

## Research Protocol

The proposed research study is part of a PhD that is taking a phased approach (MRC, 2008) to develop, pilot, and evaluate an exercise referral scheme (ERS) for inactive individuals with health conditions. Study 1 [REF 16/EM/0157] involved the co-development of the intervention in collaboration with a multidisciplinary steering group (e.g. researchers, GP's, commissioners etc.). Study 2 (REF 16/WA/0231) explored the feasibility of the ERS and tested potential outcome measures to inform a subsequent evaluation trial. **Study 3 (this application) will be a pragmatic, quasi-experimental trial to test the effectiveness of the ERS.** The research will be conducted in collaboration with Liverpool NHS Clinical Commissioning Group (CCG) and Liverpool City Council (LCC). **This protocol relates to study 3 only.**

**Formal study title:** “Clinical and cost-effectiveness of a co-developed, evidence-based physical activity referral scheme for the treatment and prevention of health conditions: a pragmatic trial”

**Lay study title:** “Evaluation of a co-developed physical activity referral scheme”

**Aim:** *To test the pragmatic effectiveness and cost-effectiveness of a co-developed, evidence-based physical activity referral scheme, with embedded process evaluation.*

### **Objectives:**

- To investigate the relative effectiveness (for improving cardiorespiratory fitness at 12 weeks) and cost-effectiveness (PA levels at 6 months) of two delivery modes of ERS (1. co-developed physical activity referral scheme; 2. standard ERS)
- To explore who each intervention reaches, patient adherence levels, fidelity of intervention delivery and acceptability of the intervention to patients and staff.

### **Study Design**

A three-arm quasi-experimental trial involving: 1. co-developed physical activity referral scheme (intervention); 2. standard ERS (usual care); and 3. no treatment control. Process evaluation will be embedded to establish reach, adherence, fidelity and acceptability of the intervention and usual care conditions.

## Participants and recruitment

There are two types of participants within the study design:

### 1. Patients

#### *Inclusion Criteria:*

≥18 years old and have a health-related risk factor (e.g. high blood pressure, hyperglycaemia, obesity etc.) or a health condition (diabetes, cardiovascular disease, anxiety, depression etc.) that may be alleviated by increasing current PA levels.

#### *Exclusion Criteria:*

- Uncontrolled health-conditions (Cardiac, metabolic, respiratory etc.) and/or any recent traumatic events (e.g. myocardial infarction).
- Unstable angina or aortic stenosis.
- Severe psychological or neurological conditions.
- Participation in an ERS at any location other than the research centres (at the time of recruitment).

### 2. ERS staff

#### *Inclusion Criteria:*

- Qualified exercise referral practitioner (ERP)
- Involvement in the delivery of the ERS at Centre A (intervention) or Centre B (usual care)

#### *Exclusion Criteria:*

- None

## Recruitment

### ***Intervention and usual care conditions***

Eligible patients will be recruited from Centre A and Centre B (after they have been referred to the ERS by a health professional). Once referred, it is standard protocol that ERS patients visit their chosen *Lifestyles* fitness centre to book an ERS induction with administrative staff. During this initial contact, administrative staff will introduce the study briefly and provide the individual with a summary poster (attached). If the patient is interested, administrative staff will gain verbal consent to pass the patient's contact details to the researcher (NB this is consent for sharing details only, the participant will still have the opportunity to opt out before full research consent is sought). Administrative staff will then provide patients with the participant information sheet to take away and have some time to consider. Patients will be informed that the researcher will contact them within one week to discuss the study and check if they want to take part. Researcher contact details will be provided on the poster and information sheet in case the participant has any questions in the meantime.

For patients who consent to speak to the researcher, the administrative staff will book an ERS induction 2-3 weeks later (to allow time for the patient to undergo baseline testing prior to starting the ERS). The researcher will then contact the patient to arrange a visit to Liverpool John Moores University (LJMU) laboratories for baseline collection of health measures.

Patients who opt out of the study at this stage will continue with the ERS as usual.

#### ***No treatment control condition***

Participants in the no treatment control group will be recruited via posters placed around LJMU, electronic invitations on LJMU research recruitment websites, email communications to LJMU staff and students, and LJMU social media output (see attached documents). Interested participants will contact the researcher for further information, who will e-mail them a full participant information sheet. If the participant then decides to take part the researcher will arrange a date and time to visit LJMU laboratories for baseline collection of health measures.

**Participant blinding.** Due to the nature of the study, it will not be possible to fully blind patients to their study condition (as they will know whether they are signed up to attend an ERS or not) or to blind ERS staff (who will know whether their centre is the intervention or the usual care condition). Patients within the two active conditions (intervention and usual care) will not however be informed whether their centre is the intervention or the usual care condition.

#### **Conditions**

##### ***Intervention (Centre A)***

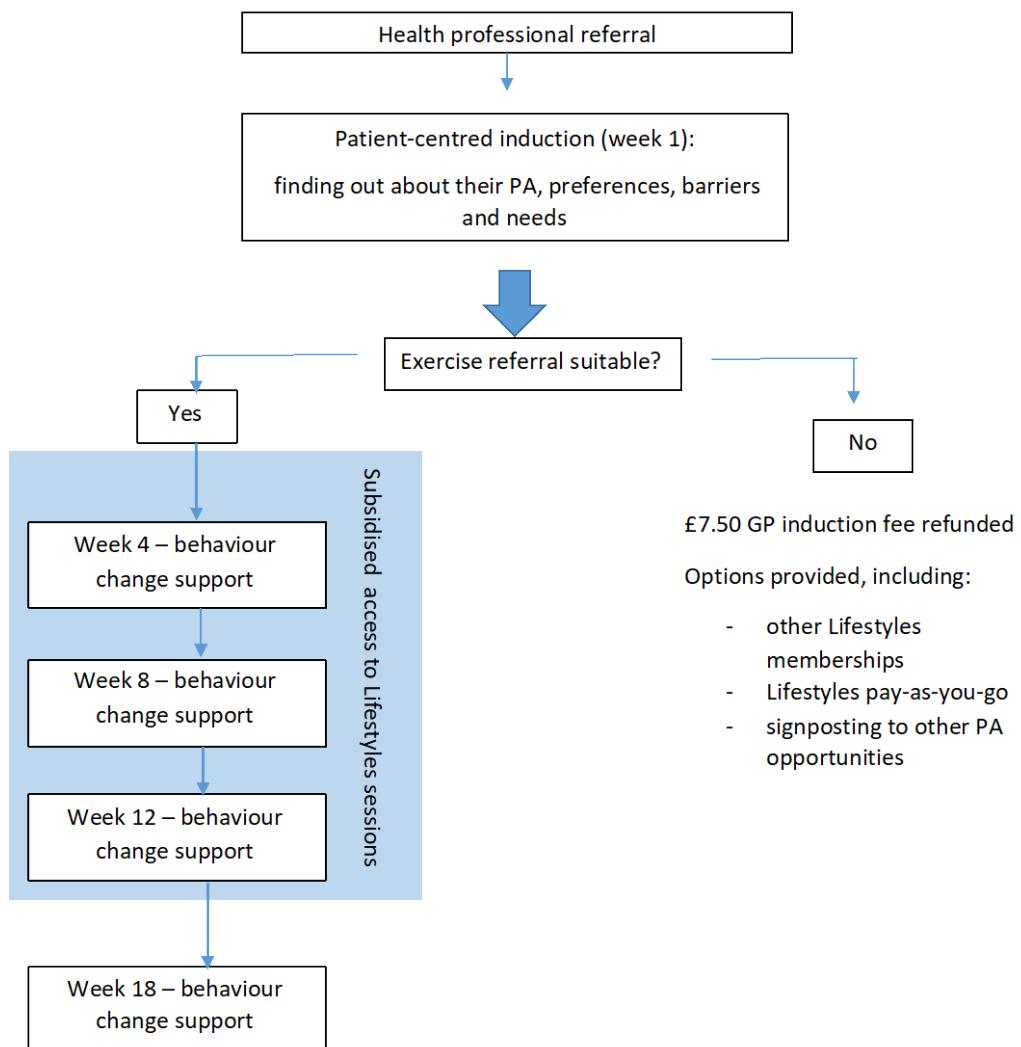
Both the co-developed scheme and standard ERS offer subsidised access to a fitness centre for 12 weeks. However, in addition to this the co-developed intervention (centre A) will offer:

- more physical activity options that include both daily opportunities to increase PA and activities available at the fitness centre;
- more individual progress meetings, during which the GP exercise referral practitioner will provide behaviour change support (Week 0, 4, 8, 12 and 18); and
- more efforts to refer patients to optional additional support from a 'Health Trainer' service qualified to provide advice on multiple health-related behaviours.

These adaptations are in line with the current NICE guidelines as well as a local evaluation study that fed into the development of the scheme. The aim of the co-developed ERS is a person-centred approach to improve overall well-being and quality of life through PA. As the intervention is drawing on an existing scheme, delivered/guided by qualified ERPs, and has been developed by a multidisciplinary stakeholder group involved with the existing scheme, it is deemed that there are no additional risks to the users compared to the existing

scheme in operation. The key aspect of the intervention is that the participant has choice but is supported through the process.

It was found during the pilot study that some patients were referred inappropriately to the ERS who were already active or were seeking subsidised access to certain activities (e.g. swimming) without a need for additional behaviour change support. In an attempt to provide more targeted support, patient eligibility for the ERS will be explored through the patient-centred induction. If it is deemed by both the instructor and patient that the intensive 18-week intervention is not the most appropriate for the patient's needs, alternative options will be offered (see figure 1). Since this study aims to investigate the real-world effectiveness of an ERS that is tailored to patient needs, patients referred to the ERS at Centre A who opt not to take part in the 18-week intervention will remain in the research study (i.e. an intention to treat approach).



**Figure 1.** Co-developed referral scheme that will run at Centre A (intervention centre).

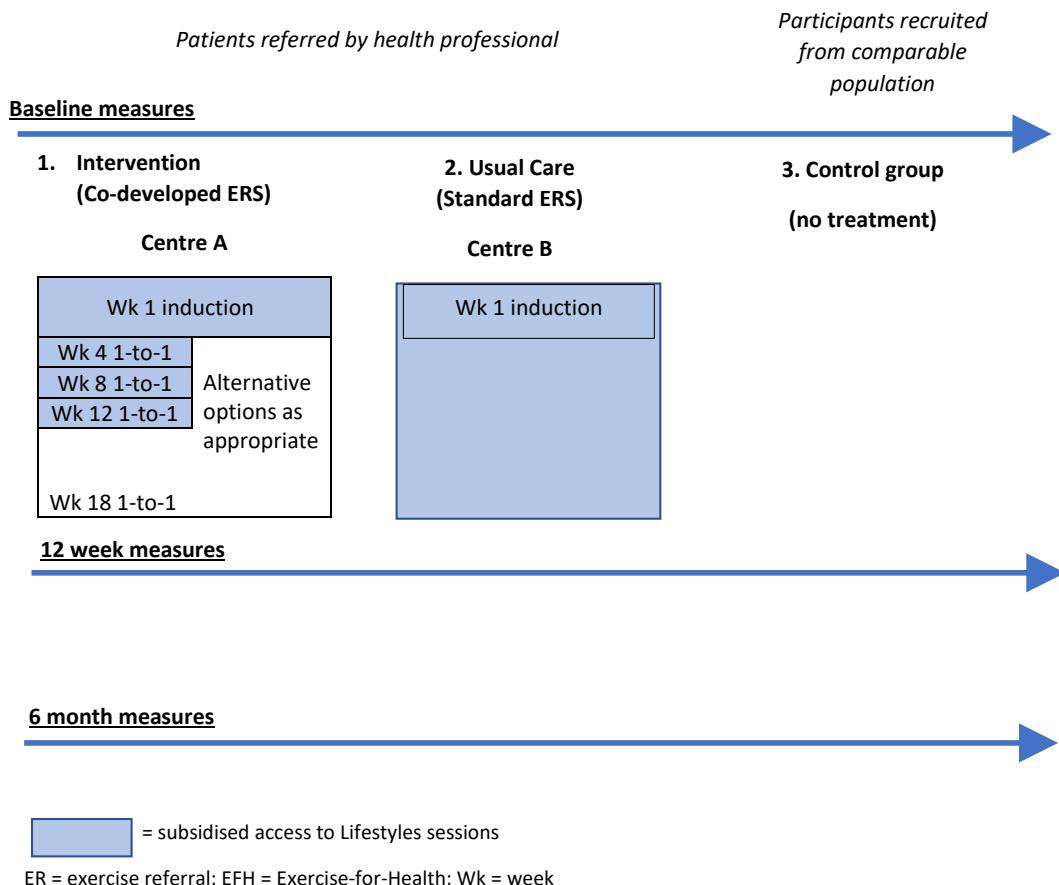
*Theoretical underpinning and behaviour change support.* All behaviour change support is underpinned by self-determination theory (SDT, Ryan and Deci, 2000) and aimed at supporting patients to feel autonomously motivated to keep up physical activity in the long-term.

### ***Usual care (Centre B)***

The usual care arm will follow a standard ERS model of 12-week access to a *Lifestyles* fitness centre. Patients referred from a health professional (GP, physiotherapist, nurse etc.) will meet an ERP at the leisure centre for an initial induction (week 1). A personalised exercise intervention will be provided to the patient based on their referral reason/health condition. The patient will have 12 weeks of subsidised access to the gymnasium and group classes. This system is already in place and is considered standard exercise referral care for the local area.

### ***No treatment control***

These participants will receive a lifestyle advice booklet only (provided to all groups at the baseline data collection point).



**Figure 2.** Overview of intervention measure time points for each arm.

## Sample size estimation

### *Between-group effects (intervention vs usual care)*

Required sample size was estimated by using effect sizes of a previous pilot study that demonstrated a mean change in CRF  $3.6 \pm 3.2 \text{ ml.kg.min}^{-2}$  (REF 16/WA/0231) and existing epidemiological evidence. A change in cardiorespiratory fitness of  $3.5 \text{ ml.kg.min}^{-2}$  has been deemed clinically meaningful with an associated reduction in all-cause mortality (13%) and cardiovascular disease risk (15%; Lee et al., 2010). Yet, it has also been demonstrated that small increases in fitness (Males:  $0.5 \text{ ml.kg.min}^{-2}$ ; Females  $1.0 \text{ ml.kg.min}^{-2}$ ) are associated with significant reductions in clustered-cardiometabolic risk in at-risk individuals (Simmons et al., 2008).

Therefore, we decided a moderate-large effect size (based on pilot baseline CRF SD of  $3.2 \text{ ml.kg.min}^{-2}$  equivalent to a change of  $1.98 \text{ ml.kg.min}^{-2}$ , would be clinically meaningful. This is between the clinically meaningful change of 3.5 units reported by Lee et al. (2010) and the smaller increases of 0.5 to 1 unit reported by Simmons et al. (2008) in at-risk individuals. Thus, to detect a difference of 1.98 units ( $\text{ml.kg.min}^{-2}$ ) between groups, it was estimated that a total sample of 84 would be needed ( $f=0.25$ ,  $p=0.05$ , power = 0.8). Factoring for dropout witnessed in the pilot study (40%) this yields a sample of 140 patients (70 per ERS arm).

### *Between-group effects (ERS arms vs no treatment control)*

It is estimated that a larger effect size would occur between the ERS arms and the no treatment control, it was therefore decided we did not need to recruit as many participants. To identify a difference of 3.2 units ( $\text{ml.kg.min}^{-2}$ ; 0.3 units smaller than the within-subjects change seen in the previous pilot for fitness to allow for some variance) between the ERS arms and a no treatment control arm a sample of 17 would be required ( $f=0.5$ ,  $p=0.05$ , power = 0.8). Factoring for dropout witnessed in the pilot study (40%) this yields a sample of 30 patients for the no treatment control arm.

In summary, the study will aim to recruit 70 patients for the intervention condition, 70 for the usual care condition and 30 for the no treatment control.

*ERPs.* All ERPs responsible for delivering the ERS at Centre A (n=4-5) and Centre B (n=2-3) will be invited to take part.

## **Measures**

### **Demographic measures**

Demographic measures collected at baseline will include: date of birth, sex, postcode, employment status, ethnicity, referral reason, referring professional, and number of previous referrals.

### **Outcome measures**

<sup>a</sup>All patient outcome data will be collected at two time-points: pre-intervention (prior to an induction with an ERP) and at Week 12 (post 12-week consultation with an ERP). <sup>b</sup>At 6-month follow-up, **questionnaire-based measures and PA levels** (determined by an accelerometer worn for 7 days), **only** will be collected. All data will be collected and analysed by a researcher at LJMU. All outcome measures were piloted in a previous study (REF 16/WA/0231) and were deemed acceptable by patients and demonstrated adequate sensitivity to detect change.

<sup>a</sup> Collected at Baseline and week 12

<sup>b</sup> Collected at Baseline, week 12 and 6-month follow-up

<sup>a</sup> **Cardiorespiratory Fitness.** A sub-maximal VO<sub>2</sub> test (Astrand Rhyming test) will be carried out to estimate cardiorespiratory fitness. The Astrand Rhyming test allows you to predict VO<sub>2</sub>max from work intensity and heart rate. Following a warm-up (unloaded cycling 3-5 minutes at 50-60 rpm) the procedure will begin. Using a Polar Heart Rate Monitor to measure heart rate, the individual will begin cycling at 60 rpm with a workload of 60 watts (female) or 90 watts (male). The participant will then cycle at this workload for 6 minutes. Heart rate will be measured each minute; blood pressure will be measured at each 3-minute period as well as pre- and post-test. If the mean heart rate is between 125 and 170 beats per minute at minute 5 and 6, the test can be terminated. If the mean heart rate is less than 125 beats per minute, the workload will be increased by 30 watts (0.5 kg). If the mean heart rate is less than 125 beats per minute at minute 5 and 6 the test will be continued for a further 3 minutes. This procedure will be repeated until the required heart rate is achieved. The test will be stopped if the participant experiences any adverse effects, their heart rate exceeds recommended max heart rate values for this test, or if the participant wants to stop.

<sup>b</sup> **Objective PA levels.** Objective PA will be analysed using an accelerometer (ActiGraph software), which will be fitted during baseline testing at LJMU. A baseline 7-day monitoring period will occur before participants engage with the scheme. During the 7-day monitoring period, each participant will complete a diary to record hours of use as well as distinguish between work and leisure hours.

<sup>a</sup> **Endothelial function.** Flow-mediated dilation (FMD) and carotid vasoreactivity (cold pressor test) will measure artery function. These tests have been deemed non-invasive and strong predictors of CVD risk (Cunningham & Gotlieb, 2005; Rubenfire *et al.*, 2000). The primary researcher will conduct these ultrasound tests with assistance and training from experts in the field of cardiovascular physiology (Prof Dick Thijssen).

*Flow mediated dilation.* Endothelium dependent vasodilatation of the brachial arteries will be examined using ultrasound. Brachial artery baseline diameter and blood flow will be assessed in one arm. An ultrasound probe is placed on the bicep for 1 minute before a blood pressure cuff (placed around the forearm)

is inflated to suprasystolic pressure (~220 mmHg) for 5 minutes. Immediately after the cuff is deflated, changes in arterial diameter and flow will be assessed continuously for 3 minutes using the ultrasound probe.

**Carotid vasoreactivity.** The carotid vasoreactivity (cold pressor) test will measure the carotid artery's response to a stimulus. Similar to the method above, an ultrasound probe will be placed on the patient's left side of their neck, positioned in such a way to allow a clear image of the right common carotid artery to be displayed on the ultrasound monitor screen. The cold pressor procedure involves submersion of the left hand to wrist in ice slush for 180-seconds. Ultrasound data will then be analysed post hoc.

**<sup>a</sup> Blood Profiles.** A 15ml blood sample will be taken. The primary researcher for this study will complete all phlebotomy and has completed the relevant LJMU training as well as having previous experience working as a physiologist collecting blood samples among other health-related measures. Blood profiles will be analysed as a measure of cardiometabolic health. Analysis will be conducted at LJMU. Patients will be made aware of the storage and use of their tissue. Blood analysis will include: glucose, insulin, cholesterol (Total, HDL and LDL), lipids, triglycerides, CRP and homocysteine.

**<sup>b</sup> Lifestyle questionnaire.** Information regarding patients' lifestyle will be collected via questions related to dietary habits (e.g. number of fizzy drinks per week, amount of processed meat etc.), alcohol consumption, smoking status, as well as any services the patient may be receiving lifestyle support from.

**<sup>b</sup> Self-reported PA.** Patients' perceived PA levels will be recorded with the short version of the International Physical Activity Questionnaire (IPAQ, Craig et al., 2003). The short-IPAQ is a 7-day recall self-administered tool that measures intensity, frequency and duration of PA and provides a total estimate of energy expenditure. A total score of MET-minutes/day/week and sedentary behaviour minutes/day/week will be calculated according to the IPAQ scoring protocol.

**<sup>b</sup> Psychological wellbeing.** Psychological wellbeing will be measured using the Warwick-Edinburgh Mental Well-being Scale (WEMWBS, Tennant et al., 2007). WEMWBS is a 14-item positively worded instrument containing items related to psychological functioning (e.g. "I've been thinking clearly") and subjective well-being (e.g. "I've been feeling cheerful"). Participants are asked to rate on a Likert scale of 1 (none of the time) to 5 (all of the time) how well each statement describes their experiences over the last two weeks.

**<sup>b</sup> PA motivation.** The Behavioural Regulation in Exercise Questionnaire (BREQ-2, Markland & Tobin, 2004) plus 4 additional items (Wilson et al., 2006a) will be used to assess PA motivation. The BREQ-2 is a widely-used instrument comprised of 19 items describing reasons why people exercise (e.g. "I think exercising is a waste

of time”; “I feel ashamed when I miss an exercise session”; “I exercise because it’s fun”). Participants answer on a likert scale of 0 (not true for me) to 4 (very true to me) to indicate how true each item is for them.

<sup>b</sup> **Psychological needs satisfaction.** Psychological need satisfaction will be measured using the Psychological Need Satisfaction in Exercise Scale (PNSE, Wilson et al., 2006b). The PNSE is an 18-item instrument designed to measure participants’ perceived autonomy (e.g. “I feel free to exercise in my own way”), competence (e.g. “I feel capable of completing exercises that are challenging to me”) and relatedness (e.g. “I feel connected to the people who I interact with while we exercise together”) in an exercise context. Participants are asked to answer on a 6-point likert scale (1 = false, 6 = true) to indicate how they typically feel when they exercise.

<sup>b</sup> **Perceived needs support.** Needs support will be measured using a 15-item needs support (NS) tool developed by Markland and Tobin (2010) to measure the extent to which participants perceive their exercise instructors provide support for autonomy, structure (linked to competence) and involvement (linked to relatedness).

<sup>b</sup> **Intentions to engage in PA.** Three items developed by Edmunds et al. (2007) will be used to assess patients’ intentions to engage in PA (e.g. “I plan to regularly engage in PA during the next 3 months”).

### Process Measures (intervention and usual care groups, unless otherwise noted)

**Attendance at consultations.** Patient attendance records will be collected by ERPs at the following time-points:

- Intervention centre: induction, 4,8,12 and 18 weeks;
- Usual care centre: induction and 12 weeks.

**Attendance at fitness centre.** The number of times patients sign in at the leisure centre to go to either the gym or a class will be recorded on a weekly basis for weeks 1 to 12, then on a monthly basis up to 6 months. This information is automatically recorded at leisure centres when patients visit.

**Patient focus groups.** Focus groups will be conducted with a purposeful subsample of patients after approximately 6-12 weeks of attending the scheme (e.g. those with low attendance, high attendance, significant health changes, no change etc.). Two focus groups will be conducted with patients attending the intervention centre (approx 5-8 participants per group) and two focus groups will be conducted with patients attending the usual care centre (approx 5-8 participants per group) (20-32 participants in total). Focus groups will be conducted at the individual fitness centres and will last approximately 60 minutes. Discussion will focus on the extent to which, and how, patients feel each ERS is facilitative (or not) in helping them become more

physically active, with questions about staff interactions, activities on offer, and the impact of the scheme on their likely continuation with PA.

**ERP interviews (intervention group only).** ERPs from the *intervention centre only* will take part in a semi-structured interview (after over half of patients have reached the 18-week point) to explore the acceptability of the co-developed intervention and any challenges of delivery, areas that require further development etc.

**Fidelity.** Fidelity of intervention delivery will be measured in two ways:

1. ERPs from both intervention and usual care centres will be asked to monitor the number of consultations offered (measured by appointment bookings or records of appointments offered but declined by participants), and the number of consultations conducted for each patient.
2. A random sample of ERS inductions from both intervention and usual care centres (approx 10 per centre) plus a random sample of 4, 8, 12 and 18-week consultations from the intervention centre only will be audio-recorded and coded for the use of “needs-supportive” communication strategies (using a coding manual developed through a previous pilot study (REF 16/WA/0231)). In addition, all intervention centre recordings will be coded for fidelity to an agreed protocol, e.g. asking required questions about physical activity, setting an action plan, giving out patient log book etc.

## **Economic evaluation measures**

*Please refer to the detailed economic evaluation information sheet attached if you require more information.*

### **Methods**

A trial- and model-based economic evaluation will be conducted from the public sector perspective, which will include the costs and consequences to the: local authority, NHS and PSS, and local authority leisure centre. Results from all analyses will be reported in the form of an incremental cost-effectiveness ratio. Firstly, a cost-utility analysis will be carried out with the results being presented as cost per quality adjusted life year. Secondly, a cost-effectiveness analysis will be carried out with the results being presented as cost per active participant. Lastly, a cost-consequence analysis will be conducted from a broader perspective, which will highlight relevant public sector and participant costs and consequences. More specifically, the main analysis will be done by exploring the costs and effects over a lifetime horizon, using a decision-analytic model. All costs and effects over the lifetime horizon will be discounted at a rate of 3.5% as recommended in the NICE reference case (NICE, 2017). The 6-month effectiveness data for change in physical activity level, as well as published secondary data sources on change in disease state will be input into the model. The extrapolated analysis will aim to estimate the relative risk of participants being in one of the following six health states 10 years after the intervention: healthy, dead, has had a stroke, has coronary heart disease (CHD), or has type 2 diabetes (T2D). The 10-year duration of effect period is a conservative approach, which has been based on a recently published study (Campbell et al. 2015) that was identified in the systematic review. All

epidemiological data along with additional published secondary data on the life expectancy, health-related quality of life and treatment costs associated with each of the six health states will be input into a Markov Model. Uncertainty will be assessed through deterministic and probability sensitivity analyses.

#### ***Data collection***

**Resource use measures.** Direct costs to the local authority will be measured, these will include the annual cost of operating the intervention, and the set up costs. A breakdown of these costs will be requested from the local authority. Any additional costs will be captured through a questionnaire completed by key staff coordinating the Exercise Referral Scheme at the local authority, local authority leisure centre, and research institute delivering the training. Indirect short-term cost savings to the NHS and PSS will be captured via health care utilisation questionnaires completed by the participants at baseline, and at 6 months follow up. The long-term indirect cost savings to the NHS and PSS through a reduction in coronary heart disease, stroke and type 2 diabetes will be sources from secondary data. A short telephone interview will be conducted with the leisure centre manager to identify whether the centre experienced a loss in revenue as a result of providing the Exercise Referral Scheme. Participant out of pocket and productivity costs will be captured through self-reported questionnaires at baseline, 12 weeks, and 6 months from baseline. All questionnaires and telephone interview questions are adapted from validated measurement tools from the Database of Instruments for Resource Use Measurement. Apart from room hire, primary data will not be collected for common overhead operating costs, such as lighting and heating; however, these costs will be explored in the sensitivity analysis, for instance by estimating the hours of the intervention and increasing the salary rates of staff by 10% to include overheads. Unit cost prices will be sources from secondary sources.

**<sup>b</sup>Economic evaluation measures (attached: located at the end of Booklet 2):**

**Health-related quality of life measure.** Participants' change in health-related quality of life (HRQoL) will be measured at baseline, 12 weeks, and 6 months. The EQ-5D will be used, this is a validated tool for measuring HRQoL. This tool has been applied successfully in a recent UK trial-based economic evaluation of exercise referral schemes (Edwards et al. 2013).

**Intervention operating and set up costs.** Captured via telephone interview with Exercise Referral Scheme Personnel from (organisation e.g. local authority/ leisure centre/ research institute; questions adapted from validated questionnaire).

**Loss in revenue costs.** Captured via telephone interview with leisure centre manager and/or coordinators (questions have been used in previous research).

**Patient costs.** Captured via patient questionnaire during lab testing (questions adapted from validated questionnaire).

**Patient Health care utilisation costs.** Captured via questionnaire (questions adapted from validated questionnaire).

### **Patient procedure**

*LJMU lab-based measures.* Written informed consent will be gained prior to the commencement of testing, when patients arrive at LJMU for baseline testing with a researcher. Patients will need to be rested for 20 minutes prior to initiation of the ultrasound techniques. During this period, demographic data will be collected in addition to information about PA levels, mental wellbeing, diet, smoking and alcohol habits, psychological questionnaires and economic-related questions (~30 minutes; see attached Booklet 1 and Booklet 2). Ultrasound measures will then be conducted (FMD and CAR): 25 minutes. A 15ml blood sample will be taken from the antecubital fossa (5 minutes). The participant will then be able to drink and eat, if they wish, prior to completing a sub-maximal fitness test (20 minutes). The patient will then be informed about the accelerometry protocol and given the Actigraph monitor with accompanying diary to be completed over a seven-day period (5 minutes). For the ERS arms, the accelerometer and accompanying diary will be returned to the ERP when the patient attends their referral induction at Centre A or Centre B to begin their programme. The control group participants will return the monitors to LJMU in person or by pre-paid mail. The expected period to complete baseline testing is ~90-120-minutes.

Lab based testing will be repeated at week 12 as per the protocol for baseline data collection described above. At 6 months from baseline, participants will be sent (by mail) a questionnaire pack (booklet 2) and an activity monitor. These will be returned via pre-paid mail or as otherwise organised with the researcher.

### **Protocol for incidental disclosures or abnormal test results**

*Disclosure of unhealthy lifestyle* – Whilst it is not deemed appropriate for researchers to pass on lifestyle information disclosed in confidence, or to provide individual advice, it is recognised that the research team have a responsibility to provide evidence-based information to allow patients to make informed decisions about their health. Therefore, after completing their baseline assessments at LJMU participants will each be given a simple information sheet that outlines the recommended guidance on PA and diet as well as risks associated with smoking and alcohol. On the sheet participants will be signposted to relevant government

websites for further information and will be advised to contact their GP if they have any concerns about their own lifestyle.

*Abnormal test results.*

The laboratory-based testing is not diagnostic in nature and is therefore not likely to find anything alarming. However, if any abnormal blood results (analysed following week 12 testing) are identified, the researcher will write to the individual participant and ask them to see their GP. Refer to attached patient letter.

**Analyses**

Statistical analysis of the primary and secondary outcomes will be conducted using linear mixed models in SPSS Statistics Version 23 (SPSS Inc., IBM Corp., Armonk, NY), with alpha levels set at  $P < .05$ . The models will be used to assess the impact of treatment (co-developed ERS, usual care ERS, and no treatment control), time (baseline and post-tests), and Group  $\times$  Time interactions. Mixed models are robust to the biases of missing data and provide appropriate balance of Type 1 and Type 2 errors. Mixed-model analyses are consistent with the intention-to-treat principle, assuming the data are missing at random. Appropriate variables including baseline values will be included as covariates in the models. The data will be screened for skewness and kurtosis prior to commencing any analyses. Magnitude-based inferences will be used to investigate 'clinical meaningfulness' of results (Batterham and Hopkins 2006).

Focus groups and interviews will be recorded and transcribed verbatim (where they will be anonymised). They will then be analysed using NVivo electronic software using a thematic approach to allow common themes to arise from the data collected. Members of the research team will review the data independently and meet to reflect on the emerging themes, discuss rationale for coding decisions, areas of disagreement and theoretical concepts that emerge.

**REFERENCES:**

Anokye, N., Lord. J., Fox-Rushby. J. (2012). National Institute for Health and Clinical Excellence Public Health Intervention Guidance on Physical Activity- Brief advice for adults in primary care: Economic Analysis. Available at: <https://www.nice.org.uk/guidance/ph44/chapter/about-this-guidance> Accessed 01.11.2017

Batterham, A.M., Hopkins, W.G. (2006) 'Making meaningful inferences about magnitudes.', *International journal of sports physiology and performance*, 1(1), 50–7.

Beecham, J., and Knapp. M. (1997). *Client Service Receipt Inventory*. Available at: <http://www.dirum.org/assets/downloads/634462388066137028-CSRI.pdf> Accessed 01.11.2017

Beck, F., Gillison, F., Koseva, M., Standage, M. (2016) 'The systematic identification of content and delivery style of an exercise intervention', *Psychology & Health*, 31(5), 605–621.

Craig, P., Dieppe, P., Macintyre, S., Michie, S., Nazareth, I., & Petticrew, M. (2008). Developing and evaluating complex interventions: the new Medical Research Council guidance. *BMJ*, 337, a1655.

Cunningham, K., & Gotlieb, A. (2005) 'The role of shear stress in the pathogenesis of atherosclerosis.', *Laboratory investigation; a journal of technical methods and pathology*, 85(1), 9-23.

Drummond, M. F., Schulpher, M.J., Claxton, K., Stoddart, G.L., et al. (2015). *Methods for the Economic Evaluation of Health Care Programmes (Fourth Edition)*. Oxford: Oxford University Press.

Edmunds, J., Ntoumanis, N., & Duda, J. L. (2007). Adherence and well-being in overweight and obese patients referred to an exercise on prescription scheme: A self-determination theory perspective. *Psychology of Sport and Exercise*, 8, 722-740.

Edwards, T. E., Linck, P., Hounsome, N., Raisanen, L., et al. (2013). Cost-effectiveness of a national exercise referral programme for primary care patients in Wales: results of a randomised controlled trial. *BMC Public Health*. 13, pp.1021

Elley, C. R., Garrett, S., Rose, S.B., O'Dea, D., et al. (2010). Cost-effectiveness of exercise on prescription with telephone support among women in general practice over 2 years. *British Journal of Sports Medicine* 45, pp. 1223-1229

Hancox, J. E., Quested, E., Thøgersen-Ntoumani, C. & Ntoumanis, N. (2015). An intervention to train group exercise class instructors to adopt a motivationally adaptive communication style: a quasi-experimental study protocol, *Health Psychology and Behavioral Medicine*, 3:1, 190-203.

Hardcastle, S., & Hagger, M. S. (2011). "You Can't Do It on Your Own": Experiences of a motivational interviewing intervention on physical activity and dietary behaviour. *Psychology of sport and exercise*, 12(3), 314-323.

Kodama S, Saito K, Tanaka S, et al. Cardiorespiratory fitness as a quantitative predictor of all-cause mortality and cardiovascular events in healthy men and women: a meta-analysis. *JAMA*. 2009;301(19):2024-2035.

Lee, D.C., Artero, E.G., Sui, X., Blair, S.N. (2010) 'Mortality trends in the general population: the importance of cardiorespiratory fitness.', *Journal of psychopharmacology (Oxford, England)*, 24(4 Suppl), 27–35.

Markland, D. & Tobin, V. (2004). A modification to the behavioural regulation in exercise questionnaire to include an assessment of amotivation. *Journal of Sport and Exercise Psychology*, 26, 191-196.

Markland, D. & Tobin, V. (2010). Need support and behavioural regulations for exercise among exercise referral scheme clients: The mediating role of psychological need satisfaction. *Psychology of Sport and Exercise*, 11, 91-99.

Medical Research Council (MRC; 2008). Developing and evaluating complex interventions: the new Medical Research Council guidance. *BMJ*, 337, a1655.

National Institute for Health and Care Excellence. (2014). *Exercise referral schemes to promote physical activity: NICE public health guidance 54*. Available from [guidance.nice.org.uk/ph54](http://guidance.nice.org.uk/ph54).

National Institute for Health and Care Excellence. (2017). *Incorporating economic evaluation*. National Institute for Health and Care Excellence. <https://www.nice.org.uk/process/pmg20/chapter/incorporating-economic-evaluation>. Updated April 2017. Accessed 01.11.2017.

Nobles, J., Griffiths, C., Pringle, A., Gately, P. (2016) 'Design programmes to maximise participant engagement: a predictive study of programme and participant characteristics associated with engagement in paediatric weight management', *International Journal of Behavioral Nutrition and Physical Activity*, 13(1), 76.

Pavey, T.G., Anokye, N., Taylor, A.H., Trueman.P., et al. (2011). The clinical effectiveness and cost-effectiveness of exercise referral schemes: a systematic review and economic evaluation. *Health Technology Assessment*. 15 (44), pp. 1366-5278.

Rubenfire, M., Rajagopalan, S., & Mosca, L. (2000). Carotid artery vasoreactivity in response to sympathetic stress correlates with coronary disease risk and is independent of wall thickness. *Journal of the American College of Cardiology*, 36(7), 2192-2197.

Ryan, R. M. & Deci, E. L. (2000). Self-determination theory and the facilitation of intrinsic motivation, social development and well-being. *American Psychologist*, 55 (1), 68-78.

Sanders, G.D., Neumann, P.J., Basu, A., Brock, D. W., et al. (2016). Recommendations for Conduct, Methodological Practices, and Reporting of Cost-effectiveness Analyses. Second Panel on Cost-Effectiveness in Health Medicine. *JAMA*. 316 (10): 1093-1103.

Teixeira, P. J., Carraça, E. V., Markland, D., Silva, M. N. & Ryan, R. M. (2012). Exercise, physical activity, and self-determination theory: A systematic review. *International Journal of Behavioural Nutrition and Physical Activity*, 9, 78. doi:10.1186/1479-5868-9-78.

Thompson, S., and Wordsworth, S. (2001). *An annotated cost questionnaire for completion by patients. HERU Discussion Paper*. Available at: <http://www.dirum.org/assets/downloads/634432307461163116-An%20annotated%20cost%20questionnaire%20for%20completion%20by%20patients.pdf> Accessed 01.11.2017.

Weatherly, H., Drummond, M., Claxton, K., Cookson, R., et al. (2009). Methods for assessing the cost-effectiveness of public health interventions: Key challenges and recommendations. *Health Policy*. 93, pp. 85-92.

Wilson, P. M., Rodgers, W. M., Loitz, C. C. & Scime, G. (2006a). "It's who I am...really!" The importance of integrated regulation in exercise contexts. *Journal of Applied Biobehavioral Research*, 11(2), 79-104.

Wilson, P. M., Rogers, W. T., Rodgers, W. M. & Wild, T. C. (2006b). The psychological need satisfaction in exercise scale. *Journal of Sport and Exercise Psychology*, 28, 231-251.