Submission to the Special Committee on Covid-19 Response
from
ExWell Medical CLG

1. EXECUTIVE SUMMARY

- Covid has had profound effects on both Covid and non-Covid cohorts. The work of the Special Committee should address the needs of both.
- Chronic illness management is the biggest challenge facing the health service.
- The socio-economic burden of chronic illness management is becoming untenable
- ExWell Medical is a social enterprise committed to delivering life-transforming exercise-based chronic illness rehabilitation in community settings. The work of ExWell, has been ongoing for 12 years. A HSE-funded evaluation of the programme confirms its efficacy across a wide range of clinically important outcomes.
- The challenge facing the Special Committee is to accommodate both Covid and non-Covid cohorts in an accessible, comprehensive, community-based, medically-led chronic illness rehabilitation service structure
- ExWell has a model of care that could, with initial financial support of c €1.5 million,, deliver its service to all of Ireland within 5 years, through community partnerships
- ExWell has developed a specific community-based Covid rehabilitation programme
- We would welcome an opportunity to make a presentation to the Special Committee

2. INTRODUCTION

ExWell Medical, a social enterprise funded currently by Rethink Ireland (formerly Social Innovation Fund Ireland) was established in January 2019 as a follow on to a pre-existing service located in DCU which was called MedEx. MedEx offered community-based chronic illness rehabilitation, on medical referral, to people with diverse chronic illnesses though structured exercise classes. The MedEx centre rapidly grew to become the biggest centre of its kind in Europe, hosting 700 participant visits weekly and receiving up to 1000 new referral annually. Over time, pressure grew to offer the service outside DCU and across Ireland. A decision was made by DCU to not become involved in the national roll out. For this reason a new corporate entity (ExWell Medical CLG) was formed in January 2019 with the aim of bringing the medically-led service to all parts of Ireland. Details of the corporate structure of ExWell Medical and the composition of its advisory board are separately attached

3. THE RATIONALE

A large part of the unwellness, disability and poor quality of life that occurs with any chronic illness is caused by becoming deconditioned through physical inactivity. This starts a downward spiral of reduced fitness, impaired mobility, social isolation, loneliness and poor mental health, loss of confidence and motivation, increasing fear of exercise and an even greater reduction in physical activity…and so the spiral continues. Appropriately designed and delivered exercise programmes can fix and reverse this trend, without needing to fix the illness. This transforms the lives of the

patients and of their families, who struggle with (often hidden) distress and frustration. The impact is restoration of mobility, fitness, enthusiasm, enjoyment and hope.

4. CHRONIC ILLNESS REHABILITATION IN THE COVID ERA: IT'S NOT JUST ABOUT COVID

The understanding of the rehabilitation needs of **Covid survivors** is an evolving work in progress. It is clear that the needs will have physical, psychological, emotional, neurological, psychiatric and social elements. Fatigue is a prominent symptom and there is a concern that we may the see the emergence of a persisting post-viral fatigue syndrome. Carefully designed, personalised exercise programmes with monitored progression will have an important role to play.

It is critical also to continue to cater for **non-Covid chronic illness cohorts**, whose need to start and continue exercise based rehab i8litaiin in community settings remains an essential part of chronic illness management. Unfortunately, the cocooners have suffered greatly in terms of loss of mobility and fitness, as well as increased loneliness, during the shut-down. A way must be found to facilitate a re-entry into community based, socially enrichening group exercise for these people

5. THE EXWELL MEDICAL COVID REHABILITATION PROGRAMME

The standard ExWell programme is focused on exercise. It is recognised that a dedicated Covid rehabilitation programme will require additional inputs (specifically nutritional and psychological elements) and that the participants will require a higher level of support than is offered in the standard programme. These amendments have been incorporated. The programme accommodates group exercise classes and also an on-line option. The Home Programme model is attached.

6. RELEVANT FACTS

- Chronic illness management is the biggest challenge facing the health service in Ireland. It affects 40% of the entire population, 80% of those aged over 65 yrs, and consumes 75% our €18 billion national health spend.

- With an aging population, and a parallel increase in the prevalence of chronic illness, the socioeconomic burden on chronic illness management is becoming untenable

- A HSE-funded evaluation of the MedEx (now ExWell) programme in DCU, carried out over 3 years, showed that participation for 1 year, even with low attendance rates, was associated with significant improvements in a wide range of highly relevant clinical outcomes, including aerobic fitness, strength, physical activity levels, blood pressure control, blood sugar control, levels of inflammation, blood lipid levels, psychological wellness, quality of life and cognitive function. So we have the evidence base confirming that, min an Irish context, the ExWell programme works.

- Follow on analysis of the data from this study demonstrates the potential for a €1500 per participant reduction in health care utilisation costs annually, thereby allowing a very significant increase in the capacity of the health care system to

- Exercise has been identified by the HSE's Integrated Care programme for Older Persons (ICPOP) as the single most effective intervention for healthy aging

7. SLAINTECARE

It is not possible to deliver the required programme of exercise based chronic illness reabi8oitatiin in hospitals. The resources are simply too scarce, too busy and too expensive. The entire thrust of Slaintecare is to shift chronic illness management into community settings.
ExWell offers a model form delivering this service based on a track record of growth, a strong evidence based, and a vision form how a nationwide, accessible service could be in place within 5 years.

8. RECOMMENDATIONS

ExWell makes the following recommendations

1. Exercise based rehabilitation in community settings should be available to Covid survivors, as part of a multi-expert service that would also include nutritional, psychological and emotional support strategies
2. A model of care to offer community based chronic illness rehabilitation through exerciser in the Covid era must be developed and evaluated
3. Detailed financial modelling suggest that ExWell could expand to operating 40 sites across Ireland within 5 years with initial funding support of 1.5 million over 3 years, after which a self-sustaining financial status would be attained. These details can be shared

Covid-19 Home Exercise Rehabilitation Programme

1. BACKGROUND

ExWell Medical is now offering a dedicated Covid-19 home-based rehabilitation programme. While most people who contract Covid-19 infection have a relatively mild illness and recover fully, a significant minority experience a different pathway characterised by more severe symptoms and much greater disability, sometimes requiring hospitalisation, including intensive care treatment. This may involve sedation and assisted ventilation. The illness can have serious medical consequences, including organ failure, stroke and myocardial infarction. Even without these complications, many patients become profoundly deconditioned because of long periods of bed rest and complete immobility. Difficulty swallowing is quite common after intubation for ventilation and this presents a big nutritional challenge. In addition, significant psychological sequelae can include relatively minor anxiety, loss of confidence, fear of social engagement, survivor guilt and apprehension about re-infection.

Acknowledging these diverse needs, and building on our successful home exercise programme (ExWell@Home) for our existing client base (comprising people with chronic illness who are referred medically tumour service), we have developed a specific programme for Covid survivors.

2. THE EXWELL COVID REHABLTIATION PROGRAMME TEAM

Dr Noel McCaffrey MB:	Sports and Exercise Medicine Specialist, CEO ExWell Medical
Dr Sharon Madigan, PhD:	Clinical and Sports Nutritionist
Dr Siobhan McArdle PhD:	Clinical Psychologist
Dr Emmett Byrne MB;	Medical Officer, ExWell Medical
Aodhahan O'Deasmhunaigh:	Chartered Physiotherapist
Dr Lauri McDermott PhD:	Operations Officer, ExWell Medical

3. THE PROGRAMME

The programme is structured as follows:

1. **Medical referral**…. referrals are accepted from hospital teams or GPs and will include brief details of the treatment pathway, complications arising, progress to date, status on discharge / referral, issues of concern and any specific recommendation

2. **Initial contact from ExWell**….this will be a phone call from one of the ExWell physicians, introducing ExWell to the patient and family, and explaining the steps that will follow

3. **Support material sent to patient**…. This will include the home exercise booklet and instructions for carrying out self-administered tests, including
    - 6 minute walk test
    - Biceps strength test
    - Timed up and go test
    - QoL questionnaire (EQ-5D)
    - Nutritional status assessment
    - Psychological wellness assessment
    - Links to podcasts / min-lectures from
        a. Dr Noel McCaffrey (the induction talk on line)
        b. Dr Sharon Madigan (intro to healthy nutrition)
        c. Dr Siobhan McArdle (intro to psychological challenges in Covid patients)

4. **Follow up phone call**…. after receiving the baseline test results, and after the patient has viewed the podcasts, a follow up call from the ExWell team will take place in which general goal setting and expectations and exercise preferences will be discussed

5. **Personalised programme design**…. based on the medical referral, the results of baseline testing and issues arising in the initial phone calls, a personalised programme will be designed and sent to the patient

6. **Programme delivery**….. the programme will involve the following elements:
    - daily exercise, which will include a mixture of watching and participating in published video classes as well carrying out other prescribed exercises
    - completion of a daily exercise diary
    - completion of a weekly 'wellness' report to assist the ExWell team in programme design, with other specific monitoring to be implemented as per pending expert advice
    - watching a series of educational talks on healthy nutrition
    - receiving personalised nutritional advice as appropriate
    - watching a series of talks on aspects of psychological wellness
    - receiving personalised psychological support as appropriate

7. **Support phone calls**…. This will involve 2 separate supports:
    - Regular phone calls from trained ExWell staff
    - Support phone calls from peer participants

8. **Chat groups**…. will be established, offering an opportunity for social interaction with other participants

9. **Programme progression**…. the content of the exercise programme will be adjusted at regular intervals, based of participant feedback

10. **Retesting and reporting**…. The baseline tests (including psychological wellness and nutritional status) will be repeated after 2 months and summary reports will be provided to the participants and to the referrers

4. THE COST

Cost for 4 month programme: €1,150

Month One fee: €400

Includes:

- Induction and baseline testing
- Physician phone call
- Covid-specific Booklet
- Nutritional status assessment and lecture
- Psychological status assessment and lecture
- Programme design, including video
- ExWell podcasts weekly
- Phone support weekly
- One live-streamed class weekly

Monthly fee thereafter: €250

Includes:

- Access to dedicated classes (pre-recorded)
- One live streamed class weekly
- Access to podcasts
- ExWell support calls
- Peer support calls
- Facilitated chat lines
- Ongoing nutritional support as needed
- Ongoing psychological support as needed
- Repeat testing once / month
- Reports based on re-testing
- One physician call

Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

An Evaluation of the Effectiveness of the MedEx Programme

Final Report

December 2017

MedEx Wellness

Trial Governance

Stakeholders

Project Sponsor: Health Service Executive (HSE)

Project/Medical Director: Dr. Noel McCaffrey, Dublin City University (DCU)

Project Manager: Dr. Bróna Furlong and Dr. Lisa Loughney, DCU

Project Personnel: Ms Fiona Skelly (PhD candidate) and Dr. Lisa Loughney, DCU

Research Support: Ms Olivia Mason and Prof Leslie Daly, CSTAR, University College Dublin (UCD)

Service Delivery Staff: DCU Sport Staff

Project Review Committee

HSE representatives: Mr Dougie Beaton and Dr. Anne O'Farrell

Project/Medical Director: Dr. Noel McCaffrey, DCU

Project Managers: Dr. Bróna Furlong and Dr. Lisa Loughney, DCU

CSTAR representative: Prof. Leslie Daly, UCD

Project Management Team

Project/Medical Director: Dr. Noel McCaffrey, DCU

Project Managers: Dr. Bróna Furlong and Dr. Lisa Loughney, DCU

Project Personnel: Ms Fiona Skelly and Dr. Lisa Loughney, DCU

Executive Summary

MedEx is a large, community-based chronic illness rehabilitation service based at Dublin City University. The mission of MedEx is *to transform the lives of people with chronic illness through physical-activity based rehabilitation.* It offers structured, supervised exercise classes to people with diverse chronic illnesses including heart disease, lung disease, peripheral vascular disease, diabetes, neurodegenerative conditions, chronic pain and cancer. Participants are referred to MedEx by their GPs or by hospital medical teams (mainly in the Mater, Beaumont and Connolly Hospitals). MedEx has been operating for 10 years, is novel in scale (currently hosting nearly 700 participant visits per week) and concept (drawing all chronic illness cohorts together in a common programme) and is one of the largest centres of its kind in Europe. MedEx recruits 600-800 new participants annually.

Study rationale: The growing burden of chronic illness requires the development and roll-out of evidence-based, accessible and sustainable services. While previous work suggests that MedEx is financially self-sustaining and the model lends itself to being scalable across Dublin and Ireland, the missing piece in the MedEx story to date has been the scientific evidence-base for its clinical effectiveness. The purpose of this trial was to address this gap by conducting a 2-year prospective trial to evaluate the effect of participating in MedEx over 12 months on physical, clinical and psychological health and wellbeing.

Methodology: 403 participants were recruited. Participants underwent assessment at baseline and commenced the MedEx programme. Repeat assessments were conducted at 3 month, 6 months and 12 months. Two hundred and seventeen participants completed the 12-month follow-up assessment. The primary outcome was cardiorespiratory fitness, measured using the 6 minute time trial. Secondary and tertiary outcomes included selected physical, clinical, and psychological outcomes.

Results: There was a significant improvement in cardiorespiratory fitness following 12 months of the MedEx programme. MedEx was also associated with significant improvements in other measures of physical fitness (strength, flexibility, body composition, falls risk), clinical outcomes (blood pressure, blood glucose, inflammatory status and healthcare utilization) and psychological outcomes (quality of life and cognitive function). Table 1 presents a summary of the significant findings.

Implications: MedEx has been a great success story in terms of sustained growth and service delivery over a 10-year period. It has become a significant resource to the surrounding community including to individuals living with chronic illness, their families and local healthcare professionals.

This trial provides the evidence to support its clinical effectiveness. MedEx can now be described as a clinically effective public health chronic illness rehabilitation intervention with potential for sustainability and scalability.

Future work: Two broad pathways of work are recommended: (1) translation of this research into practice, by exploring strategies to provide support for the immediate roll-out of MedEx across Ireland; (2) evaluation of the effectiveness of MedEx in other settings, including in other supervised settings and the Home Programme environment.

Table 1: Summary of significant findings

Outcome	Baseline	12 months	p-value
Physical Outcomes			
Physical fitness			
Cardiorespiratory fitness: 6MTT (m)	482 (403-541)	540 (452-639)	<0.001
Leg strength: sit to stand test (s)	20.2 (17-23.4)	16.5 (13-20)	<0.001
Arm strength: hand grip (kg)	26.1 (19.9-32.3)	27.1 (20-34.1)	<0.05
Flexibility: sit and reach test (cm)	8 (1-16)	9 (2-16)	<0.001
Falls Risk			
Timed up and go test (s)	7.9 (5.6-10.2)	6.6 (5.2-8.1)	<0.05
Body composition			
BMI (kg/m^2)	28.5 (25.2-31.7)	27.8 (24.3-31.3)	<0.001
Waist-hip ratio	1.0 (0.9-1.1)	1.0 (0.5-1.5)	<0.001
Clinical Outcomes			
Blood pressure			
SBP daytime (mmHg)	156 (135-177)	145 (137-153)	<0.001
Hypertensive participants			
SBP daytime (mmHg)	156 (135-177)	145 (137-153)	<0.001
SBP night-time (mmHg)	144 (129-159)	133 (122-152)	<0.001
SBP 24 hour (mmHg)	150 (137-163)	141 (131-151)	<0.05
DBP daytime (mmHg)	82 (72-92)	78 (72-84)	<0.05
DBP night-time (mmHg)	71 (63-79)	66 (60-72)	<0.05
DBP 24 hour (mmHg)	78 (69-86)	73 (68-78)	<0.05
Biomarkers			
Total cholesterol (mmol/L)	4.5 (3.8-5.2)	4.4 (3.7-5.1)	<0.05
Glucose (mmol/L)	3.8 (1.3-6.3)	1.9 (0.3-3.5)	<0.001
CRP (mg/L)	6.0 (5.4-6.6)	5.7 (5.0-6.4)	<0.05
Health care utilisation			
GP visits (no. in 12 mth)	5 (3-7)	4 (3-6)	<0.001
Hospital outpatient visits (no. in 12 mth)	7.0 (3.0-10.0)	4.0 (2.0-4.0)	<0.001
Psychological Outcomes			
Quality of life			
Depressive symptoms score	4 (1-7)	3 (0-7)	<0.001
Overall health scale	70 (55-80)	70 (70-80)	<0.001
Satisfaction with life score	26 (20-29)	27 (26-28)	<0.001
Mental wellbeing score	27 (24-29)	28 (28-29)	<0.001
Cognitive function			
*Working memory (*Luck & Vogel Task)			
Reaction time to small set	1245.5 (1000.8-	1063.5(894.5-1232.5)	<0.001
Reaction time to large Set	1226.5(969.6-1483.4)	1058.0 (880.5-1235.5)	<0.001
Attention (Attention Networking Task)			
Reaction time	834.7(32.7-36.7)	801.9(699.4-14.3)	<0.01
Alerting correct	30.89 (8.97-2.81)	39.4 (13.8-65.1)	<0.05
Executive control correct	127.9 (95.0-60.8)	106 (76.5-135.4)	<0.001

Values are reported as median (interquartile range). 6MTT, six minute time trial; BMI, body mass idex; CRP, c-reactive protein; DBP, diastolic blood pressure; GP, general practitioner; LIPA, light-intensity physical activity; MVPA, moderate-intensity physical activity; SBP, systolic blood pressure.

Impact Statement

The Patient

Participation in MedEx was associated with improvements in physical, clinical and psychological health in individuals with chronic illness. The programme increased cardiorespiratory fitness, one of the strongest independent predictors of morbidity and mortality in both primary and secondary prevention. Even small increases in cardiorespiratory fitness are associated with significant reductions in risk. The risk profile of participants was further improved through MedEx by reductions in body composition, blood pressure, cholesterol, glucose and inflammation. These are the leading risk factors for the development of many chronic conditions and for mortality. In secondary prevention, risk factor reduction can slow or halt disease progression and prevent recurrence, further complications and the development of comorbidities, and increase longevity.

Improvements in cardiorespiratory fitness and in other components of health-related physical fitness, specifically strength and flexibility, achieved through MedEx can enhance the ability to perform activities of daily living. These improvements and the reduction in falls risk associated with MedEx can contribute to the maintenance of functional independence. Cognitive function, specifically memory and attention, were enhanced through participation in MedEx. These outcomes may counteract the cognitive decline associated with ageing and again contribute to the maintenance of functional independence. Overall, the physical, clinical and psychological effects of MedEx indicate that the programme reduces the impact and burden of the disease on the patient's life. This is ultimately reflected in the improvements reported in quality of life.

The Health System

The MedEx programme was associated with reductions in healthcare service utilisation, including GP visits, emergency department visits, outpatient visits and nights spent in hospital. Chronic disease represents the major component of activity and expenditure within the healthcare system. Approximately three quarters of healthcare expenditure is attributed to the management of chronic disease. Strategies to restore health and reduce risk profile such as MedEx can reduce reliance on healthcare services and may ultimately contribute to lessening the economic and health system burden of chronic disease.

The MedEx programme has become an valuable resource to the local medical community. It provides a referral pathway for hospital specialists and their teams and local GPs. MedEx is not a fixed duration programme, participants attend on a continuous basis. This model allows for a

lifelong relationship with the programme, which can often not be provided by other healthcare services.

Policy

Referral to MedEx (or similar programmes) should be embedded in routine clinical management of all individuals with a chronic illness. To date, exercise rehabilitation has focused on cardiac and pulmonary rehabilitation programmes. The MedEx model expands the concept to include a broad range of chronic illnesses. The evidence-based for this model has now been established and it has the potential to inform HSE policy and best practice guidelines. The MedEx model is also scalable and sustainable. A National MedEx Network has been established, with the objective of developing centre-based programmes in third level academic institutions throughout Ireland. The long-term impact of a successfully rolled-out MedEx programme will be transformative for community-based chronic illness rehabilitation policy and practice in Ireland. Based on the proven acceptability, efficacy and safety of MedEx, it is hoped that the HSE will adopt major policy developments to support all potential patients to access MedEx.

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Acknowledgements

The MedEx team are grateful to the participants who gave so generously of their time in order to provide an important data set for this trial. Without their participation, it would not have been possible.

The authors also gratefully acknowledge the following:

The Health Service Executive (HSE) which funded the trial and the HSE representatives for their support and advice throughout the trial period;

The trial steering and management committee groups who advised on this trial.

Glossary of Abbreviations

Abbreviation	Definition
6MTT	Six minute time trial
BMI	Body mass index
BP	Blood pressure
CAT	COPD assessment
COPD	Chronic obstructive pulmonary disease
CR	Cardiac rehabilitation
CRP	C-reactive protein
CSTAR	Centre of Support and Training in Analysis and Research
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
DCU	Dublin City University
EQ-5D-3L	EuroQol-5 dimensions-3 levels of severity health status measure
FACT	Functional assessment of cancer therapy
GP	General practitioner
HDL	High density lipoprotein
HP	Home programme
HRQoL	Health-related quality of life
HSE	Health Service Executive
IPAQ	International physical activity questionnaire
LDL	Low density lipoprotein
LIPA	Low-intensity physical activity
MET	Metabolic equivalent task
MPVA	Moderate-vigorous physical activity
NCD	Non-communicable disease
PA	Physical activity
PHQ8	Patient health questionnaire
RT	Reaction time
SBP	Systolic blood pressure
SF-12	12-item short form survey
SOP	Standard operating procedures
SWEMWBS	Short Warwick-Edinburgh Mental-Wellbeing Scale
SWLS	Satisfaction with Life Scale
TG	Triglycerides
TILDA	The Irish Longitudinal Study on Ageing
TUG	Timed up and go test
UCD	University College Dublin
WHO	World Health Organisation
WIQ	Walking impairment questionnaire
WP	Work package

Chapter 1 Introduction

1.1 Background

Chronic disease, comprising cardiovascular (CVD), chronic obstructive pulmonary disease (COPD), cancer and diabetes, is the leading cause of death worldwide, accounting for 60% of all deaths. In Ireland, chronic disease accounts for 76% of deaths[1] and 75% of the annual health budget is attributed to the treatment of such illnesses[2]. Three quarters of the Irish population aged over 75 years have at least one chronic disease and one third of men aged over 60 years have at least two[3]. Ireland has an ageing population, with a 30% increase in the population >65 years in the period 2006-2015, twice the European average[4]. With the growing and ageing population, it can be expected that the burden of chronic disease will rise by 40% by 2020[5]. Chronic disease poses a large threat to population health with implications including decreased health-related quality of life (HRQoL) and physical functioning, polypharmacy, increased healthcare utilization and costs and premature mortality[6].

'Exercise is medicine' and there is irrefutable evidence of the effect of exercise in the secondary prevention of several chronic diseases. Exercise is associated with a reduction in the risk of morbidity and mortality in those with an established chronic condition[7,8]. The beneficial effects of exercise on the leading risk factors for mortality are clearly established, namely hypertension, high blood glucose, physical inactivity, overweight and obesity, and high cholesterol[9]. Regular exercise may mitigate or reverse disease progression. For example, an energy expenditure of ~1600 kcal per week can halt disease progression in individuals with coronary artery disease and an energy expenditure of ~2200 kcal per week is associated with plaque reduction[10,11]. The reduction of recurrent events, future complications and hospital readmissions through exercise[7] can help to reduce the burden of chronic disease.

Exercise can also restore health and maintain functional independence in those with an established chronic disease. Chronic disease and ageing are associated with a decline in physical function. For example, a loss of muscle mass, a decline in balance ability and a reduction in muscle strength and endurance[12] impact on the ability to perform activities of daily living and ultimately functional independence[13]. In a cycle of decline, reduced musculoskeletal fitness leads to inactivity and further decline and dependence[14]. A recent review of 85 meta-analyses of randomized controlled trials in 22 different chronic conditions concluded that exercise improves functional capacity and reduces disability in individuals living with a chronic disease[15].

Exercise is also associated with substantial psychological benefits. Exercise can have a positive impact on depression, anxiety, self-esteem, quality of life and cognitive function[16]. This is of particular importance in individuals with chronic disease because of the adverse affect the disease can have on quality of life[17]. Individuals with chronic disease have 2-3 fold higher rates of major depression compared to age-matched healthy controls[18]. Exercise can also have social benefits by providing opportunities and an environemnt for social interactions which can help develop social support and reduce social withdrawl[8].

Accumulation of evidence over the last several decades illustrates that there are exceptionally few chronic diseases, in which the burden of the disease, comorbidities related to the disease or the disease-related quality of life are not improved with exercise[19]. This knowledge supports the significance of exercise as a first-line treatment for many chronic diseases[8].

1.2 MedEx

MedEx is a community-based exercise rehabilitation programme for chronic disease located at Dublin City University (DCU). MedEx was established to meet the needs of the local hospitals and community for an exercise rehabilitation service that was i) community-based; ii) scalable and iii) sustainable. It's mission is *to transform the lives of people with chronic illness through physical-activity based rehabilitation.* MedEx offers group exercises classes in a medically supervised environment and physical activity education and support for people with a variety of chronic illnesses, including cardiovascular disease, pulmonary disease, diabetes, and cancer. Individuals with chronic illness are referred to MedEx by hospital specialists (and their teams) and GPs. The programme has gained the confidence of and become a significant resource for referring GPs in the North Dublin region and the Mater Misericordiae University Hospital, Beaumont Hospital, and Connolly Hospital. The programme boasts a strong and steady referral base, with approximately 40 new referrals every month.

MedEx is novel in scale and concept. Hosting over 700 participant visits per week, it has grown exponentially since its inception in 2006 to become one of the largest centres of its kind in Europe. It has become a significant resource to the surrounding community for individuals (and their families) living with the burden of chronic illness. The MedEx model is unique with regard to shared common infrastructure and content across chronic illnesses, including facilities, staffing, operating procedures and standards, patient information handling and exercise prescription and programme content. This brings all chronic illnesses together in a single programme. The model is also unique in terms of

programme duration. Participants can attend the programme on a continuous basis and are encouraged to establish a lifelong relationship with MedEx.

MedEx has a robust business model and is financially self-sustaining. Finally, MedEx is scalable. There is an established national network of third level institutions that have developed or are developing a MedEx programme onsite and the roll-out of MedEx to public leisure centres in the Dublin area has commenced. These features combine to make the MedEx model uniquely scalable as a sustainable, financially viable delivery model for chronic illness rehabilitation at national level, with real potential for rapid, inexpensive roll-out.

1.3 Hypothesis

Participation in the MedEx programme for 12 months will be associated with significant improvements in physical, clinical and psychosocial health and wellbeing.

1.4 Aim

To determine the effect of participating in the MedEx programme for 12 months on:

i. Physical health (cardiorespiratory fitness, strength, flexibility, falls risk, body composition, physical activity levels);

ii. Clinical health (blood pressure, lipids, glucose, inflammatory markers, healthcare utilisation);

iii. Psychosocial health and wellbeing (QoL, cognitive function and psychosocial determinants of physical activity).

Chapter 2 Work Packages

This trial included three separate (although related) work packages (WP).

Work Package 1: Project Management	
1.1	**Deliverable:** Project plan **Due:** 04/2015 **Delivered:** 04/2015
1.2	**Milestone:** Project review committee meetings **Due:** Monthly from month 1-3, every 3 months thereafter **Delivered:** Weekly from week 1-6, bimonthly from month 2-6, quarterly thereafter
1.3	**Milestone:** Project management team meetings **Due:** Monthly **Delivered:** Weekly
Work Package 2: Optimizing Operations	
2.1	**Deliverable:** Confirmation of the guidelines and standard operating procedures for programme content and delivery, including all aspects of safety standards and procedures **Due:** 07/2015 **Delivered:** 03/2016
2.2	**Deliverable:** Refinement of the MedEx outcome measurement battery for a comprehensive, relevant battery, which includes measures of psychological wellbeing, functional capacity, physical activity, and disease specific outcomes. **Due:** 08/2015 **Delivered:** 08/2015
2.3	**Deliverable:** Identification of a valid and appropriate method of determining health care utilization. **Due:** 08/2015 **Delivered:** 11/2015
2.4	**Deliverable:** Design and development of an efficient data capture and management system **Due:** 08/2015 **Delivered:** 11/2017 Overview of system including figure illustration of system snapshot is presented in Appendix 1.
2.5	**Deliverable:** Interim report I **Due:** 09/15 **Delivered:** 03/16
Work Package 3: Evaluation Trial	
3.1	**Milestone:** Recruitment of 300 trial participants **Due:** 08/2016 **Delivered:** 07/2016

3.2	**Deliverable:** Assessment of baseline measures of physical and psychological health **Due:** 08/2016 **Delivered:** 07/2016
3.3	**Deliverable:** Retrospective capture of healthcare utilisation data **Due:** 08/2016 **Delivered:** 07/2016
3.4	**Deliverable:** Interim report 2 **Due:** 09/2016 **Delivered:** 10/2016
3.5	**Milestone:** Implementation of the MedEx programme **Due:** 09/2015 – 09/2017 **Delivered:** 09/2015 – 07/2017
3.6	**Deliverable:** Data collection of outcome variables at 3, 6, and months **Due:** 10/2017 **Delivered:** 07/2017
3.7	**Deliverable:** Interim report 3 **Due:** 10/2017 **Delivered:** 10/2017
3.8	**Deliverable:** Data analysis **Due:** 01/2018 **Delivered:** 10/2017
3.9	**Deliverable:** Dissemination of findings **Due:** 03/3018 **Delivered:**
3.10	**Deliverable:** Final report **Due:** 03/2018 **Delivered:** 12/2017

Chapter 3 Methods

3.1 Participants

Adults with established non-communicable diseases were recruited at induction to the MedEx programme. Participants were recruited between September 2015 and July 2016 following referral to the MedEx programme through the pre-existing referral process in place between MedEx and partner hospitals and GPs. Exclusion criteria included uncontrolled CVD conditions, significant musculoskeletal or neurological condition, cognitive decline, or a significant mental illness or intellectual disability that restricted participation in a physical training programme. Participants were fully informed of the experimental procedures and provided with a plain language statement before giving informed consent in accordance with the Research Ethics Committee at Dublin City University. The trial was registered as a clinical trial on the ISRCTN registry (ISRCTN10351412).

3.2 Research Design

Figure 3.1 outlines the research design. The design was a prospective single arm intervention trial. Repeat assessments were conducted at 3, 6 and 12 months, however the focus was a pre-post design assessing the change from baseline to 12 months.

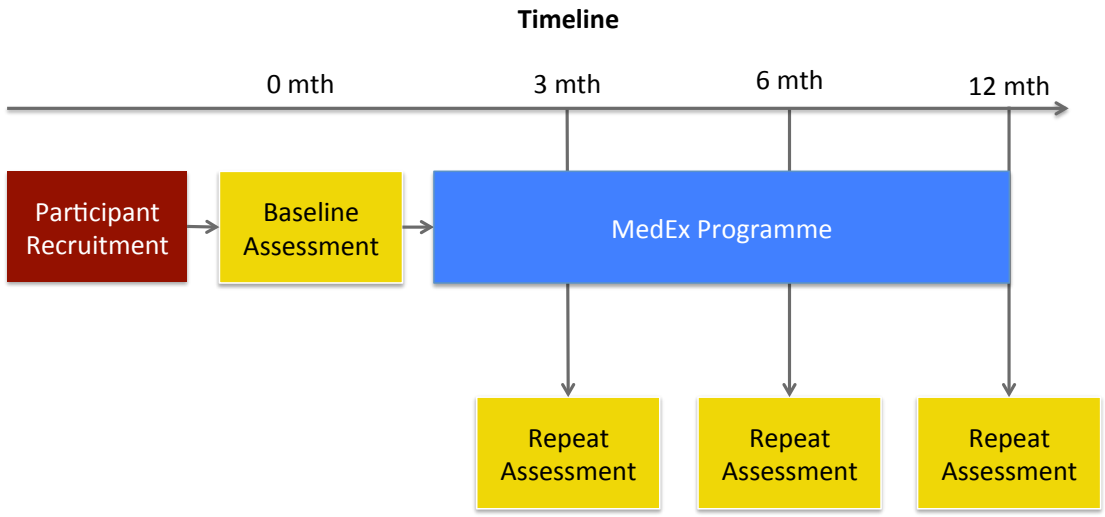

Figure 3.1: Research design

3.3 Intervention

Participants were inducted into the MedEx programme at DCU and advised to attend 2 MedEx supervised exercise classes per week on a continuous basis. Classes are scheduled during the day, evening and weekends to provide numerous options for participants. Classes consist of 15 to 75

participants grouped together based on primary condition. The 60 minute classes consist of a combination of aerobic and resistance exercise. The format is as follows:

- **Warm Up:** 10 min of aerobic exercise and range of motion/flexibility exercises
- **Aerobic exercise:** using a variety of exercise ergometers to accumulate 20 min of exercise. Participants are instructed to exercise at a moderate intensity at which they feel modestly breathless, have a red face and sweat.
- **Strength:** A circuit of 8-10 stations alternating upper and lower body exercises using both cable machines and light hand-weights. Participants select an intensity to allow them to perform continuous repetitions for 60s at each station. The circuit is completed twice.
- **Cool down:** 10 min of aerobic exercise and range of motion/flexibility exercises
- **Social tea and coffee**

Adherence to the programme is monitored as the number of sessions attended, electronically collected by swipe access to the facility.

Group exercise consultations were conducted at induction to the programme, and at 4 weeks, and 3 and 6 months. Researchers trained in exercise consultation delivery delivered the consultations and adhered to a motivational interviewing style. The aim of the consultations was to use behaviour change techniques to improve exercise adherence. The consultants focused on the benefits of exercise, barriers to exercise, problem solving, goal setting, and action planning. The group setting fostered peer social support. Each subsequent consultation built on the previous consultation delivered at earlier time points and involved a review of behaviour goals and feedback on progress.

Induction to the MedEx programme included a beginner exercise class. The beginner class followed the same format as regular MedEx classes but involved smaller group sizes and included demonstrations and teachings on the exercise techniques and equipment. The aim was to improve self-efficacy and foster social support to improve programme initiation and adherence.

3.4 Outcome Measures

Table 3.1 presents the outcome variables and the measurement tools used. The primary outcome was cardiorespiratory fitness assessed using the 6-minute time trial (6MTT). Secondary outcomes were quality of life (QoL), physical activity (PA) and health care utilisation. Tertiary outcomes were blood pressure (BP), biomarkers, other measures of physical fitness (strength, flexibility, body composition), falls risk and cognitive function. Exploratory outcomes were psychosocial

determinants of physical activity. A detailed description of data collection protocols is outlined in Appendix 2.

Table 3.1: Outcome measures

Outcome	Subsections	Measurement Tool
Primary outcome		
Cardiorespiratory fitness		6 minute time trial
Secondary outcomes		
Quality of life	Health status	Medical Outcomes Study Short Form-12, EuroQoL-5D-3L
	Depressive symptoms	Patient Health Questionnaire-8
	Psychological wellbeing	Satisfaction with Life Scale, Warwick Edinburgh Mental Wellbeing Scale
	Disease-specific	COPD Assessment Test, Functional Assessment of Cancer Therapy, Walking Impairment Questionnaire
Physical activity		Accelerometer, International Physical Activity Questionnaire
Healthcare utilization		12 month recall questionnaire
Tertiary outcomes		
Blood pressure		24-hour blood pressure monitor
Blood markers		Lipids, glucose, inflammation (CRP)
Physical fitness	Body composition	Body mass index, waist-to-hip ratio
	Strength	Sit-to-stand test, handgrip test
	Flexibility	Sit-and-reach test
	Claudication time	Claudication treadmill test
Falls risk		Timed get up and go test
Cognitive function	Attention	Attention Network Task
	Memory	Luck & Vogel Visual Working Memory Task
	Cognitive reserve	Cognitive Reserve Questionnaire
Exploratory outcomes		
Psychosocial outcomes	Self-efficacy	Self-regulatory self-efficacy, barrier self-efficacy
	Social support	Social support for exercise - family and friends
	Intentions	Intentions for exercise

Outcome measures were assessed at baseline, and 3, 6 and 12 months. The assessments were conducted over 2 visits, separated by 6 days, and 3 visits for participants with intermittent claudication (day 2 and 3 were separated by 24 hr). Figure 3.2 provides an overview of assessment procedure. Visit 1 involved a fasting blood sample, questionnaire completion and assessment of body composition, strength and flexibility. Participants were provided with a take home questionnaire and an accelerometer to wear for 6 days. Visit 2 involved assessments of cognitive function, cardiorespiratory fitness and falls risk. Participants were provided with an ambulatory BP monitor to wear for 24 hours and a take home questionnaire. Participants with intermittent claudication performed a treadmill test before the start of the first class at Visit 3.

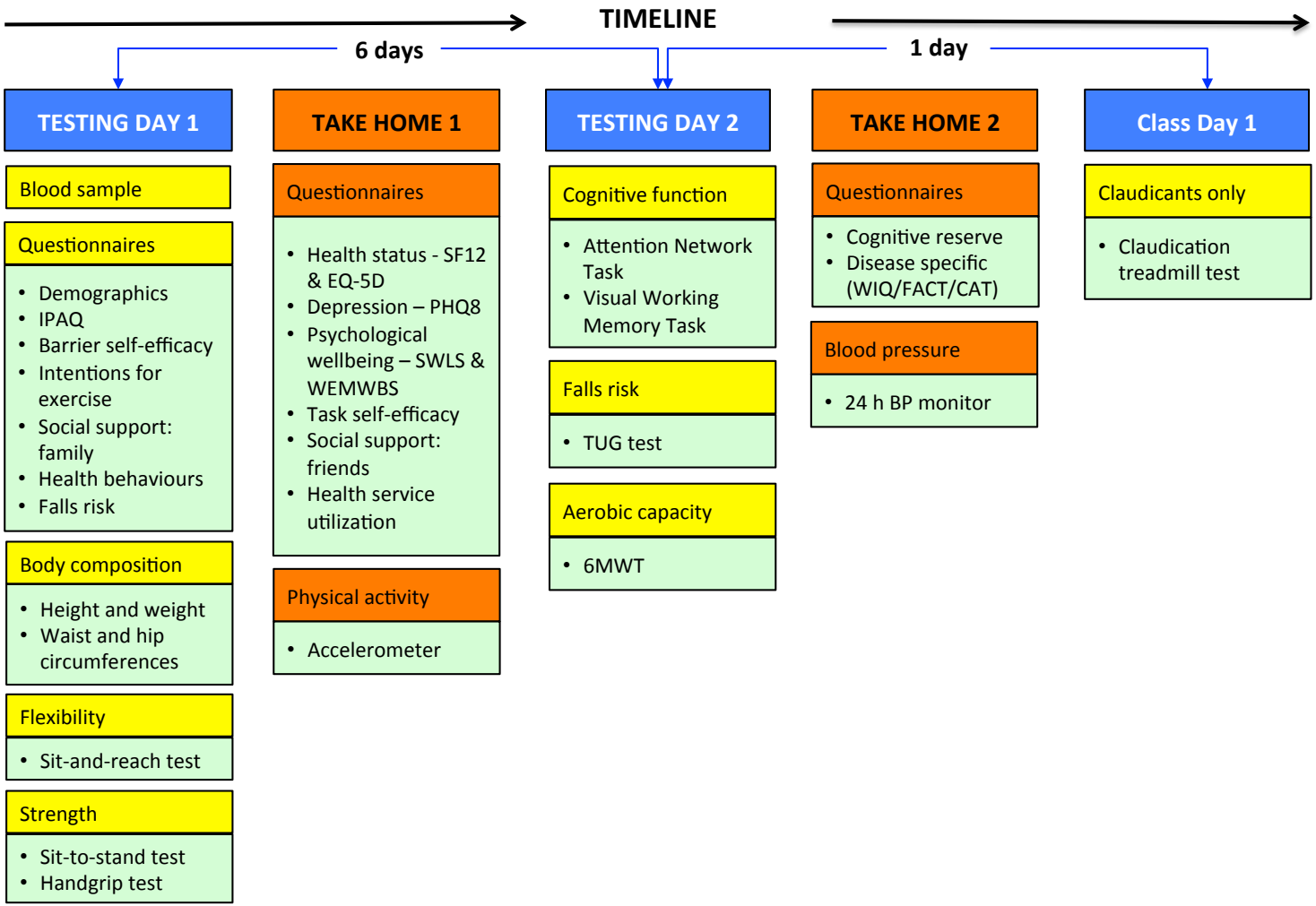

Figure 3.2: Algorithm of assessment process

3.5 Data Handling and Analysis

3.5.1 Sample size

The critical determination of the sample size was the standard deviation of the change in 6MWT distance from time 1 (baseline) to time 2 (12 months). The standard deviation estimate used is 90 m (Polkey *et al.,* 2013). The minimum difference to be detected is 25 m as described in the literature (Holland & Nici, 2013). For a power of 80% and two-sided significance of 5%, a sample size of 104 participants was required. To account for drop out 400 participants were recruited.

3.5.2 Data handling

Primary and secondary outcome data for physical fitness, QoL and psychosocial outcomes were handled using double data entry and cleaning. All other outcome measures underwent single data entry.

3.5.3 Data analysis

Data analyses were conducted by Ms. Olivia Mason, CSTAR (Centre of Support and Training in Analysis and Research), University College Dublin. Analyses were performed using IBM SPSS Statistics 24. Intention-to-treat analysis was performed on data from a number of the questionnaires by using data imputation. Questionnaire responses were imputed for the EQ-5D, Satisfaction with Life Scale, Warwick Edinburgh Mental Wellbeing Scale, health care utilisation, self-efficacy for exercise, intentions for exercise and social support for exercise using SAS 9.4. Descriptive statistics are displayed in either n (%) for counts or median (IQR) for numeric data. The Wilcoxon Rank-Sum test and Friedman's test were used to assess difference between time points for paired participants, and Mann-Whitney U or Kruskal Wallis were used for independent data.

Chapter 4 Findings

4.1 Participants

Four hundred and three participants were recruited. Participant demographics are presented in Table 4.1. The mean age was 63 (range 28-96) years and 203 participants were male and 200 were female. Forty-nine percent of participants were referred to MedEx by hospital consultants and a further 14% were referred from phase IV cardiac rehabilitation teams within the hospitals. GPs were responsible for 26% of referrals. Two-hundred and twenty-one participants completed the trial, 97 dropped out and 86 were lost to follow up at 12-months. The trial flow diagram is illustrated in Figure 4.1, including reasons for drop-out and loss to follow-up. This highest risk period for drop-out was within the first 3 months, with 19% of participants dropping out during this period. This includes 19 (4.7%) partipants who dropped out following induction and prior to commencing the programme and 59 (14.7%) participants who dropped out between commencing the programme and 3 months. Drop-out rate for 3–6 months and 6–12 months were 2.7% and 2%, respectively. More females (n=60) than males (n=30) dropped out. There was no difference in the mean age of completers and drop-outs. Educational status was also similar. Eleven percent of completers and 11% of drop-outs had primary education only; 35% of completers and 45% of drop-outs had secondary education; and 37% of completers and 38% of drop-outs had higher education. On average, trial completers attended 31 MedEx exercise classes in the 12 month period. Twenty-five percent of completers attended ≥46 sessions in 12 months.

Table 4.1: Participant demographics (n=403)

Age (yr)		64 (56-71)
Gender, male		203 (50.5)
BMI (kg/m^2)		28.9 (8.4)
Marital status		
	Married	237 (62.0)
	Living with partner	20 (5.2)
	Single, never married	59 (15.4)
	Separated	16 (4.2)
	Divorced	14 (3.7)
	Widowed	34 (8.9)
Education		
	None	3 (0.8)
	Some primary	42 (10.8)
	Junior certificate (or equiv.)	81 (20.8)
	Leaving certificate (or equiv.)	79 (20.3)
	Diploma/certificate	80 (20.6)
	Primary degree	48 (12.3)
	Postgraduate/higher degree	47 (12.1)
Chronic illness		
Cardiovascular disease		**152 (37.7)**
	Heart disease	*107 (26.6)*
	Heart failure	*7 (1.7)*
	Peripheral arterial disease	*38 (9.4)*
Respiratory disease		**76 (18.9)**
	COPD/chronic bronchitis/emphysema	*42 (10.4)*
	Asthma	*25 (6.2)*
	Other lung disease	*16 (4.0)*
	Pulmonary hypertension	*4 (1.0)*
Diabetes		**54 (13.4)**
	Type 1	*46 (11.4)*
	Type 2	*8 (2.0)*
Cancer		**97**
	Breast	*50 (12.4)*
	Colorectal	*15 (3.7)*
	Prostate	*14 (3.5)*
	Lung	*3 (0.7)*
	Other	*14 (3.5)*
Mental health condition		**23 (5.7)**
	Depression	*12 (3.2)*
	Anxiety/emotional mental health condition	*23 (5.7)*
Other		**311 (77.2)**
	Hypercholesterolaemia	*46 (11.4)*
	Hypertension	*62 (15.4)*
	Arthritis/rheumatic disease	*46 (11.4)*
	Chronic pain	*14 (3.5)*
	Other conditions	*143 (35.5)*

Continuous variables are presented as median (IQR); categorical variables are presented as n (%). Data on chronic illness were obtained from referral letters.
Note: Medical history was reported from participant referral letters.

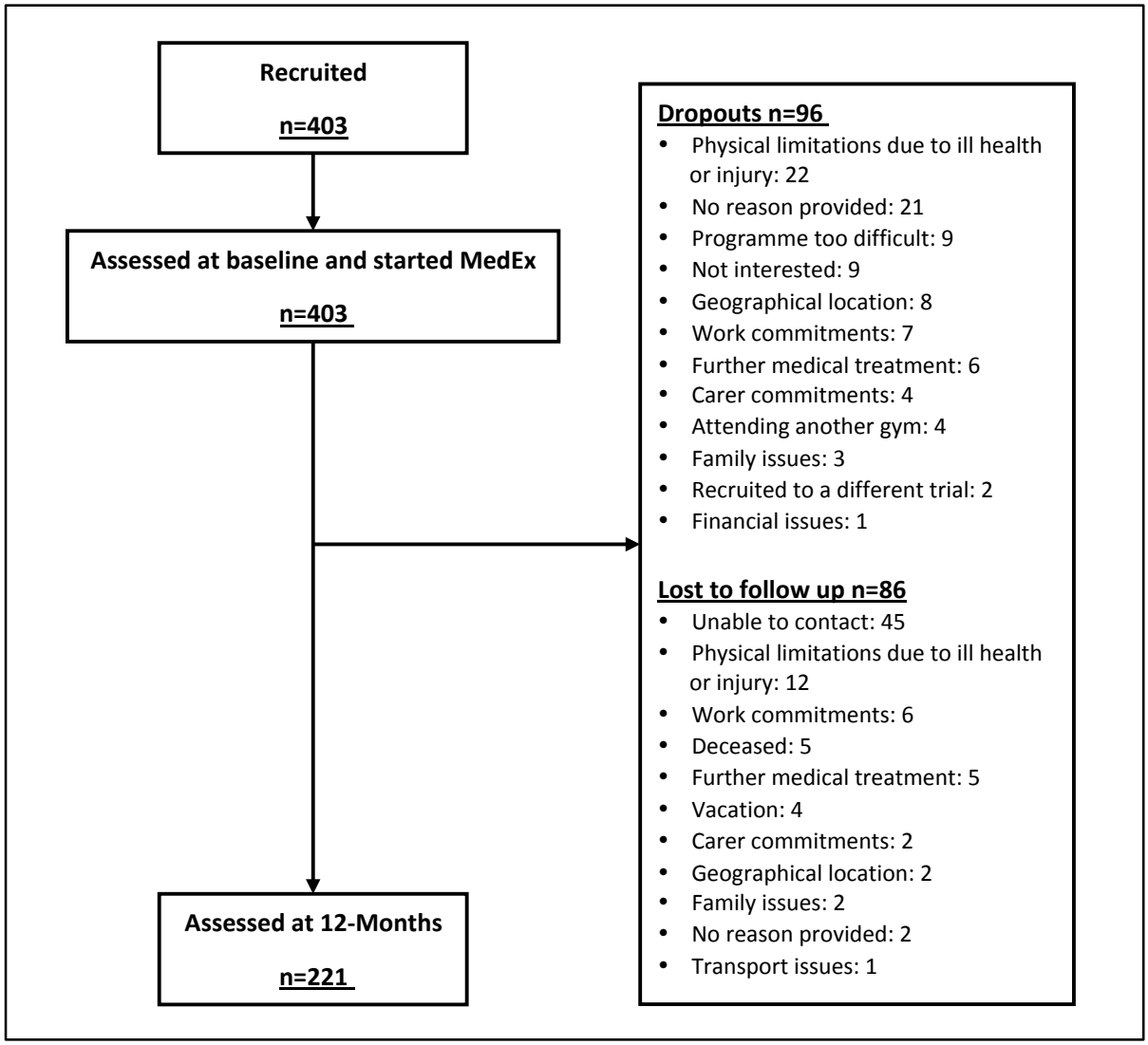

Figure 4.1: Trial flow diagram

4.2 Primary Outcome

There was a statistically significant increase in 6MTT distance between baseline and 12 months [482.0 m (403-541) vs. 540 m (452-639); p<0.001] (Figure 4.2). Significant improvements in 6MTT distance were found in both participants who had a high attendance at MedEx (≥1 session per week/≥46 sessions per year) and those who had a low attendance (≤1 session per week/≤46 sessions per year) (Table 4.2). A time (baseline and 12 months) x attendance (high and low) ANOVA found no significant interaction effect.

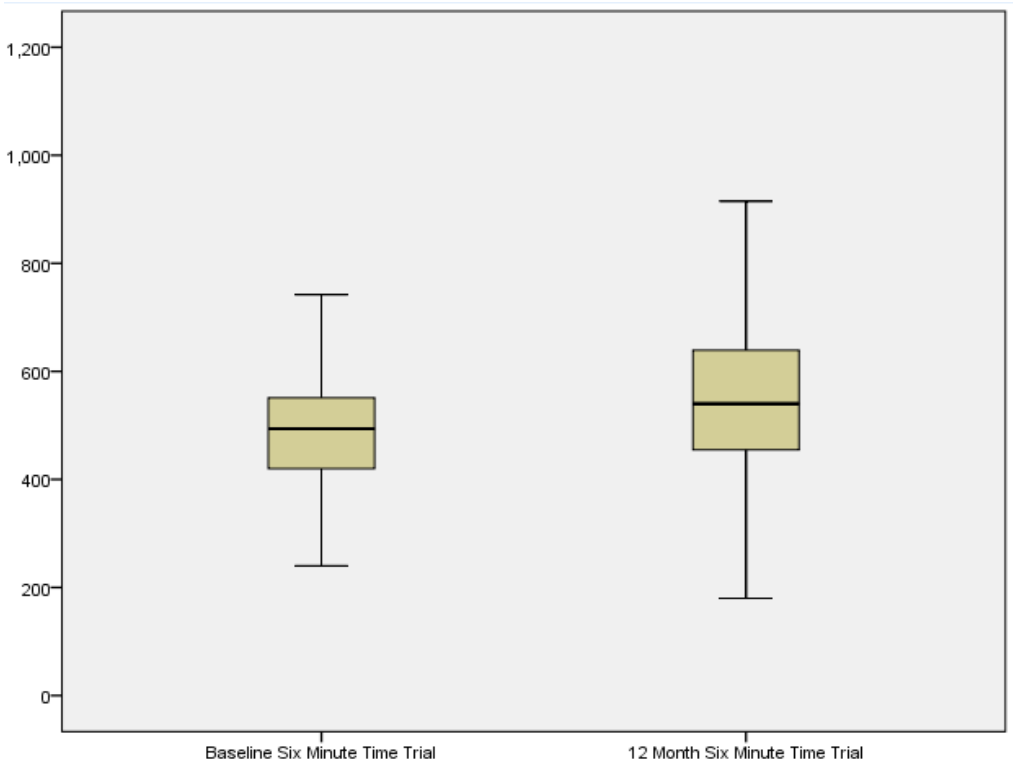

Figure 4.1: 6MTT at baseline and 12 months

Table 4.2: 6MTT at baseline and 12 months for high and low attenders

Attendance	n	Baseline (m)	12 Months (m)	p-value
<46 sessions*	143	485 (405-551)	539 (434-633)	<0.001
≥ 46 sessions*	52	506 (438-540)	563 (481-694)	<0.001

Data are reported as median (IQR). p<0.05 was taken as *statistical significance following P┼ Wilcoxon Ranked Sum test for change between baseline to 12-months.

4.3 Secondary Outcomes

4.3.1 Physical activity

4.3.1.1 Accelerometers

There were no statistically significant differences in PA variables between baseline and 12-months (Table 4.3). In high attenders, there was a significant increase in light-intensity physical activity and a trend towards an increase in step count between baseline and 12 months.

Table 4.3: Physical activity at baseline and 12 months

Variable	n	Baseline	12 Months	P†
Waking sedentary time*				
All participants	118	9.6 (8.2-10.5)	9.6 (8.7-10.9)	0.873
<46 sessions	82	9.7 (8.4-10.5)	9.6 (8.7-10.9)	0.386
>46 sessions	36	9.3 (8.1-10.7)	9.2 (8.2-11)	0.838
LIPA*				
All participants	118	1.2 (1.0-1.4)	1.2 (0.9-1.4)	0.247
<46 sessions	82	1.2 (1.0-1.4)	1.2 (0.9-1.4)	0.582
>46 sessions	36	1.1 (0.9-1.5)	1.2 (1.0-1.6)	0.016
MVPA*				
All participants	118	15.9 (2.7-16.6)	17.4 (7.8-29.4)	0.913
<46 sessions	82	15.3 (6.4-30.9)	16.6 (7.0-28.9)	0.846
>46 sessions	36	18.4 (7.8-36.3)	18.4 (13.4-34.9)	0.460
Step-count*				
All participants	118	6607 (5105-9210)	7058 (5177-8964)	0.507
<46 sessions	82	6598 (5164-8812)	6943 (4698-8430)	0.600
>46 sessions	36	6683 (4681-10364)	7445 (5841-10582)	0.088

*Data are presented as median (IQR). P<0.05 was taken as *statistical significance. P† Wilcoxon Ranked Sum test for change between baseline to 12-months, P≠ Mann Whitney U test for the difference between high and low attenders at 12-months.*

4.3.1.2. International Physical Activity Questionnaire (IPAQ)

There was a significant difference between baseline and 12 months for metabolic equivalent task (MET) minutes of PA per week [1071.5 (436.5-2700.8) vs. 2102.3 (854.5-4412.3), p<0.001]. At 12 months, significantly more participants were classified as active (meeting the PA recommendations) than inactive or minimally active compared to baseline (p<0.001).

4.3.2 Quality of life

There were statistically significant improvements in all QoL measures between baseline and 12 months (Table 4.4). There was a significant reduction in depressive symptoms (PHQ8). Self-reported health status (EQ-5D) significantly improved for mobility, self-care, usual activities, anxiety/depression and pain/discomfort. Significantly fewer participants were reporting problems in each of these domains at 12 months. Overall health state also significanly improved. There were significant improvements in satisfaction with life total score and mental well-being total score. There were also significant improvements in COPD and cancer-specific quality of life measures. Item 1 only of the SF-12 was used and Figure 4.2 illustrates how participants rated their health at baseline and 12-months.

Table 4.4: QoL at baseline and 12 months

QoL Measures	n	Baseline	12 Months	p-value
Depressive symptoms (PHQ8)	139	4 (1-7)	3 (0-7)	<0.001[F]
Self-reported health status (EQ-5D)				
Mobility	403			<0.001[c]
No problems		177 (44)	255 (63)	
Some problems		207 (51)	146 (36)	
Confined to bed		19 (5)	1 (0.2)	
Self-care	402			<0.001[c]
No problems		363 (90)	393 (98)	
Some problems		33 (8)	7 (2)	
Unable to wash/dress self		6 (2)	1 (0.2)	
Usual activities	399			<0.001[c]
No problems		179 (45)	292 (73)	
Some problems		196 (49)	107 (27)	
Unable to perform usual		24 (6)	4 (1)	
Anxiety/depression	403			
Not anxious/depressed		261 (65)	352 (87)	<0.001[c]
Moderately		132 (33)	46 (11)	
Extremely		10 (3)	4 (1)	
Pain/discomfort	400			<0.001[c]
No pain/discomfort		106 (27)	67 (17)	
Moderate pain/discomfort		258 (65)	324 (81)	
Extreme pain/discomfort		36 (9)	12 (3)	
Overall health state	403	70.0 (55.0-80.0)	70.0 (70.0-80.0)	<0.001[w]
Satisfaction with life scale	397	26 (20-29)	27 (26-28)	<0.001[w]
Mental well-being scale	396	27 (24-29)	28 (28-29)	<0.001[w]
Walking impairment score	10	39.9 (23-80)	52.6 (18-249)	ns[F]
COPD assessment Test*	14	20.0 (6-33)	16.5 (4-33)	<0.05[F]
FACT				
*FACT General**	27	80 (42-103)	93 (49-107)	<0.001[F]
FACT Colorectal	6	123 (74-130)	118.3 (98-134)	ns[F]
*FACT Breast**	15	99 (62-131)	119 (67-133)	<0.05[F]

*P-value 0<0.05 taken as statistical significance following (c) Chi-square test, (w) Wilcoxon Rank Sum Test and (F) Friedman test.

Description of scores: PHQ8 – Personal Health Questionnaire (0-4 no depression; 5-9 mild depression; 10-14 moderate; 15-19 moderately severe; 20-24 severe); EQ-5D-3L data are reported as n (%). Overall health state scored on a VAS anchored at 0: worst imaginable health state and 100: best imaginable health state). Satisfaction with life scale (range:5-9: extremely dissatisfied with life to 31-35 extremely satisfied); Mental wellbeing scale (range: 7 to 35, higher scores indicate more positive mental well-being). For the COPD assessment test, the higher the score the more severe the condition: >30 very high, >20 high, 10-20 medium, <10 low.

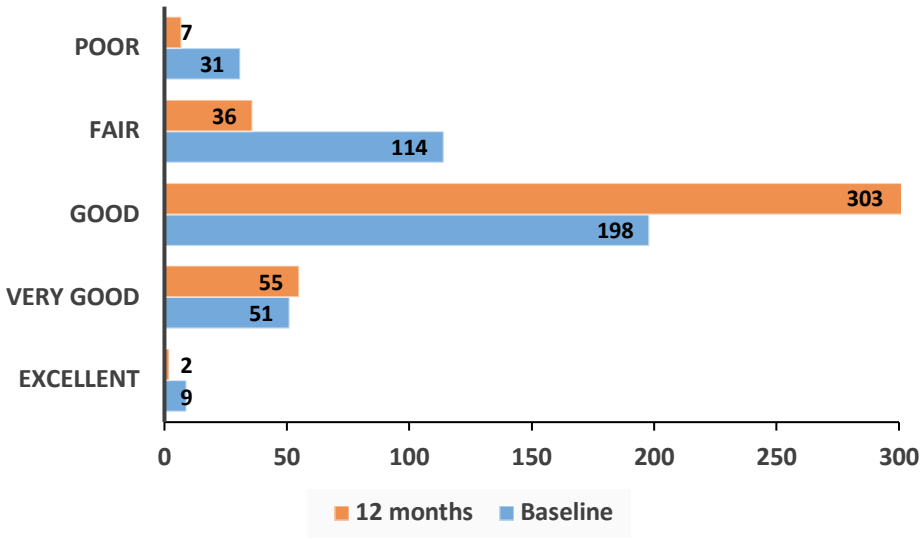

Figure 4.2: SF-12 Item 1: Self-rating of health
Data are reported as frequencies.

4.2.3 Health care utilisation

There were significant reductions in 12-month recall of the number of GP visits, emergency department visits, outpatient visits and nights spent in hospital at 12 months compared with baseline (Table 4.5).

Table 4.5: Health care utilisation at baseline and 12 months

Health care variable	n	Baseline	12 Months	p-value
GP visits*	398	┼5.0 (3.0-7.0) ‡42 (185)	4.0 (3.0-6.0) 26 (137)	<0.001[w]
ED visits as patient*	395	0.0 (0.0-1.0) ┼13 (109)	0.0 (0.0-0.0) 7 (61)	<0.001[w]
Hospital visits as outpatient*	386	‡7.0 (3.0-10.0) ┼76 (230)	4.0 (2.0-4.0) 23 (104)	<0.001[w]
Nights spent in hospital*	393	‡ 1.0 (0.0-6.0) ┼29 (138)	0.0 (0.0-0.0) 14 (85)	<0.001[w]

*P-value <0.05 taken as statistically significant following (w) Wilcoxon Signed Rank test. ┼Values are given in median (IQR), ‡ Values are given in mean (SD).

4.3 Tertiary Outcomes

Table 4.6 outlines the data for teritary outcomes.

4.3.1 Blood pressure

24 hour blood pressure data was available on a sub-sample of participants (n=58). There was a significant reduction in the average daytime systolic BP between baseline and 12 months. Subgroup analysis was conducted for participants who were hypertensive. This subgroup showed a significant reduction in all BP measures (average day time, night time and 24 hour systolic and diastolic BP) between baseline and 12-months (Table 4.7).

4.3.2 Blood markers

There were significant reductions in total cholesterol, glucose and C-reactive protein between baseline and 12-months.

4.3.3 Other measures of physical fitness

There were significant reductions in BMI and waist:hip ratio between baseline and 12-months. There were significant improvements in the sit-to-stand test, handgrip test and sit-and-reach test. In participants with intermittent claudication, there were significant improvements in time to the onset claudication between baseline and 12 months.

4.3.4 Falls risk

There was a significant improvement in the timed up and go test between baseline and 12 months. Significant fewer participants reported falling in the previous year and reported a fear of falling at 12 months compared to baseline.

4.3.4 Cognitive function

From baseline to 12 months, there were significant improvements in the Luck & Vogel Visual Working Memory Task. Average reaction time (RT) for the small set and large set conditions significantly improved. In the Attention Network Task, average RT and executive control to correct detections significantly improved. There was a significant increase in mean RT in the alerting correct condition between baseline and 12-months.

Table 4.6: Teritary outcomes at baseline and 12 months

Outcomes	n	Baseline	12 Months	p-value
Blood pressure (mm/Hg)				
*Avg daytime SBP**	58	151 (121-181)	141 (132-140)	<0.05[w]
Avg night-time SBP	58	133 (117-149)	127 (114-140)	ns[w]
Avg 24-hour SBP	58	142 (128-157)	137 (126-148)	ns[w]
Avg daytime DBP	58	78 (61-95)	77 (70-84)	ns[w]
Avg night-time DBP	58	67 (59-75)	66 (60-72)	ns[w]
Avg 24-hour DBP	58	73 (66-80)	72 (66-78)	ns[w]
Blood markers				
LDL (mmol/L)	83	1.3 (0.7-1.9)	1.3 (0.7-1.9)	ns[w]
HDL (mmol/L)	83	2.2 (1.9-4.1)	2.3 (2.1-2.5)	ns[w]
Total cholesterol (mmol/L)*	83	4.5 (3.8-5.2)	4.4 (3.7-5.1)	0.005[w]
TG (mmol/L)	83	1.0 (0.7-1.3)	1.0 (0.7-1.3)	ns[w]
Glucose (mmol/L)*	83	6.0 (5.4-6.6)	5.7 (5.0-6.4)	0.003[w]
CRP (mg/L)*	83	3.8 (1.3-6.3)	1.9 (0.3-3.5)	<0.001[w]
Physical fitness				
BMI (kg/m$^{2)}$*	159	28.5 (25.2-31.7)	27.8 (24.3-31.3)	<0.001[w]
*Waist:hip ratio**	159	1.0 (0.9-1.1)	1.0 (0.5-1.5)	<0.001[w]
Sit and reach (cm)*	159	8 (1-16)	9 (2-16)	<0.001[w]
Sit to stand (secs)*	159	20.2 (17-23.4)	16.5 (13-20)	<0.001[w]
Handgrip test (kg)*	159	26.1 (19.9-32.3)	27.1 (20-34.1)	0.002[w]
*Onset claudication time (min)**	10	2.8 (1.1-30.3)	7.3 (2.2-11.4)	<0.05[F]
Max. claudication time (min)	10	6.9 (3.3-10)	12.8 (3-25)	
Falls risk				
TUG test (secs)	27	7.9 (5.6-10.2)	6.6 (5.2-8.1)	p<0.05
Cognitive function				
Visual Working Memory				
% Accuracy to small Set	119	93.0 (88.0-98.0)	93.0 (90.0-96.0)	ns[w]
Reaction time to small Set(ms)*	121	1245.5 (1000.75-1490.0)	1063.5 (894.5-1232.5)	<0.001[w]
% Accuracy to large set	120	68.0 (61.5-74.5)	68.0 (62.5-73.5)	ns[w]
*Reaction time to large set (ms)**	119	1226.5 (969.6-1483.4)	1058.0 (880.5-1235.5)	<0.001[w]
Attention Networking				
% Accuracy to ANT	86	98.3 (96.8-99.8)	98.6 (96.6-101.6)	ns[w]
*Reaction time to ANT (ms)**	86	834.7 (32.7-936.7)	801.9	<0.01[w]
Alerting correct	83	30.9 (9.0-52.8)	39.41 (13.8-65.1)	<0.05[w]
Orienting correct	83	43.46 (14.5-72.5)	43.98 (21.3-66.7)	ns [w]
*Exec control correct**	80	127.94 (95.0-160.8)	106 (76.5-135.4)	<0.001[w]
Cognitive reserve score	136	113.0 (89.8-136.2)		

*P-value <0.05 taken as statistically significant following (w) Wilcoxon Signed Rank test or (F) Friedman test. Values are given in median (IQR). Mean (standard deviation) reported for Cognitive Reserve)

Note: For the Attention Network Task separate RT difference measures (Alerting: RT to No Cue – RT to Double Cue; Orienting: RT to Central – RT to Spatial Cues; Executive: RT to Incongruent – RT to Congruent), the higher the score, the greater the attentional cost to no cues in alerting; central cues in orienting and incongruent trials in executive. It takes more time to pay attention to these types of conditions. For the Cognitive Reserve task, the higher the overall score, the higher the inferred reserve capacity level. Reserve was measured at baseline only.

Table 4.7: Subgroup analysis of blood pressure for hypertensive participants

Blood pressure variable	**n**	**Baseline** (mm/Hg)	**12 Months** (mm/Hg)	**p-value**
Avg daytime SBP *	49	156 (135-177)	145 (137-153)	<0.001
Avg night-time SBP *	49	144 (129-159)	133 (122-152)	<0.001
Avg 24-hour SBP *	49	150 (137-163)	141 (131-151)	<0.001
Avg daytime DBP *	49	82 (72-92)	78 (72-84)	<0.05
Avg night-time DBP *	49	71 (63-79)	66 (60-72)	<0.05
Avg 24-hour DBP *	49	78 (69-86)	73 (68-78)	<0.05

*P-value <0.05 was taken as statistical significance. Baseline hypertension was classified as: average 24-hour BP ≥130/80; average daytime BP ≥135/85; average night-time BP≥120/70.

4.4 Exploratory Outcomes

4.4.1 Psychosocial determinants of physical activity

There was a significant improvement in social support for exercise from friends between baseline and 12 months (Table 4.8). However, there were significant reductions in self-efficacy (self-regulatory and barrier), intentions to exercise and social support for exercise from family between baseline and 12-months.

Table 4.8: Psychosocial determinants of physical activity at baseline and 12 months

Outcomes	n	Baseline	12 Months	p-value
Self-regulatory self-efficacy*	395	78.3 (66-89.1)	72.7 (71.4 – 83.6)	<0.001[F]
Barriers to self-efficacy*	395	59.2 (45.4-73.9)	56.5 (51.5-63.9)	0.002[F]
Intentions to exercise*	395	3.5 (3.0-3.9)	3.3 (3.0-3.6)	<0.001[F]
Social support (family)*	395	2.5 (1.5-3.63)	2.3 (1.9-2.6)	<0.001[F]
Social support (friends)*	395	1.75 (1.3-2.6)	2.00 (1.6-2.3)	<0.001[F]

Note: For all psychosocial outcome scores, the higher the score, the more positive the response.

Chapter 5 Discussion

5.1 Summary of Findings

Participation in the MedEx programme over a 12-month period was associated with a significant improvement in cardiorespiratory fitness. Significant improvements were also evident in other measures of physical fitness, including strength, flexibility, body composition, and falls risk; clinical outcomes, including health care utilisation, BP, and blood markers; and psychological outcomes, including QoL and cognitive function.

5.2 Cardiorespiratory Fitness

Cardiorespiratory fitness is one of the strongest independent predictors of morbidity and mortality in both primary and secondary prevention of cardiovascular disease[20,21]. Even small improvements in cardiorespiratory fitness are associated with significant reductions in risk. For example, an increase in cardiorespiratory fitness of 1 metabolic equivalent (MET) is associated with a 13% reduction in all-cause mortality and a 15% reduction in cardiovascular disease[22]. The most commonly used test of functional exercise capacity for patient management and research in patients with moderate-to-severe cardiopulmonary disease is the 6-minute walk test[23]. This trial used the same standardised protocol as the walk test with the exception that participants could walk/jog depending on each individual's ability. This was to account for the range of abilities in the MedEx cohort and enhance the ability of the test to detect inter-individual differences and the responsiveness of the test to change. Participation in MedEx over a 12-month period led to a significant and clinical improvement in cardiorespiratory fitness. A change in 6-minute walk test of more than 50 m is clinically significant in most diseases[24] and 25-33 m in respiratory disease[25]. The MedEx programme was associated with a mean improvement of 58 m (11%) in 6MTT distance. Improvements were found in both high and low attenders to the MedEx programme. This has been similarly reported in a previous CR study, in which there was no difference in 6-minute walk test between people who attended supervised once-weekly vs. twice-weekly exercise sessions[26].

5.3 Physical Activity and Sedentary Behaviour

There was no significant change in physical activity or sedentary behaviour between baseline and 12 months. In high attenders, there was a significant increase in LIPA and a trend towards to an increase in daily step count. Participating in >300 minutes of LIPA per week has been found to be associated with more favourable body composition, blood pressure, inflammatory markers, glucose

and insulin compared to <300 min[28]. High attenders at MedEx were participating in >500 min of LIPA at the 12-month point.

A recent systematic review of community-based PA interventions for older adults provided some evidence for effectiveness to increase physical activity[27]. However, there are many factors that determine physical activity behaviour including psychosocial factors, which may help to explain the lack of an improvement in PA following MedEx. MedEx had a positive effect on social support for exercise from friends. Social isolation is common among elderly adults and it has been reported that elderly females have difficulty in finding physically active friends[29]. The MedEx environment (group- and community-based) provides opportunity for social interaction and making new friends. However, social support for exercise from family decreased over the 12-month period. It has been previously reported that compared with men, the majority of women aged 45 and older have less support from their spouse and generally experienced declining encouragement to be active with their advancing years[29]. There was also a decrease in exercise self-efficacy and exercise intentions, the reasons for which are unclear.

5.4 Quality of Life

Living with a chronic disease has been shown to adversely affect health-related QoL (HRQoL). Furthermore, chronic disease is associated with depressive symptoms, insomnia and cognitive impairment, and all are associated with reduced HRQoL[17]. Participation in the MedEx programme resulted in significant improvements in QoL and positive mental well-being and a significant reduction in depressive symptoms. A recent meta-analysis addressed the antidepressant effects of exercise in older adults and reported that exercise had a large and significant effect on depression following i) mixed aerobic and anaerobic exercise interventions; ii) moderate intensity exercise; iii) group-based exercise; iv) mixed/unsupervised exercise sessions in people with other clinical morbidities[30], all of which are similar to the MedEx Model.

5.5 Blood Pressure

Hypertension is the leading risk factor for global mortality. Aerobic exercise has been recently suggested to be one of the non-pharmacological treatments for hypertension and is recommended by European and American hypertension guidelines to reduce BP[31,32]. The average reduction in SBP and DBP for hypertensive individuals following aerobic exercise is 6/7 mmHg[33]. MedEx was associated with a reduction of almost 10 mmHg in both SBP and DBP values in hypertensive participants. These findings are of major clinical significance. It has been estimated, on a population

level, that a 5 mmHg decrease in SBP is associated with a 7%, 14% and 9% reduction in all-cause mortality, mortality due to stroke and CHD mortality, respectively[34].

5.6 Other Clinical Outcomes

Participation in the MedEx programme was associated with a significant reduction in total cholesterol and fasting blood glucose levels (means were within the normal range at baseline) and CRP (higher than normal range at baseline). The American College of Cardiology and the American Heart Association emphasize lifestyle, including regular exercise, as the foundation for atherosclerotic CVD risk reduction efforts[35]. Lifestyle modification is recommended both prior to and concurrently with the use of pharmacotherapy[35,36]. CRP is a marker for inflammation and CRP levels above 2.4 mg/L is associated with a doubled risk of a coronary event compared to CRP levels below 1 mg/L[37]. Previous research investigated the effect of a 12-month moderate-intensity exercise intervention on CRP levels in elderly individuals (aged 70-89) and reported a 32% reduction in CRP[38]. MedEx was associated with a 47% reduction in CRP from a median of 3.8 mg/L to 1.9 mg/L.

5.7 Other Measures of Physical Fitness

MedEx was associated with a significant and positive change in both arm and leg strength. Sarcopenia is the age related loss of skeletal muscle mass and is a major factor associated with declining strength with age[39]. Sarcopenia has been shown to be exacerbated by certain chronic conditions, and can also increase the burden of chronic disease. Moreover lower levels of arm and leg strength are related to mortality[40]. Regular strength training has been shown to preserve bone density, independence and vitality with age, as well as improvements in sleep and reductions in depression[41]. There was also an improvement in the TUG test, an indicator of falls risk, and a reduction in self-reported incidence and fear of falls. In Ireland, one in three older people fall every year and two-thirds of them fall again within six months. Older people are more likely to suffer serious injuries, disability, psychological consequences and death following a fall[42].

Flexibility improved with the MedEx programme. Flexibility reduces with advancing age, which has detrimental effects on activities of daily living, mobility and functional decline[43]. Exercise, including general aerobic and resistance exercise has previously been shown to have beneficial effects on flexibility in older adults[43].

There were also improvements in body composition, including BMI and waist-to-hip ratio. Overweight/obesity is a central risk factor for many chronic conditions[44].

5.8 Cognitive Function

Prior research on the acute and chronic effects of aerobic exercise on cognitive processes such as executive function, point to significant improvements in both healthy ageing and young populations[45,46,47] and also more recently in chronic illness populations[48,49]. MedEx extends this line of evidence as significant improvements in processing efficiency were found in both visual working memory and attentional networks. Whilst both tasks show that performance accuracy is not significantly improved, processing efficiency is significantly improved in Working Memory and Attention. Both tasks dovetail with the argument that physical exercise enhances cognitive function via brain-derived neurotropic factors (BDNF); and point to the benefits of exercise not only in working memory ability to detect change; but also in the alerting and executive aspects of attention. Similar to prior studies, this study ground a significant effect on the executive system following chronic exercise. However, we also report a selective effect on alerting, and not orienting attention. The clinical significance of our results relates to the effects of chronic exercise on executive components of cognition. These executive components are part of the brain's cognitive control system and are implicated in general goal-directed reasoning, emotion regulation and other cognitive abilities.

5.9 Clinical Significance

It has been demonstrated that participation in the MedEx programme has positive effects on selected physical, clinical and psychosocial health outcomes. This combination of effects contributes to an overall improved health risk profile in a chronic illness cohort. In the context of secondary prevention, an improved health risk profile may slow or halt the progression of the disease, prevent recurrence or further complications, reduce the impact of the disease and restore health and function. These findings are highly significant and provide a strong evidence-base for the clinical effectiveness of a model of chronic illness rehabilitation that is community-based, scalable and sustainable, and accommodates all chronic illnesses.

5.10 Economic Significance

Although this research did not include a cost-benefit analysis, some of the findings may indicate a potential economic benefit from the MedEx programme. Particularly in relation to healthcare utilisation, there was a significant decrease in the number of GP visits, emergency department visits, outpatient visits and nights spent in hospital. In chronic illness populations, exercise has been found to be effective in reducing hospital readmission[7]. The improvement in the health profile of participants may be responsible for the reduced reliance on healthcare services.

5.11 Limitations

Limitations of the trial include the nature of the single arm design resulting in a high risk of random sequence and allocation concealment bias. However this was a pragmatic real-life approach on an already established service. In addition, participants and personnel delivering the programme were not blinded to the trial and medication lists were not collected at baseline.

Chapter 6 Conclusion

A strong evidence base has been provided for the efficacy of MedEx and the clinically-relevant impact of the MedEx Programme. This trial demonstrates that participation in the MedEx programme for 12 months is associated with significant improvements in physical, clinical and psychosocial health and wellbeing in men and women with established chronic illness.

In addition to be clinically-impactful, MedEx as a novel community-based chronic illness rehabilitation model that is both sustainable and scalable. The financial self-sufficiency has been described in the National Exercise Referral Framework (NERF) document produced for the HSE by DCU team (Lead: Prof Catherine Woods with Dr Noel McCaffrey as collaborator). The business plan detailed in the NERF document is based directly on the MedEx model and experience. Separately, a recent detailed independent financial analysis of a proposed MedEx roll out in Dublin has been carried out and demonstrates viability using quite conservative assumptions, themselves drawn from the 10 year MedEx experience to date. A very strong argument for scalability can be made because of both the financial self-sufficiency of the model and the wide availability of state-owned exercise facilities inside and outside third level institutions. For this reason, the up-scaling and roll out of MedEx model is viable and could happen quickly and inexpensively.

Chapter 7 Future work

This trial reported significant benefits in several important outcome measures for people with chronic illness. Due to the strong evidence-base presented along with the continued growth of the MedEx DCU programme, there is an urgent need for similar programmes in other areas of Dublin and other counties of Ireland. The MedEx Team strongly suggest immediate and significant activity in the following key areas:

1. Development, delivery and evaluation of a MedEx service throughout Dublin, located primarily in state-owned public leisure facilities with close links to local hospitals, GPs and other health care professionals;
2. Development, delivery and evaluation of a MedEx Home Programme for people who, for various reasons, cannot or will not attend a supervised programme (Appendix 3). Substantial work has been carried out by the MedEx Team on this important programme, focusing on delivering the connected health pillars (information, education, interaction and monitoring) while providing expert-given telephone support, peer support and regular (but infrequent) face-to-face visits;
3. Development of a medical data and information handing system that is user friendly (for staff, participants and referrers), compliant with standards and data protection regulations and compatible with existing hospital and GP patient record systems. This work is ongoing in collaboration with MedEx industry partner Acquis (Appendix 1);
4. Exploration of innovative behaviour change strategies to include incentive schemes, optional competitive structures (leader boards etc), self-assessment of selected outcomes and self-management of exercise prescription.

The MedEx Team will continue to strive to achieve the MedEx vision of *offering life transforming chronic illness rehabilitation through a network of supervised and home based physical activity programmes that are effective, enjoyable, financially self-sustaining and scalable at local, national and international levels.*

References

1. HSE, 2014a. 'Preventing chronic disease: defining the problem.' [online] Available at: http://www.lenus.ie/hse/bitstream/10147/338212/3/PreventingChronicDisease_DefiningtheProblem.pdf Accessed 24/10/17.
2. HSE, 2014b. 'Tackling Chronic Disease A Policy Framework for the Management of Chronic Diseases.' [online] Available at: http://health.gov.ie/wp-content/uploads/2014/03/tackling_chronic_disease.pdf Accessed 01/11/17.
3. TILDA, 2016. 'Health and Wellbeing: Active Ageing for Older Adults in Ireland' [online] Available at: https://tilda.tcd.ie/publications/reports/pdf/w3-key-findings-report/TILDA%20Wave%203%20Key%20Findings%20report.pdf Accessed 01/11/17 .
4. Department of Health, 2016. 'Health in Ireland - Key Trends.' [online] Available at:http://health.gov.ie/wp-content/uploads/2016/12/Health-in-Ireland-Key-Trends-2016.pdf Accessed 09/11/17.
5. Barnett, K., Mercer, S.W., Norbury, M., Watt, G., Wyke, S. and Guthrie, B., 2012. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. The Lancet, 380(9836), pp.37-43.
6. Balanda, K.P., Barron, S. and Fahy, L., 2010. 'Making Chronic Conditions Count.' '[online] Available at: https://www.publichealth.ie/files/chronic_executive.pdf Accessed 01/11/17.
7. Heran, B.S., Chen, J.M.H., Ebrahim, S., Moxham, T., Oldridge, N., Rees, K., Thompson, D.R., Taylor R.S. Exercise-based cardiac rehabilitation for coronary heart disease. Cochrane Database of Systematics Reviews, 2011.
8. Pedersen, B.K. and Saltin, B. Exercise as medicine – evidence for prescribing exercise as therapy in 26 different chronic diseases. Scand J Med Sci Sports, 2015 (Suppl 3) 25: 1-72.
9. Myers, J. Exercise and cardiovascular health. Circulation, 2003: 107: e2-e5.
10. Hambrecht R, Niebauer J, Marburger C, Grunze M, Kälberer B, Hauer K, Schlierf G, Kübler W, Schuler G. Various intensities of leisure time physical activity in patients with coronary artery disease: effects on cardiorespiratory fitness and progression of coronary atherosclerotic lesions. J Am Coll Cardiol. 1993 Aug; 22(2):468-77.
11. Franklin BA, Swain DP, Shephard RJ. New insights in the prescription of exercise for coronary patients. J Cardiovasc Nurs. 2003 Apr-Jun; 18(2):116-23.
12. Sakuma, K, Yamaguchi A., 2012. Sarcopenia and age-related endocrine function. International Journal of Endocrinology, 10.
13. Durstine, J.L., Gordon, B., Wang, Z. and Luo, X., 2013. Chronic disease and the link to physical activity. Journal of Sport and Health Science, 2(1), pp.3-11.
14. Warburton DE, Glendhill N, Quinney A. The effects of changes in musculoskeletal fitness on health. Can J Appl Physiol. 2001 Apr; 26(2):161-216.
15. Pasanen, T., Tolvanen, S., Heinonen, A., and Kujala, U.M. Exercise therapy for functional capacity in chronic diseases: an overview of meta-analyses of randomised controlled trials. Br J Sports Med 2017;51:1459–1465.
16. Fletcher, G., Balady, G., Blair, S.N., Blumenthal, J., Caspersen, C., Chaitman, B., Epstein, S., Sibarajan Froelicher, E.S., Froelicher, V.F., Pina, I.L., and Pollock, M.L. Statement on Exercise: Benefits and Recommendations for Physical Activity Programs for All Americans. A Statement for Health Professionals by the Committee on Exercise and Cardiac Rehabilitation of the Council on Clinical Cardiology, American Heart Association. Circulation, 1996; 94:857-862.
17. Megari K., 2013. Quality of life in chronic disease patients. Health Psychology Research, 1,3,:e27.
18. Katon, W. Epidemiology and treatment of drepression in patients with chronic medical illness. Dialogues Clin Neurosci, 2011 Mar; 13(1): 7-23.

19. American College of Sports Medicine (ACSM). ACSM's Exercise Management for Persons with Chronic Diseases and Disabilities. 4th Edition. Moore, G.E., Durstine, L.J. and Painter, P.L. Human Kinetics, Champaign , Illinois, 2016.
20. Blair, S.N., Kohl, H.W., Paffenbarger, R.S., Clark, D.G., Cooper, K.H., Gibbons, L.W., 1989. Physical fitness and all-cause mortality: A prospective study of healthy men and women. JAMA, 262(17), pp.2395-2401.
21. Katzmarzyk, P.T., Church, T.S., Blair, S.N., 2004. Cardiorespiratory fitness attenuates the effects of the metabolic syndrome on all-cause and cardiovascular disease mortality in men. Archives of Internal Medicine American Medical Association, 164(10), pp.1092-1097.
22. Kodama S, Saito K, Tanaka S, Maki M, Yachi Y, Asumi M, Sugawara A, Totsuka K, Shimano H, Ohashi Y, Yamada N, Sone H, 2009. Cardiorespiratory fitness as a quantitative predictor of all cause mortality and cardiovascular events in healthy men and women: a meta-analysis. JAMA 301(19), pp.2024-35.
23. Luxton N, Alison JA, Wu J, et al. Relationship between field walking tests and incremental cycle ergometry in COPD. Respirology 2008; 13: 856–862.
24. Rasekaba, T., Lee, A.L., Naughton, M.T., Williams, T.J., Holland, A.E., 2009. The six-minute walk test: a useful metric for the cardiopulmonary patient. Internal Medicine Journal, 39(8), pp.495-501.
25. Holland, A.E., Spruit, M.A., Troosters, T., Puhan, M.A., Pepin, V., Saey., et al. An official European Respiratory Society/American Thoracic Society technical standard: field walking tests in chronic respiratory disease. European Respiratory Journal, 44, pp.1428-1466.
26. Bellet, R.N., Francis, R.L., Adams, L., Morris, N.R., 2015. Six-Minute Walk Test Distances in Fast-Track and Traditional Cardiac Rehabilitation: A 3-YEAR DATABASE REVIEW. Journal of Cardiopulmonary Rehabilitation, 35, 6, pp.417-22.
27. Moore M, Warburton J, O'Halloran P,D., Shields N, Kingsley M. Effective community-based physical activity interventions for older adults living in rural and regional areas: A systematic review. J Aging Phys Act. 2016;24(1):158-167.
28. Loprinzi PD, Lee H, Cardinal BJ. Evidence to support including lifestyle light-intensity recommendations in physical activity guidelines for older adults. Am J Health Promot. 2015;29(5):277-284.
29. Cousins, S.0., 1995. Social support for exercise among elderly women in Canada. Health Promotion International, 10, 4, pp.273-282.
30. Schuch, F.B., Vancampfort, D., Rosenbaum, S., Richards, J., Ward, P.B., Veronese, N., et al. Exercise for depression in older adults: a meta-analysis of randomised controlled trials adjusting for publication bias. Revista Brasileira de Psiquiatria, 38, 3, pp.247-54.
31. Mansia, G., De, B.G., Dominiczak, A., et al., 2007 ESH-ESC Guidelines for the management of arterial hypertension: the task force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). European Heart Journal, 34, pp.2159–219.
32. Weber, M.A., Schiffrin, E.L., White, W.B., et al., 2014. Clinical practice guidelines for the management of hypertension in the community: a statement by the American Society of Hypertension and the International Society of Hypertension. Journal of Hypertension, 32, pp.162–70.
33. Fagard, RH. Exercise characteristics and the blood pressure response to dynamic physical training. *Med Sci Sports Exerc* 2001;**33**(Suppl. 6):S484—492
34. Whelton PK, He J, Appel LJ, Cutler JA, Havas S, Kotchen TA, et al. Primary prevention of hypertension: clinical and pub- lic health advisory from The National High Blood Pressure Education Program. *JAMA* 2002;**288**(15):1882—8.
35. Stone NJ, Robinson J, Lichtenstein AH, Bairey Merz CN, Blum CB, Eckel RH, Goldberg AC, Gordon D, Levy D, Lloyd-Jones DM, McBride P, Schwartz JS, Shero ST, Smith SC Jr, Watson K, Wilson PWF. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce

atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2013.

36. Standards of medical care in diabetes – 2017: summary of revision. Diabetes Care 2-17; 40:S4-5.
37. Hirschfield, G.M, Pepys, M.B., 2013. C-reactive protein and cardiovascular disease: new insights from an old molecule. An International of Journal Medicine, 96, pp.793-807.
38. Nicklas, B.J, Fang-Chi, H, Brinkley, T.J, Church, T, Goodpaster, B.H, Kritchevsky, S.B, Pahor, M., 2008. Exercise Training and Plasma C-reactive Protein and Interleukin-6 in the Elderly. Journal of the American Geriatrics Society, 56 (11), pp. 2045-2052.
39. Thompson, D., 2007. Aging and sarcopenia. Journal of Musculoskeletal and Neuronal Interactions, 7, 4, pp.344.
40. Laukkanen, P., Heikkinen, E., Kauppinen, M., 1995. Muscle strength and mobility as predictors of survival in 75–84-year-old people. Age Ageing, 24, 6, pp.468-473.
41. Seguin, R., Nelson, M.E., 2003. The benefits of strength training for older adults. American Journal of Preventative Medicine, 25, 3, pp.141-149.
42. HSE, 2008. Strategy to Prevent Falls and Fractures in Ireland's Ageing Population. [online] Available at: http://www.hse.ie/eng/services/publications/olderpeople/Executive_Summary_-_Strategy_to_Prevent_Falls_and_Fractures_in_Ireland%E2%80%99s_Ageing_Population.pdf. Accessed 30/11/2017.
43. Holland, G.J., Tanaka, K., Shigematsu, R., and Nakagaichi, M. Flexibility and Physical Functions for Older Adults: A Review. Journal of Aging and Physical Activity, 2002; 10: 169-206.
44. Australian Institute of Health and Welfare. Impact of overweight and obesity as a risk factor for chronic conditions: Australian Burden of Disease Study. 2017.
45. Hillman, C. H., Erickson, K. I., & Kramer, A. F. (2008). Be smart, exercise your heart: exercise effects on brain and cognition. Nature Reviews Neuroscience,9(1), 58-65.
46. Guiney, H., & Machado, L. (2013). Benefits of regular aerobic exercise for executive functioning in healthy populations. Psychonomic bulletin & review,20(1), 73-86.
47. Kelly, M. E., Loughrey, D., Lawlor, B. A., Robertson, I. H., Walsh, C., & Brennan, S. (2014). The impact of exercise on the cognitive functioning of healthy older adults: A systematic review and meta-analysis. Ageing research reviews, 16, 12-31.
48. Barha, C. K., Hsiung, G. Y. R., Best, J. R., Davis, J. C., Eng, J. J., Jacova, C., ... & Liu-Ambrose, T. (2017). Sex Difference in Aerobic Exercise Efficacy to Improve Cognition in Older Adults with Vascular Cognitive Impairment: Secondary Analysis of a Randomized Controlled Trial. Journal of Alzheimer's Disease, 60(4), 1397-1410.
49. Kennedy, G., Hardman, R. J., Macpherson, H., Scholey, A. B., & Pipingas, A. (2017). How does exercise reduce the rate of age-associated cognitive decline? A review of potential mechanisms. Journal of Alzheimer's Disease, 55(1), 1-18.

Appendix 1: Deliverable 2.4

Design an efficient data capture and data management system

System Overview

The MedEx patient management system is a secure cloud-based solution that integrates patients' personal, medical and exercise records in a distributed encrypted database architecture to facilitate uniform information access by multiple healthcare professionals and patients. A patient's personal data is randomly distributed across multiple relational database servers while their medical data is stored in multiple NoSQL (Not Only Structured Query Language) database servers. Each relational database and NoSQL server utilizes different encryption algorithms to ensure complete anonymization of a patient's data records. Data security is further enhanced by using a master time based encryption technique that continuously modifies the encryption processes for each server. This MedEx application has the following capabilities:

1. Integrated User Identity Management module. This allows GP's, Consultants and other healthcare professionals to register their practices/clinics on the MedEx system. All registrations are automatically verified against the appropriate medical professional registration databases such as the MCRN, ICGP, GMS, RCPI or RCSI registration databases.

2. Electronic Referral to MedEx. Healthcare professionals can submit a patient's relevant information electronically to MedEx, triggering automatic notification of the referral to the referring physician. The referring GP or consultant or the MedEx medical officer can subsequently log on and add additional details or update notes Updates are also automatically notified to the referring physician.

3. Integrated International Disease Classification Standards. During the electronic referral process doctors can classify each patient's illness using multiple disease classification standards including SNOMED, ICD10, ICPC, and DSM 5. All diagnoses/surgical procedures/allergies are classified and automatically cross referenced within the MedEx patient database. Medications can be selected from the MIMS and BNF drugs databases which are fully integrated into the MedEx database.

4. Levels of Access. The MedEx system has a comprehensive roles and permissions hierarchy that ensures a strict control of who can access to a patient's personal and medical record. i.e. data access can be controlled to a single data entry. For example. MedEx exercise personnel can view a patient's demographic details but cannot access any medical information. Doctors can only access their own patient records. However, doctors do have the option to allow other doctors to access their patient records. For example, a patient may develop another condition which results in new consulting doctor interacting with the patient. In this circumstance the GP can simply add the new doctor to the list of doctors who can access the patients records.

5. Integrated Notification System. The MedEx system allows multiple healthcare professionals and the MedEx team to continuously update the patients record. For example. When the results of a patients MedEx assessment are added to the patients record, the system will automatically notify the patients GP and Consulting Doctors that the patient has attended and completed the MedEx

induction process and whether the patient has started attending the MedEx classes. Doctors can opt out of such notifications if they do not wish to receive them.

6. Health Intelligence and MedEx Reports. All patient diagnoses, surgical procedures, allergies and medications are coded to international classification standards. This classification approach enables the MedEx system to generate reports based on a comprehensive range of reporting criteria.. The MedEx system will also enable authorized users to view patients progress and graph their test results from quarterly assessments and other tests that may be added to future MedEx programs. i.e. blood tests.

7. Patient Portal. Upon receipt of a doctor referral the MedEx system will automatically notify the patient that they have been referred to the MedEx program and invite them to log on and confirm their intention to attend or not attend the MedEx assessment. Patients will be able to view and select the most convenient date to attend the MedEx induction program. They will also be able to view their demographic data, complete application forms and patient surveys online i.e. the EQ-5D patient questionnaires. They will also be able to schedule which MedEx classes they will be attending. In future releases patients will be able to submit specific medical data (e.g. blood pressure, as documented before and after every MedEX class) or comments about their daily routines. This information may be useful in facilitating exercise prescription or exercise self-management.

8. MedEx Home-based programme (HBP). The HBP is an extension of the patient portal. Patients will be able to download the MedEx home application to either the Smart Phone/Tablet or Computer (access to manual/DVD electronically). The MedEx Home application will be an interactive messaging/chat facility and will deliver the Home Programme through the four pillars of connected health, namely, information, education, interaction and monitoring. All data collected by the MedEx home application will be maintained in the core MedEx system and will be available for analysis by healthcare professionals responsible for each patient's healthcare.

Appendix 1 Cont'd

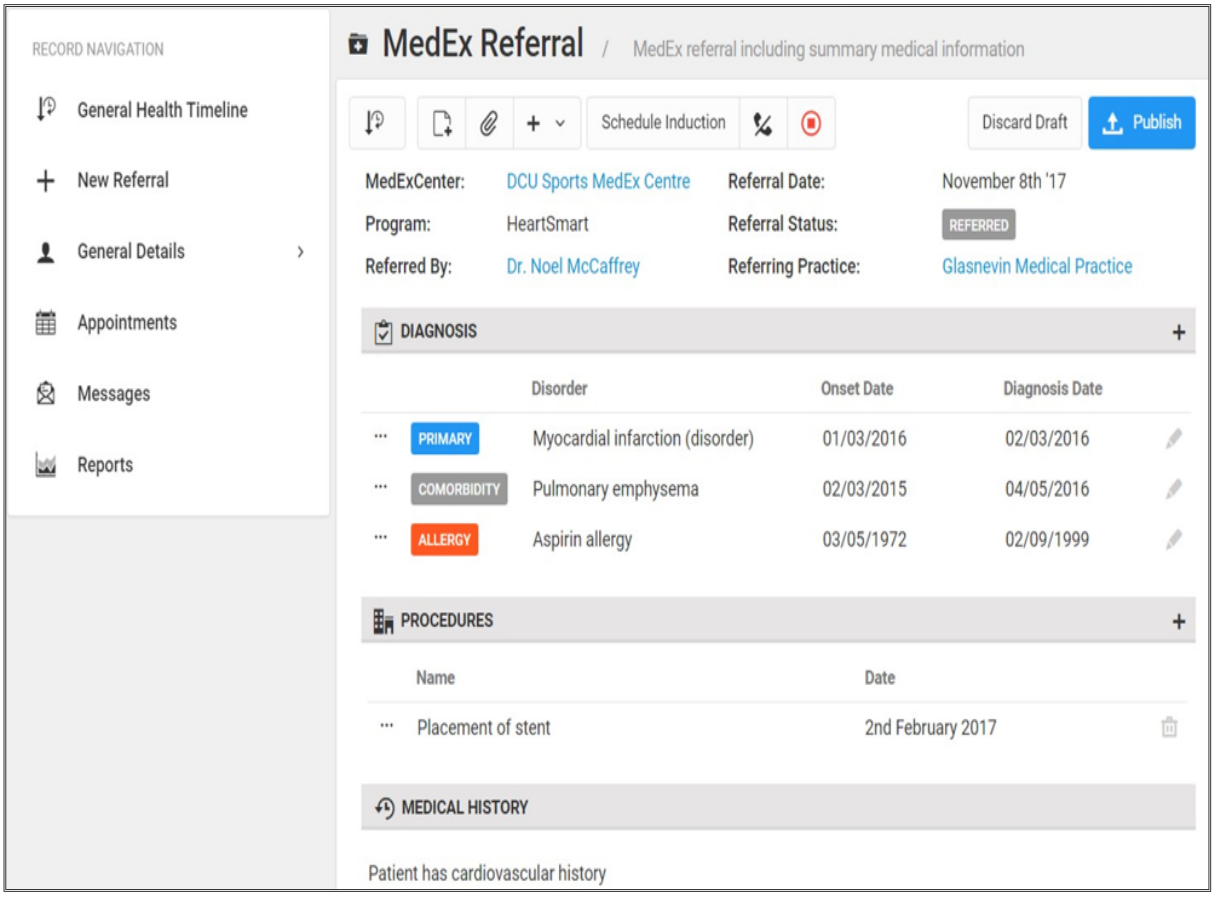

Figure 1. Screen shot of MedEx patient database system

Appendix 2: List of Outcome Measures

Primary Outcome

Six-minute time trial: is an exercise test in which participants were instructed to cover as much ground as possible up and down a flat indoor 20 m course in 6 minutes by walking, running or a combination of both. Participants received a standard set of instructions and standard encouragement. The total distance covered was recorded.

Secondary Outcomes

Quality of life

Participant Health Questionnaire (PHQ8): is a validated and widely used diagnostic and severity measure for depression.

EuroQoL (EQ-5D-3L): is a health status measure consisting of a descriptive system and a visual analogue scale (EQ VAS). The descriptive system comprises 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has 3 levels: no problems, some problems and extreme problems. The EQ VAS records the patient's self-rated health on a vertical visual analogue scale where the endpoints are labelled 'best imaginable health state' and 'worst imaginable health state'.

Medical Outcomes Study Short Form (SF-12): is a 12-item health-related quality of life assessment tool which captures patient-reported general health and well-being, including the impact of any and all illnesses on a broad range of functional domains.

Satisfaction with Life Scale: is a 5-item scale designed to measure global cognitive judgement of subjective wellbeing.

Warwick Edinburgh Mental Wellbeing Scale: is a 14-item positively worded scale covering both feeling and functional aspects of mental wellbeing.

COPD Assessment Test (CAT): is an 8-item COPD-specific questionnaire designed to quantify the impact of COPD symptoms on the health status of patients.

Functional Assessment of Cancer Therapy (FACT): is a 40-item questionnaire, which includes five domains: physical, social/family, emotional, function and cancer-specific, to evaluate quality of life and fatigue in patients with cancer.

WIQ: A 3-item claudication-specific questionnaire measuring functional capacity with regards to distance, speed, and stair climbing.

Physical activity

Accelerometer: Participants wore an ActivPAL^3 micro accelerometer on the midpoint of the anterior aspect of the right thigh for 6 consecutive days The device measures bodily accelerations using a triaxial accelerometer and identifies the posture of the wearer using an inbuilt inclinometer, which can objectively and directly measure sedentary behaviour.

International Physical Activity Questionnaire (IPAQ): is a self-report measure of physical activity over the previous 7 days. It measures types of intensity of physical activity and sitting time and estimates total physical activity in MET – min/week and time spent sitting.

Health service utilisation

Health care utilisation: was assessed using 8 questions drawn from the TILDA study and focusing on 12 month recall of the usage of healthcare services, specifically i) whether participant had medical card cover; ii) number of GP visits; iii) number of hospital emergency service visits; iv) number of outpatient hospital visits; v) whether an outpatient hospital visit was a public/private visit; vi) number of nights spent in hospital; vii) whether nights spent in hospital were a public/private visit; viii) number of days taken off work due to illness.

Teritary Outcomes

Blood pressure

Participants wore an ambulatory blood pressure monitor for 24 hours.

Blood markers

A fasting blood sample was taken and analysed for lipids, blood glucose and CRP.

Other measures of physical fitness

Body composition: BMI was calculated as weight ÷ (height^2). Waist-to-hip ratio was calculated as waist circumference ÷ hip circumference.

Strength: lower body strength was assessed using the s*it-to-stand test*, which records the time taken to stand up from sitting 10 times. Upper body strength was measured using a handgrip dynamometer.

Flexibility: was measured using the s*it and reach test*, in which the participant sits on a bench with the soles of their feet against the sit and reach box, and flexes forward to reach fingertips as far as possible along the measurement scale.

Claudication time: Participants with peripheral arterial disease performed a disease-specific incremental treadmill walking test. The Gardner protocol is 3.2 km.h^{-1} and 0% grade, with a

subsequent 2% increase in grade every 2 min to absolute claudication. Time and distance to the onset of claudication and to maximal claudication were recorded.

Falls risk

Patients reporting haven fallen once or more in the last year or reporting a fear of falling or problems with balance or walking performed the Timed Get Up & Go (TUG) Test. This test assesses the time taken to stand from a chair, walk 3m, turn, walk back, and sit down again.

Cognitive Function

Attention Network Task (Posner & Peterson, 1990): Computerized task measuring three functionally and independent aspects of attention control crucial to everyday cognitive functioning by recording performance accuracy and average reaction time to correctly detected targets: (1) alertness, (2) how orient attentional orienting, and (3) executive function.

Luck Vogel Task (Luck & Vogel, 1997): Computerised task measuring visual working memory by capturing performance accuracy and average reaction times to correctly detecting a change in a visual array of objects. The set size of the object array varies from small to large.

Both tasks were used with open permissions from the Psychology Experiment Building Language (PEBL) site: http://peblblog.blogspot.ie/2014/07/overview-of-some-of-new-tests-in-pebl.html; and these benchmark tasks are studied within various populations to establish timing precision. See Mueller & Piper (2014) for further details.

Cognitive Reserve Questionnaire (Nucci et al., 2012): Questionnaire measuring cognitive reserve or the construct that is used to explain differences among individuals in their ability to cope with pathology and challenging cognitive tasks. Questionnaire measures demographics, education, and working activity including physical, social and intellectually challenging activity. It is an open source measure available at http://www.cognitivereserveindex.org/.

Exploratory Outcomes

Intentions for exercise: This 6 item intention for exercise questionnaire measures an individual's intention to exercise.

Self-efficacy for self-regulation of exercise: This 11 item self-efficacy for exercise scale is used to measure an individual's self-efficacy for exercise itself, and self-efficacy for overcoming barriers and relapses to return to exercise.

Barrier self-efficacy: This 9 item proxy efficacy scale is used to measure an individual's confidence in a proxy agent (MedEx team) to assist them in order that the participant can exercise, adhere to exercise, and overcome barriers and relapses to exercise.

Social support for exercise: The social support for exercise scale is a 13 item scale measuring frequency of support received by participant in relation to exercise.

Appendix 3. Sample of the home programme including sample pages of the manual and a screenshot of the video.

CONTENTS

MedEx Wellness

PROGRAMME A: MEDEX AEROBIC EXERCISE PROGRAMME

	BEGINNER	INTERMEDIATE	LONG TERM EXERCISER
WEEKS 1-3 TARGET	Walk continuously for 10 minutes on at least 5 days of the week.	Walk continuously for 20 minutes, on at least 5 days of the week.	Walk continuously for 30 minutes, on at least 5 days of the week. During your walk, alternate the intensity of your walk between a brisk walk and a slow jog for 1-2 minutes for the 30 min period.
WEEKS 4-6 TARGET	Walk continuously for 10 minutes, twice per day, on at least 5 days of the week.	Walk continuously for 25 minutes, on at least 5 days of the week.	Gradually increase the number of minutes jogging and decrease the minutes walking while maintaining and even increasing the total time exercising.
WEEKS 6-9 TARGET	Walk continuously for 10 minutes, 3 times per day on at least 5 days of the week.	Build up to 30 minutes of continuous brisk walking on at least 5 days of the week.	Continue to gradually increase the number of minutes jogging and decrease the minutes walking while maintaining and even increasing the total time exercising. Work towards jogging for 30 minutes on at least 5 days each week.

HALF JACKS

- Place your right hand on your right hip.
- Tap the left toe out to the side and raise your left arm upwards.
- This movement should reflect one half of a jumping jack.
- Change to the opposite side.
- Repeat.

HEEL FLICKS

- Stand with your feet shoulder width apart and your hands on your hips.
- Bending your leg at the knee, bring your right leg behind you as shown.
- Change to the opposite leg.
- Repeat.

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Note: The solid black line images contains a sample of pages taken from the home programme manual. The image above is a screenshot from the welcome video to the MedEx home programme