (769)	10.4 (549)	10.1 (220)
High activity: ≥60minutes		10.7 (800)	10.6 (563)	10.9 (237)
	≥120minutes	1.6 (118)	1.5 (78)	1.8 (40)

Key: MVPA moderate to vigorous physical activity

N.B. The activity categories were created based on the PA recommendations that CYPwCF should be aiming to achieve 60minutes of MVPA each day (Department of Health and Social Care, 2019). Highly active meant achieving or exceeding the recommendations.

On average, participants were active at a similar level on weekdays and weekend days: median (IQR) 17 (6-35) minutes for weekdays and 18 (7-36) minutes for weekend days. There were no clear differences in the proportion of days spent in each activity level category comparing weekdays to weekend days (Table 29). This was supported by a Chi-squared test for independence which indicated no significant association between weekday/weekend day and time spent in MVPA: $\chi^2(3, n = 7473) = 5.443, p 0.142$.

The median time spent in MVPA per day for individual participants for their own duration in the study ranged from 2minutes (IQR: 0-8minutes) to 63minutes (IQR: 43-91minutes), mean±SD 18.8±12.0minutes (Figure 64). Only 1 participant achieved median time spent in MVPA per day of ≥60minutes. A total of 49 participants (63%) achieved median time spent in MVPA per day of <20minutes, however the majority of these low active participants had recorded at least some extremely active days (marked as outliers in Figure 64) with time spent in MVPA per day ≥60minutes. Only 14 participants (18%) did not achieve 60minutes of MVPA on a single day of their participation.

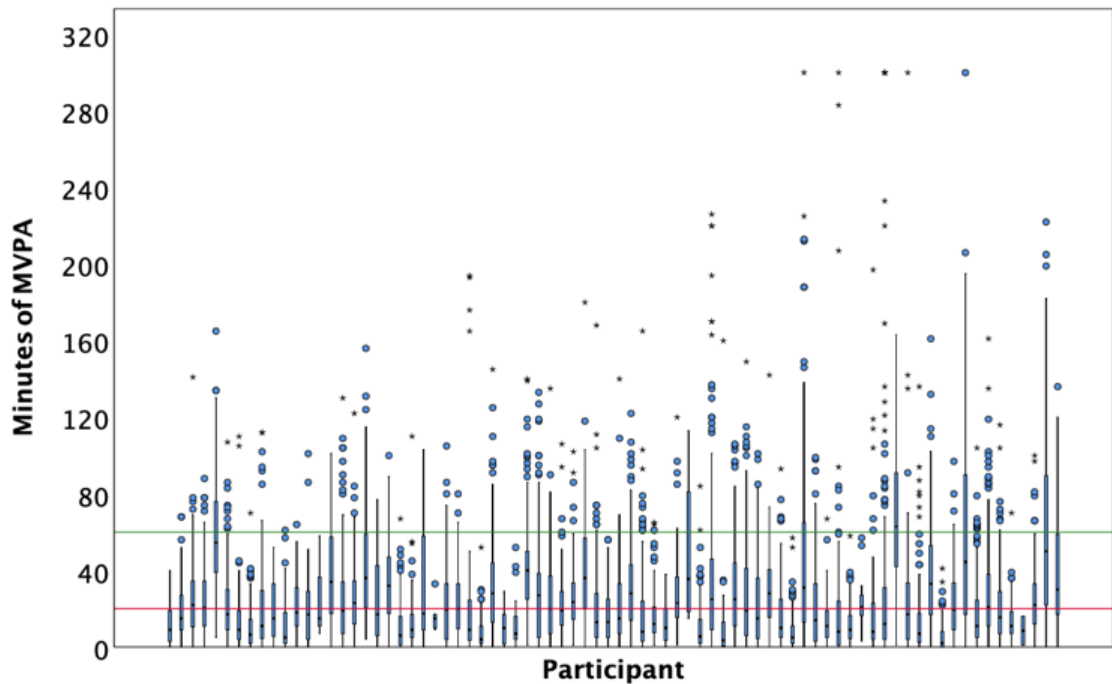


Figure 64: Boxplot of time spent in MVPA (minutes) for each participant of phase 2 for their own study duration. Green line indicates 60minutes of MVPA, red line indicates 20minutes of MVPA

Half of all participants ($n = 39$) spent, on average, more time in MVPA on weekend days than weekdays, with the difference between time in MVPA on weekend days and weekdays ranging from 1-34minutes. A total of 30 participants (38%) spent, on average, more time in MVPA on weekdays than weekend days, with the difference ranging from 1-28minutes. The remaining 9 participants (12%) spent, on average, the same amount of time in MVPA on weekdays and weekend days, although PA levels varied for these participants with the median time spent in MVPA ranging from 2 to 31minutes.

8.4.2.2.1 Time spent in MVPA: comparing males and females

The 35 male participants contributed 3392 valid days (≥ 500 minutes of wear-time) and the 43 female participants contributed 4081 days. Time spent in MVPA ranged from:

- Males: 0minutes to 226minutes (median: 19minutes, IQR: 7-39minutes),
- Females: 0minutes to 300minutes (median: 16minutes, IQR: 6-33minutes).

Female participants appeared to be less active than male participants with a greater proportion of days in the lower 2 activity categories (Table 30). A Chi-square test for independence indicated a significant association between sex and proportion of

days in the different activity categories with females less active than males, albeit with a small effect size: $X^2(3, n = 7473) = 39.2, p < 0.0001$, Cramer's $V = 0.073$. This pattern remained true for both weekdays and weekend days. The only anomaly to this was a slight increase in the proportion of extremely active days (≥ 120 minutes of MVPA) recorded by female participants on weekdays and weekend days compared to males. This also represented more extremely active days on weekend days compared to weekdays for females, however the number of days reported in this category were small.

Table 30: Table of amount of days by time spent in MVPA comparing males and females for phase 2 participants

Time spent in MVPA per day category	Upper and lower extremes	All days		Weekdays		Weekend days	
		Males % (n = 3392 days)	Females % (n = 4081 days)	Males % (n = 2402 days)	Females % (n = 2891 days)	Males % (n = 990 days)	Females % (n = 1190 days)
<20mins		50.9 (1728)	57.0 (2326)	51.1 (1227)	58.1 (1681)	50.6 (501)	54.2 (645)
	0mins	5.5 (187)	6.6 (268)	5.4 (129)	7.3 (212)	5.9 (58)	4.7 (56)
20-39mins		25.1 (852)	24.5 (998)	25.0 (600)	23.3 (673)	25.5 (252)	27.3 (325)
40-59mins		12.0 (407)	8.9 (362)	11.7 (282)	9.2 (267)	12.6 (125)	8.0 (95)
≥ 60 mins		11.9 (405)	9.7 (35)	12.2 (293)	9.3 (270)	11.3 (112)	10.5 (125)
	≥ 120 mins	1.4 (47)	1.7 (71)	1.4 (33)	1.6 (45)	1.4 (14)	2.2 (26)

Key: mins minutes, MVPA moderate to vigorous physical activity

The median time spent in MVPA per day for individual participants for their own duration in the study ranged from:

- Males: 4minutes (IQR: 2-11minutes) to 63minutes (IQR: 42.5-91minutes), mean \pm SD 21.0 \pm 13.0minutes,
- Females: 2minutes (IQR: 0-8minutes) to 50minutes (IQR: 22-89.5minutes), mean \pm SD 17.0 \pm 11.0minutes (Figure 65).

The participant who achieved median time spent in MVPA per day of ≥ 60 minutes was male. The majority of the 49 participants who achieved median time spent in MVPA per day of <20minutes were female (n = 30).

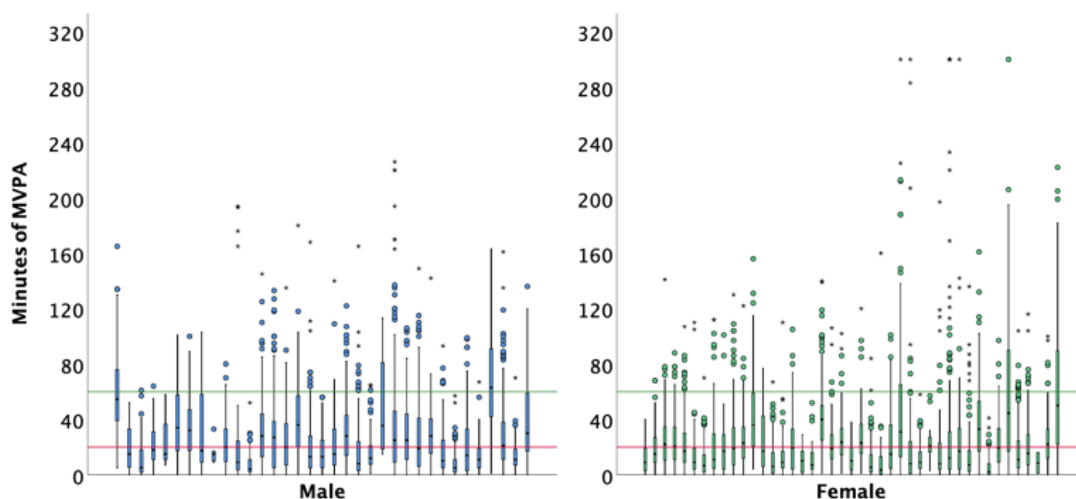


Figure 65: Boxplots of time spent in MVPA (minutes) for each participant of phase 2 for their own study duration, left: male participants, right: female participants.
Reference lines: 60minutes of MVPA (green, top), 20minutes of MVPA (red, bottom)

Weekday/weekend day activity patterns varied between males and females. A total of 54% (n =19) of male participants spent, on average, more time in MVPA on weekdays than weekend days (range of difference between time in MVPA on weekdays and weekend days: 1-28minutes), compared to 26% (n = 11) of female participants (range: 1-15minutes). However, 40% (n = 14) of male participants spent, on average, more time in MVPA on weekend days than week days (range: 1-20minutes) compared to 58% (n = 25) female participants (range: 1-34minutes). Of the 9 participants who spent, on average, the same amount of time in MVPA on weekdays and weekend days, 7 were female and 2 male. Females were generally more active on weekend days than weekdays. The difference in the proportion of males being more active on weekdays than weekend days, and vice versa, was smaller suggesting that the pattern was more varied for males than females.

8.4.2.2.2 Time spent in MVPA: differences between age groups

The 36 participants in age category 1 (6-8years) contributed 3454 valid days (≥ 500 minutes of wear-time), the 24 participants in age category 2 (9-11years) contributed 2435 valid days and the 18 participants in age category 3 (12+years) contributed 1584 valid days. Time spent in MVPA ranged from:

- 6-8-year olds: 0minutes to 300minutes (median: 18minutes, IQR: 7-34minutes),

- 9-11year olds: 0minutes to 300minutes (median: 16minutes, IQR: 6-37minutes),
- 12+year olds: 0minutes to 300minutes (median: 18minutes, IQR: 5-39minutes).

All age groups followed a similar pattern with proportions of days in each activity category reducing with an increase in time in MVPA (Table 31). The only exception to this was the second age group (9-11years) where there was an increase of proportion of days in the most active category (≥ 60 mins of MVPA) compared to the previous category. The youngest age group generally appeared to be active to a low/moderately low level more frequently than the older 2 age categories with a larger proportion of days in the 2 lower active categories (<20mins and 20-30mins of MVPA) (Table 31). The youngest age group also had the lowest proportion of days in the most active category (≥ 60 mins of MVPA). However, the oldest age group achieved the highest proportion of days with no MVPA for both weekdays and weekend days. A Chi-square test for independence indicated a significant association between age group and proportion of days in the different activity categories with the younger age group being more consistently active to a low or moderately low level whilst the older participants achieved more active days, albeit with a small effect size: $X^2(6, n = 7473) = 41.6, p < 0.0001$, Cramer's V 0.053. This pattern remained true for both weekdays and weekend days. The youngest and oldest age groups (6-8years and 12+years) appeared to be more active on weekend days than weekdays. The middle age group (9-11years) were active to a similar level on weekdays and weekend days.

Table 31: Table of amount of days by time spent in MVPA comparing age groups for phase 2 participants

Time spent in MVPA per day category	Upper and lower extremes	All days			Weekdays			Weekend days		
		6-8 years % (n = 3454 days)	9-11 years % (n = 2435 days)	12+ years % (n = 1584 days)	6-8 years % (n = 2445 days)	9-11 years % (n = 1726 days)	12+ years % (n = 1122 days)	6-8 years % (n = 1009 days)	9-11 years % (n = 709 days)	12+ years % (n = 462 days)
<20mins		54.1 (1870)	54.9 (1337)	53.5 (847)	55.0 (1345)	54.9 (948)	54.8 (615)	52.0 (525)	54.9 (389)	50.2 (232)
	0mins	5.8 (199)	5.3 (130)	8.0 (126)	6.3 (155)	5.3 (92)	8.4 (94)	4.4 (44)	5.4 (38)	6.9 (32)
20-39mins		27.2 (939)	23.0 (560)	22.2 (351)	26.5 (647)	23.0 (397)	20.4 (229)	28.9 (292)	23.0 (163)	26.4 (122)
40-59mins		9.7 (336)	9.9 (240)	12.2 (193)	9.6 (234)	10.0 (173)	12.7 (142)	10.1 (102)	9.4 (67)	11.0 (51)
≥60mins		8.9 (309)	12.2 (298)	12.2 (193)	9.0 (219)	12.1 (208)	12.1 (136)	8.9 (90)	12.7 (90)	12.3 (57)
	≥120mins	1.3 (45)	2.1 (50)	1.5 (23)	1.2 (29)	2.0 (35)	1.2 (14)	1.6 (16)	2.1 (15)	1.9 (9)

Key: mins minutes, MVPA moderate to vigorous physical activity

The median time spent in MVPA per day for individual participants for their own duration in the study ranged from:

- 6-8year olds: 5minutes (IQR: 2-11minutes) to 36minutes (IQR: 20-56.75minutes), mean±SD 17.6±8.5minutes,
- 9-11year olds: 4minutes (IQR: 4-11minutes) to 63minutes (IQR: 42.5-91minutes), mean±SD 20.2±13.8minutes,
- 12+year olds: 2minutes (IQR: 0-8minutes) to 54.5minutes (IQR: 39-75.75minutes), mean±SD 19.5±15.6minutes (Figure 66).

Median time spent in MVPA for individual participants appeared to become more widely varied in the oldest age group. The 12+years age group demonstrated the greatest proportion of participants recording a median daily time in MVPA of <20minutes (66.7%, compared to 62.5% and 61.0% for 9-11year olds and 6-8year olds respectively) and also ≥40minutes (16.7%, compared to 8.3% and 0% for 9-11year olds and 6-8year olds respectively). The oldest age group also represented the smallest proportion of participants who did not achieve 60minutes of MVPA on a single day, 11.1% compared to 20.8% and 22.2% for 9-11year olds and 6-8year olds respectively.

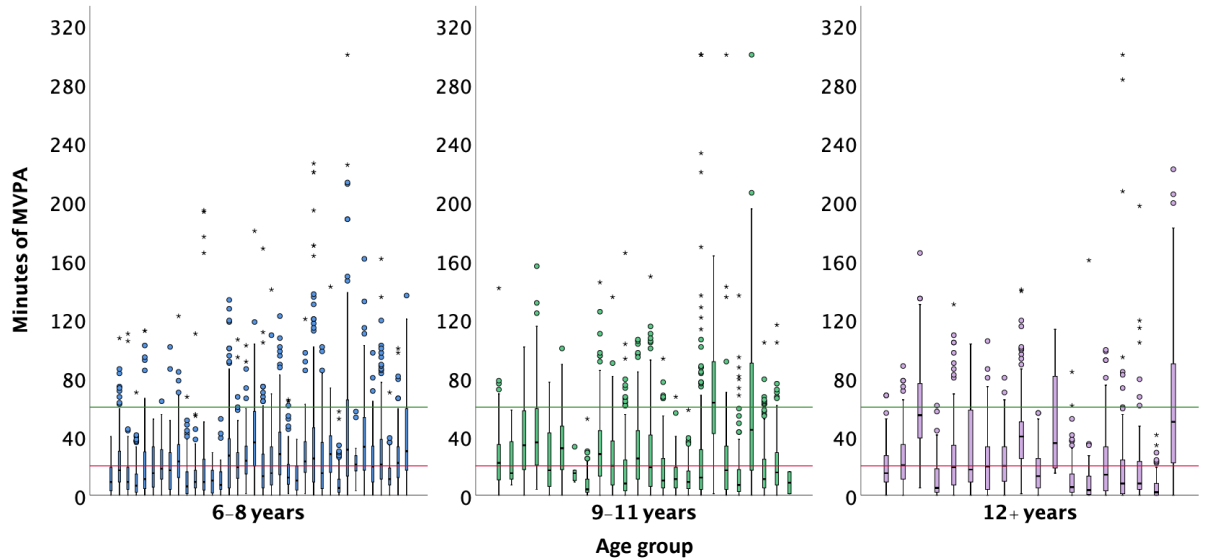


Figure 66: Boxplots of time spent in MVPA (minutes) for each participant of phase 2 for their own study duration, left: 6-8-year olds, middle: 9-11-year olds, right: 12+year olds. Reference lines: 60minutes of MVPA (green, top), 20minutes of MVPA (red, bottom)

Age groups followed different patterns when comparing the differences between weekday and weekend day levels of MVPA. Most participants in the youngest age group (6-8years) spent, on average, more time in MVPA on weekend days than weekdays:

- 58.3% (n = 21) spent, on average, more time in MVPA on weekend days than weekdays, range of difference: 1-15minutes,
- 27.8% (n = 10) spent, on average, more time in MVPA on weekdays than weekend days, range of difference: 1-10minutes,
- 13.9% (n = 5) spent, on average, the same amount of time in MVPA on weekdays and weekend days.

However, the largest proportion of participants in the middle age group (9-11years) spent, on average, more time in MVPA on weekdays than weekend days:

- 41.7% (n = 10) spent, on average, more time in MVPA on weekend days than weekdays, range of difference: 1-18minutes,
- 50.0% (n = 12) spent, on average, more time in MVPA on weekdays than weekend days, range of difference: 1-21minutes,
- 8.3% (n = 2) spent, on average, the same amount of time in MVPA on weekdays and weekend days.

The oldest age group (12+years) were equally split between those who spent more time in MVPA on weekend days than weekdays and those who spent more time in MVPA on weekdays than weekend days:

- 44.4% (n = 8) spent, on average more time in MVPA on weekend days than weekdays, range of difference: 3-34minutes,
- 44.4% (n = 8) spent, on average, more time in MVPA on weekdays than weekend days, range of difference: 1-28minutes,
- 11.1% (n = 2) spent, on average, the same amount of time in MVPA on weekdays and weekend days.

These results demonstrated the variability of weekday/weekend day PA patterns. There were some age and sex-based differences, however the trends were not great enough to enable prediction of CYPwCF weekday/weekend day PA pattern by these characteristics alone.

8.4.2.3 Patterns of physical activity over time

The number of days with the required amount of PA data (at least 500minutes) contributed by individual participants ranged from 2days to 219days (mean±SD: 96±51days), which equated to 1% to 99% of days of participation (median: 67%, IQR: 42-86%). Patterns of PA over time varied between participants with some participants regularly achieving high levels of PA, some participants regularly achieving low levels of PA and other participants fluctuating between high and low levels (Figure 67).

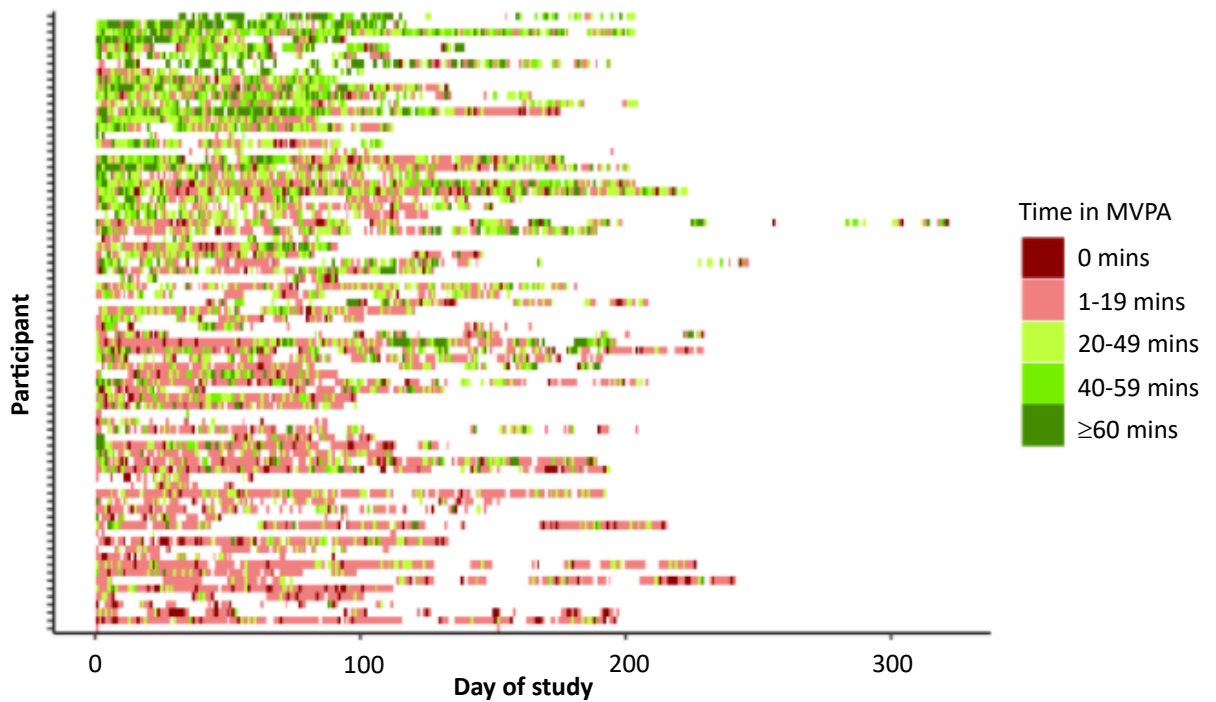


Figure 67: Patterns of physical activity over time by participant of phase 2. Red indicates low level of physical activity, green indicates high level of physical activity

A Latent Class Growth Analysis (LCGA) model was used to explore patterns of PA. The LCGA enabled the identification of multiple sub-groups classified by the longitudinal change in amount of MVPA within the sub-group and the between sub-group differences in change in amount of MVPA (Jung and Wickrama, 2008). The model was developed using PA tracker data from the first 100 days of participation from all participants. A total of 61 participants (78%) contributed PA tracker data beyond 100 days. Therefore, restricting the model to use only the first 100 days enabled more equitable representation of all participants by avoiding over-representation of the participants who had longer study duration and under-representation of the participants with shorter study duration. A 5-class model with non-linear transformation (splines with 5 nodes at quantiles) demonstrated the most reasonable representation of the observed data (Bayesian Information Criteria (BIC): 42815) (Figure 68 and Table 32).

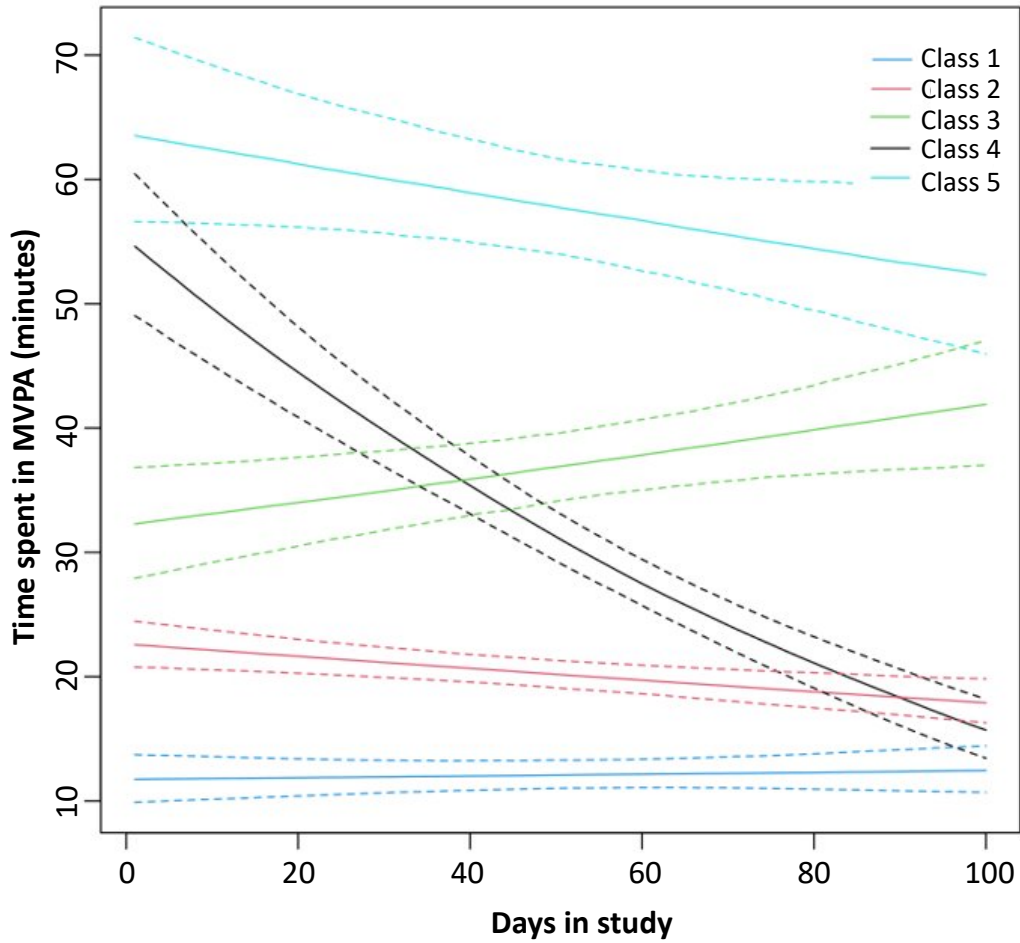


Figure 68: 5-class LCGA model depicting changes in time spent in MVPA by each class over the first 100 days of participation in phase 2

Table 32: Posterior classification table for the 5-class LCGA model depicting changes in time spent in MVPA by each class for phase 2 participants: average posterior probability

Class	Description	N (%)	Probability 1	Probability 2	Probability 3	Probability 4	Probability 5
1	Low, stable	18 (23)	0.9405	0.0556	0.0031	0.0006	0.0002
2	Moderate, slight decrease	33 (42)	0.0323	0.9096	0.0402	0.0169	0.0010
3	Moderate, slight increase	9 (12)	0.0000	0.0121	0.9839	0.0038	0.0002
4	High to low	11 (14)	0.0000	0.0093	0.0083	0.9640	0.0185
5	High, slight decrease	7 (9)	0.0000	0.0000	0.0181	0.0009	0.9809

The 5 classes demonstrated different patterns in PA over the first 100 days of the study: class 1 remained low throughout, classes 2 and 3 started at a moderate level but class 2 decreased whilst class 3 increased over time Table 33. Class 4 demonstrated the most substantial drop from a high level to low level, possibly as a result of a novelty effect of the PA tracker. Class 5 started high and demonstrated only a small decrease in PA over time to remain at a high level at the end of the 100 days. Class 5 represented the smallest proportion of participants of all classes (9%). Class 3 was the only class with a positive trajectory or increase in PA over time. The majority of participants (65%) were allocated to the 2 lowest active level classes, 1 and 2.

Table 33: Start and end values for each class of 5-class LCGA model depicting changes in time spent in MVPA by each class for phase 2 participants

Class	Time spent in MVPA per day (minutes)		
	Start value (day 1)	End value (day 100)	Direction of change
1	12	13	Nil
2	23	18	Slight decrease
3	32	42	Slight increase
4	55	16	Substantial decrease
5	64	52	Slight decrease

8.4.2.4 Patterns of physical activity over time: comparing males and females

The PA patterns were then examined by male/female groups (Table 34). A greater proportion of females were in the consistently low and consistently high active level classes (1 and 5): 35% and 12% respectively compared to 9% and 6% for males. A greater proportion of males were in the moderately active classes (2 and 3): 71% compared to 40% for females. It was not possible to confirm these differences with a Chi-square test for independence because the assumption of minimum expected cell frequency was violated (5 cells with $n \leq 5$).

Table 34: Table of activity patterns comparing males and females for phase 2 participants

Class	Males n = 35 (%)	Females n = 43 (%)
1	3 (9)	15 (35)
2	19 (54)	14 (33)
3	6 (17)	3 (7)
4	5 (14)	6 (14)
5	2 (6)	5 (12)

8.4.2.5 Patterns of physical activity over time: differences between age groups

The PA patterns were then explored by age group (Table 35). There did not appear to be much effect of age group on PA pattern class allocation. The younger age groups (6-8 and 9-11 years) tended to be slightly less likely to be in the higher active level classes (4 and 5) than those in the oldest age group (12+ years) but, again, this was unable to be tested with a Chi-square test for independence due to the small cell frequencies.

Table 35: Table of activity patterns comparing age groups for phase 2 participants

Class	6-8 years n = 36 (%)	9-11 years n = 24 (%)	12+ years n = 18 (%)
1	9 (25)	5 (21)	4 (22)
2	14 (39)	11 (46)	8 (44)
3	6 (17)	3 (13)	0 (0)
4	6 (17)	2 (8)	3 (17)
5	1 (3)	3 (13)	3 (17)

8.5 Self-reported activity levels compared to measured activity levels

Not all participants contributed a day of valid PA tracker data on the days that they chose to discuss for their self-report of PA (HAES), therefore direct comparison was not possible for all participants. A total of 50 participants contributed paired self-reported PA and PA tracker data days for weekdays (28 missing pairs) and 49 for weekend days (29 missing pairs). Of those with missing pairs, 21 participants did not have either weekday or weekend day pairing. A further 3 participants were excluded from analysis for each weekday and weekend day because of insufficient PA tracker wear-time on that day, and therefore a lack of valid PA data. Therefore, there were 49 participants included in analysis for direct comparison of self-

reported MVPA and MVPA measured by PA tracker for weekdays and 47 for weekend days.

8.5.1 Comparison between self-reported and physical activity tracker measured time spent in MVPA

There were substantial differences between self-reported time spent in MVPA and time spent in MVPA measured by PA tracker for the paired days, with self-reported time spent in MVPA far exceeding time spent in MVPA measured by PA tracker:

- Weekdays:
 - self-reported time spent in MVPA (median(IQR)): 162 (90-290) minutes,
 - time spent in MVPA measured by PA tracker (median(IQR)): 20 (7.5-43) minutes,
- Weekend days:
 - self-reported time spent in MVPA (median(IQR)): 139 (35-243) minutes,
 - time spent in MVPA measured by PA tracker (median(IQR)): 23 (3-43) minutes.

These differences were confirmed by Wilcoxon Signed Rank Tests which revealed statistically significant differences between self-reported time spent in MVPA and that measured by PA tracker for both weekdays and weekend days:

- $z = -5.90, p < 0.001$, with a large effect size ($r = 0.60$) for weekdays
- $z = -5.11, p < 0.001$, with a large effect size ($r = 0.53$) for weekend days.

In addition, there did not appear to be a clear or consistent relationship between self-reported time spent in MVPA and that measured by PA tracker (Figure 69).

Bland and Altman plots (Figure 70) indicated wide limits of agreement for both weekdays and weekend days suggesting large variations in differences, with some participants reporting similar time spent in MVPA to that measured by PA tracker, but others reporting MVPA that was usually much more than that measured by PA tracker. These differences appeared to be greatest for those with a higher mean of self-reported MVPA and PA tracker measured time spent in MVPA. This

inconsistency remained true when time spent in MVPA measured by PA tracker was categorised (Figure 71).

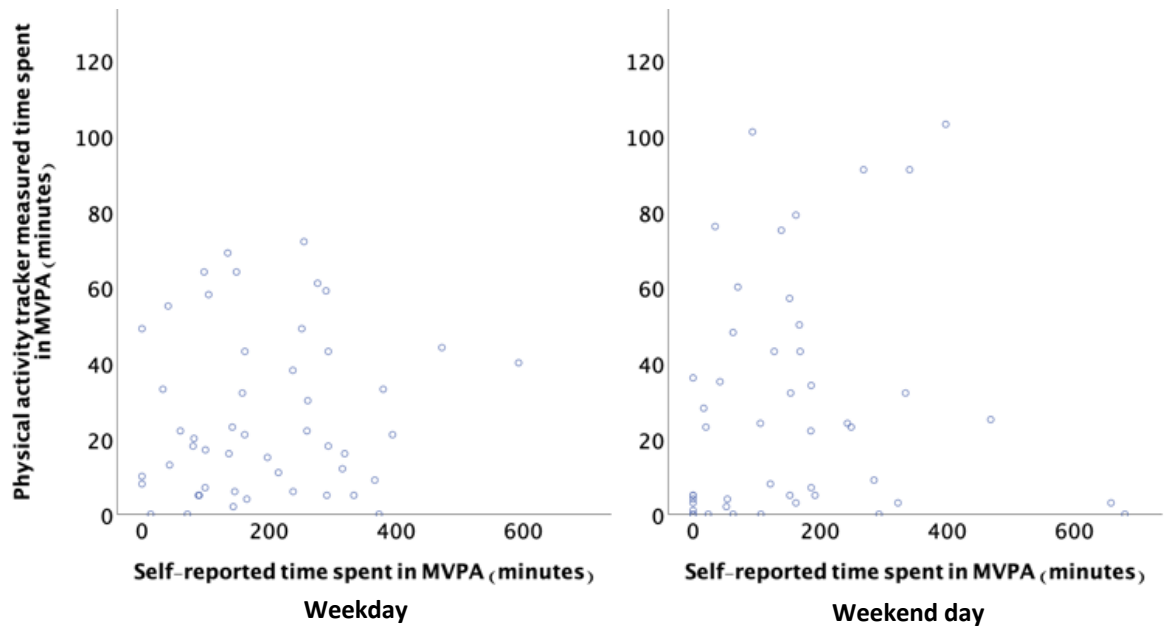


Figure 69: Scatterplots of self-reported time spent in MVPA (measured by HAES) compared to physical activity tracker measured time spent in MVPA for phase 2 participants for weekdays (left) and weekend days (right)

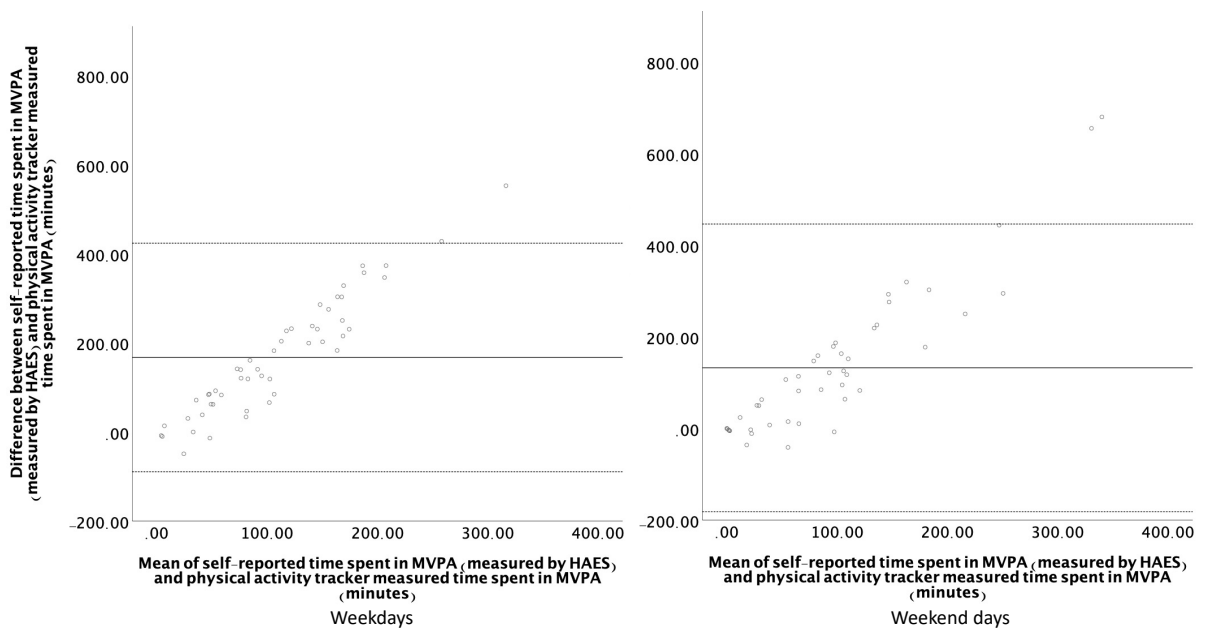


Figure 70: Bland and Altman plot of self-reported time spent in MVPA and physical activity tracker measured time spent in MVPA for phase 2 participants for weekdays (left) and weekend days (right)
Y axis = self-reported time spent in MVPA – physical activity tracker measured time spent in MVPA, therefore values >0 indicate more self-reported MVPA than physical activity tracker measured MVPA and values <0 indicate more physical activity tracker measured MVPA than self-reported MVPA.
Solid line indicates mean difference of 167minutes for weekdays and 132minutes for weekend days, with limits of agreement from -1.96SD to +1.96SD represented by dotted lines

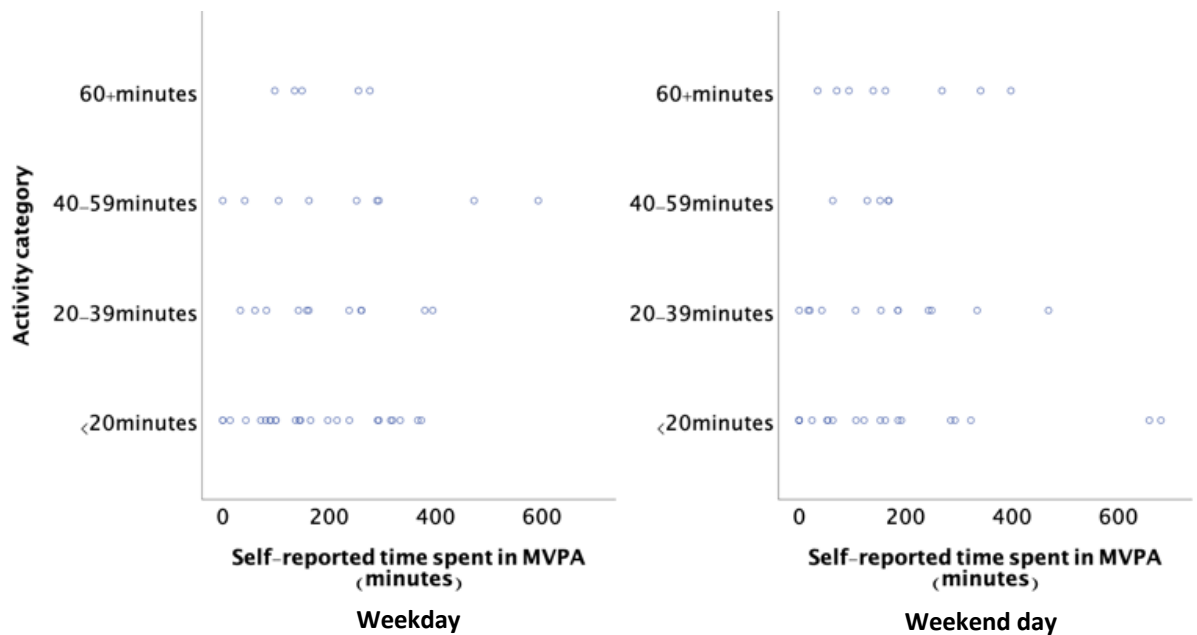


Figure 71: Scatterplots of self-reported time spent in MVPA (measured by HAES) compared to categorised physical activity tracker measured time spent in MVPA for phase 2 participants for weekdays (left) and weekend days (right)

The majority of participants over-reported time spent in MVPA when compared to that measured by PA tracker (n = 44 for weekdays and n = 36 for weekend days). This ranged from 14-553 minutes for weekdays and 8-680 minutes for weekend days. Only 4 participants under-reported their time spent in MVPA when compared to that measured by PA tracker for weekdays. This ranged from 8-49 minutes. There were 10 participants who under-reported time spent in MVPA for weekend days, 6 of which were within 5 minutes of the time spent in MVPA as measured by PA tracker. The remaining 4 ranged from 7-41 minutes under-reporting. Only 1 participant reported exactly the same time spent in MVPA as that measured by PA tracker on weekdays, 5 minutes of MVPA. However, 2 participants reported exactly the same time spent in MVPA as that measured by PA tracker on weekend days, both reported no MVPA for that particular day.

Only 6 of the 49 participants who contributed paired days of self-reported and PA tracker measured MVPA for both weekdays and weekend days appeared to be fairly accurate in their self-report, i.e. within 40minutes. There were no clear predictors for who might report more accurately. They tended to be older (range 11.5-15.2years), female (5 females vs 1 male) and all achieved within 1SD of the mean for distance achieved during 10m-MSWT standardised by age (range -0.95-

0.38). However, both median time spent in MVPA per day (measured by PA tracker) and self-efficacy for PA (measured by CSAPPA) varied (ranges 5.5-40minutes and 33-69 respectively). These results tended to be low with only 2 participants recording above the sample mean \pm SD for time spent in MVPA (18.8 \pm 12.0minutes) and only 1 participant above the sample median(IQR) for self-efficacy for PA (62.5(53-68)). These were not recorded by the same participant.

8.5.2 Comparison between self-identified level of physical activity and time spent in MVPA measured by physical activity tracker

In addition to reporting time spent in MVPA, participants also identified their perception of their activity level for the weekday and weekend day that they described when completing the HAES. These results were compared to time spent in MVPA measured by PA tracker for the same weekday and weekend day. Again, there appeared to be no consistent relationship between how active a participant was as measured by PA tracker and how active they identified themselves to be (Figure 72). Some participants appeared to fairly accurately identify their activity level (examples identified within the green boxes in (Figure 72)). A total of 13 (27%) of the 49 self-identified activity levels for weekdays were fairly accurate:

- 4 (27%) of 15 participants who self-identified as somewhat inactive or somewhat active achieved 20-40minutes of MVPA as measured by PA tracker for the same weekday,
- 9 (27%) of 33 participants who self-identified as active or very active achieved more than 40minutes of MVPA as measured by MVPA for the same weekday.

A total of 17 (36%) of the 47 self-identified activity levels for weekend days were fairly accurate:

- All 3 of 3 participants who self-identified as very inactive or inactive achieved less than 20minutes of MVPA as measured by PA tracker for the same weekend day,

- 4 (27%) of 15 participants who self-identified as somewhat inactive or somewhat active achieved 20-40minutes of MVPA as measured by PA tracker for the same weekend day,
- 10 (34%) of 29 participants who self-identified as active or very active achieved more than 40minutes of MVPA as measured by MVPA for the same weekend day.

Only 4 participants (8%) appeared to be fairly accurate at self-identifying activity level of both weekday and weekend day. However, the majority of participants did not accurately identify their activity level when compared to time spent in MVPA as measured by PA tracker (Figure 72). As with self-reported time spent in MVPA, participants appeared more likely to identify themselves as being more active than was measured by PA tracker, and there was only 1 participant (2%) who self-identified as inactive on a day (weekday) when PA tracker recorded a higher level of time spent in MVPA (62minutes).

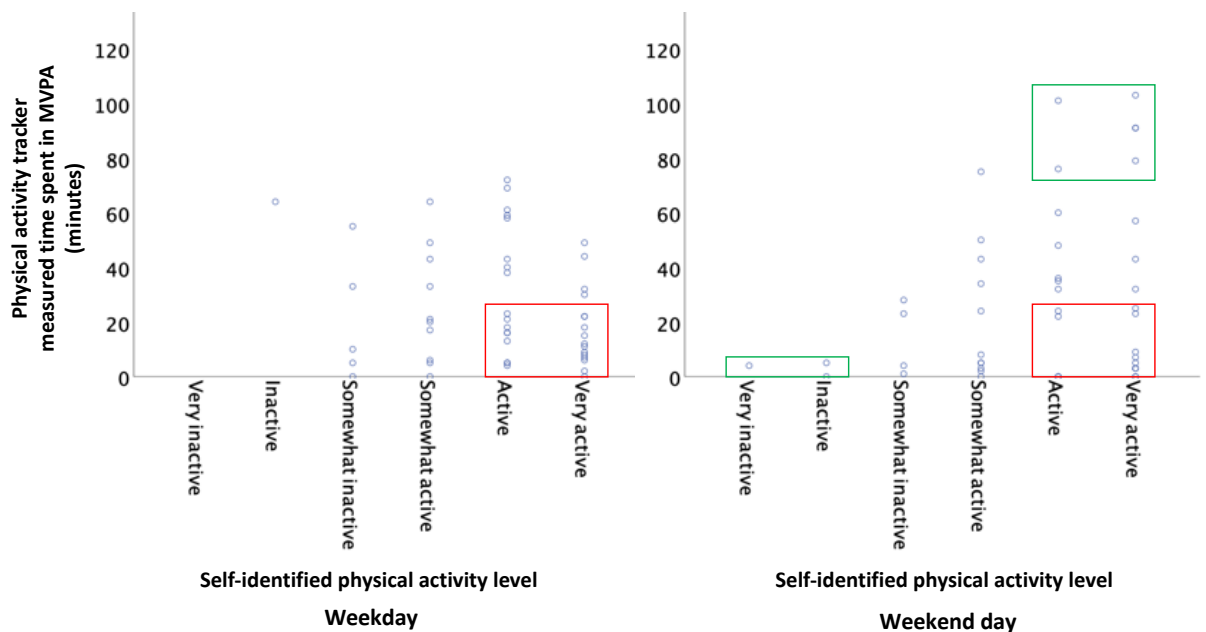


Figure 72: Scatterplots of self-identified physical activity level (collected by HAES) compared to physical activity tracker measured time spent in MVPA for phase 2 participants for weekdays (left) and weekend days (right), with examples of less accurate self-identified activity level marked by the red boxes and examples of more accurate self-identified activity levels marked by the green boxes

8.6 Participant profiling

Individual participant profiles were developed in order to explore if any relationships existed between the 4 different variables (Figure 73). The first step was to decide on categorisation thresholds for each variable.

What physical activity CYPwCF CAN do Exercise capacity measured by 10m-MSWT	How confident CYPwCF FEEL about physical activity Self-efficacy for physical activity measured by CSAPPA
What physical activity CYPwCF ACTUALLY do Physical activity levels measured by activity tracker	What physical activity CYPwCF SAY they do Self-reported physical activity levels measured by HAES

Figure 73: Figure describing the purpose of the objective and subjective outcome measures used in phase 2

8.6.1 Variable categorisation thresholds

To date, there have not been any agreed normative values for CYPwCF for any of the outcome measures used in this research. Therefore quartiles for the study population were used to create four categories for each variable: low, moderate-low, moderate-high and high. This facilitated the identification of whether participants occupied the same quartiles (low, moderate-low, moderate-high or high) for each of the outcome measures, or if there was no consistency to quartile allocation. If there were clear patterns to quartile allocation, i.e. participants were either allocated to low and moderate-low or high and moderate-high for all outcome measures, then that would have provided some confidence that PA maintenance might be predicted by 1 or a combination of these outcome measures.

8.6.1.1 Self-reported levels of physical activity measured by HAES

All 78 participants completed the HAES thus each generating a self-report for time spent in MVPA for a weekday and a weekend day. The average of weekday and weekend day values was used for a single summary value for this variable and thresholds created using population quartiles (Figure 74). The data were not normally distributed therefore there was not an equal spread of values for each of the population's quartiles.

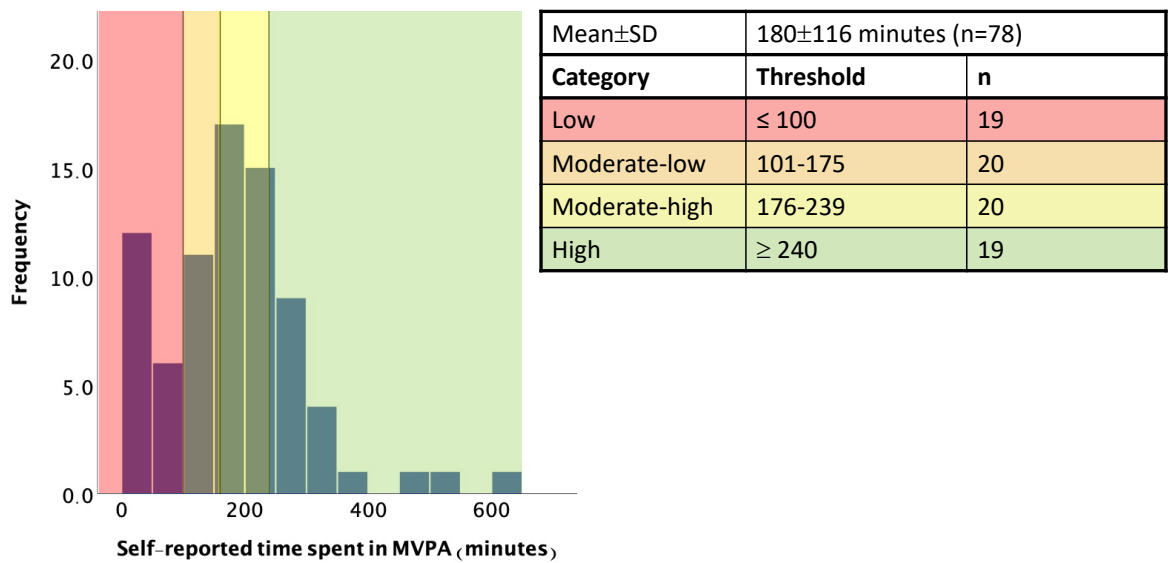


Figure 74: Histogram demonstrating the spread of self-reported minutes of MVPA per day by each participant of phase 2(HAES) for average of week days and weekend days. Table indicates the category thresholds and number of participants in each category

8.6.1.2 Self-efficacy for physical activity measured by CSAPPA

The possible score range for the CSAPPA is 19-76. Again the data from this sample were not normally distributed with the majority scoring well above the midpoint of 47.5 (mean±SD 60±10) and thus quartiles represented an uneven distribution of values (Figure 75). This was consistent across both phases of this research although participants in phase 2 scored on average slightly higher than those in phase 1.

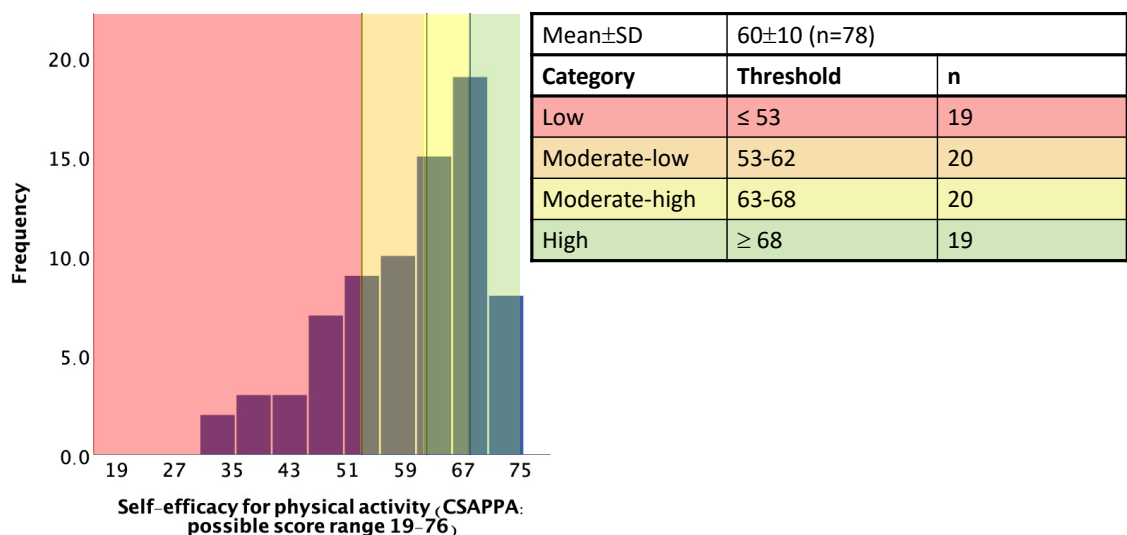


Figure 75: Histogram demonstrating the spread of self-efficacy for physical activity reported by each participant of phase 2 (CSAPPA). Table indicates the category thresholds and number of participants in each category

8.6.1.3 Exercise capacity measured by 10m-MSWT

Only 74 of the 78 participants completed a maximal effort 10m-MSWT therefore the categories were generated using the quartiles of 74 for exercise capacity (Figure 76).

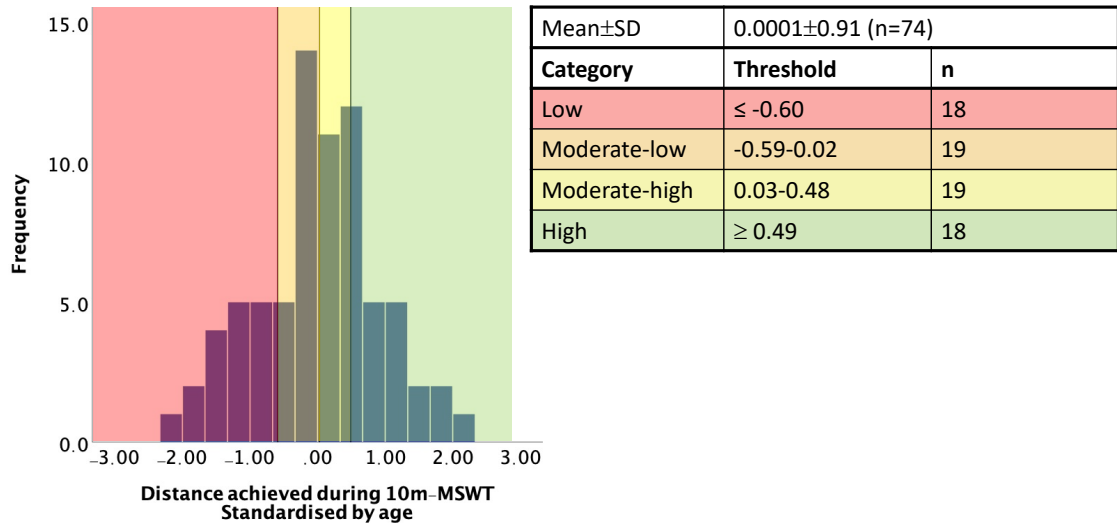


Figure 76: Histogram demonstrating the spread of exercise capacity per participant of phase 2 (10m-MSWT-distance standardised by age). Table indicates the category thresholds and number of participants in each category

8.6.1.4 Time spent in MVPA measured by activity tracker

This is the first research to date that has collected detailed data on the daily PA levels in CYPwCF over a long study duration. Again, the data were not normally distributed therefore there was unequal spread of values in the categories generated by population quartiles (Figure 77).

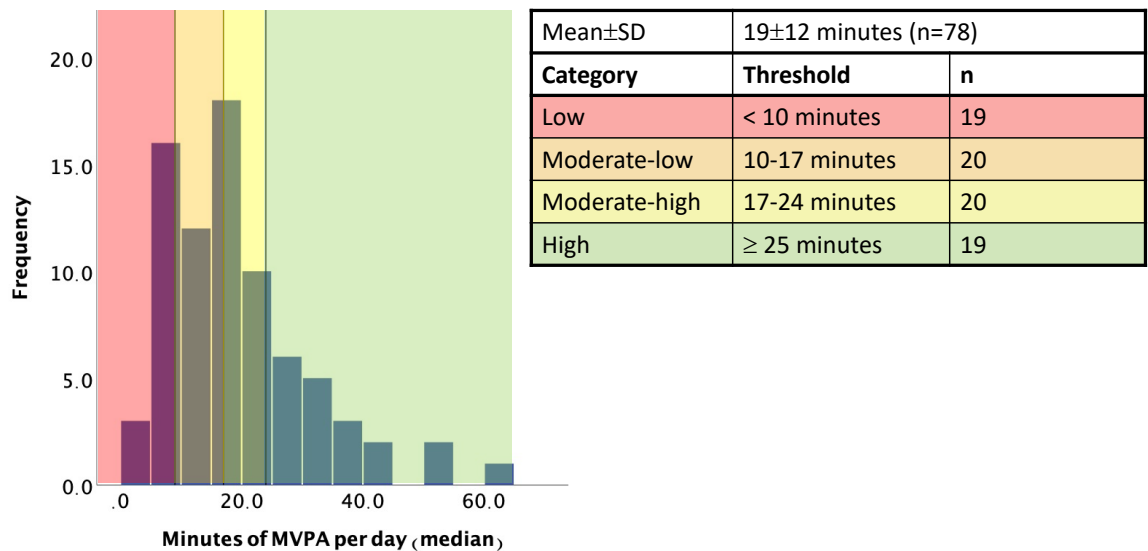


Figure 77: Histogram demonstrating the spread of median time spent in MVPA per day for each participant of phase 2 (measured by activity tracker). Table indicates the category thresholds and number of participants in each category

8.6.2 Participant profiles

Individual participant profiles exploring the relationships between the 2 objective and 2 subjective measures were developed using the categories described above (Figure 78). It was clear that there was no consistent pattern between the subjective and objective outcome measures, although there did appear to be a slight trend that those who achieved higher values for the objective measures also tended to achieve higher values for the subjective measures. Likewise, some participants who achieved lower values for the objective measures also tended to achieve lower values for the subjective measures. However, there was no way of identifying who was likely to achieve similar category allocation as some participants were allocated to different categories for each of the outcome measures.

Participant	What PA CYPwCF ACTUALLY does: PA tracker	What PA CYPwCF CAN do: exercise capacity	How confident CYPwCF FEEL about PA: self-efficacy for PA	What PA CYPwCF SAY they do: self-reported PA
41	High	High	High	High
37	Moderate-high	High	Moderate-high	High
5	Moderate-high	High	Moderate-high	High
67	Moderate-high	High	Moderate-high	High
53	Moderate-high	High	Moderate-high	Moderate-low
15	Moderate-high	High	Moderate-high	High
18	Moderate-high	High	Moderate-high	High
50	Moderate-high	High	Moderate-high	High
78	Moderate-high	High	Moderate-high	Low
29	Moderate-high	High	Moderate-high	High
64	Moderate-high	High	Moderate-high	High
46	Moderate-high	High	Low	Moderate-low
33	Moderate-high	High	High	High
70	Moderate-high	Moderate-low	High	High
20	Moderate-high	Moderate-low	Moderate-high	Moderate-low
77	Moderate-high	Moderate-low	Moderate-high	Low
56	Moderate-high	Low	High	Moderate-high
48	Moderate-high	Low	Moderate-high	Moderate-high
32	Moderate-high	Low	Low	Low
13	Moderate-high	High	High	Moderate-low
17	Moderate-high	High	High	High
6	Moderate-high	High	High	Moderate-high
23	Moderate-high	High	Moderate-high	High
25	Moderate-high	High	Low	Low
35	Moderate-high	High	High	High
36	Moderate-high	High	High	Moderate-high
69	Moderate-high	High	Moderate-high	High
34	Moderate-high	High	High	High
16	Moderate-high	High	Moderate-high	Low
45	Moderate-high	Moderate-low	High	High
72	Moderate-high	Moderate-low	High	Moderate-low
19	Moderate-high	Moderate-low	Moderate-high	Moderate-low
12	Moderate-high	High	Low	High
3	Moderate-high	Moderate-low	Low	Moderate-high
51	Moderate-high	Low	High	High
76	Moderate-high	Low	Moderate-high	High
61	Moderate-high	Low	Moderate-high	Moderate-high
26	Moderate-high	Low	Low	Low
4	Moderate-high	Low	Low	Low
73	Moderate-high	High	High	High
14	Moderate-high	High	High	Moderate-low
44	Moderate-high	High	Moderate-high	Moderate-high
57	Moderate-high	High	High	Moderate-high
43	Moderate-high	High	High	Moderate-high
10	Moderate-high	High	High	High
58	Moderate-high	Moderate-low	Moderate-high	Moderate-low
54	Moderate-high	Moderate-low	Moderate-high	Moderate-low
52	Moderate-high	Moderate-low	Moderate-high	Low
71	Moderate-high	Moderate-low	Moderate-high	Moderate-low
39	Moderate-high	Moderate-low	Low	Low
74	Moderate-high	Low	High	Moderate-high
30	Moderate-high	Low	Moderate-high	Moderate-high
9	Moderate-high	Low	Low	Moderate-high
2	Moderate-high	Low	Low	Moderate-high
38	Moderate-high	Low	Low	Moderate-high
40	Moderate-high	Low	Low	Low
65	Moderate-high	Not available	High	Low
63	Moderate-high	Not available	Moderate-high	Moderate-high
24	Moderate-high	Not available	Moderate-high	Moderate-high
60	Moderate-high	Not available	High	High
7	Low	High	High	High
75	Low	High	High	Moderate-low
31	Low	High	Moderate-high	Moderate-high
68	Low	High	Moderate-high	Low
8	Low	Moderate-high	Moderate-high	Moderate-high
27	Low	Moderate-high	Low	Low
62	Low	Moderate-high	Low	Low
22	Low	Moderate-high	High	Moderate-high
28	Low	Moderate-high	Moderate-high	Moderate-high
42	Low	Moderate-high	Moderate-high	Moderate-high
59	Low	Moderate-high	Low	Low
21	Low	Moderate-high	Low	Low
49	Low	Moderate-high	Low	Low
1	Low	Low	Moderate-high	Moderate-high
66	Low	Low	High	High
47	Low	Low	Low	Low
11	Low	Low	Low	Low
55	Low	Not available	Moderate-high	Moderate-high

Key:

- High
- Moderate-high
- Moderate-low
- Low
- Not available

CYPwCF: children and young people with cystic fibrosis
PA: physical activity

Figure 78: Individual participant outcome measure profiles for phase 2 participants

CAN and DOES

A total of 23 (31%) participants were categorised as high or moderate-high for both exercise capacity and measured PA levels (CAN and DOES). Of those, 10 (43%) were also categorised as high or moderate-high for self-efficacy for PA and self-reported activity levels. However, 13 (57%) participants were either categorised as low or moderate-low for self-reported activity levels (n = 3, 13%) or self-efficacy for PA (n = 5, 22%), or both (n = 5, 22%).

CAN but DOES NOT

This pattern was similar for the 14 (19%) participants who were categorised as high or moderate-high for exercise capacity but low or moderate-low for measured levels of PA (CAN but DOES NOT). Again, half of participants in this group (n = 7, 50%) were also categorised as high or moderate-high for self-efficacy for PA and self-reported activity levels. Only 3 (21%) were categorised as high or moderate-high for self-efficacy but low or moderate-low for self-reported PA levels, 1 participant (7%) was categorised as low or moderate-low for self-efficacy for PA but high or moderate-high for self-reported PA levels and 3 participants (21%) were categorised as low for both.

CANNOT but DOES

There were 16 (22%) participants who were categorised as low or moderate-low for exercise capacity but high or moderate-high for measured levels of PA (CANNOT but DOES). Only 4 (25%) of these participants were categorised as high or moderate-high for self-efficacy for PA and self-reported activity levels. However, 6 participants (38%) were categorised as low or moderate-low for self-efficacy for PA but high for self-reported activity levels and 3 participants (19%) were categorised as low or moderate-low for both. Only 2 participants (13%) were categorised as high or moderate-high for self-efficacy for PA and low for self-reported PA levels.

CANNOT and DOES NOT

Finally, there were 21 (28%) participants who were categorised as low or moderate-low for both objective measures (CANNOT and DOES NOT). Only 4 (19%) of these

participants were categorised as high or moderate-high for self-efficacy for PA and self-reported PA levels with the majority of participants (n = 12, 57%) categorised as low or moderate-low for both subjective measures. A total of 5 (24%) participants were categorised as high or moderate-high for self-efficacy for PA but low or moderate-low for self-reported activity levels, and no participants were categorised as high or moderate-high for self-reported activity levels but low or moderate-low for self-efficacy for PA.

There were 4 participants who did not achieve a maximal 10m-MSWT and were therefore not categorised for exercise capacity. All 4 of these participants were categorised as low or moderate-low for measured levels of PA (DOES NOT). Only 1 participant was categorised as high or moderate-high self-efficacy for PA but low or moderate-low self-reported levels of PA, 2 participants were categorised as low or moderate-low self-efficacy for PA but high or moderate-high self-reported PA levels, and the remaining participant was categorised as low for both subjective measures.

8.6.2.1 Identifying the characteristics of participants in each profile group

The characteristics of the participants in each of the profile groups were then explored. Again, scores within the high and moderately high categories were considered as positive for each outcome, and low and moderately low were considered as negative for each outcome. Figure 79 depicted the sex and age characteristics of the participants in each profile group relating to the subjective and objective outcome measures. Sex and age were the 2 characteristics identified from phase 1 of this research as having an impact on the outcomes under investigation. Figure 79 has been colour-coded to indicate the results of the objective outcome measures because high exercise capacity is known to have a positive impact on the long-term health and prognosis of CYPwCF and high PA levels are known to have a positive impact on exercise capacity. Phase 1 of this research demonstrated that self-efficacy for PA can be impacted by an appropriate exercise intervention, and phase 2 of this research has demonstrated that self-reported levels of PA are variable and unpredictable, and do not reliably reflect objectively measured PA. Therefore, the 2 objectively measured variables (what PA

CYPwCF actually DO and what PA CYPwCF CAN do) may have more potential to effect a desirable impact on the health of CYPwCF and are therefore the most important to identify. Green indicated high exercise capacity and levels of PA thus positive health behaviours, amber identified high exercise capacity but low levels of PA or vice versa, suggesting that there is some level of risk to health, and red signified low exercise capacity and levels of PA and therefore greater risk to health.

Male participants were more likely to achieve positive exercise capacity and levels of PA than females, regardless of self-efficacy for PA and self-reported levels of PA. Females reported lower self-efficacy for PA than males particularly when associated with either low exercise capacity or levels of PA, or both. It also appeared that the oldest age group were more likely to report low levels of self-efficacy for PA and self-reported activity levels compared to the other 2 age groups, even when levels of PA and/or exercise capacity were high.

		Subjective			
Objective		Self-efficacy: HIGH	Self-efficacy: HIGH	Self-efficacy: LOW	Self-efficacy: LOW
		Self-reported physical activity: HIGH	Self-reported physical activity: LOW	Self-reported physical activity: HIGH	Self-reported physical activity: LOW
	Exercise capacity: HIGH	n= 10 Males/females (%): 5/5 (50/50) Age distribution (%): 6-8yrs 6 (60) 9-11yrs 3 (30) 12+yrs 1 (10)	n= 3 Males/females (%): 2/1 (67/33) Age distribution (%): 6-8yrs 2 (67) 9-11yrs 1 (33) 12+yrs 0 (0)	n= 5 Males/females (%): 3/2 (60/40) Age distribution (%): 6-8yrs 2 (40) 9-11yrs 2 (40) 12+yrs 1 (20)	n= 5 Males/females (%): 3/2 (60/40) Age distribution (%): 6-8yrs 2 (40) 9-11yrs 0 (0) 12+yrs 3 (60)
	Physical activity: HIGH				
	Exercise capacity: HIGH	n= 7 Males/females (%): 3/4 (43/57) Age distribution (%): 6-8yrs 5 (71) 9-11yrs 1 (14) 12+yrs 1 (14)	n= 3 Males/females (%): 1/2 (33/67) Age distribution (%): 6-8yrs 0 (0) 9-11yrs 3 (100) 12+yrs 0 (0)	n= 1 Males/females (%): 0/1 (0/100) Age distribution (%): 6-8yrs 1 (100) 9-11yrs 0 (0) 12+yrs 0 (0)	n= 3 Males/females (%): 1/2 (33/67) Age distribution (%): 6-8yrs 1 (33) 9-11yrs 0 (0) 12+yrs 2 (67)
Physical activity: LOW					
Exercise capacity: LOW	n= 4 Males/females (%): 1/3 (25/75) Age distribution (%): 6-8yrs 2 (50) 9-11yrs 1 (50) 12+yrs 0 (0)	n= 2 Males/females (%): 2/0 (100/0) Age distribution (%): 6-8yrs 1 (50) 9-11yrs 1 (50) 12+yrs 0 (0)	n= 6 Males/females (%): 3/3 (50/50) Age distribution (%): 6-8yrs 4 (67) 9-11yrs 1 (17) 12+yrs 1 (17)	n= 4 Males/females (%): 0/4 (0/100) Age distribution (%): 6-8yrs 0 (0) 9-11yrs 1 (25) 12+yrs 3 (75)	
Physical activity: HIGH					
Exercise capacity: LOW	n= 4 Males/females (%): 2/2 (50/50) Age distribution (%): 6-8yrs 3 (75) 9-11yrs 1 (25) 12+yrs 0 (0)	n= 5 Males/females (%): 3/2 (60/40) Age distribution (%): 6-8yrs 2 (40) 9-11yrs 3 (60) 12+yrs 0 (0)	n= 0 Males/females (%): 0 Age distribution (%): 6-8yrs 0 9-11yrs 0 12+yrs 0	n= 12 Males/females (%): 4/8 (33/67) Age distribution (%): 6-8yrs 4 (33) 9-11yrs 2 (17) 12+yrs 6 (50)	
Physical activity: LOW					

Male/female ratio for participants included in this analysis n = (%): 33/41 (45/55)

Age group distribution for participants included in this analysis n = (%): 6-8yrs 35 (47), 9-11yrs 21 (28), 12+yrs 18 (24)

Figure 79: Figure representing the characteristics of participants of phase 2 in each profile group

8.6.3 Can level of physical activity be predicted by exercise capacity, self-efficacy for physical activity and self-reported physical activity?

A standard multiple regression was performed to investigate whether level of PA (median daily MVPA in minutes measured by PA tracker), as the dependent variable, could be predicted statistically by exercise capacity (measured by distance achieved during 10m-MSWT standardised by age), self-efficacy for PA (measured by CSAPPA total score) or self-reported levels of PA (measured by HAES summary), as independent variables. Results of evaluation of assumptions led to transformation of the variables to reduce skewness, reduce the number of outliers and improve the normality, linearity and homoscedasticity of residuals. Reflect and square root transformations were used for CSAPPA total score and square root for HAES summary. No outliers were identified by using $p < 0.001$ criterion for Mahalanobis distance. A total of 4 of the 78 participants had missing data, all exercise capacity results. Variance in level of PA (median daily MVPA measured by PA tracker) explained by the model was only 9.5% and the model did not reach statistical significance, $F(3, 70) = 2.44$, $p = 0.071$. This suggested that level of PA taken as the median daily time spent in MVPA could not be predicted by exercise capacity, self-efficacy for PA and self-reported PA.

8.6.4 Identifying the physical activity patterns in each profile group

Median daily MVPA provides limited insight into the maintenance of PA in each participant. Pattern of PA and how the amount of PA changes over time is more important to consider in relation to health and how to support the maintenance of PA in the clinical setting. Therefore, the final stage of analysis investigated the relationship between the measured variables and identified PA patterns. The participant profiles and PA patterns were examined to discover if the profile of subjective and/or objective outcome measures could predict the PA pattern of CYPwCF. Figure 80 identified the frequency of each PA pattern being identified in the subjective and objective outcome measure profiles.

There was a greater proportion of classes 3 and 5 activity patterns (moderate with a slight increase and high with a slight decrease respectively) in the high exercise

capacity and PA (CAN/DOES) and high self-efficacy for PA and self-reported levels of PA profile. There were small participant numbers in all other profile groups in the high exercise capacity and PA (CAN/DOES) category, but there did not appear to be a clear indication of PA pattern.

There was a greater proportion of participants identified with classes 1 and 2 activity patterns (low and stable, and moderate with slight decrease respectively) in the low exercise capacity and PA levels (CANNOT/DOES NOT) and low self-efficacy for PA and self-reported levels of PA group. All 21 participants in the low exercise capacity and PA levels category (CANNOT/DOES NOT) were identified as classes 1 or 2 activity patterns, but these occurred in all subjective outcome measure groups suggesting that they could not be predicted by subjective outcome measures results.

There was a relatively high proportion of participants identified with class 3 activity pattern (moderate and slight increase) in the high exercise capacity and PA levels (CAN/DOES) but all combinations of self-efficacy for PA and self-reported levels of PA profiles suggesting that this pattern could not be predicted by the subjective measure.

		Subjective			
Objective		Self-efficacy: HIGH	Self-efficacy: HIGH	Self-efficacy: LOW	Self-efficacy: LOW
		Self-reported physical activity: HIGH	Self-reported physical activity: LOW	Self-reported physical activity: HIGH	Self-reported physical activity: LOW
	Exercise capacity: HIGH	n= 10 (%) Class 1: 0 (0) Class 2: 3 (30) Class 3: 3 (30) Class 4: 2 (20) Class 5: 2 (20)	n= 3 (%) Class 1: 0 (0) Class 2: 1 (33) Class 3: 1 (33) Class 4: 1 (33) Class 5: 0 (0)	n= 5 (%) Class 1: 0 (0) Class 2: 1 (20) Class 3: 2 (40) Class 4: 1 (20) Class 5: 1 (20)	n= 5 (%) Class 1: 0 (0) Class 2: 3 (60) Class 3: 1 (20) Class 4: 1 (20) Class 5: 0 (0)
	Physical activity: HIGH	n= 7 (%) Class 1: 4 (57) Class 2: 3 (43) Class 3: 0 (0) Class 4: 0 (0) Class 5: 0 (0)	n= 3 (%) Class 1: 1 (33) Class 2: 2 (67) Class 3: 0 (0) Class 4: 0 (0) Class 5: 0 (0)	n= 1 (%) Class 1: 1 (100) Class 2: 0 (0) Class 3: 0 (0) Class 4: 0 (0) Class 5: 0 (0)	n= 3 (%) Class 1: 1 (33) Class 2: 1 (33) Class 3: 0 (0) Class 4: 1 (33) Class 5: 0 (0)
	Exercise capacity: LOW	n= 4 (%) Class 1: 0 (0) Class 2: 1 (25) Class 3: 0 (0) Class 4: 1 (25) Class 5: 2 (50)	n= 2 (%) Class 1: 0 (0) Class 2: 1 (50) Class 3: 1 (50) Class 4: 0 (0) Class 5: 0 (0)	n= 6 (%) Class 1: 0 (0) Class 2: 3 (50) Class 3: 0 (0) Class 4: 3 (50) Class 5: 0 (0)	n= 4 (%) Class 1: 0 (0) Class 2: 1 (25) Class 3: 0 (0) Class 4: 1 (25) Class 5: 2 (50)
Physical activity: LOW	n= 4 (%) Class 1: 3 (75) Class 2: 1 (25) Class 3: 0 (0) Class 4: 0 (0) Class 5: 0 (0)	n= 5 (%) Class 1: 1 (20) Class 2: 4 (80) Class 3: 0 (0) Class 4: 0 (0) Class 5: 0 (0)	n= 0 (%) Class 1: 0 Class 2: 0 Class 3: 0 Class 4: 0 Class 5: 0	n= 12 (%) Class 1: 5 (42) Class 2: 7 (58) Class 3: 0 (0) Class 4: 0 (0) Class 5: 0 (0)	

Activity pattern distribution for participants included in profiles n = 74 (%):
Class 1: 16 (22), Class 2: 32 (43), Class 3: 8 (11), Class 4: 11 (15), Class 5: 7 (9)

Figure 80: Figure representing the subjective and objective outcome measure profiles of participants of phase 2 and their physical activity pattern

LDA was conducted to investigate if PA pattern class could be predicted statistically by the raw values of exercise capacity (measured by 10m-MSWT), self-efficacy for physical activity (measured by CSAPPA total score) or self-reported amount of physical activity (measured by HAES summary) rather than the categorised profiles. Time spent in MVPA measured by PA tracker (median daily MVPA) was not included in this analysis because daily MVPA data were used to construct the LCGA classes therefore would have resulted in a violation of the assumption of singularity. As identified in section 8.6.3, the assumption of normality was violated by both CSAPPA total score and HAES summary (Shapiro Wilk 0.002 and 0.001 respectively). These data were transformed to achieve normal distribution: reflect and square root for CSAPPA (Shapiro Wilk 0.604) and square root for HAES summary (Shapiro Wilk 0.081). No other assumptions were violated. Table 36 presented the mean values for each variable by LCGA class. Class 3 appeared to have the most notable difference in each variable compared to all other classes. This was the only PA pattern class with a positive trajectory over time (increase in amount of daily MVPA). However, the 3 functions returned by the LDA all achieved poor fit and lacked statistical significance (function 1 achieved the best fit: Eigenvalue 0.142 and

$p = 0.334$). The model was only able to correctly classify 44.6% of the originally grouped cases (40.5% of cross-validated grouped cases). This further indicated that it was not possible to predict PA pattern from exercise capacity, self-efficacy for PA and self-reported levels of PA.

Table 36: Table of outcome measure averages by LCGA class for phase 2 participants

LCGA class	n	Distance achieved during 10m-MSWT (standardised residual) (mean±SD)	Self-efficacy for physical activity (CSAPPA total score) (mean±SD)	Self-reported physical activity measured by HAES summary (minutes) (mean±SD)
1	16	-0.04±0.98	60.1±11.0	153±110
2	32	-0.07±0.79	59.7±11.6	161±90
3	8	0.66±0.73	65.4±6.3	274±177
4	11	-0.16±1.25	57.9±8.8	204±131
5	7	-0.07±0.79	60.7±11.0	212±116

LCGA: Latent class growth analysis

9 Phase 2 discussion

9.1 Introduction

The findings from Phase 1 of this research identified that:

- A supervised exercise intervention can have a positive impact on functional exercise capacity, but this benefit only lasted as long as the participation was maintained,
- Independent maintenance of PA was difficult for many CYPwCF after the withdrawal of the supervised exercise training,
- Some CYPwCF did manage to maintain PA, some without even having experienced the supervised exercise training,
- Self-efficacy for PA was higher in those CYPwCF who appeared to manage to maintain PA independently.

However, the research conducted in Phase 1 did not directly measure PA participation or maintenance. Phase 2 of this research aimed to directly measure PA maintenance patterns, and also to assess whether PA maintenance can be predicted by 3 clinical outcome measures (10m-MSWT measuring exercise capacity, CSAPPA measuring self-efficacy for PA and HAES measuring self-reported levels of PA). Being able to identify CYPwCF who will and won't maintain adequate levels of PA independently would be useful for CF clinical teams. This would enable the identification of the support required by individual CYPwCF to improve or maintain engagement in PA without adding further burden of assessment in the clinical setting.

The research questions addressed in this phase of work were:

4. What are the patterns and maintenance of PA over time in CYPwCF?
5. Can the maintenance of PA in CYPwCF be predicted?

The anticipated outputs from this phase of the programme of research are identified in Figure 81.

- Identification of the patterns of physical activity in CYPwCF.
- The relationships between self-efficacy for physical activity, reported activity levels, actual activity levels and exercise capacity in CYPwCF.
- Identification of the predictors for exercise and physical activity maintenance behaviours in CYPwCF.

Figure 81: Research outputs anticipated from phase 2 study

The key findings identified in chapter 8 will be discussed in line with the literature and the strengths and limitations of this research. Conclusions will then be drawn with implications for clinical practice and future research identified.

9.2 What are the patterns and maintenance of physical activity over time in children and young people with CF?

To date, research projects investigating PA amongst CYPwCF have been of relatively short duration, and thus reported on level of PA rather than pattern of maintenance over time. The length of participation, and therefore PA tracker data collection, in this study enabled the development of the PA maintenance classes by LCGA model. However, in order to place the findings within the literature, the summarised levels of PA recorded by CYPwCF will be discussed first, followed by patterns of PA maintenance over time.

9.2.1 Levels of physical activity in children and young people with CF

The majority of participants in this study appeared to be active to a low or moderately low level with many more low active days recorded by the sample than high active days. A total of 54% of days recorded <20minutes of MVPA but only 11% of days recorded ≥60minutes of MVPA. Furthermore, 49 participants (63%) recorded a median daily time in MVPA of <20minutes as recorded by PA tracker, and 14 (18%) did not achieve >60minutes of MVPA on a single day of participation. However, a small number of participants were active to a higher level with 1 participant achieving a median daily time in MVPA of >60minutes. It is important to highlight that comparing to data reported by other studies was problematic because of the huge variations in measurement tools, data processing techniques and outcome measures selected. Nonetheless, it was clear from this sample that levels of PA were varied with the majority achieving short durations of daily MVPA. This was in agreement with the conclusion of a systematic review conducted by

Puppo et al. (2020). This review examined 20 randomised controlled trials and observational studies investigating PA in CYPwCF. The authors also identified the difficulty of direct comparison of data due to the variety of outcomes used: 11 studies used objective measures of PA but there was even further variety with 9 using accelerometers (with a minimum of 3-7days data collected), 2 used indirect calorimetry, 1 used double labelled water and 1 used flex HR method. A further 9 studies used subjective measures of PA only. Despite the limitations of the studies reviewed, the authors concluded that the majority of studies reported 'insufficient levels of MVPA' (Puppo et al., 2020). Furthermore, the review identified that the levels of PA recorded by CYPwCF were comparable to those of the non-CF control groups investigated in some of the reviewed studies (Kilbride et al., 2012, Aznar et al., 2014, Mackintosh et al., 2018, Mackintosh et al., 2019).

A more recent study conducted by Valencia-Peris et al. (2021) investigated PA and sedentary behaviours in school-aged children with CF and healthy controls. Participants were required to wear a hip-worn accelerometer during waking hours for 7 days, similar to the requirements of the studies reviewed by Puppo et al. (2020). Valencia-Peris et al. (2021) reported agreement with the findings of the systematic review, that there was no statistically significant difference between CF and non-CF groups in MVPA (54 vs 59minutes/day respectively) or sedentary behaviour (558 vs 553minutes/day respectively). The sample size (CF group n = 44, control group n = 45) was comparable or larger than those in the studies reviewed by Puppo et al. (2020) (Kilbride et al., 2012, Aznar et al., 2014, Mackintosh et al., 2018, Mackintosh et al., 2019). Elmesmari et al. (2022) compared the 24-hour movement patterns of children with a number of different diseases, including CF, to those of healthy controls, matched by age, gender and week of measurement. Participants were requested to wear an accelerometer continuously for 7 days. Data were only included in analysis if there was ≥ 4 days with >10 hours of wear-time including at least 1 weekend day and night. The CF group recorded the same amount of PA to their matched peers (2.4hours of PA for each group) but appeared to spend more time sitting (8.1hours compared to 7.2hours). Whilst there has been some debate, as discussed above, it appeared from the literature that the levels of

PA for CYPwCF were comparable with those of non-CF peers, but levels were generally low.

This conclusion remained true of adults with CF. Shelley et al. (2019) conducted a systematic review of the literature pertaining to the PA levels of adults with CF. The authors concluded that PA levels were comparable between adults with CF and non-CF peers, but that both failed to meet PA guidelines.

However, in the current study, over 1 in 10 days of data captured by PA tracker (11%) recorded ≥ 60 minutes of MVPA and, whilst this was only a relatively small proportion, it indicated that levels of PA were varied and not all low. Furthermore, only 14 participants (18%) did not achieve 60 minutes of MVPA on a single day of their participation. The majority of participants were very active on some days, but these were the exception with a predominance of low activity resulting in their low median daily time in MVPA. There were 5 participants who achieved a median daily MVPA of ≥ 40 minutes providing evidence that the levels of PA of individual CYPwCF were not all low and that these more active individuals were not obvious when only group level analysis was conducted. The volume of PA tracking data yielded by this study enabled more detailed analysis including comparisons of weekdays with weekend days, differences between males and females, and differences by age groups.

9.2.1.1 Comparing weekday and weekend day levels of physical activity in children and young people with CF

There was no statistically significant difference in the amount of MVPA recorded by PA tracker when comparing weekdays to weekend days. This finding was in contradiction to previous literature. For example Mackintosh et al. (2018), who used Actigraphs to compare the levels of PA of 18 CYPwCF aged 6-17 years to those of 18 age-matched healthy controls, reported that participants in both CF and control groups were more active on weekdays than weekend days. This was also the conclusion drawn from 4 other studies investigating the difference between weekday and weekend day activity levels in 425 young German girls (Bachner et al., 2020), 36 urban American Indian children (Grant et al., 2020), 470 Taiwanese

adolescents (Wang et al., 2019) and 136 CYP living in Scotland (McLellan et al., 2020). These 4 studies did not investigate CYPwCF but the levels of PA of CYPwCF appeared to be comparable to those without CF therefore discussion of this literature was pertinent. Participants in all 5 of these studies were requested to wear the accelerometer for at least 7 days, although data were included in analysis if participants contributed as little as 8hours (Bachner et al., 2020), 9hours (Mackintosh et al., 2018) or 10hours (Wang et al., 2019, McLellan et al., 2020) of accelerometer data for 4 days (including 1 weekend day). Even the maximum duration of 7 days was much shorter than the minimum of 2 months collected by the current study and may have contributed to the difference in findings. The short duration of monitoring may have led to participants behaving differently during the assessment period, and therefore may not have reflected the true habitual levels of PA and weekday/weekend patterns.

When analysed as a group, there was no difference in time spent in MVPA on weekdays to weekend days in the current study. However, when the patterns of individuals were investigated it became apparent that there was a difference in number of individual participants who spent more time on MVPA on weekdays (n = 30, 38%) and those who spent more time in MVPA on weekend days (n = 39, 50%). Therefore, it was not accurate to conclude that there was no difference in time spent in MVPA between weekdays and weekdays, rather that it varied by individual participants. Thus, assessment by PA tracking may provide a more accurate picture of the individual weekly pattern of PA of all CYPwCF. Beemer et al. (2021) collected accelerometer data in 21 7-11year olds to examine the duration and intensity of habitual PA and sedentary time at and away from school. The investigators employed the common protocol of issuing hip-worn accelerometers for 7 days and including data in analysis if a participants contributed at least 10hours of wear-time on at least 4 days including 1 non-school day. The small sample size and short duration sparked concerns about the reliability of the findings. The non-participating population may have performed different amounts of MVPA (substantially more or less) and in different settings (in school or away from school), and the participants may have performed atypical amounts of MVPA on the small

number of monitored days (again, either substantially more or less). It remains difficult to be convinced about the confidence in habitual PA that 4-7 days of PA tracking can really generate. The authors concluded that the amount of MVPA recorded by the participants was comparable for school days and non-school days. Whilst this was in line with the key group-level finding of the current study, it may well have reflected the same pattern, that weekday/weekend day or school day/non-school day PA patterns varied between individuals, but this was not identified by Beemer et al. (2021).

In addition to directional variation, there was also a notable disparity in amount of difference. For some participants there was only a difference of 1 minute between median time spent in MVPA for weekdays and weekend days. However, other participants recorded a difference of as much as 34 minutes. The longer duration of PA monitoring employed in this study has facilitated the more detailed investigation of the relationship between weekday and weekend day PA levels which has not been possible to assess reliably before with only single weekend days included in analysis.

9.2.1.2 Comparing the levels of physical activity of male and female participants

On average, female participants achieved less time in MVPA than male participants: the mean of individual participants' median daily time in MVPA was 17 minutes for females and 21 minutes for males. Furthermore, females occupied a greater proportion of the inactive group than males with 61% (30 of 49) of the participants achieving a median time spent in MVPA of <20 minutes being female. This was supportive of literature discussed in chapter 2 (Selvadurai et al., 2004, Baker and Wideman, 2006). The systematic review conducted by Puppo et al. (2020) concluded that females tended to have less PA than males, and that this remained true for CYPwCF and the non-CF control groups. Valencia-Peris et al. (2021) also reported that the male participants in their study did 30 minutes per day more MVPA than the female participants, and that the healthy males were the most active group and females with CF were the least active. The different approaches to measuring MVPA (accelerometers vs HR tracking) and different duration of

participation meant that direct comparison of daily time spent in MVPA between this study and the Valencia-Peris et al. (2021) study was not possible. However, the common finding that female CYPwCF were less active than male CYPwCF, and that this remained true for the non-CF populations involved in PA studies albeit with substantial differences in magnitude of difference, suggest that this finding was important to note (Sallis et al., 2000, Blaes et al., 2011, Ruiz et al., 2011, Cooper et al., 2015, Jago et al., 2017, Farooq et al., 2017, Wang et al., 2019, Llorente-Cantarero et al., 2020, McLellan et al., 2020, Farooq et al., 2020).

However, there appeared to be more extreme PA behaviours in the female participants than male. Females occupied a greater proportion of both the extremely inactive days (0minutes of MVPA: 6.6% of female days, 5.5% of male days) and extremely active days (≥ 120 minutes of MVPA: 1.7% of female days, 1.4% males days) than males, albeit by fairly small margins. This finding warrants further investigation in future research.

Further sex-based differences were also noted. Interestingly, at a group level, the male participants in this study recorded more time in MVPA on weekdays than weekend days whilst the opposite was true for the female participants. When the weekday/weekend day patterns of PA were examined for individual participants, it was clear that a small majority (54%) of males were more active on weekdays than weekend days but only 26% of females. There were more notable increases in the proportions of active and very active days for female participant on weekend days over weekdays which did not occur with the male participants. This suggested that the weekly patterns of PA may be different for males and females, as well as overall levels of PA. This detail was not reported by Mackintosh et al. (2018) as the investigators did not find any significant differences in key anthropometric or lung function measurements between boys and girls so pooled all accelerometer data for analysis. Similarly, Blaes et al. (2011) pooled the PA data from their male and female participants (non-CF) thus were not able to analyse differences in weekday and weekend day levels of PA between males and females. Wang et al. (2019) and McLellan et al. (2020) did analyse the weekday/weekend day PA patterns by males and females. The authors of both studies reported that boys achieved more time in

MVPA than girls on weekdays and weekend days, and that, in contrast to the findings of the current study, both males and females were more active on weekdays than weekend days. Participants were only required to wear the hip-worn (Wang et al., 2019) or wrist-worn (McLellan et al., 2020) accelerometer for 3 weekdays and 1 weekend day for their data to be included in analysis. The longer duration of PA monitoring in the current study may have resulted in the inclusion of many more weekend days, compared to only a single weekend day collected by Wang et al. (2019) and McLellan et al. (2020), and thus more variety of amount of MVPA recorded on these days leading to the varied levels identified in the female participants.

9.2.1.3 Comparing the levels of physical activity of the different age groups

There were also differences in time spent in MVPA by the different age groups. Participants in the youngest age group, 6-8years old, achieved more low/moderately low PA days (0-39minutes of MVPA) than the 2 older age groups (9-11years and 12+years). The youngest age group also achieved the smallest proportion of very active days (≥ 60 minutes MVPA) when compared to the 2 older age groups. The oldest age group demonstrated the most varied PA levels with the highest proportion of days with no MVPA recorded as well as also achieving the highest proportion of active days (≥ 40 minutes MVPA). This remained true when the median daily time spent in MVPA of individual participants was explored. The oldest age group (12+years) had the greatest proportion of participants with median daily time spent in MVPA of < 20 minutes or ≥ 40 minutes compared to either of the other 2 age groups. However, the oldest age group had the smallest proportion of participants who did not achieve 60minutes of MVPA on a single day of participation (11.1%). This was almost half of those in the younger 2 age groups (20.8% in 9-11year olds and 22.2% in 6-8year olds). Overall the results suggested that daily time spent in MVPA changes with age, that younger participants were more consistently active but at a low or moderately low level and the older age group demonstrated more variety with some only occasionally achieving active days but others regularly achieving a larger amount of MVPA each day. This could be explained by participation in structured activities which last an hour or more,

such as team sport training and/or matches, which younger children are less likely to participate in. This would also account for the variability, in the older age group, as some young people participate and others do not. This finding is not entirely in line with previous literature. As discussed in chapter 2, there have been a large number of studies reporting that levels of PA fall with age (Blaes et al., 2011, Ruiz et al., 2011, Cooper et al., 2015, Van Dijk et al., 2016, Jago et al., 2017, Farooq et al., 2017, Llorente-Cantarero et al., 2020). Furthermore, a systematic review and meta-analysis conducted by Farooq et al. (2020) concluded that amount of MVPA declines annually from the age of 6years in girls and 9years in boys. This comprehensive review considered 52 studies with a subset of 31 contributing change in amount of MVPA data of at least 1 year duration to the meta-analysis. Whilst these cited studies and systematic review were all investigating CYP who do not have CF, Valencia-Peris et al. (2021) investigated the PA levels of CYPwCF and also concluded that time in MVPA reduced with age, by 13minutes per day from 6 to 17 years old for the CYPwCF group.

There were a number of possible reasons for the difference in this key finding. The current study involved tracking PA over a longer period of time. Participants in all of the other cited studies (and those included in the systematic review) wore the PA tracker for a maximum of only 8 days. It is possible that the longer duration of tracking enabled the detection of more variety of PA behaviours in the older age group. The cross-sectional nature of the PA tracking may have resulted in different findings when compared to studies which used longitudinal PA tracking repeated at various time intervals in the same participants (repeated at 1years (Van Dijk et al., 2016, Farooq et al., 2020), 3years (Jago et al., 2017), pre-pubertal and pubertal (Llorente-Cantarero et al., 2020), and 2, 5 and 8years (Farooq et al., 2017)). However, studies that employed a cross-sectional design reported comparable findings indicating that this was not the sole reason for the additional finding of varied PA levels of older participants of this current study (Blaes et al., 2011, Ruiz et al., 2011, Cooper et al., 2015, Valencia-Peris et al., 2021). The older CYPwCF who participated in this study may have demonstrated different patterns of PA, with the notable variety of levels, compared to those investigated previously. There are a

number of potential reasons for this finding. This may represent PA maintenance behaviours which have not been identified before in a general population of young people. Or it may be specific to young people with CF who have received specific support from clinical services over the years. This support may have worked for some participants, thus some participants demonstrated high levels of PA, but did not work for others who demonstrated low levels of PA.

The weekday/weekend PA patterns also varied by age group although there was not a clear relationship between age and weekday/weekend pattern of PA. The majority (58%) of the 6-8 year old participants were more active on weekend days than weekdays and only 28% of this youngest age group were more active on weekdays than weekend days. This was perhaps the most defined link between age group and weekday/weekend PA pattern. Half of the participants aged 9-11years were more active on weekdays than weekend days compared to 42% who were more active on weekend days than weekdays. And the oldest age group, 12+years, were split equally with 44% more active on weekdays and 44% more active on weekend days. This was in line with the finding that the levels of PA of older CYPwCF were more varied between individuals and therefore weekday/weekend day patterns were also less predictable. This finding was different to the published literature. Blaes et al. (2011) aimed to investigate changes in different levels of PA from childhood to adolescence using accelerometers, and reported the differences between school days and non-school days. The 361 participants from a peri-urban area of France (94 from pre-school aged ~4years, 156 from primary school aged ~9years and 111 from junior high school aged ~12years) contributed PA data from 4 school days and 3 non-school days. The authors reported that more PA occurred on school days than non-school days across the range of age groups, and that the decrease in levels of PA associated with age was greater for non-school days than school days. Khawaja et al. (2019) also investigated the differences in PA behaviours and location of PA (including in or out of school) according to gender and age. This mixed-methods study used global positioning system (GPS) and HR monitoring in 119 CYP from 2 age groups (9-11years and 11-13years) from a single school in the West Midlands, UK. The authors concluded that time spent in MVPA was similar on

days in school and days out of school. They also reported that participants in the older age group spent more time in MVPA than the younger age group, and that girls spent more time in MVPA than boys. These findings were in contrast to much of the reported literature but may be as a result of the study design. Participants were asked to wear the GPS and HR tracking device for 4 consecutive days, however data were included in analysis if a single hour of GPS and HR data were returned. Only 60 participants returned at least 1hour of GPS and HR data thus raising questions about how representative the findings were of the whole population. The work developing wear-time inclusion criteria in this current study (section 8.4.2.1) has demonstrated the importance of valid wear-time for establishing patterns of PA. The limited wear-time (as low as 1hour) may have resulted in over- or under-estimations of time spent in MVPA thus limiting the reliability of the findings. Furthermore, the longer duration of PA tracking in this current study resulted in far more weekdays and weekends being included in analysis. This might have led to a more accurate representation of habitual levels and patterns of PA on different days of the week. Studies that only included a single weekend day may have inadvertently captured an unusually active or inactive day for individual participants and less indication of habitual PA.

9.2.2 Patterns of physical activity maintenance in children and young people with CF

The longer duration of PA tracking employed by this study meant that it was possible to detect how levels of PA changed within and between CYPwCF over time. There is a dearth of literature exploring the longitudinal patterns of PA, or maintenance of PA, in CYPwCF. Studies have been conducted and reported on the patterns of PA maintenance in samples of healthy CYP, however there are many differences in how the authors define 'pattern' of PA. Gomes et al. (2020) conducted a systematic review of literature (published to October 2019) pertaining to the concept, operational definitions, measurement tools, statistical analyses and health implications of children's PA patterns. The review included literature relating to healthy children rather than those with CF and was limited to a slightly younger cohort (6-11year olds) than the CYPwCF included in this study, but the findings may

be transferable to the CF population given the proven similarities in levels of PA between CF and non-CF populations. The authors concluded that there have been many different approaches to defining and analysing patterns of PA in children and suggested that the term PA pattern should be used when investigating similarities or differences between children as well as stability or changes at an intra-personal level. The LCGA model reporting 5 classes of PA in this study fulfils those criteria (by identifying intra-personal stability/changes and inter-personal similarities/differences), and thus could be considered an appropriate method of reporting patterns of PA in CYPwCF.

It is clear that the health and well-being benefits associated with MVPA are only realised in those CYPwCF who maintain adequate levels of MVPA regularly (Radtke et al., 2017, Hebestreit et al., 2019). Guidelines for PA in the UK recommend that CYP should achieve an average of 60minutes of MVPA per day across each week to experience important health and well-being benefits (Department of Health and Social Care, 2019). The studies reviewed by Gomes et al. (2020), reporting on patterns of PA in CYP, all collected PA data for a much shorter duration than this study. Length of PA data collection ranged from 3hours to 2weeks, with only 7 of the 76 reviewed studies monitoring on more than 1 occasion. It was questionable as to whether the short durations of PA data collection employed in these studies would be able to detect reliable levels of habitual MVPA, or if some or all of the participants changed their PA behaviour for the short duration of monitoring. Furthermore, there were few studies that employed data analysis strategies to identify different patterns of PA within study samples. The unique longevity of continuous PA data collected in this study enabled the analysis of patterns of PA maintenance in CYPwCF over time by LCGA. The LCGA model identified that patterns of PA maintenance were varied in this sample. The majority of participants were fairly consistently active to a low or moderately low level: 65% were allocated to classes 1 (low level of daily MVPA and no change over time) and 2 (moderately low with a slight fall in daily MVPA). This significant proportion of CYPwCF would have been missing the important health and well-being benefits associated with higher levels of PA.

A small but notable proportion (14%) demonstrated a substantial fall in daily MVPA from a relatively high level (55minutes per day) to a low level (16minutes per day). This dramatic fall in recorded daily MVPA may represent the novelty effect of tracking PA which diminished over time, or it may be as a result of a real fall in habitual PA. Either way, the participants allocated to this class were at significant risk of losing the health and well-being benefits associated with higher levels of PA. Furthermore, this class demonstrates the importance of PA tracking over a longer continuous duration. Tracking PA for a shorter duration, as many other studies have reported, would have resulted in these participants being allocated to a high PA level class and the risk that they face would be missed. Clinicians need to be aware of this and assess levels of PA over an appropriate duration, or even better continuously, if they are to identify CYPwCF who are in need of support to achieve and maintain high levels of PA.

Only 12% of participants were allocated to class 3 which was the only pattern of PA maintenance that demonstrated any increase over time. Furthermore, 9% of participants were allocated to class 5 which represented high levels of PA which fell slightly. The relatively small proportion of participants allocated to these 2 classes of the LCGA model maintained a moderate to high level of PA, associated with health and well-being benefits.

The small number of studies that explored patterns of PA were conducted in non-CF populations. Armstrong et al. (2021) used cluster analysis to identify 4 distinct clusters of different patterns of PA, and the relationships between different activity states on school days and non-school days, in a sample of 240 children from a single school district in South Carolina, USA. The study design was similar to that of the current study: HR data were collected by Fitbit Charge 2 as indication of activity. In total, 196 children (mean age 7years) contributed 6642days of HR data (median 22days/child) from which the investigators calculated daily time spent in MVPA (as well as other activity states) using threshold values from the heart rate reserve (HRR) ($HRR = HR_{peak} - RHR$) of each participant. The 4 clusters of different patterns of behaviours identified by the investigators did not indicate change in amount of MVPA over time which was achieved in the current study. In agreement with the

findings of the current study, Armstrong et al. (2021) reported that the links between activity states and school/non-school day varied in magnitude and direction between individuals. The similarities in study design, instruments used and processing techniques resulted in some useful comparisons. The different group-level and individual-level findings were congruent. For example, the current study identified that, at a group level, levels of MVPA were comparable for weekdays and weekend days. However, the individual-level analysis revealed notable differences in direction and magnitude of difference in amount of time in MVPA on weekdays and weekends for individual participants. Armstrong et al. (2021) also concluded that activity patterns were different on school days compared to non-school days, but the magnitude and direction of these effects differed across individuals.

Volmut et al. (2021) investigated the longitudinal changes in PA and inactivity associated with school summer holidays by measuring PA (by hip-worn accelerometer) on 2 occasions during the school year, once during school summer holiday and then repeating at 1 year from the initial assessment point. The 93 participants, aged 6-9 years at baseline, were recruited from 9 schools in 5 areas of Slovenia. The authors reported that MVPA fell during summer holidays and remained low for a while after, but had returned to baseline level at 1 year re-assessment. The investigators employed the common accelerometer protocol of including data for analysis if participants contributed a minimum of 2 weekdays and 1 weekend day, maximum of 5 days in total. Minimum wear-time was set at 9.6 hours per day. The value of comparing this study to the current study is limited as Volmut et al. (2021) did not report differences in trajectories of PA over time. However, the authors were able to identify change in levels of PA at a group level over the course of a year, and the notable impact of the long school summer holiday.

9.2.2.1 Comparing the patterns of physical activity maintenance of male and female participants

As with levels of PA, there were differences in pattern of PA maintenance class allocation associated with sex. There was a higher proportion of females than males in the low and stable PA level class 1 (35% vs 9% respectively) and the high with a slight decrease in PA level class 5 (12% vs 6% respectively). This further supports the finding that female participants demonstrated more extreme PA behaviours than males who were perhaps more likely to be consistently active to a moderate level. Importantly, there was a greater proportion of male participants allocated to class 3, the only class to demonstrate any increase in level of PA (17% compared to 7% of females). Sex-based differences in levels and patterns of PA maintenance are particularly important when considering CYPwCF given that females with CF are already experiencing a significantly lower life expectancy than males (UK Cystic Fibrosis Registry, 2020). The results of this study suggested that some females were able to maintain PA at a high level but others seemed less able than males to be active or increase PA. It was interesting to note that both sexes occupied class 4, the group whose PA levels fell from high to low levels, equally (14% for both males and females).

Farooq et al. (2017) managed to identify different patterns of PA by group-based modelling. The investigators repeatedly monitored PA (using accelerometers) in the same cohort of CYP at ages 7, 9, 12 and 15 years, 545 in total but only 217 at all 4 time points. They analysed PA by sex and were able to identify different trajectories of daily minutes of MVPA, 4 for males and 3 for females. Females achieved less time in MVPA than males at each time point. The majority of participants were in the lower 2 MVPA trajectories (which also both fell with age), 64% of males and 81% of females. A total of 19% of females were in the highest MVPA trajectory although this still fell with age. There was a similar trajectory for 17% of the male participants, however 19% of males demonstrated stable MVPA across the study at a relatively high level. This supported the findings of the current study, that there are different trajectories in changes in amount of MVPA achieved by different CYP over time. However, again, Farooq et al. (2017) collected 'habitual' PA data for a

maximum of 7 days at each assessment point. This resulted in some clear changes in amount of MVPA recorded between time points, but did not identify the detailed level of patterns of PA maintenance that the current study did with continuous monitoring. Furthermore, the age-related findings differed from those detected by the current study.

9.2.2.2 Comparing the patterns of physical activity of the different age groups

There was little impact of age on PA maintenance pattern class allocation with fairly even representation of each age group in each of the 5 LCGA model PA maintenance pattern classes. The exception to this was the absence of any participant from the oldest age group (12+ years) in class 3, the only class to demonstrate any increase in daily MVPA.

A number of studies have reported the age-related patterns of PA in CYP, particularly across the transition to secondary school. Chong et al. (2020) conducted a systematic review of longitudinal studies investigating change in PA from primary to secondary schools. From the 6 studies reviewed, there was limited but consistent evidence of a decrease in total daily PA over the school transition period, however the evidence relating to MVPA was more conflicting with 1 study reporting a fall in daily MVPA (Marks et al., 2015), others demonstrating an increase as a result of active travel to and from school (Cooper et al., 2012, De Meester et al., 2014) and 1 study reporting an increase in MVPA on weekends but a decrease after school (Jago et al., 2012). The variety of these findings could be considered in line with those of the current study where all age groups were fairly well represented in each class of PA maintenance pattern.

Dunton et al. (2020) aimed to quantify changes in day-level PA and sedentary behaviour pattern metrics across 3 years in mid-childhood, in a US-based sample (greater Los Angeles). Participants were aged 8-12 years at baseline and contributed data at 6 monthly time intervals, on 6 occasions. A total of 169 participants contributed accelerometer data with at least 1 day of ≥ 10 hours wear-time during at least 2 of the assessment points. The majority of participants contributed significantly more than that minimum standard (mean 4.95 days/assessment point,

25.39days/study). The authors reported the common finding that boys were more active than girls at each assessment point, and also that MVPA fell from age 8 to 13years by about 30minutes. More recently, Pate et al. (2022) aimed to describe patterns of age-related change in total PA and MVPA in children transitioning from elementary school to high school. The investigators recruited children from 2 school districts in South Carolina, USA. A total of 951 children contributed all baseline data and accelerometer data, collected by hip-worn accelerometers, from at least 2 of the 5 assessment points, aged 10-17years old. Participants were requested to wear the device for 7 consecutive days at each assessment point, but accelerometer data were included in analysis if there was at least 8hours of wear-time recorded on a minimum of 2 days. The authors used growth curve analysis to identify that MVPA fell with age and that males achieved more time in MVPA than females, in line with the literature discussed in relation to levels of PA. The rate of decline varied by age with an apparent plateau by the time the female participants reached the age of 16 and 17years old, and even a slight reverse for the male participants by the same age. However, the authors acknowledged that the numbers of participants contributing by this age was substantially smaller than the younger ages and thus these results may be less reliable. Both of these studies reported a single pattern and compared males and females, but did not identify sub-groups as the LCGA model did in the current study. The varied findings may be as a result of the slightly older participants in Pate et al. (2022), or it may be the acknowledged limitation of small sample size in the older age group of that study. However, it could be that Pate et al. (2022) detected the more varied levels of PA in the older ages that were also identified in the current study.

Similar findings were reported by studies conducted elsewhere in the world. Downing et al. (2021) investigated the longitudinal changes in volume and patterns of different activity states in children from ages 3-5 to 9-11years in Melbourne, Australia. The sample size fell from 758 at the first assessment point (aged 3-5years) to 473 at the second point (6-8years) and then remained stable at the third assessment point (9-11years). PA data were collected using hip-worn accelerometers and standard protocol of 4-8days (including 1 weekend day) of

≥6hours wear-time at the first assessment point and ≥8hours at the second and third assessment points. The investigators used GEE to predict each variable based on age at the first assessment point and time between measurements. The authors reported that girls achieved less MVPA than boys at each time point, but that amount of MVPA remained stable across the 3 assessment points for girls and boys. Again, this study reported a trajectory of PA for females and males (albeit it separate trajectories for different activity states), but did not identify any sub-group patterns.

A European study conducted by Remmers et al. (2020) investigated the changes in PA patterns in transition from primary to secondary school. They analysed accelerometer and GPS data from 175 participants who wore a hip-worn accelerometer for 7days on 2 occasions, 1 year (and school transition) apart. In line with the findings of other studies, the authors concluded that boys recorded more MVPA than girls, and that MVPA fell with age and across the transition from primary to secondary school. This was more notable for weekend days (55.1minutes/day to 34.3minutes/day) than weekdays (43.9minutes/day to 34.0minutes/day). Interestingly, this was the only study to report more time in MVPA on weekend days than weekdays, albeit only at the first assessment point. This study was conducted in the Netherlands where the PA behaviours and opportunities may be different to those of other populations. Data were collected in April to July of 2 consecutive years. This time of year, spring to early summer in the Netherlands, is associated with better weather and therefore weekend activity levels may be increased. The authors appeared to use the term 'pattern' to refer to the relationship between the amount of MVPA achieved on weekdays and weekend days, and commented on the changes in this relationship over the course of the year. This was less detailed than the patterns identified in the current study.

All of these studies, as with the vast majority of PA pattern studies, only required a short duration of accelerometer data at each assessment point. It was possible that this short duration did not capture true habitual PA and therefore misrepresented the levels of PA of the participants. It is difficult to be convinced of the ability to detect true patterns with only occasional assessment for short duration.

Furthermore, whilst claiming to identify patterns of PA, each of the studies discussed above only reported single group-level findings rather than the different clusters or group trajectories identified by Armstrong et al. (2021) and Farooq et al. (2017).

Farooq et al. (2021b) did recognise different sub-groups of patterns of PA. The investigators further analysed the PA data reported in Farooq et al. (2017) (discussed in more detail in section 9.2.2.1) and used multi-trajectory modelling to identify latent groups for time spent in MVPA and sedentary behaviour jointly across childhood and adolescence, and test the associations with adiposity outcomes in adolescence. In this later work, Farooq et al. (2021b) combined PA data for males and females, stating that the attrition of participants by age 15years was too great to analyse sexes separately. The 4 MVPA trajectories for this combined group were similar to those identified by the current study: group 1 had low MVPA at baseline and continued to fall across the duration of the study (7% of sample), group 2 started higher at baseline but then started to decline by the second assessment point at age 9years (61%), group 3 started high still and declined from age 12 onwards (26%) and group 4 started at the highest level of MVPA, fell at each assessment point, but remained ≥ 60 minutes of MVPA daily by age 15years (6%). The combined MVPA and sedentary behaviour multi-trajectories identified 3 distinct groups of: high but declining MVPA with increasing sedentary time, low and stable MVPA with high and increasing sedentary time, and high and stable MVPA with low and stable sedentary time. Shull et al. (2020) also identified different trajectories of MVPA, although the investigators defined the different sub-groups by sport participation rather than recognising sub-groups as in Farooq et al. (2021b) and the current study. Shull et al. (2020) examined the associations between sport participation and PA in youth transitioning from middle to high school, and reported the differences in trajectories by sport participation classification. A total of 306 participants contributed accelerometer data with a minimum of 8hours wear-time for at least 2 days (maximum 7days). Participants were classified as being a sport 'participant' if they reported being part of at least 1 school or community sports team in the preceding year, otherwise they were classified as a

sport 'non-participant'. The authors reported that sport participation and MVPA fell across the transition from middle to high school (grades 7 to 9). Perhaps unsurprisingly, MVPA remained higher in sport participants than non-participants by 0.2minutes/hour (about 11%). These patterns remained true for both male and females. These findings supported those of the current study, that different and varied MVPA patterns existed in CYP, albeit with the limitations of short PA monitoring discussed throughout this chapter.

In summary, it was clear from the findings of the current study, and discussion of relevant literature, that the patterns of MVPA in CYP(wCF) were varied. A small proportion of participants (12%) increased MVPA over time. However, the majority of participants demonstrated negative changes over time, some by a large amount (14%) and others only small changes (51%). A minority (23%) remained stable over time, albeit at a low level of MVPA. Participants demonstrating these different patterns are likely to require different types and amount of support for each individual to maintain adequate levels of PA to experience the associated health and well-being benefits. Therefore, it would be helpful to accurately identify which class of PA maintenance pattern each individual is closest to.

9.3 Can the maintenance of physical activity in children and young people with CF be predicted?

As discussed in section 2.3.2, a number of correlates and determinants of levels of PA have been identified, including:

- Gender (being male) (Sallis et al., 2000, Bauman et al., 2012, Farooq et al., 2017),
- Age (inverse correlation) (Sallis et al., 2000, Bauman et al., 2012, Farooq et al., 2017),
- Education level, ethnic origin, overweight (inversely) and perceived effort (inversely) (Bauman et al., 2012),
- Positive self-efficacy for PA (Sallis et al., 2000, Spink et al., 2006, Moola et al., 2012, Bauman et al., 2012, Patterson et al., 2016),

- Finding activities enjoyable/fun (Spink et al., 2006, Moola et al., 2012, Poobalan et al., 2012),
- Positive body image (Poobalan et al., 2012),
- Temperament- those who enjoy high intensity stimulus activities (high intensity pleasure) and are highly active, impulsive and quick to respond (high surgency) (Janssen et al., 2017),
- Parental support and facilitation (Sallis et al., 2000, Prasad and Cerny, 2002, Spink et al., 2006, Moola et al., 2012, Bauman et al., 2012),
- Support from peers and others (Sallis et al., 2000, Prasad and Cerny, 2002, Spink et al., 2006),
- Activity provision at school and longer breaks (Morgan et al., 2016),
- Proximity to facilities (Prasad and Cerny, 2002, Spink et al., 2006).

Whilst the correlates and determinants listed above were identified in the non-CF population, it is pertinent to consider them in relation to CYPwCF and may be useful to identify individuals who may be at risk of struggling to maintain adequate levels of PA. Farooq et al. (2021a) investigated the factors associated with patterns of PA, having established the different trajectories of MVPA and sedentary behaviours in Farooq et al. (2021b). This was perhaps the first time that the factors associated with maintaining PA over time were identified. In the later study, Farooq et al. (2021a) explored the factors associated with being in the most favourable trajectory across childhood and adolescence. The authors reported that non-modifiable factors, including being male and higher socio-economic status (SES), and modifiable factors, including commuting to school at age 7, access to a safe play environment at age 7 and sports club participation at age 12, resulted in a twice greater probability of being in the most favourable trajectory. There was some agreement with the findings of the current study, where female participants were found to be less active than male participants. However, the key finding that female participants actually demonstrated more extreme variety of PA meant that more detail was required to try and accurately predict pattern of PA maintenance in CYPwCF. The current study demonstrated agreement between a number of correlates with levels of PA and those of PA patterns (changes in PA over time), but

to-date, there was no evidence of factors that could be used to predict pattern of PA maintenance, and specifically in CYPwCF. The current study aimed to investigate whether 3 easy-to-use clinical tests and questionnaires could. Each outcome measure, and its value in predicting level and pattern of PA maintenance in CYPwCF, will be discussed in turn, followed by the impact of combining results for all outcome measures.

9.3.1 Exercise capacity

Exercise capacity was measured by 10m-MSWT, a functional, maximal exercise test which has been validated for use with CYPwCF. Analysis of data indicated that there was no sex-based difference in performance, female participants performed as well as male participants. A number of studies have demonstrated a positive association between exercise capacity and PA, or time spent in MVPA, in adults with CF (Cox et al., 2016, Troosters et al., 2009, Savi et al., 2015, Savi et al., 2013). However, Curran et al. (2022) conducted a systematic review of investigating the effect of interventions on levels of PA and other secondary outcomes, including aerobic capacity in people with CF. Of the 6 studies identified by the investigators that examined the impact that an increase in PA had on aerobic capacity, 3 demonstrated an associated increase in aerobic capacity and 3 demonstrated no increase in aerobic capacity. The authors concluded that it should not be assumed that an increase in PA results in an increase in aerobic capacity. This was in line with the findings of the current study where the link between levels of PA and exercise capacity was not clear. Figure 78 displayed the range of low to high exercise capacity achieved by highly active participants, and the range of levels of PA recorded by participants who achieved a high exercise capacity. Whilst some participants who were highly active achieved a high exercise capacity result, others did not, and vice versa.

9.3.2 Self-efficacy for physical activity

The results of this study identified that self-efficacy for PA (measured by CSAPPA) was lower for participants in the older age group (12+years) than those in the younger 2 age groups. This remained true for male and female participants.

Interestingly, the lower total score appeared to be driven by a fall in predilection and enjoyment domains, but the adequacy domain score remained more stable across the age groups. This was in contrast to previous literature. Adank et al. (2021) investigated the longitudinal associations between motor competence (measured using a series of validated locomotor and stability tasks) and PA enjoyment with daily MVPA in 359 CYP aged 10years at baseline in the Netherlands. Participants underwent assessment annually over 3 school years (aged 12years at final assessment point). PA data were collected by hip-worn accelerometers, worn for the standard protocol of 7days at each assessment point. PA data were included in analysis if a participant contributed at least 480minutes of wear-time on at least 2 weekdays. PA enjoyment and satisfaction of basic psychological needs (BPN), including competence, autonomy and relatedness, in physical education were measured using validated questionnaires. The authors reported that perception of competence reported by female participants declined at a steeper rate between the second and third assessment points than males. The sample investigated by Adank et al. (2021) did not have CF. It is feasible that CYPwCF could have different self-efficacy for PA when compared to non-CF peers as a result of the previous PA or exercise support that they have received as a result of having CF (either by their clinical team or another source, such as personal training). This might be a contributing factor in the contrasting findings that perception of competence/adequacy fell in older participants in the study by Adank et al. (2021) but did not in the current study. Furthermore, the outcome measures used were different. Whilst perception of competence (measured by Adank et al. (2021)) and the adequacy domain of the CSAPPA (measured in the current study) sounded comparable, the outcome measures may have actually measured a slightly different construct. There were also methodological differences between the studies which may have resulted in the difference in findings. Adank et al. (2021) conducted a longitudinal study, thus repeated measurement of perception of competence in the same cohort of participants for 3years. The current study used a cross-sectional design for this element and then compared the results of different participants in different age groups.

Adank et al. (2021) also reported that males demonstrated a fall in MVPA across the study duration which was not observed in females, although the authors noted that females already recorded low levels of MVPA at baseline. This further difference in findings may not be a true reflection of different patterns of MVPA in CYPwCF, but may be as a result of differences in PA tracking between the studies. The current study has demonstrated that there were differences in levels of PA between weekday and weekend day, although direction and magnitude of difference for individual participants was unpredictable. Adank et al. (2021) only tracked PA on weekdays, and for a much shorter duration, thus different levels and patterns of PA maintenance may have been detected. The authors also reported that the repeated-measures linear mixed model analyses identified that PA enjoyment and motor competence were positive predictors of MVPA in girls, but motor competence alone predicted MVPA in boys. There was no clear relationship between self-efficacy for PA and levels of PA in CYPwCF identified by the current study.

Zhanbing Ren et al. (2020) aimed to examine the associations of social support and self-efficacy with levels of PA in adolescents, and the mediating effect of self-efficacy on the relationship between social support and PA. Data were collected from 2500 adolescents (aged 12-17years) from 10 schools in Shenzhen, China, although 159 datasets were incomplete and therefore excluded from analysis. Level of PA, exercise self-efficacy and social support were all measured by validated questionnaire. The authors reported that males scored higher for levels of PA and exercise self-efficacy than females. A regression analysis identified that exercise self-efficacy and social support were significant predictors for the PA level after controlling for age and gender. This remained true for females and males when analysed separately. The authors also concluded that exercise self-efficacy had a significant mediating effect on the relationship between social support and levels of PA. These findings demonstrated some congruence with the findings from the qualitative element of Phase 1 of this study: that an adult facilitator and impact of other people (including sociability of exercise) were important factors in the maintenance of exercise. However, Zhanbing Ren et al. (2020) measured levels of

PA by self-report only. The current study has demonstrated how inaccurate this can be when compared with objectively measured PA. This may be the reason that a statistically significant link was identified between exercise self-efficacy and level of PA by Zhanbing Ren et al. (2020), but not in the current study when levels of PA were more objectively measured, by PA tracker.

9.3.3 Self-reported physical activity

Self-reporting of levels of PA is an easy and frequently-used method of collecting information in the clinical setting. Studies have been published demonstrating a correlation between questionnaire-measured levels of PA and objectively measured PA (Wells et al., 2008, Ruf et al., 2012). A systematic review, conducted on behalf of the European CF Society Exercise Working Group, concluded that there was evidence of convergent validity for the HAES (Bradley et al., 2015). Furthermore, an editorial authored by an international group of PA researchers stated that self-report measures of PA continue to have an important role in the measurement of PA, and suggested that they should be used for 'screening and promoting PA in healthcare', for example 'a short questionnaire administered to patients to determine whether they are sufficiently physically active' (Sattler et al., 2021). However, the results of Phase 2 of this work clearly demonstrated that self-report, even using a validated tool such as HAES, usually resulted in important over-estimations of actual PA levels. It is important to acknowledge that the Fitbit data collection and processing methods employed in this study may have underestimated time in MVPA, therefore direct comparison of minutes spent in MVPA may be unfair. Whilst most participants seemed to over-report time spent in MVPA, some under-reported, and 6 participants were fairly accurate in their self-reported levels of PA. They tended to be female and older participants, although not exclusively, therefore it was not possible to predict who might be able to self-report accurately by other means.

The HAES reports 2 constructs. As well as measuring self-reported minutes in MVPA, it also records self-identified PA level for the day in question. The construct of self-identified PA level incorporates self-perception. An individual may consider a

day to have been active but a different individual may consider the same day, with the same number of minutes in MVPA, to have been inactive. Comparing self-identified level of PA is not likely to be a fair representation of objectively measured levels of PA. There appeared to be over-estimation of levels of PA by both HAES constructs. Furthermore, the relationship between the 2 constructs was also inconsistent. Savi et al. (2013) compared HAES reported PA with accelerometer recorded PA in adults with CF. A total of 20 adults with CF (recruited from 1 CF clinic in Rome, Italy) and 11 age-matched controls contributed 4 days of accelerometer data (2 weekdays and 2 weekend days, collected by arm-worn accelerometer) and HAES data (self-reported PA for a weekday and a weekend day). The authors reported that the HAES questionnaire over-estimated levels of PA. This study was conducted in adults with CF, but the findings of the current study demonstrated that this finding was not limited to adults and was similar in CYPwCF as well.

There was no pattern identified when self-reported time spent in MVPA for weekdays and weekend days were compared. Some participants demonstrated similarities whilst others were very different. Participants in the oldest age group (12years+) reported that they were less active for both weekdays and weekend days than the younger age groups, and the difference was greater for female participants than male participants. This pattern remained true for self-identified level of PA as well. There was no evidence found to either support or refute this finding in the literature.

The significant differences and lack of consistent pattern between HAES and Fitbit measured MVPA, and self-identified levels of PA, for the same days, indicated that HAES was not an accurate measure of time spent in MVPA. There are a number of other measurement tools (questionnaires and diaries) available that are designed to collect data on self-reported levels of PA. However, they are all subject to the individual's perception of different activity levels and the risk of recall and reporting biases. Therefore, self-reported PA should not be considered to report the same construct as objectively measured time in MVPA. This is important for clinical teams to be aware of, simply asking CYPwCF about their levels of PA will not always generate an accurate picture of actual levels of PA.

9.3.4 Predicting levels of physical activity

The results of this study have demonstrated that exercise capacity (measured by 10m-MSWT), self-efficacy for PA (measured by CSAPPA) or self-reported levels of PA (measured by HAES) alone could not predict level of PA in CYPwCF. The standard multiple regression demonstrated that the combination of all 3 outcome measures could not statistically predict level of PA either.

The profiles presented in Figure 78 demonstrate the variety of combinations of outcome measure scores. For example, participant 53 achieved high scores (green) for median daily MVPA and exercise capacity but moderately low (amber) for self-efficacy for PA and self-reported PA. In other words, this participant CAN and DOES high levels of PA and therefore was likely to experience the associated health and well-being benefits. However, this individual did not have an accurate perception of his/her levels of PA, as indicated by moderately low self-reported PA score, and did not have high self-efficacy for PA. This individual would need careful monitoring to ensure that this lack of perception and lack of self-efficacy did not have an impact on actual levels of PA in the future, and the right support implemented at the right time to maintain adequate levels of PA. In contrast, participant 60 achieved high scores (green) for exercise capacity, self-efficacy for PA and self-reported PA but low (red) for levels of PA. In other words, this participant CAN but DOES NOT achieve high levels of PA, and had confidence but an inaccurate perception of his/her levels of PA. This participant was at risk of losing the health and well-being benefits associated with physical fitness if he/she did not increase levels of PA. He/she would require specific support to recalibrate his/her perception of activity. Finally, participant 55 achieved a low score (red) for levels of PA, did not complete a maximal exercise capacity test and scored moderately low for self-efficacy for PA but moderately high for self-reported levels of PA. In other words, this participant was missing out on the health and well-being benefits associated with high levels of PA. He/she was unable to complete a maximal exercise capacity test, perhaps because the sensation of physical exertion was unfamiliar to him/her. And he/she was not confident in his/her abilities yet perception of levels of PA were inaccurate.

This individual needed different support, to develop confidence and skills in higher intensity PA and the associated sensations.

There were some participant characteristics that appeared to be more frequently associated with outcome measure categories. Male participants were more likely to achieve high or moderately high scores for median daily MVPA (DOES) and exercise capacity (CAN) than females, regardless of self-efficacy for PA and self-reported PA. Females achieved lower scores for self-efficacy for PA than males especially when associated with low median daily MVPA (DOES) and/or exercise capacity (CAN). Finally, the participants in the oldest age group (12years+) were more likely to score low or moderately low for self-efficacy for PA and self-reported levels of PA than participants in the younger 2 age groups. This remained true regardless of categorisation of median daily MVPA (DOES) and exercise capacity (CAN). However, these associations were not proven statistically and were not clear enough to enable prediction of levels of PA in CYPwCF in the future.

In summary, from a clinical perspective, those who CAN and DO high levels of PA are less at risk and therefore are not the priority for support, 31% of the sample in this study. Those who CAN but DO NOT are concerning (19% of the sample in this study), they are at risk in the future. Those who CANNOT but DO (22% of the sample in this study) may be at risk because their levels of PA have not resulted in a positive effect on their exercise capacity which is known to be a prognostic indicator in CYPwCF. This group of CYPwCF perhaps require more detailed medical assessment and management to establish the cause of their reduced exercise capacity in view of the high levels of PA. Those who CANNOT and DOES NOT (28% of the sample in this study) are at immediate risk. Importantly, any red or amber score in Figure 78 should raise concern to a clinical team and instigate appropriate support. However, the 2 objective measures (measurement of PA tracking and exercise capacity) should be considered the key outcomes for suggesting level of concern and immediacy of action required, and both must be measured if clinical teams are to be able to identify those who require support. It was not possible to predict levels of PA (DOES) in this study, thus they must be measured objectively if CF clinical teams are to identify those CYPwCF who are at risk. However, single or

limited interval measurement of level of PA have limited value and patterns of PA maintenance should be identified in order to understand the level of risk and type of support required by individual CYPwCF.

9.3.5 Predicting patterns of physical activity maintenance

The LDA conducted in this study identified that it was also not possible to predict pattern of PA maintenance by the combination of exercise capacity, self-efficacy for PA and self-reported levels of PA. There was some indication that those participants who increased PA over the duration of the study (allocated to class 3 of the LCGA model) scored higher in all 3 outcome measures, but the lack of distinct patterns in average scores for all other classes meant that this did not reach statistical significance. It may be possible to speculate that CYPwCF who score highly on all outcomes may be maintainers of PA and so don't require as much support as other CYPwCF, but this was not confirmed by this study. Furthermore, only 12% of all participants were allocated to this group, thus the vast majority (88%) of participants displayed patterns of PA maintenance that were not predictable at all. Figure 80 demonstrated that there was perhaps some association between the objective outcome measures (median daily time spent in MVPA measured by PA tracker and exercise capacity measured by 10m-MSWT) and LCGA pattern of PA maintenance class. However, this needs to be considered with caution as daily time spent in MVPA was used to generate the LCGA model, thus the median daily time spent in MVPA and LCGA class allocation were closely related.

This was the first study to identify patterns of PA maintenance in CYPwCF over at least a 2month duration, and explore the relationships between exercise capacity, self-efficacy for PA, self-reported time in MVPA, and objectively measured levels and patterns of PA maintenance. Therefore, there was no other literature available to compare findings with to answer whether pattern of PA maintenance could be predicted. The results of this study suggested that PA maintenance behaviours are complex and unpredictable, and thus level of PA was not predictable by the 2 subjective measures and pattern of PA maintenance was not predictable by the combination of subjective and objective measures. CF clinical teams must measure

PA as well as exercise capacity and consider self-efficacy for PA in the CYPwCF that they care for if they are to identify who requires support to maintain PA participation to an adequate level to result in health and well-being benefits, and who is already achieving adequate levels independently. The clinical team would then need to respond to the support requirements of each individual CYPwCF, and repeat measurements regularly to ensure the changing needs of the CYPwCF are met. Self-reported PA, as used by many clinical teams, is not sufficient and will likely result in an over-estimation of actual levels of PA in many, but not all, CYPwCF.

9.4 Methodological strengths and limitations

This study was the first to identify patterns of PA maintenance in CYPwCF. Evidence suggested that levels of PA are comparable between CYPwCF and those without CF, therefore it was feasible to consider literature pertaining to CYP who do not have CF and their patterns of PA maintenance. However, it remains important to conduct research and develop specific understanding of the patterns of PA maintenance in CYPwCF and factors associated with these. This will enable the development of appropriate support and advice which addresses the specific and more complex needs of CYPwCF over and above those of the non-CF population. This unique study has identified that it is possible to detect patterns of PA maintenance in CYPwCF but it was not possible to predict level or pattern of PA maintenance by 3 simple and frequently used clinical tools.

This study had a number of methodological strengths. According to the sample size calculation, identified in 7.5.1, data from 74 participants were required to conduct LDA (independent variables: exercise capacity, self-efficacy for PA and self-reported time in MVPA). A total of 78 participants contributed data to this study, with 74 participants each providing a full dataset. Therefore, the sample size was sufficient for LDA.

Curran et al. (2022) identified that studies reporting PA used a variety of variables, and the lack of a single or consistent variable meant that it was not possible to conduct a pooled effects analysis of PA interventions in CF as part of the systematic

review that they conducted. The authors highlighted the importance of working towards the development of a single validated measure of PA for CYPwCF. The current study was the first to analyse PA data collected using a commercially available PA tracker over a longer period of time in CYPwCF. This study has proven that this method of data capture, transfer and processing is feasible and generates useful data which can be used to determine the different PA levels and maintenance patterns of different CYPwCF. The large and multi-professional team, which collaborated on the technical framework for this study and Project Fizzyo, has developed a comprehensive data processing pipeline and enabled the use of personalised MVPA thresholds, which varied between participants, and which responded to within-participant change over time. This was responsive to varying health state and level of fitness/PA. Furthermore, the length of PA tracking undertaken by this study resulted in a unique insight into the PA maintenance patterns and behaviours of CYPwCF. Short-term tracking may result in the detection of PA that is not typical for the individual being monitored, either because of a conscious change in PA as a result of being monitored, or a coincidental unusually low or high active day. Tracking for a longer duration enables a more reliable detection of true habitual PA. The device selected was appropriate to use from 6years of age and throughout life, and thus could be a feasible and sensible option for tracking PA in the future, be that for clinical or research purposes.

This study also had a number of limitations. The sample, although an adequate size, may not be representative of the population of CYPwCF. Participants were recruited from 3 London CF centres and were all also participating in Project Fizzyo, a longitudinal study investigating PA and airway clearance technique behaviours. CYPwCF who were more active may have been more likely to volunteer to take part in this study as they had more interest in PA and monitoring their own levels of PA. However, the results demonstrated a wide variety of levels and patterns of PA maintenance, exercise capacity, self-efficacy for PA and self-reported levels of PA suggesting that the sample represented a spectrum of PA behaviours.

As identified earlier in this chapter, the time spent in MVPA as measured by PA tracker may have been an underestimation. The multi-professional research team,

which collaborated on the technical framework, developed this new method of data capture, transfer and processing through exploration of the data, consultation with available literature and experts, and discussion within the team. Pragmatic decisions were made when support from the evidence-base did not exist. For example, the personalised MVPA threshold by HRR was evidence-led, but the definitions of RHR and HR_{peak} were pragmatic. The details of the study by Armstrong et al. (2021) have since been published and there were some similarities in methods used, for example, Fitbits collecting HR and HRR being used to calculate a personalised MVPA threshold. However, Armstrong et al. (2021) used 50% of HRR as MVPA threshold in comparison to 40% used in the current study. This difference may be of limited impact though as the HR_{peak} used for HRR calculation in the current study was measured for each participant during maximal exercise test whereas Armstrong et al. (2021) used 197bpm for all participants. Development of a validated standardised protocol for measuring MVPA by continuous HR monitoring would add value to future research and clinical monitoring. The likely underestimation of time spent in MVPA in the current study meant that the number of participants meeting the guideline recommendations of 60minutes of MVPA per day would probably have been underestimated. Comparison of this to data reported by other studies would not have been reasonable. Furthermore, it was not possible to compare time spent in MVPA in the sample to that of other studies. It was, however, possible to compare levels and patterns of PA maintenance within the sample.

All studies involving PA tracking are limited by device wear-time. If the device is not being worn, then data is not being captured and the amount of MVPA occurring is unknown. The longer duration of this study resulted in a large volume of PA data being yielded from each participant, far more than the standard protocol of at least 3 weekdays and 1 weekend day employed by many other studies. The decisions made about required daily wear-time have been justified in this thesis and seemed similar to those made by other investigators. As discussed in section 8.4.2.1, Cooper et al. (2015) conducted an analysis of data from the ICAD. The investigators stipulated a minimum of 500minutes per day wear-time for a day to be considered

valid and included in analysis, as in the current study. This resulted in 19% of days being excluded by Cooper et al. (2015), but only 12.6% of days in the current study. This suggested that, whilst data were limited by wear-time, a relatively small number of days were lost with the vast majority meeting the requirements for inclusion and raising confidence in the findings.

The HAES was not the only measure of self-reported PA but was selected because it had the most reliability data available in the CF population (Bradley et al., 2015). The CSAPPA was also not the only measure of self-efficacy for PA in CYP, but there was limited reliability and validity data in CYP (and none in CYPwCF) in all measures, and the CSAPPA had some in a different population (Hay et al., 2004). Phase 1 of this research then demonstrated some discriminate validity as participants who identified as 'sporty' scored higher than those who identified as 'not sporty'. It is simple and easy to use so a practical tool to use in the clinical setting, therefore understanding its value in predicting maintenance of PA was important. However, it was not possible to predict levels or patterns of PA maintenance by the results of these outcomes measures, in combination with 10m-MSWT. The variety of patterns and characteristics of participants allocated to each PA maintenance pattern class suggests that it is the complexities of human behaviour that make this unpredictable and that other self-reported PA and self-efficacy for PA measures would not prove to be any better as prediction tools.

9.5 Summary

Despite, or perhaps as a result of, the methodological strengths and limitations, this study demonstrated a number of key findings:

- Levels of PA maintenance of CYPwCF were varied with the majority at a lower level. This was in line with previous literature.
- The patterns of weekday and weekend day PA varied between individual CYPwCF. This had not been demonstrated before.
- Female participants generally maintained less activity than male participants. This was in line with previous literature.

- Female participants demonstrated more extreme PA behaviours, both in terms of levels of PA and patterns of PA maintenance. This had not been demonstrated before in the CYP literature, and not been investigated before specifically in CYPwCF.
- Female participants were more likely to be active or extremely active on weekend days, whereas males were more consistently active, and slightly more active on weekdays than weekend days. This was in contradiction to previous literature.
- The oldest age group (12+years) demonstrated more varied levels of PA maintenance. This level of detail had not been identified before.
- It was possible to detect patterns of PA maintenance by LCGA, patterns were varied but the majority reduced MVPA over time. This has not been identified in CYPwCF before.
- Self-efficacy for PA was lower in the older age group but this was driven by the predilection and enjoyment domain scores. The adequacy domain scores did not show this fall. This had not been identified in CYPwCF before and was in contradiction to previous literature investigating CYP.
- Self-reported PA usually resulted in an over-estimation when compared to objectively measured PA, but there was no consistent pattern and self-report should not be considered an alternative to objectively measured PA. This was in line with previous literature.
- It was not possible to predict levels or patterns of PA maintenance in CYPwCF, these must be measured. This had not been identified before.

The key findings from phase 2 contributed to answering research questions 4 and 5, and to the overall study findings.

10 Discussion of research programme

The primary aim of this clinical research and resultant thesis was to investigate the predictors of PA maintenance in CYPwCF. The findings of Phase 1 of this project suggested that self-efficacy for PA was the strongest factor, and therefore the most likely predictor. However, the work conducted in Phase 2 of this project demonstrated that human behaviour is more complex and nuanced, thus the maintenance of PA, at least in CYPwCF, was not predictable by the outcome of 3 easy-to-administer clinical tools, including self-efficacy for PA.

This thesis addressed 5 research questions, 1-3 in Phase 1 and 4-5 in Phase 2. Discussion of the findings with the focus on addressing the research questions were presented in chapters 6 (Phase 1) and 9 (Phase 2). This final chapter provides an overview and assimilation of the findings, discussions and answers to the research questions, discusses the strengths and limitations of the research programme, and identifies implications for clinical practice.

10.1 Research questions

The first 3 research questions were addressed in Phase 1 (methods were presented in chapter 4, and results were presented in chapter 5 and discussed in chapter 6). The participants involved in this phase of work had been involved in an exercise intervention RCT, INSPIRE-CF. Research questions 4 and 5 were addressed in Phase 2 (methods presented in chapter 7, and results were presented in chapter 8 and discussed in chapter 9). An overview of the research questions and key findings is presented in Table 37.

Table 37: Summary of the research questions and key findings

Research question	Relevant study	Key finding and statistical result (where appropriate)
1. What happened to the health, well-being and PA maintenance of CYPwCF after withdrawal of a supervised exercise intervention?	Phase 1 Part A	Exercise capacity (10m-MSWT) increased during the intervention for those who received the exercise training, but this was not sustained after withdrawal ANCOVA: $p < 0.0005$ FEV ₁ z score, HRQoL and self-reported levels of PA were not affected However, trajectories for individual CYPwCF were notably varied
2. What affects the maintenance of exercise and PA in CYPwCF?	Phase 1 Part B	Self-efficacy for PA scores were higher for maintainers than non-maintainers Mann-Whitney U test: $p = 0.001$ with large effect size (0.5) Self-reported PA and parent/carer exercise barriers were not associated with the maintenance of exercise and PA in CYPwCF
3. What are the barriers to and facilitators for maintaining exercise and PA in CYPwCF?	Phase 1 Part C	Thematic analysis: Intrinsic barriers were cited more frequently than extrinsic barriers Maintenance of PA can be facilitated by sociability, fun, developing skills and achieving goals, and an adult facilitator
4. What are the patterns and maintenance of PA over time in CYPwCF?	Phase 2	LCGA identified 5 classes of maintenance of PA which varied by amount of daily MVPA and change in MVPA over time
5. Can the maintenance of PA in CYPwCF be predicted?	Phase 2	PA maintenance pattern could not be predicted by exercise capacity, self-efficacy for PA and self-reported levels of PA LDA: Eigenvalue 0.142 and $p = 0.334$

Key: CYPwCF children and young people with cystic fibrosis, FEV₁ forced expiratory volume in 1s, HRQoL health-related quality of life, LCGA latent class growth analysis, LDA linear discriminant analysis, PA physical activity, 10m-MSWT 10m Modified Shuttle Walk Test

10.1.1 Research question 1: What happened to the health, well-being and physical activity maintenance of children and young people with CF after withdrawal of a supervised exercise intervention?

This research utilised a unique opportunity to measure and report on the long term impact of an intensive supervised exercise intervention for CYPwCF. This study identified that the exercise intervention had a detectable impact on functional exercise capacity (as measured by 10m-MSWT) during the course of the intervention. This was demonstrated by a statistically significant difference between the trajectories of distance achieved during 10m-MSWT for the exercise

training and control groups during INSPIRE-CF: the exercise training group had a greater increase compared to the control group. However, this benefit was lost by the point of PA maintenance assessment: the trajectories of distance achieved during 10m-MSWT for exercise training and control groups between the end of INSPIRE-CF and PA maintenance assessment point remained statistically significantly different, but the direction was reversed. The exercise intervention did not appear to impact the lung function (as measured by FEV₁ z-score), HRQoL (as measured by CFQ-R) or PA participation (as measured by a simple unvalidated questionnaire) of the CYPwCF who took part. These findings align with the conclusion from the most recent systematic review investigating PA and exercise training in people with CF (Radtke et al., 2022). A total of 9 studies were identified as meeting the inclusion criteria, in addition to the 15 included in the previous systematic review (Radtke et al., 2017). All 9 studies involved CYPwCF, either exclusively (n = 6) (del Corral et al., 2018, Alexander et al., 2019, Gupta et al., 2019, Hatziagorou et al., 2019, Donadio et al., 2020, Gungor et al., 2021), or in combination with adults with CF (n = 3) (Carr et al., 2018, Sawyer et al., 2020, Hebestreit et al., 2022). The exercise interventions remained heterogenous in terms of type (included Tai Chi, active video gaming, pulmonary rehabilitation programme, whole-body vibration and combinations of resistance and aerobic training), level of supervision (4 supervised, 5 part-supervised), and duration (range 8 weeks to 12 months). However, none of these later studies assessed participants as part of an off-intervention follow-up design. The authors concluded with moderate certainty that PA and exercise training conducted for 6 months or more resulted in a positive impact on exercise capacity, and with low certainty that there was little or no effect on FEV₁ or HRQoL.

When the trajectories of individual participants for each outcome measure were examined in the Part A study it became apparent that there were notable variations within and between participants. There were participants in both control and exercise training groups whose exercise capacity increased at each assessment point, and others whose trajectories fluctuated between assessment points. These variations in trajectories were also apparent in lung function, HRQoL and PA

participation. This suggested that individuals within the study followed many different trajectories both during and after INSPIRE-CF. This change to understanding of the impact that PA has on the health and well-being of CYPwCF is important. Previous research has reported group-level findings with some studies demonstrating benefit to physical and/or psychosocial measures and others reporting either temporary or limited effect. The current study has clarified that group-level analysis does not explain the whole picture and that the impact that PA can have on individual CYPwCF is varied. Therefore, identifying the impact on individual CYPwCF and personalising subsequent PA advice and prescription is of paramount importance.

10.1.2 Research question 2: What affects the maintenance of physical activity in children and young people with CF?

All participants reported doing some form of PA regularly. Most of the participants who were interviewed (12 of 20) preferred informal physical activities to organised, structured sports or exercise. Half of those interviewed took part in structured exercise but only 8 of 20 reported enjoying them. Personal training was reported as being particularly useful for CYPwCF who disliked formal sports and enabled them to also experience the benefits of effective exercise. Self-efficacy for PA was the only variable which demonstrated a significant difference between those who maintained PA participation and those who did not, indicated by maintenance or increase in distance achieved during 10m-MSWT between the end of INSPIRE-CF and the PA maintenance assessment point. Barriers to PA and exercise for parents and CYPwCF self-reported time spent in MVPA and were not associated with the PA maintenance status of CYPwCF. However, parents who acted as PA facilitators for their CYPwCF had a positive impact on the maintenance of PA participation, but this status was unrelated to the parent's own levels of PA. Active parents did not appear to always result in active CYPwCF, an important aspect to note for clinicians. Exercise identity was discussed by 17 of the participants who were interviewed, and importantly appeared to be positively modifiable in 27% of the sample. However, having a positive exercise identity, either as a result of personal training or not, did not appear to indicate that an individual was more likely to maintain PA

participation. The 6 CYPwCF who were interviewed and managed to maintain PA participation had self-efficacy scores of $\geq 50/76$, suggesting that self-efficacy for PA was a stronger indicator of maintaining PA than exercise identity.

10.1.3 Research question 3: What are the barriers to and facilitators for maintaining PA in children and young people with CF?

Interestingly, the barriers that have been most frequently cited by previous studies were only mentioned in the current study in relation to parent PA participation, not the PA participation of CYPwCF. Time, will-power, energy and expense were frequently reported as barriers for parent PA, but skill, resources or fear of injury were not. For CYPwCF, the most notable barriers were intrinsic and included feeling bored with physical activities, having low self-efficacy for PA, poor skills and experience, poor attitude to PA, fear of pain and other negative sensations, and difficulties arising directly as an impact of CF. Competition was cited as a barrier for some CYPwCF but a facilitator for others, further highlighting the need for individual, personalised assessment and support. Extrinsic barriers included the influence of others, other commitments (such as homework), availability of a parent facilitator and the impact of weather/seasons. Intrinsic facilitators were also cited more frequently than extrinsic facilitators. Physical activities being fun, the positive impact of others (sociability, accountability to another and receiving praise or acknowledgement), and having skills or experience were key to supporting the maintenance of PA in CYPwCF. Recognition and a sense of achievement were important facilitators for those with lower self-efficacy for PA. Interestingly, some participants with lower self-efficacy for PA were unable to identify barriers to their own PA, suggesting that CYPwCF may first need to experience and understand supported exercise, such as personal training, in order to identify barriers to maintaining participation. Being unable to identify barriers to maintenance does not mean that there are no barriers, simply that the individual may not be aware of them.

In 15% of the parent/CYPwCF interview pairs, there was conflict between an active parent and CYPwCF who was reluctant to participate in PA. This further supported

the finding that active parents did not appear to always result in active CYPwCF. In fact in some instances, this seemed to be more of a barrier.

10.1.4 Research question 4: What are the patterns and maintenance of physical activity over time in children and young people with CF?

In line with previous literature, the findings of this research identified that some CYPwCF maintain PA whilst others do not. Furthermore, of those who did maintain, a small proportion maintained high levels of PA (12% of the sample of Phase 2) whilst the majority maintained low levels of PA (23% of the sample). The remaining 65% of participants of Phase 2 did not maintain PA and demonstrated a fall in PA over time. Half of all participants (51%) demonstrated a fall from an already low level of PA, whereas 14% exhibited a large fall from high to low levels of PA. Male participants were generally more active than female participants, however females demonstrated more extremes of levels and patterns of PA maintenance, both low and high. The oldest participants (12+years) also demonstrated more extreme low and high PA behaviours. The participants in Phase 1 of this work demonstrated that personal training was successful in assisting some CYPwCF to maintain PA by developing skills and experience, whilst it did not impact the maintenance of PA in other CYPwCF.

10.1.5 Research question 5: Can the maintenance of physical activity in children and young people with CF be predicted?

The final research question was addressed in Phase 2 of this work. The results from Phase 2 corroborated those of previous literature, that self-reported levels of PA usually resulted in an over-estimation when compared to objectively measured levels of PA. There was no consistent pattern, therefore this should not be considered an alternative to objectively measured levels of PA. PA must be measured directly in order to ascertain accurate levels of habitual PA. Findings also suggested that there were no consistent relationships between exercise capacity, self-efficacy for PA, self-reported levels of PA and levels or patterns of PA maintenance in CYPwCF. There was some indication that differences in these outcomes were detectable for the small proportion (12%) of participants who

demonstrated a slight increase in PA over time and were therefore allocated to class 3 of the LCGA, all mean scores were higher than for other classes of LCGA. However, the LDA confirmed that this was inconsistent and it was not possible to predict pattern of PA maintenance from the relationships between exercise capacity, self-efficacy for PA and self-reported levels of PA.

10.2 Strengths and limitations of the research programme

This research programme and resultant thesis had a number of novel aspects and strengths. The mixed methods design enabled the exploration of the maintenance of PA in CYPwCF, the development of the theory that self-efficacy for PA was an important factor, and then exposed that this was not strong enough to predict the maintenance of PA in CYPwCF. It also allowed the voices of CYPwCF with a unique exercise and PA experience to be heard providing a new insight into the factors affecting the maintenance of PA. Using a commercially available PA tracker facilitated the significant duration and volume of continuous PA tracking data collected during Phase 2 of this study. The data collection, transfer, cleaning, processing and analysis pipeline developed by this study provided a unique insight into the maintenance of PA in CYPwCF. PA maintenance behaviours were varied but distinct patterns were detectable with LCGA, and thus identified in this sample. This pipeline can potentially be used for ongoing data collection indefinitely.

There were also a number of limitations. The parallel design of Phase 1 of this work limited the opportunity to identify the maintenance status of participants before conducting the interviews. By identifying status of PA maintenance prior to interview (by analysing the outcome measures collected in phase 1 of this work), further interview topics may have been covered, and in greater detail, to understand the factors affecting maintenance of PA in CYPwCF. However, the design of this clinical research minimised burden to participants, and facilitated useful and unbiased insights into the factors affecting maintenance of PA in the interviewed subgroup.

The novel use of a commercially available PA tracker as a data collection tool meant that the data transfer, cleaning and processing pipeline had to be developed, and

decisions made about the cut-point for MVPA threshold. These decisions were made by the research team after exploring the evidence and data, and were largely pragmatic decisions based on consensus where the evidence-base was lacking. A change to these decisions may result in very small changes to the amount of MVPA detected. However, should improvements in process be identified in the future, it is possible to make changes within the pipeline and thus improve the process going forwards.

This method of PA tracking resulted in the quantification of time spent in MVPA. Lower intensity PA may also have an impact on the health and well-being of CYPwCF, however it was not possible to quantify time spent in lower intensity PA using HR alone with this study design. HR values above RHR but below the MVPA threshold could have been caused by factors other than lower intensity PA, thus it was not possible to accurately quantify PA at intensities less than moderate to vigorous. Incorporating accelerometry with HR tracking may facilitate the quantification of time spent in different PA intensities in the future.

10.3 Comments on the study population and generalisability of the findings

The CYPwCF who participated in this research were all receiving CF care from 3 London CF centres (only GOSH for Phase 1, and GOSH, RBH and RLH for Phase 2). This may have limited the generalisability of the findings as CYPwCF from elsewhere in the UK may have different PA experiences and opportunities. However, in terms of CF outcomes, the sample appeared to be similar to the UK population of CYPwCF (UK Cystic Fibrosis Registry, 2020). CYPwCF living in other parts of the world may receive different CF care as well as have access to different PA opportunities. The findings from this study may have limited transferability to these populations. However, the discussion of literature demonstrated that the levels, and likely patterns of maintenance, of PA are similar between CYPwCF and CYP without CF. The literature pertaining to levels and patterns of PA maintenance in the general population was international suggesting that the findings of this current research may be generalisable, albeit with some caution, to the wider international population of CYPwCF, and to some degree, CYP without CF as well.

Since undertaking this research, highly effective CFTR modulator therapies have been introduced as part of standard CF care for most CYPwCF living in the UK, and resulted in significant changes to current and future health status. It is not yet known what impact this will have on the patterns of PA maintenance in CYPwCF, however, the literature to-date has suggested that levels of PA appear unchanged in adults with CF who have had access to modulator therapies for longer than CYPwCF (Savi et al., 2019, Quon et al., 2020, Gruet et al., 2022). Furthermore, the similarities in levels and patterns of PA maintenance between CYPwCF and CYP without CF suggest that the findings of this current study will still be relevant for CYPwCF on long-term modulator therapies, as well as the 10% of CYPwCF who are not eligible for modulator therapies.

10.4 Implications for clinical practice and future directions

The findings of this clinical research have a number of implications for all stakeholders and clinical practice, as well as raising further questions to address in future research. Table 38 presents a summary of the value that this programme of research has for each stakeholder, recommendations that can be made as a result of the findings, and how the findings and recommendations will be disseminated.

Table 38: Key findings, value and recommendations identified by this research programme for all stakeholders

Stakeholder	Key finding, value or benefit	Recommendation	Mode of dissemination
Research and PPIE participants	As a direct result of the contribution of all participants, this research has identified the key findings detailed below. This has resulted an important contribution to the knowledge-base and progress towards being able to support all CYPwCF to experience the benefits of being physically fit and active.		All participants were thanked for their important contribution
CYPwCF (including research and PPIE participants)	Maintenance of PA is important for health	Maintain PA that is enjoyable and sociable	CF service newsletter
	Patterns of PA vary between CYPwCF but may also change over a lifetime	CF teams have the ability to support CYPwCF to maintain PA. Ask for help	Contact with CF team at clinic or other appointments Social media, especially through the CF Trust
Parents/carers of CYPwCF (including research and PPIE participants)	Some CYPwCF maintain PA and others do not	Engaging CYPwCF in PA from a young age, find fun and sociable activities	CF service newsletter Contact with CF team at clinic or other appointments
	Barriers can be mitigated with the right facilitator, in many cases this was an adult facilitator but often not a parent	Discuss with CF team and other support systems (such as family, friends, school, activity groups) to share the responsibility for ensuring CYPwCF maintains adequate PA	Social media, especially through the CF Trust Conference presentations and publications

Key: CF cystic fibrosis, CYPwCF children and young people with cystic fibrosis, PA physical activity, PPIE public and patient involvement and engagement

Table 38: Key findings, value and recommendations identified by this research programme for all stakeholders continued

Stakeholder	Key finding, value or benefit	Recommendation	Mode of dissemination
Healthcare professional	Self-reported PA does not give an accurate indicator of objectively measured PA	Simply asking CYPwCF does not provide a useful insight into levels or patterns of PA. Efforts should be focused on monitoring objectively	Contact through network Conference presentations Publications
	Patterns of PA cannot be predicted by the 3 clinical outcome measures used in this research.	PA must be objectively measured if CF teams want to know with some certainty about levels and patterns of PA	
	Self-efficacy and exercise identity are important for the maintenance of PA and modifiable in some people	Assess and identify the PA support requirements of each CYPwCF, build a network of adult facilitators to support CYPwCF to maintain PA and provide social support, and praise and acknowledgement to empower many to combat their barriers to the maintenance fo PA	
Wider healthcare and academic community	Patterns of PA maintenance are measurable, varied and distinct	This novel method of collecting long-term continuous PA data with personalised rather than generic thresholds of MVPA is feasible and reproducible and could lead to a single standardised outcome measure. This is not limited to the CF population and will enable future academic research into the longer-term patterns of PA in any population	Contact through network Collaboration Conference presentations Publications
	Different people require different support to maintain PA. Some will maintain independently without any support, some will not maintain even with the most intensive support, but the maintenance of others is modifiable	Identifying whose behaviour can be modified with the right support for skill or confidence, providing social support, facilitating access to facilities or resources, or providing education about effective PA in order to adjust perception of PA	

Key: CF cystic fibrosis, CYPwCF children and young people with cystic fibrosis, PA physical activity, PPIE public and patient involvement and engagement

10.4.1 Implications for clinical practice

First and foremost, the benefits of high levels of PA for CYPwCF are only experienced as long as they are maintained. However, for some CYPwCF, maintenance of PA is not the first priority, but a change in behaviour and building up any amount of PA is required first. Current guidance of an average of 60minutes of MVPA per day across each week is based on generic guidelines which are not specific to CYPwCF (Department of Health and Social Care, 2019).

Recommendations specifically pertaining to people with CF were developed by a large, international and multidisciplinary expert group and published as a consensus document (Williams et al., 2022). However, this document did not include specific recommendations about frequency, intensity, time or type of PA required to be beneficial to the health and well-being of people with CF, perhaps due to the difficulty with producing robust evidence. There has been some suggestion that at least 150minutes per week of MVPA is associated with clinically important benefits to FEV₁ in CYPwCF (Main et al., 2022). MVPA data were reconciled with longitudinal clinical data for each CYPwCF. The effect of habitual MVPA on FEV₁ was estimated using a linear mixed effects model which accounted for disease severity, age, use of intravenous antibiotic and use of modulator therapies. The model identified that 25-150minutes of MVPA per week was associated with 2% benefit to FEV₁ over the course of a year, but 150minutes of MVPA per week produced >5% benefit to FEV₁ over a year. Achieving 150minutes of MVPA per week is more feasible than 60minutes per day for CYPwCF who already have substantial time burden of additional CF treatments.

The current research has also identified that self-efficacy for PA and exercise identity are important for PA maintenance, in line with the PAM proposed by Nigg et al. (2008) (Figure 1). Furthermore, self-efficacy for PA and exercise identity are modifiable with the right support, but do not predict patterns of PA maintenance. Personalised assessment is required to enable clinical teams to recognise those CYPwCF who need assistance and support to build up healthy levels of PA and then maintain participation, and those who are active enough and able to maintain without the investment of limited resources. Self-reported levels of PA are not an

accurate representation of actual level of PA. Clinical teams should not just ask what PA is being done. Routine objective assessment of PA is important if a clinical team want to gain an accurate understanding of the levels of PA of their individual patients. Long term PA tracking is feasible and generates useful insights into levels of PA. The Fitbit data processing pipeline has been developed and can be used to continuously monitor PA. Patterns of maintenance of PA exist and are identifiable by LCGA. The LCGA model developed in this research can be used to identify PA patterns in CYPwCF in the clinical setting. Whilst this could provide useful insights for CYPwCF and their clinical support teams, this level of assessment will require significant resources and infrastructure to facilitate continuous measurement of PA, storage and analysis of the data, as well as training and staffing to support personalised PA prescription, and to support to change and maintain behaviours.

Healthcare providers may ask whether supporting PA should be the priority for CF clinical teams when this is a public health issue relevant beyond the CF community, and consideration should be given as to why CF should have the priority over other long-term health conditions. However, the benefits of PA to CYPwCF are well documented and supporting PA has been identified in UK standards of care guidelines (Cystic Fibrosis Trust, 2020). Thus, it is important that CF clinical teams do provide some level of support to their patient groups to enable all CYPwCF to achieve adequate levels of PA and to realise the associated health and well-being benefits. CF clinical teams need to know, with more certainty, the threshold of frequency, intensity, time and type of PA required for health and well-being benefits in order to support their patient groups effectively, but not over-commit valuable and limited resources. Supporting the achievement of elite athlete status for all CYPwCF is not the responsibility of resource-limited clinical teams.

Understandably, self-report methods have been widely used by clinical teams due to their ease and low cost. This programme of research has demonstrated the limited value of this method of PA measurement. The regular measurement of self-efficacy for PA and patterns of maintenance of PA, possibly as part of the annual assessment, would facilitate the detection of changes or problems in PA maintenance at an early stage and enable the provision of personalised support to

mitigate any associated difficulties. However, the frequency of measurement has not been analysed as part of this research so could be considered for research in the future. Investigation into how frequently PA maintenance patterns or behaviours change, and if there are key time periods, or ages/stages, where this is more likely to happen could help the focus for repeat assessment.

The package of assessment suggested by this research will be substantially more costly, both financially and in time, and staffing resources. However, if CF clinical teams are going to continue to prescribe PA then accurate measurement must be implemented. The CF community in the UK is relatively small but well-coordinated. This offers an opportunity for the infrastructure required for continuous PA tracking to be developed providing access to all CF clinical centres, thus optimising benefit and minimising cost. Many CF centres adopted the use of CPET as an annual assessment of exercise capacity. Whilst the expensive facilities are often already available in hospital settings, there are substantial costs associated with conducting these tests regularly, and time and skill is required for thorough and appropriate data interpretation. However, this research has demonstrated that assessing exercise capacity alone does not provide enough information to adequately prescribe and support PA in CYPwCF. The Capability, Opportunity, Motivation, Behaviour (COM-B) model of behaviour provides a useful framework to contextualise the findings and suggested package of assessments (Michie et al., 2011). The direct objective measurement of PA pattern could identify CYPwCF who require support to maintain adequate levels of PA. Measuring exercise capacity, self-efficacy for PA and self-reported levels of PA would then provide insight into which component requires focus (Figure 82).

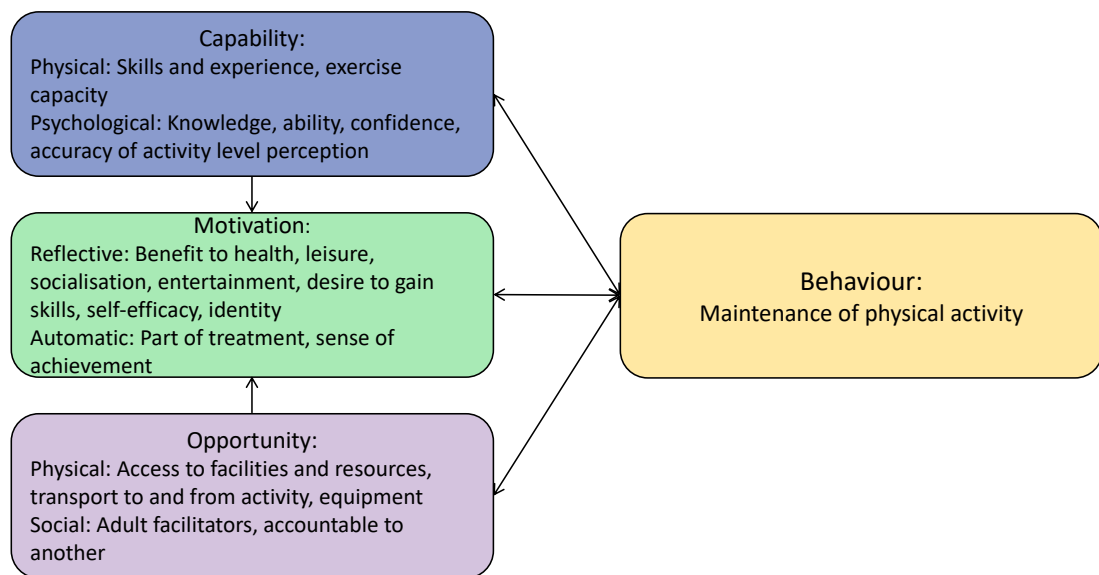


Figure 82: Key findings of this programme of research mapped to the COM-B model of behaviour (Chater et al., 2020, Michie et al., 2011)

Finally, this research has demonstrated that people are important: an adult facilitator, social support, praise and acknowledgement all seem to mitigate barriers in the maintenance of PA in CYPwCF. Clinical teams can foster this advice and facilitate appropriate and valuable support for CYPwCF.

These findings and recommendations for clinical practice are in line with behaviour maintenance theories and published literature. As previously identified, Nigg et al. (2008) suggested the importance of 5 factors when considering PA maintenance: goal-setting (satisfaction, attainment, commitment), motivation (self-motivation, pros/cons) and self-efficacy (relapse self-efficacy and barrier self-efficacy) are potentially modifiable and should be considered for intervention design, and life stress and PA environment should be considered as potential influencing factors. These factors were identified in this 2 phase research programme. Kwasnicka et al. (2016) also suggested 5 factors that should be considered in relation to supporting maintenance of behaviour (Table 39). Whilst these theories relate to adults and there are other factors that must be considered when the focus is on CYP (examples include impact of parents, limited independence, restricted choices), there are important similarities with the findings of the current research and recommendations for clinical practice: enjoyment, identity, self-efficacy, provision of physical and psychosocial resources, and providing social support.

Table 39: The 5 maintenance processes identified by Kwasnicka et al. (2016)

1	Helping individuals to maintain positive behaviour change maintenance motives, emphasising positive outcomes of a new health behaviour, providing behavioural options which are enjoyable, inspiring individuals to redefine themselves in line with new healthy lifestyle principles.
2	Facilitating behaviour self-regulation; for instance through self-monitoring behaviour and helping individuals to develop effective strategies to overcome behavioural barriers and to prevent relapse.
3	Facilitating habit development and maintenance for positive health behaviour changes; for instance by reshaping the environment and making healthy options salient and by cuing individuals towards healthy behaviours.
4	Providing individuals with resources that are needed to successfully maintain a new health behaviour. Resources can be physical (e.g., sport facilities, health products) or psychological (e.g., self-regulation training, mindfulness and relaxation methods).
5	Reshaping the environment at individual, social and community levels. Providing social support and introducing social changes that are in line with positive health behaviour change maintenance.

10.4.2 Future research

This programme of research has confirmed that group-based analysis provides limited insight into the maintenance of PA behaviours of individual CYPwCF, and that different behaviour patterns exist, thus a personalised approach is important. Future research should aim to explore the trajectories of individuals or subgroups rather than whole group analysis, and therefore development and utilisation of single case research methodologies. Whilst this project generated a unique dataset of long-term PA data in CYPwCF, further work should be conducted to understand how the patterns of PA maintenance change in the same CYPwCF over time, i.e. longitudinal continuous PA tracking. Future research should aim to validate a package of assessments, and frequency of re-assessment, to identify the type and level of PA support required by individual CYPwCF, and develop advice and recommendations about appropriate resources and interventions.

10.5 Summary and conclusions

In summary, this study has confirmed that the supervised exercise interventions, such as INSPIRE-CF, work for some CYPwCF but not others, and that the overall

average benefits of the exercise intervention only last as long as participation is maintained. Patterns of PA maintenance in CYPwCF vary over time: some maintain participation and some do not. This is in line with the general population of CYP. Phase 1 demonstrated that self-efficacy for PA can be affected by the right intervention. However, no clear predictors of maintenance of PA were identified in this sample, thus it may be important to directly measure exercise capacity (as a key health indicator), levels of PA (as a predictor of future health) and self-efficacy for PA (as an indicator for future levels of PA) to get a rounded picture of the factors affecting the levels of PA of each individual child or young person with CF. Measurement should be repeated regularly as human behaviour is complex and unpredictable, and support requirements are liable to change within individuals.

Future research is needed to establish appropriate targeted interventions for affecting each issue. The range of interventions may include supervised exercise interventions, social support such as online groups, adult facilitators such as mentors or youth workers, PA coaching to target behaviour change, or financial and practical support to participate in sports clubs, groups and teams. However, as with all care, any intervention needs to be personalised, especially in the age of HEMT. Furthermore, the CYPwCF who are not eligible for HEMT are at risk of feeling left behind and the health benefits of maintaining PA are of paramount importance for them to continue to benefit.

In conclusion, the maintenance of PA behaviours is not predictable. To guide PA prescription to appropriately support the maintenance of PA, levels and patterns of PA maintenance must first be measured, and clinical teams should respond accordingly. Resource intensive interventions need to be sustained for some CYPwCF but may not even need to be implemented for others. Measurement should be repeated regularly because behaviour, and therefore the support required to maintain adequate levels of PA, is likely to change as the circumstances of individual CYPwCF change.

11 References

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INSPIRE- CF TRIAL FOLLOW-UP
Information Sheet
(To be read by the child/young person and their parent/carer)

Date: 21/04/2017

REC Reference:	12/LO/1135	NHS R&D Reference:	11AR13
Funders Reference:	V1252		
Title of study:	INSPIRE-CF: a randomised controlled trial investigating the clinical and economic benefits of an alternative model of physiotherapy care for children with Cystic Fibrosis FOLLOW-UP		
Investigators:	Helen Douglas and Professor Eleanor Main		

You will be asked to complete some of tests that are familiar to you- you will have done them for INSPIRE-CF in the past. This time we would like you to do:

Child/young person

- The bleep test (you will not need to do the i-step test as well if you are attending your annual assessment on the same day)
- Lung function tests (you will not need to repeat this if you are also attending the CF clinic or annual assessment on the same day)
- Quality of life questionnaire
- Physical activity questionnaire
- A questionnaire asking what you think about exercise and INSPIRE-CF
- We would like to check what exercise you are doing by phoning you or your parent/carer in two weeks' time
- We would also like to interview a few children/young people and a parent/carer about your experiences of exercise and INSPIRE-CF

Parent/carer

- Quality of life questionnaire- about YOUR CHILD'S quality of life
- A questionnaire asking about YOU and what think about exercise
- A questionnaire asking you what YOUR CHILD thinks about exercise and INSPIRE-CF
- We would like to check what exercise your child is doing by phoning you or your child in two weeks' time
- We would also like to interview a few children/young people and a parent/carer about your experiences of exercise and INSPIRE-CF

All of your results will be made anonymous so that you cannot be identified from them. Only the researcher will have access to them and they WILL NOT be stored in your medical notes. The results WILL NOT have any impact on the care that you receive from the CF team.

Please complete ALL of the questions in each questionnaire. If you miss any out then we cannot use any of your results. We do not mind what your results are, it is important that they are honest. We are not looking at you as an individual but want to see the results of the whole group.

If you have any questions please ask the researcher at any time.

Helen Douglas

Participant Information Sheet for Children (6-10 years)
Research Study:
**Identifying predictors for participation in and maintenance of
exercise in children and young people with cystic fibrosis**



I would like to invite you to take part in this research.

Before you decide if you would like to join, it is really important that you understand what the study is about, why the study is being done and what it would involve for you. So please read and think about this carefully. Also talk to your family or friends about it if you want.

If something isn't clear or you have more questions you can ask your parents to give us a call and we can discuss it with you and your parents. Thank you for reading this.



There is not much information on what young people with cystic fibrosis think and feel about exercise, and how much they do.

I would like to meet with you at the hospital when you come for a clinic appointment 2-3 months after you started Project Fizzyo and get you to fill out two questionnaires.





Your answers and the information we get from your Fitbit™ and sleep test will help us to understand more about exercise for young people with cystic fibrosis.

I plan to meet other young people with cystic fibrosis to do the same thing. I will meet each person at a different time.

It is up to you whether you take part in the research project. You can say 'yes' or 'no'.



If you take part, it will take you no longer than 15 minutes to fill out each questionnaire, and you can stop at any time.





Your name would not be on the questionnaires so no-one will know that your answers are yours.

If you want to know the results of the study then we will give you a summary sheet at the end.

If you do want to take part, please ask your parent or guardian to read the information on their sheet with you.

Thank you for reading this information sheet.



Lead Investigator:	Helen Douglas  
Supervisors:	Professor Eleanor Main Dr Mandy Bryon
IRAS:	246187
NREC reference:	18/NE/0324

Participant Information Sheet for Young People (11-16 years)
Research Study:
**Identifying predictors for participation in and maintenance of
exercise in children and young people with cystic fibrosis**



I would like to invite you to take part in this research.

Before you decide if you would like to join, it is really important that you understand what the study is about, why the study is being done and what it would involve for you. So please read and think about this carefully. Also talk to your family or friends about it if you want.

If something isn't clear or you have more questions you can ask your parents to give us a call and we can discuss it with you and your parents. Thank you for reading this.



What is research?

People carry out research when they want to find out more about something and want to find answers to a question.

Why are we doing this research?

This research is finding out what young people with cystic fibrosis think and feel about exercise, and how much exercise they are doing. Exercise has been found to help young people with cystic fibrosis but many young people find it difficult to keep going. It is important to look at why this is so that medical teams can help young people to exercise more easily.

Why me?

You have been invited to take part because you are already taking part in Project Fizzyo and using a Fitbit™. Another 74 young people will be taking part in this study.

Do I have to take part?

No, it is entirely up to you. If you do decide to take part:

- You will be asked to sign a form to say that you agree to take part (an assent form).
- You will be given this information sheet and a copy of your signed assent form to keep.



What will happen to me if I take part?

If you decide to take part I will meet you at the hospital when you come for a clinic appointment 2-3 months after you started on Project Fizzyo.



- We will fill in a form with your mum, dad or guardian to confirm you have said yes to taking part (a consent form).
- You will fill out two questionnaires. This will take about 20 minutes.



We will look at the information from your Fitbit™ and bleep test from Project Fizzyo as part of this research. You don't need to do anything else.



Will anyone know I'm doing this?

The people in our research team will know you are taking part and the CF medical team will know.

All information that is collected about you during the research will be kept strictly confidential. You will be given a number which will be used instead.

What will happen to the results of the research study?

When the study has finished we will present our findings and we will put the results in medical magazines and websites that people can read. We would also like to put a brief summary on the hospital research website and charity website. They will be anonymous, which means that you will not be identified from them. If you want to know the results of the study then we will give you a summary sheet at the end.



What are the possible disadvantages of taking part?

There are no disadvantages to taking part that we can think of. It will take a bit of time to complete the two questionnaires. But we will try and do these on a day when you are coming to the hospital for another appointment anyway.

What are the possible benefits of taking part?

We cannot promise the study will help you but the information from this study will help CF teams to support young people like you with cystic fibrosis in the future.

What happens if there is a problem?

If there is a problem you should let me know, or your mum, dad or carer and then they can tell me or contact hospital complaints.

What if I don't want to do the research anymore?

Just tell your mum, dad or guardian at any time. They will not be cross with you. You still have the same care whilst you are at hospital.

Has anyone checked that the research is okay to do?

Before any research is allowed to happen, it has to be checked by a group of people called a Research Ethics Committee. They make sure that the research is fair. This project has been checked by the North East- Newcastle & North Tyneside 1 Research Ethics Committee Research Ethics Committee.

I want to take part. What should I do now?

You can let your parents know if you want to take part and they will let me know.

Please feel free to ask your doctors, nurses or physiotherapists any questions about the study or ask your parent/guardian to contact me, Helen.

Thank you for reading this information sheet.



Lead Investigator:	Helen Douglas	☎ ✉
Supervisors:	Professor Eleanor Main Dr Mandy Bryon	
IRAS:	246187	
NREC reference:	18/NE/0324	

Parent/Guardian Information Sheet

Title of study: Identifying predictors for participation in and maintenance of exercise in children and young people with cystic fibrosis

NREC reference: 18/NE/0324

IRAS Project ID: 246187

Researcher:

Helen Douglas, Physiotherapist and PhD student,
Great Ormond Street Institute of Child Health, UCL

Supervisors:

Professor Eleanor Main
Dr Mandy Bryon



I am inviting your child to take part in a research study. I am carrying out this study as part of completing a PhD funded by the Cystic Fibrosis Trust at University College London. It is important that your child understands why this study is being done and what I will ask your child to do if he/she decides to take part. Please read the information carefully with your child. You can talk about it with your family, friends and health professionals if you want to. Here are some answers to questions you and your child might want to ask:

What is this study about?

This research is finding out what young people with cystic fibrosis think and feel about exercise, and how much exercise they are doing. Exercise has been found to help young people with cystic fibrosis but many young people find it difficult to keep going. It is important to look at why this is so that medical teams can help young people to exercise more easily. I would like to understand what your child thinks and feel about exercise, and how much exercise he/she does.

Why is your child being asked to take part?

Your child has been invited to take part because he/she is already taking part in Project Fizzyo and using a Fitbit™. Another 74 young people will be taking part in this study.

Does your child have to take part?

Your child does not have to take part. It is up to your child to decide whether to take part. If your child wants to take part you will be asked to fill in a form to say that you are happy for him/her to take part. Your child can still change his/her mind and stop taking part in this study at any time. His/her care with the NHS will not be affected by any decisions about this study.

What will happen during the study?

If your child decides to take part I will meet you and your child at the hospital when he/she comes for a clinic appointment 2-3 months after starting on Project Fizzyo.

- I will explain the study to your child and check he/she understands it.
- We will fill in a form confirming that you and your child have said yes to taking part.
- Your child will fill out two questionnaires: one asking about what he/she thinks and feels about exercise, and one asking about what exercise he/she has done in the last week. This will take about 20 minutes.



We will look at the information from your child's Fitbit™ and bleep test from Project Fizzyo as part of this research. Your child doesn't need to do anything else.



What data will be collected?

This study will only collect data from the questionnaires. With your consent, we will look at this information along with the data from your child's Fitbit™ and the results of the bleep test and some of the hospital records information, all collected as part of Project Fizzyo. We will use this information to explore the relationships between exercise activity patterns and what your child thinks and feels about exercise.

How will the data be stored?

All data will be handled according to GDPR. UCL is the sponsor for this study based in the UK. We will be using information from your child and his/her medical records in order to undertake this study, and will act as the data controlled for this study. This means that we are responsible for looking after your information and using it properly. UCL will keep identifiable information about your child for 15 years after the study has finished.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to

be reliable and accurate. If your child withdraws from the study, we will keep information about your child that we have already obtained. To safeguard your child's rights, we will use the minimum personally-identifiable information possible.

Members of the research/CF team at your child's hospital will use your name, NHS number and contact details to contact you about the research study, and make sure that relevant information about the study is recorded for your child's care, and to oversee the quality of the study. Individuals from UCL and regulatory organisations may look at your child's medical and research records to check accuracy of the research study. Your child's research/CF team will pass these details to UCL along with the information collected from your child and medical records. The only people in UCL who will have access to information that identifies your child will be people who need to contact you or audit the data collection process. The people who analyse the information will not be able to identify your child and will not be able to find out your child's name, NHS number or contact details. Your child's research/CF team will keep identifiable information about your child from this study for 15 years after the study has finished.

The questionnaire data will be coded with a unique identification number (so that Project Fizzyo data can be matched to the correct questionnaire data) and transmitted to and stored in a secure cloud space. Personal and research data will be stored separately and analysed within the secure hospital data research environment (DRE). Access to the DRE will only be available to specific members of the research team. Your child's CF team will hold the code linking personal and research data. Therefore the research team will not be able to identify your child from the data. Any hardcopy records that are taken will be kept at a central location in a secure locked cabinet only accessible to the research team.

You can find out more about how we use your information by contacting us with the details on the final page of this information sheet

What is good about taking part?

Your child will be helping me to find out what young people with CF think and feel about exercise. This may help health professionals to understand how to help and support other young people with cystic fibrosis to keep exercising in the future, and therefore experience health benefits from being fit and active.

What is not so good about taking part?

It will take a bit of time to complete the two questionnaires, but we will try and do these on a day when you are coming to the hospital for another appointment anyway.

What if there is a problem?

If you have a concern about any aspect of this study, you should first ask to speak to Helen Douglas or Professor Eleanor Main (tel: 020 7905 2155). You can also speak to Dr Mandy Bryon at the CF unit, Great Ormond Street Hospital. If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Details can be obtained from the hospital patient advice and liaison service (PALS).

UCL is the sponsor of this research and the study is covered through UCL's indemnity scheme. No special compensation arrangements have been made for this study but you have the right to claim damages in a court of law if an unforeseen event occurs. This will require you to prove a fault on the hospital and/or any manufacturer involved.

Who is organising and funding the research?

This study is funded by the CF Trust. UCL is the sponsor for this study based in the United Kingdom and will act as the data controller for this study. UCL has assigned the day to day running of the study to the lead investigator and research team. This means that we are responsible for looking after your child's information and using it properly. Individuals from UCL and regulatory organisations may look at your child's medical and research records to check the accuracy of the research study. They will not be able to identify your child, find out their name, NHS number or contact details.

Who has reviewed the study?

An Independent Research Ethics Committee: North East- Newcastle & North Tyneside 1 Research Ethics Committee has reviewed this study 18/NE/0324. They believe that it is of minimal risk to your child.

Who will know about my child taking part?

Your child's CF medical team will know that your child is taking part, but to make sure people do not know who your child is, I will give your child a unique ID number for this study. Only people helping me with my project and I will see his/her answers to the questionnaires. They will not be allowed to tell anyone

what they saw. The paper copies of the questionnaires will be kept safely locked away in a filing cabinet at your child's hospital.

Limits to confidentiality:

Please note that assurances on confidentiality will be strictly adhered to unless evidence of wrongdoing or potential harm is uncovered. In such cases the University may be obliged to contact relevant statutory bodies/agencies.

Data protection privacy notice:

The data controller for this project is University College London (UCL) (ref number Z6364106/2018/09/29). The UCL Data Protection Office provides oversight of UCL activities involving the processing of personal data, and can be contacted at data-protection@ucl.ac.uk

What happens at the end of the study?

When the study has finished I will write about the results in a report for the University. I also plan to write about the study in a research brochure and talk about it at meetings. Nothing that I write will identify you or your child. At the end of this study I will start working on the next stage of research. Your child may or may not be invited to take part in this next stage. It will be up to your child to decide if he or she wants to take part in that stage at that time. If you want to know the results of the study then we will give you a summary sheet at the end.

Who can we contact about the study?

If your child would like to take part you can contact me, the researcher, **Helen Douglas** at UCL Great Ormond Street Institute of Child Health, Guilford Street, London, WC1N 1EH. My telephone number is _____ or email _____. I will be happy to talk to you about the study and will try to answer any questions you or your child have.

Thank you for reading this information sheet.





PARENT/GUARDIAN CONSENT FORM

Please complete this form after you have read the Information Sheet and/or listened to an explanation about the research.

CF Centre: _____ **Patient Study Number:** _____

Title of Project: Identifying predictors for participation in and maintenance of exercise in children and young people with cystic fibrosis

Lead Researcher: Helen Douglas

Principal Researcher: Professor Eleanor Main

UCL Data Protection Officer: Lee Shailer

data-protection@ucl.ac.uk

IRAS: 246187

NREC Reference: 18/NE/0324

Thank you for considering this research. The person organising the research must explain the project to you before you agree for your child to take part. If you or your child have any questions, please ask the researcher before you and your child decide whether to join in. You will be given a copy of this Consent Form to keep and refer to at any time.

I confirm that I understand that by ticking/initialling each box below I am consenting to this element of the study. I understand that it will be assumed that unticked/initialled boxes means that I DO NOT consent to that part of the study. I understand that by not giving consent for any one element that I may be deemed ineligible for the study.

Please initial box

1. I confirm that I have read the information sheet dated..... (version.....) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily
2. I understand that participation is voluntary and that my child is free to withdraw at any time without giving any reason and without their medical care or legal rights being affected
3. I agree to relevant data being collected from my child as part of Project Fizzyo and give permission for this to be de-identified and stored by the investigators
4. I agree to the anonymous results of the study being published in medical, academic and conference journals and websites (clinicaltrials.gov and/or www.isrctn.com)
5. I understand that relevant sections of my child's data collected during the study may be looked at by individuals from regulatory authorities or the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my child's records

Appendix 3- Consent form for phase 2

6. I understand that the data collected about my child may be used to support other research in the future, and may be shared anonymously with other researchers
7. I agree to my child's cystic fibrosis team being informed of their participation in the study
8. I am aware of who I should contact if I wish to lodge a complaint
9. I agree to take part in the above study
10. If you would like your contact details to be retained so that you can be contacted in the future by UCL researchers who would like to invite you to participate in follow up studies to this project, or in future studies of a similar nature, please tick the appropriate box below.

Yes, I would be happy to be contacted in this way	<input type="checkbox"/>
No, I would not like to be contacted	<input type="checkbox"/>

_____	_____	_____
Name of Parent or Guardian	Date	Signature
_____	_____	_____
Name of Person taking consent	Date	Signature



CHILD/YOUNG PERSON ASSENT FORM (6-16 years)

Please complete this form after you have read the Information Sheet and/or listened to an explanation about the research.

CF Centre: _____

Patient Study Number: _____

Title of Project: Identifying predictors for participation in and maintenance of exercise in children and young people with cystic fibrosis

Lead Researcher: Helen Douglas

Principal Researcher: Professor Eleanor Main

UCL Data Protection Officer: Lee Shailer

data-protection@ucl.ac.uk

IRAS: 246187

NREC Reference: 18/NE/0324

Thank you for considering taking part in this research. The person organising the research must explain the project to you before you agree to take part. If you have any questions please ask the researcher before you decide whether to join in. You will be given a copy of this form to keep and look at any time.

Child/young person to circle all they agree with:

- | | |
|--|--------|
| Has somebody else explained the project to you | Yes/No |
| Do you understand what this project is about? | Yes/No |
| Have you asked all the questions you want? | Yes/No |
| Have you had your questions answered in a way that you understand? | Yes/No |
| Do you understand it's ok to stop taking part at any time? | Yes/No |
| Are you happy to take part? | Yes/No |

If **any** answers are 'no' or you don't want to take part, don't sign your name

If you **do** want to take part, you can write your name below

Your name _____ Sign _____ Date _____

The researcher who explained this project to you needs to sign too:

Researchers name _____ Sign _____ Date _____

Thank you for your help.

Fw: IRAS 107522. Confirmation of Amendment Categorisation as Category A

Ledger, Sean <
Thu 09/02/2017 16:47
To: Main, Eleano
FYI

Sean Ledger BSc MSc
Senior Research Physiotherapist
UCL PhD Fellow
UCL Great Ormond Street Institute of Child Health
Faculty of Population health Sciences
Guilford Street
London WC1N 1EH

Email :
Mobile:

From: AMENDMENTS, Hra (HEALTH RESEARCH AUTHORITY) <hra.amendments@nhs.net>
Sent: 09 February 2017 16:44
To:
Cc:
Subject: IRAS 107522. Confirmation of Amendment Categorisation as Category A

Dear Sean Ledger,

IRAS Project ID:	107522
Short Study Title:	INSPIRE-CF ver. 1.0
Date complete amendment submission received:	01/02/2017
Amendment No./ Sponsor Ref:	1
Amendment Date:	07/12/2016
Amendment Type:	Non-substantial

Thank you for submitting the above referenced amendment. In line with the [UK Process for Handling UK Study Amendments](#) I can confirm that this amendment has been categorised as:

- **Category A** - An amendment that has implications for, or affects, ALL participating NHS organisations

You should now provide this email, together with the amended documentation, to the research management support offices **and** local research teams at your participating NHS organisations in England.

If you have participating NHS organisations in Northern Ireland, Scotland and/or Wales, you should communicate directly with the relevant research teams to prepare them for implementing the amendment, as per the instructions below. You do not need to provide this email or your amended documentation to their research management support offices, as we will pass these to the relevant national coordinating functions who will do this on your behalf.

Subject to the three conditions below, you will be able to implement the amendment at your participating NHS organisations in England **35 days after you notify them of the amendment**. A template email to notify participating NHS organisations in England is provided [here](#).

- You may not implement this amendment until and unless you receive all required regulatory approvals, including REC favourable opinion where applicable, (for participating organisations in England, please see 'Confirmation of Assessment Arrangements' below). You should provide regulatory approvals to the research management support offices and local research teams at your participating NHS organisations in England, plus to local research teams at any participating NHS organisations in Northern Ireland, Scotland or Wales*.
- You may not implement this amendment at any participating NHS organisations which inform you within the 35 day period that they require additional time to consider the amendment, until they notify you that the considerations have been satisfactorily completed.
- You may not implement this amendment at any participating NHS organisation that informs you that it is no longer able to undertake this study.

Note: you may only implement changes described in the amendment notice or letter.

If you receive required regulatory approvals (for participating organisations in England, please see 'Confirmation of Assessment Arrangements' below) after the 35 days have passed, you may then immediately implement this amendment at all participating NHS organisations that have not requested additional review time, or are no longer able to undertake this study.

There is no need for you to receive a letter of confirmation from the participating organisation that the amendment can be implemented, as the intended date of implementation is communicated through the above process. However, you may be able to implement this amendment ahead of the 35 day deadline, if all necessary regulatory approvals are in place and the participating organisation has confirmed that the amendment may be implemented ahead of the 35 day date.

* Where the study involves NHS organisations in Northern Ireland, Scotland or Wales, the HRA will forward regulatory approvals to the relevant national coordinating function to distribute to their research management support offices.

Participating NHS Organisations in England – Confirmation of Assessment Arrangements

Further to the details above, I can confirm that no HRA assessment of this amendment is needed.

- If this study has HRA Approval, this amendment may be implemented at participating NHS organisations in England once the conditions detailed in the categorisation section above have been met
- If this study is a pre-HRA Approval study, this amendment may be implemented at participating NHS organisations in England that have NHS Permission, once the conditions detailed in the categorisation section above have been met. For participating NHS organisations in England that do not have NHS Permission, these sites should be covered by HRA Approval before the amendment is implemented at them, please see below;
 - If this study is awaiting HRA Approval, I have passed your amendment to my colleague in the assessment team and you should receive separate notification that the study has received HRA Approval, incorporating approval for this amendment.

Please do not hesitate to contact me if you require further information.

Kind regards

Laura

Laura Greenfield | Amendments Coordinator
Health Research Authority

The OMNI Scales can be used for both perceived exertion and breathlessness.

If both outcomes are required ask one at a time, do not combine the question.

STANDARD INSTRUCTIONS

Please use the numbers on this scale to tell me how your body feels when you are running.

Please look at the person at the bottom of the hill who has just started to run. If you feel like this person when you are running you will not feel tired at all and your rating will be 0.

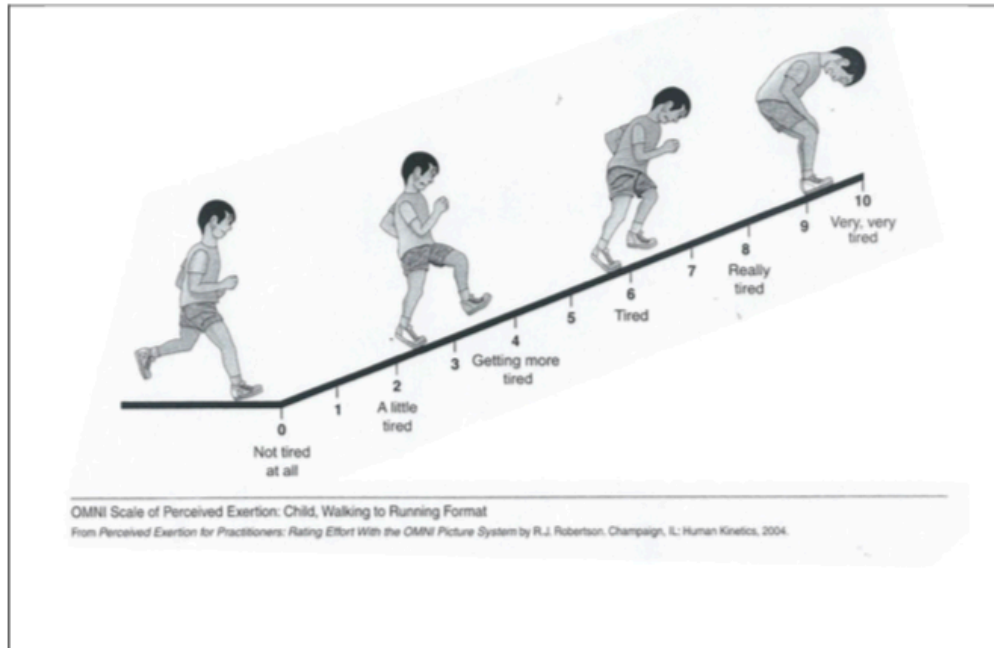
Now look at the person who is barely able to run at the top. If you feel like this person when you are running you will feel very, very tired and your rating should be the number 10.

If you feel somewhere between not tired at all and very, very tired give a number between 0 and 10.

I will ask you to point to the number that tells how your whole body feels during the test.

There are no right or wrong answers. Use both the pictures and the words to help you select a number. Use any of the numbers to tell how you feel when you are running.

How do you feel now? Please point to a number on the scale.



Tester Name: _____

Signature: _____

Date: ___/___/___

Appendix 8- INSPIRE-CF self-reported physical activity data collection sheet

INSPIRE-CF – CURRENT EXERCISE REGIMEN

Version 1.0 Date: 17.1.2013



Participant Name:

Hospital Number:



CURRENT WEEKLY PHYSICAL ACTIVITY & EXERCISE (FOLLOW-UP)

TYPE	DURATION	FREQUENCY/WK
1.	min	1 2 3 4 5 6 7
2.	min	1 2 3 4 5 6 7
3.	min	1 2 3 4 5 6 7
4.	min	1 2 3 4 5 6 7
5.	min	1 2 3 4 5 6 7
6.	min	1 2 3 4 5 6 7
7.	min	1 2 3 4 5 6 7

Nuffield membership: YES / NO

Active Luton membership: YES / NO

Local gym: _____

Telephone number: _____

Arrange to call two weeks after HAES completion to complete this form

Researcher Name: _____ Signature: _____ Date: ___/___/___

Appendix 9- Children’s Self-Perceptions of Adequacy in and Predilection for Physical Activity scale- child version

INSPIRE-CF Feedback- INSPIRE-CF ID _____

Please answer these questions to tell us what you thought about INSPIRE-CF. There are no right or wrong answers- we need your honest views. This will help us to plan and shape future exercise services for children and young people with CF. You will not be identified with your answers- no one (even the CF team) other than the researcher will see your answers, and they will NOT be stored in your notes.

Instructions:

In this survey you have to read a pair of sentences and then circle the sentence that you think is *the most like you*. For example:

Some kids have one nose on their face but Other kids have three noses on their face!

That shouldn’t be too hard for you to decide! Once you have circled the sentence that is most like you, then you have to decide if it is the SORT OF TRUE for you or REALLY TRUE for you, and put a tick in the right box. Here is another example for you to try.

Remember, first circle the sentence that is most like you and then tick if it is REALLY TRUE or only SORT OF TRUE for you.

Practice questions:

Really true for me	Sort of true for me		BUT		Sort of true for me	Really true for me
[]	[]	Some kids like to play with computers		Other kids don’t like playing with computers	[]	[]

Now you are ready to start filling in this form. There are no right or wrong answers, just what is *most like you*. Take your time and do the whole form carefully. If you have any questions just ask! If you think you are ready you can start now. BE SURE TO FILL IN BOTH SIDES OF EACH PAGE!

Part 1: Exercise and you

Really true for me	Sort of true for me		BUT		Sort of true for me	Really true for me
[]	[]	Some kids can’t wait to play active games after school		Other kids would rather do something else	[]	[]
[]	[]	Some kids really enjoy physical education class		Other kids don’t like physical education class	[]	[]
[]	[]	Some kids don’t like playing active games		Other kids really like playing active games	[]	[]
[]	[]	Some kids don’t have much fun playing sports		Other kids have a good time playing sports	[]	[]
[]	[]	Some kids think physical education is the best class		Other kids think physical education isn’t much fun	[]	[]

Child V9

Appendix 9- Children's Self-Perceptions of Adequacy in and Predilection for Physical Activity scale- child version

Really true for me	Sort of true for me				Sort of true for me	Really true for me
[]	[]	Some kids are good at active games	BUT	Some kids find active games hard to play	[]	[]
[]	[]	Some kids don't like playing sports	BUT	Other kids really enjoy playing sports	[]	[]
[]	[]	Some kids like to play active games outside	BUT	Other kids would rather read or play video games	[]	[]
[]	[]	Some kids do well in most sports	BUT	Other kids feel they aren't very good at sports	[]	[]
[]	[]	Some kids learn to play active games easily	BUT	Other kids find it hard learning to play active games	[]	[]
[]	[]	Some kids think they are the best at sports	BUT	Other kids think they aren't very good at sports	[]	[]
[]	[]	Some kids find games in physical education hard to play	BUT	Other kids are good at games in physical education	[]	[]
[]	[]	Some kids like to watch games being played outside	BUT	Other kids would rather play active games outside	[]	[]
[]	[]	Some kids are among the last to be chosen for active games	BUT	Other kids are usually picked to play first	[]	[]
[]	[]	Some kids like to take it easy during break-times	BUT	Other kids would rather play active games	[]	[]
[]	[]	Some kids have fun in physical education class	BUT	Other kids would rather miss physical education class	[]	[]
[]	[]	Some kids aren't good enough for sports teams	BUT	Other kids do well on sports teams	[]	[]
[]	[]	Some kids like to play quiet games	BUT	Other kids like to play active games	[]	[]
[]	[]	Some kids like to play active games outside on weekends	BUT	Other kids like to relax and watch TV on weekends	[]	[]

Child V9

2

Appendix 10- Children’s Self-Perceptions of Adequacy in and Predilection for Physical Activity scale- parent/carer version

INSPIRE-CF Feedback- INSPIRE-CF ID _____

Please answer these questions to tell us your thoughts about INSPIRE-CF. There are no right or wrong answers- we need your honest views. This will help us to plan and shape future exercise services for children and young people with CF. You will not be identified with your answers- no one (even the CF team) other than the researcher will see your answers, and they will NOT be stored in your child’s notes.

Instructions:

In this survey you have to read a pair of sentences and then circle the sentence that you think is *the most like your child*. For example:

Some kids have one nose on their face but Other kids have three noses on their face!

That shouldn’t be too hard for you to decide! Once you have circled the sentence that is most like your child, then you have to decide if it is the SORT OF TRUE or REALLY TRUE for your child, and put a tick in the right box. Here is another example for you to try.

Remember, first circle the sentence that is most like your child and then tick if it is REALLY TRUE or only SORT OF TRUE for your child.

Practice questions:

Really true for my child	Sort of true for my child		BUT		Sort of true for my child	Really true for my child
[]	[]	Some kids like to play with computers		Other kids don’t like playing with computers	[]	[]

Now you are ready to start filling in this form. There are no right or wrong answers, just what is *most like your child*. Take your time and do the whole form carefully. If you have any questions just ask! If you think you are ready you can start now. BE SURE TO FILL IN BOTH SIDES OF EACH PAGE!

Part 1: Your child and exercise

Really true for my child	Sort of true for my child		BUT		Sort of true for my child	Really true for my child
[]	[]	Some kids can’t wait to play active games after school		Other kids would rather do something else	[]	[]
[]	[]	Some kids really enjoy physical education class		Other kids don’t like physical education class	[]	[]
[]	[]	Some kids don’t like playing active games		Other kids really like playing active games	[]	[]
[]	[]	Some kids don’t have much fun playing sports		Other kids have a good time playing sports	[]	[]
[]	[]	Some kids think physical education is the best class		Other kids think physical education isn’t much fun	[]	[]

Appendix 10- Children's Self-Perceptions of Adequacy in and Predilection for Physical Activity scale- parent/carer version

Really true for my child	Sort of true for my child				Sort of true for my child	Really true for my child
[]	[]	Some kids are good at active games	BUT	Some kids find active games hard to play	[]	[]
[]	[]	Some kids don't like playing sports	BUT	Other kids really enjoy playing sports	[]	[]
[]	[]	Some kids like to play active games outside	BUT	Other kids would rather read or play video games	[]	[]
[]	[]	Some kids do well in most sports	BUT	Other kids feel they aren't very good at sports	[]	[]
[]	[]	Some kids learn to play active games easily	BUT	Other kids find it hard learning to play active games	[]	[]
[]	[]	Some kids think they are the best at sports	BUT	Other kids think they aren't very good at sports	[]	[]
[]	[]	Some kids find games in physical education hard to play	BUT	Other kids are good at games in physical education	[]	[]
[]	[]	Some kids like to watch games being played outside	BUT	Other kids would rather play active games outside	[]	[]
[]	[]	Some kids are among the last to be chosen for active games	BUT	Other kids are usually picked to play first	[]	[]
[]	[]	Some kids like to take it easy during break-times	BUT	Other kids would rather play active games	[]	[]
[]	[]	Some kids have fun in physical education class	BUT	Other kids would rather miss physical education class	[]	[]
[]	[]	Some kids aren't good enough for sports teams	BUT	Other kids do well on sports teams	[]	[]
[]	[]	Some kids like to play quiet games	BUT	Other kids like to play active games	[]	[]
[]	[]	Some kids like to play active games outside on weekends	BUT	Other kids like to relax and watch TV on weekends	[]	[]

IRAS: 246187

THE HAES (HABITUAL ACTIVITY ESTIMATION SCALE)

This questionnaire will ask you questions about your daily activities. Please read all of the instructions carefully and answer each question as truthfully as you can.

Name: _____

Date: _____

INSTRUCTIONS (please read!)

Please recall the activities of *one typical weekday* (choose from Tuesday, Wednesday or Thursday) and *one typical Saturday within the past 2 weeks*. For each given time period, please estimate the percentage of time that you spent in each of 4 different activity levels. For each of the time periods, the total time spent in all activity levels must add up to 100%.

The different activity levels are described below:

ACTIVITY LEVEL DESCRIPTIONS

These descriptions give you examples of activities that are typical of each activity level. You should refer back to these descriptions as often as you need when completing your estimates.

- a) **inactive** – *lying down*, sleeping, resting, napping
- b) **somewhat inactive** – *sitting*, reading, watching television, playing video games, time in front of the computer, playing games or activities which are mostly done sitting down
- c) **somewhat active** – *walking*, shopping, light household chores
- d) **very active** – *running*, jumping, skipping, bicycling, skating, swimming, games that require lots of movement and make you breathe/sweat hard

Following is a sample of a completed time period:

SAMPLE

From when you finished breakfast until when you started lunch, please estimate the percentage of time that you spent in each of the following activity levels:

a) inactive	<u>5%</u> (i.e., having a nap)
b) somewhat inactive	60% (i.e., watching TV)
c) somewhat active	25% (i.e., shopping)
d) very active	10% (i.e., riding a bicycle)
TOTAL	<u>100%</u>

Appendix 11- Habitual Activity Estimation Scale

IRAS: 246187

WEEKDAY ACTIVITY

For *one typical weekday in the past 2 weeks*, (choose from one of Tuesday, Wednesday or Thursday), please estimate the percentage of time that you spent in each activity level.

1. After getting out of bed until starting breakfast:

- a) inactive _____ %
b) somewhat inactive _____ %
c) somewhat active _____ %
d) very active _____ %

TOTAL **100%**

2. After finishing breakfast until starting lunch:

- a) inactive _____ %
b) somewhat inactive _____ %
c) somewhat active _____ %
d) very active _____ %

TOTAL **100%**

3. After finishing lunch until starting supper:

- a) inactive _____ %
b) somewhat inactive _____ %
c) somewhat active _____ %
d) very active _____ %

TOTAL **100%**

4. After finishing supper until bedtime:

- a) inactive _____ %
b) somewhat inactive _____ %
c) somewhat active _____ %
d) very active _____ %

TOTAL **100%**

Appendix 11- Habitual Activity Estimation Scale

IRAS: 246187

For the *typical weekday* that you are referring to, please answer the following questions as accurately as possible in the spaces provided.

5. At what time did you get out of bed in the morning? _____
6. At what time did you start eating breakfast? _____
7. How long did you spend eating breakfast? _____ minutes
8. At what time did you start eating lunch? _____
9. How long did you spend eating lunch? _____ minutes
10. At what time did you start eating supper? _____
11. How long did you spend eating supper? _____ minutes
12. At what time did you go to bed that evening? _____

13. For the *typical weekday* that this questionnaire has asked you about, please rate your overall level of activity (please circle one response only):

- a) very inactive
- b) inactive
- c) somewhat inactive
- d) somewhat active
- e) active
- f) very active

14. Is this "typical" Tuesday, Wednesday or Thursday that you described in this questionnaire (please circle one response only):

- a) a lot like most weekdays
- b) a little bit like most weekdays
- c) a little bit different from most weekdays
- d) a lot different from most weekdays

Appendix 11- Habitual Activity Estimation Scale

IRAS: 246187

SATURDAY ACTIVITY

For one typical Saturday in the past 2 weeks, please estimate the percentage of time that you spent in each activity level.

15. After getting out of bed until starting breakfast:

- a) inactive _____ %
b) somewhat inactive _____ %
c) somewhat active _____ %
d) very active _____ %

TOTAL 100%

16. After finishing breakfast until starting lunch:

- a) inactive _____ %
b) somewhat inactive _____ %
c) somewhat active _____ %
d) very active _____ %

TOTAL 100%

17. After finishing lunch until starting supper:

- a) inactive _____ %
b) somewhat inactive _____ %
c) somewhat active _____ %
d) very active _____ %

TOTAL 100%

18. After finishing supper until bedtime:

- a) inactive _____ %
b) somewhat inactive _____ %
c) somewhat active _____ %
d) very active _____ %

TOTAL 100%

Appendix 11- Habitual Activity Estimation Scale

IRAS: 246187

For the *typical Saturday* that you are referring to, please answer the following questions as accurately as possible in the spaces provided.

19. At what time did you get out of bed in the morning? _____
20. At what time did you start eating breakfast? _____
21. How long did you spend eating breakfast? _____ minutes
22. At what time did you start eating lunch? _____
23. How long did you spend eating lunch? _____ minutes
24. At what time did you start eating supper? _____
25. How long did you spend eating supper? _____ minutes
26. At what time did you go to bed that evening? _____

27. For the *typical Saturday* that this questionnaire has asked you about, please rate your overall level of activity (please circle one response only):

- a) very inactive
- b) inactive
- c) somewhat inactive
- d) somewhat active
- e) active
- f) very active

28. Is the “typical” Saturday that you described in this questionnaire (please circle one response only):

- a) a lot like most Saturdays
- b) a little bit like most Saturdays
- c) a little bit different from most Saturdays
- d) a lot different from most Saturdays

29. If you have any comments about your activity patterns that you think are important, please mention them on the back of this page. Thank-you.

Part 5: Exercise and YOU

A. INSPIRE-CF ID _____

B. What is your relationship to the child?

- Mother
- Father
- Grandmother
- Grandfather
- Other relative
- Foster mother
- Foster father
- Other (please describe)

C. **Definitions:**

- **Physical activity/physically active**

Any movement that is produced by contracting muscles and results in burning more calories than your body would do by resting still. It can be purposeful (sports, training), or habitual (occupational, household).

- **Exercise**

Planned, structured, repetitive and purposeful activities. It aims to improve or maintain fitness.

D. **Instructions:**

Listed below are reasons that people give to describe why they do not get as much physical activity as they think they should. Please read each statement and circle the number of the statement that most applies to you. Please answer ALL statements. If one does not directly apply to you (e.g. if you are not employed) then please consider what your response would be if it did apply to you, and give that answer.

How likely are you to say:	Very likely	Somewhat likely	Somewhat unlikely	Very unlikely
1. My day is so busy now, I just don't think I can make the time to include physical activity in my regular schedule.	3	2	1	0
2. None of my family members or friends like to do anything active, so I don't have a chance to exercise.	3	2	1	0
3. I'm just too tired after work or at the end of a busy day to get any exercise.	3	2	1	0
4. I've been thinking about getting more exercise, but I just can't seem to get started.	3	2	1	0
5. I'm getting older so exercise can be risky.	3	2	1	0

Appendix 12- Parent exercise barriers questionnaire

6. I don't get enough exercise because I have never learned the skills for any sport.	3	2	1	0
7. I don't have access to jogging trails, swimming pools, bike paths, et.	3	2	1	0
8. Physical activity takes too much time away from other commitments—time, work, family, etc.	3	2	1	0
9. I'm embarrassed about how I will look when I exercise with others.	3	2	1	0
10. I don't get enough sleep as it is. I just couldn't get up early or stay up late to get some exercise.	3	2	1	0
11. It's easier for me to find excuses not to exercise than to go out to do something.	3	2	1	0
12. I know of too many people who have hurt themselves by overdoing it with exercise.	3	2	1	0
13. I really can't see learning a new sport at my age.	3	2	1	0
14. It's just too expensive. You have to take a class or join a club or buy the right equipment.	3	2	1	0
15. My free times during the day are too short to include exercise.	3	2	1	0
16. My usual social activities with family or friends do not include physical activity.	3	2	1	0
17. I'm too tired during the week and I need the weekend to catch up on my rest.	3	2	1	0
18. I want to get more exercise, but I just can't seem to make myself stick to anything.	3	2	1	0
19. I'm afraid I might injure myself or have a heart attack.	3	2	1	0
20. I'm not good enough at any physical activity to make it fun.	3	2	1	0
21. If we had exercise facilities and showers at work, then I would be more likely to exercise.	3	2	1	0

E. Do you think your child's other parent would give different responses to yours?

- Yes, different responses
- No, the same response
- n/a

Appendix 12- Parent exercise barriers questionnaire

- F. It would be very helpful to have responses from both parents. Please provide an email address so that we can send this questionnaire to you at home so that it can be completed by both parents.

Thank you very much for answering all of these question!

INTERVIEW SCHEDULE- CYP

Introduction- conversation about INSPIRE and exercise- not formal, and NOT part of clinic. Will not affect their care or go in their notes. Not reflective of them as individuals but trying to gain an understanding of the things that affect them so that we can help children and young people with CF as a group.

Topic guide:

- Exercise and activity as a priority
 - Current exercise practices
 - Barriers
 - Facilitators
 - Impact of interventions
 - Maintaining behaviour change
 - Role of family
1. When you haven't got to go to school, or to the hospital for clinic, or anywhere else, what is your favourite thing to do with your time?
 2. Tell me about where you have done some exercise recently.
 3. What exercise activities do you most enjoy
 4. What activities do you least enjoy
 5. Who helps you to exercise and be active?
 6. What makes it difficult for you to be active?
 7. Can you think of other children and what it might be that would make it difficult for them to be active or do exercise?
 8. How did you feel when you found out you were in the exercise/control group for INSPIRE-CF
- Intervention Group
9. Tell me about the last time you went to the gym
 10. Tell me about your INSPIRE-CF training sessions, describe a typical day when you went training
 11. What did you like about them/ the best part
 12. What did you not like about them/ the worst part
 13. How did you feel when INSPIRE-CF came to an end
 14. What is different about exercise training now compared to during INSPIRE-CF

Appendix 13- Interview schedules

15. What has surprised you about the differences in your exercise and activity since finishing INSPIRE-CF
16. What is easier about exercising now
17. What is more difficult about exercising now
18. What advice would you give to other children and young people about carrying on with exercise and activity

Control

19. What do you think would be/feel different about exercising on your own compared to with a trainer or even in a group of other young people
20. What do you think is the biggest worry or reason to be put off joining a gym or sports club for young people with CF

End

21. Would you like to say/tell me anything else about exercise or INSPIRE-CF

INTERVIEW SCHEDULE- PARENT

Topic guide:

- Exercise and activity as a priority for parent
- Current exercise practices
- Barriers
- Facilitators
- Impact of interventions
- Maintaining behaviour change

1. Tell me a bit about your family and what you do when your child/children are not at school.
2. Tell me about the time in your life when you were most active or did the most exercise.
3. Tell me about some exercise activity that your child has done recently
4. Who helps your child to exercise and be active
5. What makes it difficult for your child to be active
6. How did you feel when you found out that your child had been randomised into exercise/ control group?

Intervention Group

7. Tell me about your child's INSPIRE-CF training sessions, describe a typical day when they went training
8. Did anything surprise you about your child taking part in INSPIRE-CF
9. What is different about your child's exercise and activity now compared to during INSPIRE-CF
10. What is easier about exercising now
11. What is more difficult about exercising now
12. How did you feel when INSPIRE-CF came to an end
13. What has surprised you about the differences in your exercise and activity since finishing INSPIRE-CF
14. What advice would you give to other parents of children and young people with CF about exercise and activity

End

15. Would you like to say/tell me anything else about exercise or INSPIRE-CF



Health Research Authority
North East – Newcastle & North Tyneside 1 Research Ethics Committee

Newcastle NHSBT Blood Donor Centre
Holland Drive
Newcastle upon Tyne
NE2 4NQ

Telephone: 0207 1048084

Please note: This is the favourable opinion of the REC only and does not allow you to start your study at NHS sites in England until you receive HRA Approval

12 October 2018

Ms Helen Douglas
UCL Great Ormond Street Institute of Child Health
30 Guilford Street
London WC1N 1EH

Dear Ms Douglas

Study title: Identifying predictors for maintenance of exercise participation in children and young people with cystic fibrosis
REC reference: 18/NE/0324
Protocol number: V1
IRAS project ID: 246187

The Proportionate Review Sub-Committee of the North East - Newcastle & North Tyneside 1 Research Ethics Committee reviewed the above application in correspondence.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this favourable opinion letter. The expectation is that this information will be published for all studies that receive an ethical opinion but should you wish to provide a substitute contact point, wish to make a request to defer, or require further information, please contact hra.studyregistration@nhs.net outlining the reasons for your request. Under very limited circumstances (e.g. for student research which has received an unfavourable opinion), it may be possible to grant an exemption to the publication of the study.

Ethical opinion

On behalf of the Committee, the Sub-Committee gave a **Favourable** ethical opinion of the above research on the basis described in the application form, protocol and supporting documentation, subject to the conditions specified below.

Conditions of the favourable opinion

The REC favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).

Guidance on applying for HRA and HCRW Approval (England and Wales)/ NHS permission for research is available in the Integrated Research Application System, www.hra.nhs.uk or at <http://www.rdforum.nhs.uk>.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of management permissions from host organisations.

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database. This should be before the first participant is recruited but no later than 6 weeks after recruitment of the first participant.

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to request a deferral for study registration within the required timeframe, they should contact hra.studyregistration@nhs.net. The expectation is that all clinical trials will be registered, however, in exceptional circumstances non-registration may be permissible with prior agreement from the HRA. Guidance on where to register is provided on the HRA website.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Ethical review of research sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion").

Extract of the meeting minutes

The Sub-Committee raised the following issues and the chief investigator Ms Helen Douglas responded accordingly as follows.

It was noted that the application was generally very well presented.

Recruitment arrangements and access to health information, and fair participant selection

Concern was raised regarding the initial recruitment process. The application indicated that clinic staff would be asked to identify patients and inform the researchers of the potential recruits who would then be approached by the researcher to obtain consent. That would be considered a breach of data protection and human rights legislation and the most recent GMC Good Practice Guidance on Patient Confidentiality. The Committee advised that the clinician involved should firstly seek permission from the patient and parent/guardian to divulge their identity to the research team. The relevant documentation would need to be amended accordingly.

It was confirmed that following discussion with the clinical team, it had been agreed that the initial invitation letter would be sent from the senior physiotherapist on behalf of the clinical team, who would have awareness and knowledge of good practice in recruiting to research studies. The recruitment process was revised accordingly and noted in the invitation letter and protocol.

Favourable risk benefit ratio; anticipated benefit/risks for research participants (present and future)

Clarification was requested regarding plans for dealing with potential distress (as the clinical team appeared superfluous to the study organisation).

It was clarified that the researchers worked closely with the clinical team and therefore they would be able to easily refer participants back to the psychologists who were part of the cystic fibrosis team, if needed. As all participants would be taking part in this research whilst attending the hospital for a clinic appointment, the whole cystic fibrosis team would be readily available at those times.

Care and protection of research participants; respect for potential and enrolled participants' welfare and dignity

Clarification was requested if participants would be reimbursed for refreshments, car parking charges and the additional time element involved.

It was explained that this had been discussed with the team during the planning stages, however it was not considered necessary or appropriate as the study appointments would be timed with routine clinic visits, and therefore there would be no additional financial burden. There could be a small increase in time spent at the hospital as a result of taking part in the study but if families were not happy with this then they would not participate in the study. The research team had worked closely with a number of families during the planning stages and they had been very positive regarding the research and were interested in participating in the study.

Clarification was requested if consideration has been given to any potential financial and social drawbacks to involvement in the study (especially regarding the vulnerable population which may have greater than average demand on the time and disruption to the participant and family members).

It was explained that the study had been designed with minimal burden for the participants and families by arranging the study visits to coincide with clinic appointments and involving as little time as possible.

Informed consent process and the adequacy and completeness of participant information

Issues noted to be addressed the participant information sheet:

An explanation of the term 'tool' in the context of this study would need to be included.

It was explained that for the purposes of this research, the term 'tool' referred to the measurement instrument that was being developed. It would likely include a new questionnaire and could involve other already standardised tests, scales or scores. A brief explanation was added to all participant information sheets.

An explanation of how participants would be able to access the results would need to be included.

This was added to the revised information sheets.

Consent Form – a statement for permission to record the interviews would need to be included.

It was clarified that this was already included in the consent form for part Bi (the only part with an interview) but not on the assent form, so this statement was added and a revised copy was provided.

The Sub-Committee was satisfied with the responses provided to the issues raised and the revised documentation.

Approved documents

The documents reviewed and approved were:

<i>Document</i>	<i>Version</i>	<i>Date</i>
Copies of advertisement materials for research participants [Social media recruitment poster]	V1	01 August 2018
Covering letter on headed paper [cover letter]		20 September 2018
Covering letter on headed paper		27 September 2018
Evidence of Sponsor insurance or indemnity (non-NHS Sponsors only) [Insurance letter]		25 July 2018
IRAS Application Form [IRAS_Form_27092018]		27 September 2018
Letter from funder [CF Trust SRC award letter]		23 February 2016
Letters of invitation to participant [Invitation letter Part A V2]	V2	08 October 2018
Letters of invitation to participant [Invitation letter Part B V2]	V2	08 October 2018
Other [Assent form Part A]	V3	20 September 2018
Other [Assent form Part Bii]	V3	20 September 2018
Other [Protocol]	V2.4	08 October 2018
Other [Assent form Part Bi]	V4	09 October 2018
Participant consent form [Consent form Part A]	V3	20 September 2018
Participant consent form [Consent form Part Bi]	V3	20 September 2018
Participant consent form [Consent form Part Bii]	V3	20 September 2018
Participant information sheet (PIS) [Child PIS Part A]	V4	09 October 2018
Participant information sheet (PIS) [Young person PIS Part A]	V5	09 October 2018
Participant information sheet (PIS) [Parent PIS Part A]	V5	09 October 2018
Participant information sheet (PIS) [Child PIS Part Bi]	V4	09 October 2018
Participant information sheet (PIS) [Young person PIS Part Bi]	V4	09 October 2018
Participant information sheet (PIS) [Parent PIS Part Bi]	V5	09 October 2018
Participant information sheet (PIS) [Child PIS Part Bii]	V4	09 October 2018
Participant information sheet (PIS) [Young person PIS Part Bii]	V4	09 October 2018
Participant information sheet (PIS) [Parent PIS Part Bii]	V5	09 October 2018

Summary CV for Chief Investigator (CI) [CV Helen Douglas]		02 August 2018
Summary CV for student [CV Helen Douglas]		02 August 2018
Summary CV for supervisor (student research) [CV Dr Mandy Bryon]		02 August 2018
Summary CV for supervisor (student research) [CV Prof Eleanor Main]		30 April 2018
Summary, synopsis or diagram (flowchart) of protocol in non-technical language [Flowchart Part A V1.1]	V1.1	27 September 2018
Summary, synopsis or diagram (flowchart) of protocol in non-technical language [Flow chart Part B V1.1]	V1.1	27 September 2018
Validated questionnaire [Habitual Activity Estimation Scale]		
Validated questionnaire [Children's Self-perceptions of Adequacy in and Predilection for Physical Activity]		

Membership of the Proportionate Review Sub-Committee

The members of the Sub-Committee who took part in the review are listed on the attached sheet.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study.

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website: <http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/>

HRA Training

We are pleased to welcome researchers and R&D staff at our training days – see details at <http://www.hra.nhs.uk/hra-training/>

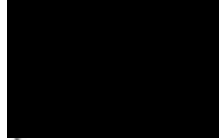
With the Committee's best wishes for the success of this project.

18/NE/0324

Please quote this number on all correspondence

Yours sincerely

pp



Dr Mike Bone
Vice Chair

Email: nrescommittee.northeast-newcastleandnorthtyneside1@nhs.net

Enclosures: List of names and professions of members who took part in the review
'After ethical review – guidance for researchers' SL-AR2

Copy to: Dr Vanshree Patel – R&D Dept, UCL Great Ormond Street
Hospital for Children NHS Trust

Professor Eleanor Main – Dept of Children Health, Great Ormond
Street Hospital for Children NHS Trust

Lead Nation - England



Health Research
Authority

London - Brighton & Sussex Research Ethics Committee

Health Research Authority
Ground Floor, Supton House
80 London Road
London
SE1 6LH

Telephone: 02071048129

Please note: This is the favourable opinion of the REC only and does not allow you to start your study at NHS sites in England until you receive HRA Approval

15 August 2018

Professor Eleanor Main
4th Floor, Wellcome Trust Building
UCL GOS Institute of Child Health
30 Guilford Street, London
WC1N 1EH

Dear Professor Main

Study title:	Project Fizzyo: Remote monitoring and gaming technology for improving physiotherapy prescription, adherence and prediction of clinical outcomes in children with cystic fibrosis.
REC reference:	18/LO/1038
Protocol number:	18/0296
IRAS project ID:	228625

Thank you for your letter of 16 July 2018, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair in consultation with Dr John Bull and Mr Maurice Marchant.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this opinion letter. Should you wish to provide a substitute contact point, require further

information, or wish to make a request to postpone publication, please contact hra.studyregistration@nhs.net outlining the reasons for your request.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Conditions of the favourable opinion

The REC favourable opinion is subject to the following conditions being met prior to the start of the study.

1. Make the wording in the third box, on page 3, of the 6-10 year old PIS clearer. It is not clear if the participants will receive all 3 items or just one of them.

You should notify the REC once all conditions have been met (except for site approvals from host organisations) and provide copies of any revised documentation with updated version numbers. Revised documents should be submitted to the REC electronically from IRAS. The REC will acknowledge receipt and provide a final list of the approved documentation for the study, which you can make available to host organisations to facilitate their permission for the study. Failure to provide the final versions to the REC may cause delay in obtaining permissions.

Management permission must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).

Guidance on applying for HRA and HCRW Approval (England and Wales)/ NHS permission for research is available in the Integrated Research Application System, at www.hra.nhs.uk or at <http://www.rdforum.nhs.uk>.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of management permissions from host organisations

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database within 6 weeks of recruitment of the first participant (for medical device studies, within the timeline determined by the current registration and publication trees).

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to request a deferral for study registration within the required timeframe, they should contact hra.studyregistration@nhs.net. The expectation is that all clinical trials will be registered, however, in exceptional circumstances non registration may be permissible with prior agreement from the HRA. Guidance on where to register is provided on the HRA website.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Non-NHS sites

The Committee has not yet completed any site-specific assessment (SSA) for the non-NHS research site(s) taking part in this study. The favourable opinion does not therefore apply to any non-NHS site at present. We will write to you again as soon as an SSA application(s) has been reviewed. In the meantime no study procedures should be initiated at non-NHS sites.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

<i>Document</i>	<i>Version</i>	<i>Date</i>
Covering letter on headed paper [Cover Letter]		09 May 2018
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [UCL Insurance Certificate]		24 July 2017
GP/consultant information sheets or letters [Doctors Letter]	1	30 April 2018
IRAS Application Form [IRAS_Form_21052018]		21 May 2018
Letter from funder [Rosetrees Funding Letter]		06 November 2017
Letter from sponsor [UCL Insurance letter 17A106]		14 May 2018
Letters of invitation to participant [Letter of Invitation]	1	30 April 2018

Appendix 15- Research Ethics Committee approval letter for Project Fizzyo

MHRA Notice of No Objection Letter (Medical Devices) and relevant correspondence [MHRA correspondence]	1	31 July 2017
Other [HEIF KEIF Funding]	1	30 November 2017
Other [UCL Finance Letter]	1	23 August 2017
Other [Letter in response to provisional opinion]	1	16 July 2018
Participant consent form [Consent]	2	13 July 2018
Participant consent form [Consent]	2	13 July 2018
Participant information sheet (PIS) [Parent Information Sheet]	4.0	13 July 2018
Participant information sheet (PIS) [Child Information Sheet 11-16y]	4.0	16 July 2018
Participant information sheet (PIS) [Child Information Sheet 6-10y]	4.0	13 July 2018
Participant information sheet (PIS) [Parent Information Sheet]	4.0	16 July 2018
Participant information sheet (PIS) [Child Information Sheet 11-16y]	4.0	16 July 2018
Participant information sheet (PIS) [Child Information Sheet 6-10y]	4.0	13 July 2018
Research protocol or project proposal [Protocol]	3.0	16 July 2018
Research protocol or project proposal [Protocol]	3.0	16 July 2018
Summary CV for Chief Investigator (CI) [CI CV E Main]		30 April 2018
Summary CV for student [Student CV]		26 January 2018
Summary CV for supervisor (student research) [Primary Supervisor CV]		30 April 2018
Summary CV for supervisor (student research) [Secondary Supervisor CV]		01 September 2017
Summary, synopsis or diagram (flowchart) of protocol in non technical language [Summary protocol]	2	08 May 2018
Validated questionnaire [CFQ-R]		

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document "*After ethical review – guidance for researchers*" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website:

<http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/>

HRA Training

We are pleased to welcome researchers and R&D staff at our training days – see details at

<http://www.hra.nhs.uk/hra-training/>

18/LO/1038	Please quote this number on all correspondence
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With the Committee's best wishes for the success of this project.

Yours sincerely



Dr Simon Walton
Chair

Email: NRESCcommittee.SECOast-BrightonandSussex@nhs.net

Enclosures: "After ethical review – guidance for researchers"

Copy to: **Ms Emma Pendleton**
Miss Stephanie De Sa Marques Basset, Great Ormond Street Hospital for Children NHS Foundation Trust