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Pragmatic evaluation of a co-produced physical activity referral scheme: A quasi-experimental study

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Contributorship Statement

BJRB contributed to the study design, data collection, data analysis, and preparation of the final document. PMW, DHJT, and RCM contributed to the study design, data analysis, and preparation of the final document. MC contributed to the data collection and approved the final version. LEFG, FG, DC, PW, and GW intellectually contributed to this paper and approved the final version.

Objectives. UK exercise referral schemes (ERSs) have been criticised for focusing too much on exercise prescription and not enough on sustainable physical activity (PA) behaviour change. Previously, a theoretically-grounded intervention (Co-PARS) was co-produced to support long-term PA behaviour change in individuals with health conditions. The purpose of this study was to investigate the effectiveness of Co-PARS compared to a usual care ERS and no treatment for increasing cardiorespiratory fitness.

Design. A three-arm quasi-experimental trial.

Setting. Two leisure centres providing a) Co-PARS, b) usual exercise referral care, and one no-treatment control.

Participants. 68 adults with lifestyle-related health conditions (e.g. cardiovascular, diabetes, depression) were recruited to Co-PARS, usual care, or no treatment.

Intervention. 16-weeks of physical activity behaviour change support delivered at 4, 8, 12, and 18 weeks, in addition to the usual care 12-week leisure centre access.

Outcome measures. Cardiorespiratory fitness, vascular health, PA, and mental wellbeing were measured at baseline, 12 weeks, and 6 months (PA and mental wellbeing only). Fitness centre engagement (Co-PARS and usual care) and behaviour change consultation attendance (Co-PARS) were assessed. Following an intention-to-treat approach, repeated-measures linear mixed models were used to explore intervention effects.

Results. Significant improvements in cardiorespiratory fitness (p=.002) and vascular health (p=.002) were found in Co-PARS compared to usual care and no-treatment at 12 weeks. No significant changes in PA or wellbeing at 12 weeks or 6 months were noted. Intervention engagement was higher in Co-PARS than usual care, though this was not statistically significant.

Conclusion. A co-produced PA behaviour change intervention led to promising improvements in cardiorespiratory and vascular health at 12 weeks, despite no effect for PA levels at 12 weeks or 6 months.

Trial registration: ClinicalTrials.gov: NCT03490747

Keywords: Cardiovascular Health; Self-Determination Theory; Exercise Referral; Behaviour Change Intervention; Translational Research.

Strengths and limitations of the study

- This study advances the literature on exercise referral effectiveness by pragmatically evaluating a co-produced physical activity referral intervention, which was underpinned by multiple stakeholders and behaviour change theory.
- The study documents the third phase of a novel and iterative approach which co-produced, piloted, and then evaluated (this study) a physical activity referral intervention that was deemed feasible to implement in practice.
- Objective and subjective measures provide insight into the potential effects for patient health.
- It is not possible to directly attribute intervention effects to the phased co-production approach, although supported by the Medical Research Council.
- A larger sample size is needed to substantiate findings.

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Competing interests

The authors declare that they have no competing interests.

Authors' contributions

BJRB contributed to the study design, data collection, data analysis, and preparation of the final document. PMW, DHJT, and RCM contributed to the study design, data analysis, and preparation of the final document. MC contributed to the data collection and approved the final version. LEFG, FG, DC, PW, and GW intellectually contributed to this paper and approved the final version.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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Ethics approval and consent to participate

Full written consent was obtained from participants and the study was approved by NHS Research Ethics Committee (REC: 18/NW/0039 - Project: 238547).

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INTRODUCTION

Physical inactivity is the fourth leading cause of death worldwide and costs the UK an estimated £7.4 billion annually, including £0.9 billion to the NHS alone[1]. Exercise referral schemes (ERSs) provide a promising framework to facilitate physical activity (PA) behaviour change in at-risk populations. Typically, UK ERSs consist of a referral from a healthcare professional to a 12-16-week tailored exercise programme provided by a qualified practitioner.

There is inconsistent evidence as to the effectiveness of ERSs on PA behaviour, mental well-being, quality of life, and physical health outcomes [2–4]. More recently, however, promising effects of ERSs have been demonstrated in Wales [5], Sweden [6], and Spain [7] and a systematic review identified promising effects of UK ERSs on self-reported PA and cardiovascular health markers [8]. Prior and colleagues [9] demonstrated that for every 11 participants referred to a 24-week ERS, 1 participant went on to report achieving ≥90 min/week of PA at 12-months. For perspective, it is estimated that 67-167 patients (categorised as ≤10% cardiovascular disease (CVD) risk) need to receive statin treatment for 5 years to prevent one major vascular event [10]. Whilst we are not suggesting PA behaviour change is a comparable outcome to a serious clinical event, it is notable that replacing 30 minutes of TV viewing time with PA across the UK population, could reduce premature mortality by 5-15%, depending on activity intensity [11]. The majority of studies evaluating ERSs, however, have drawn on self-reported PA data and future studies employing device-based measures are needed to substantiate these observations.

Despite recent promise for the effectiveness of ERSs [7–9,12], substantial heterogeneity exists in both design and delivery [13,14], reflecting varying assumptions on how best to promote health behaviour change [15,16]. This limits potential scalability of 'successful' ERSs. Traditionally, ERSs have focussed on short-term exercise prescription without appropriate evidence of effectiveness or underpinning of

behaviour change theory [17]. A recent attempt to integrate behaviour change theory into an ERS [18] however, showed no advantage over a standard ERS at 12 weeks or 6 months. The authors noted considerable implementation challenges when training staff, such as work-related demands that may have reduced the importance of the theory-based training. It is plausible that delivery staff asked to implement interventions designed by academics may lack ownership and feel less motivated/competent. One potential way to promote ownership and engagement might be to adopt a co-production approach, as a means of co-creating value across the public sector [19–21]. Though not a panacea, the involvement of practitioners, managers and service-users in co-production has potential to improve intervention relevance, fidelity, and effectiveness [22].

Previously, a theoretically-grounded PA referral scheme (Co-PARS) was co-produced by academics, policy-makers, practitioners, and service-users [23] in Liverpool, UK, with a focus on supporting sustainable PA behaviour change. Liverpool is the 3rd most deprived local authority in England and has the 2nd highest proportion of Lower Super Output Areas (LSOAs) in the most deprived 10% nationally [24]. Interventional work with at-risk patients is therefore critical and is aligned with the concept of proportionate universalism [25]. Underpinned by self-determination theory [24], the co-produced intervention differed from usual ERS care in its focus on PA behaviour change (rather than exercise prescription), and inclusion of frequent one-to-one consultations with exercise referral practitioners (compared to usual care which included formal contact at induction only). A pilot of Co-PARS [26] showed clinically meaningful improvements in cardiorespiratory fitness (CRF) and PA, although as we did not include a usual care control, it was unknown whether these effects were due to the fact participants were taking part in an ERS or due to the unique elements of Co-PARS. Furthermore, despite having very low CRF (<27.7 $ml.kg^{-1}.min^{-1}$) [26] we found 64% of the baseline pilot sample were meeting the PA guidelines [27] of at least 150 minutes moderate-intensity PA per week (measured objectively via accelerometry). This suggested CRF may be a more appropriate primary outcome measure than PA for this low-fit population (whilst changing PA behaviour was the focus of the intervention, a target health outcome of this behaviour change was improved CRF). The pilot also

allowed the opportunity to investigate delivery processes, and we noted several areas that required refinement in preparation for a controlled trial. These refinements included, increasing the number of behaviour change consultations from four to five; enhanced focus on daily PA opportunities (rather than focussing on activities offered at the fitness centre); adapting staff timetables to promote consistency of care and to allow participant one-to-one consultations to take place in a private room; and reducing practitioner paperwork. Building on our previous pilot work, the aim of the current study was to investigate the effectiveness of Co-PARS compared to a usual care ERS and a no-treatment control on change in cardiorespiratory fitness (CRF) at 12 weeks and PA and wellbeing at 6 months.

METHODS

Study Design

A three-arm quasi-experimental trial involving: 1. Co-PARS (delivered at fitness centre A); 2. usual care ERS (delivered at fitness centre B); and 3. no-treatment control. This paper reports trial outcomes (CRF, vascular health, PA, mental wellbeing) measured at baseline, 12 weeks, and 6 months (PA and mental wellbeing only). Additional data were collected to investigate psychosocial processes of change, intervention fidelity and cost-effectiveness; due to space limitations they are not considered in the present manuscript, but findings can be obtained on request from p.m.watson@ljmu.ac.uk. Full written consent was obtained from participants and the study was approved by NHS Research Ethics Committee (REC: 18/NW/0039 - Project: 238547) and registered on ClinicalTrials.gov (NCT03490747).

Patient and Public Involvement

The intervention was previously co-produced, piloted, and adapted with substantial service user input [23,26].

Participants and Recruitment

Inclusion criteria were the same for all three conditions (Co-PARS, usual care, no-treatment). Participants were eligible if aged ≥18 years with a health-related risk factor (e.g. hypertension, hyperglycaemia, obesity) and/or health condition (e.g. diabetes, cardiovascular disease, depression)

that may be alleviated by increasing PA levels. Participants with uncontrolled health conditions, severe psychological or neurological conditions were excluded. Participants for the Co-PARS and usual care arms were recruited from fitness centre A (Co-PARS) and fitness centre B (usual care) respectively (where they had been referred for exercise by a health professional). Reception staff at both centres provided study information and gained consent to pass participant details to the researcher. Participants for the no-treatment control were recruited via posters, electronic invitations, and email communications primarily at the university site. Participants were not eligible for the no-treatment control if they were currently attending an exercise referral scheme. Interested participants for all groups were sent an information sheet and baseline data collection was arranged.

Study Arms

Intervention arm components are presented in Figure 1.

Usual care exercise referral scheme (ERS – centre B). Usual care followed a standard ERS model of 12-week subsidised access to a fitness centre (swimming, gym, group classes). Participants met an exercise referral practitioner for an initial, 1-hour induction (week 1) during which a 12-week exercise programme was provided for the participant. Any further contact with a practitioner was informal and opportunistic. This system was already in place and was considered usual care for the local area. Centre B was chosen as a comparison centre due to its similarity in referral numbers and socio-economic make-up of the local population to centre A (where Co-PARS was being delivered). For example, based on areas within Liverpool ranked from 1 (most deprived) to 30 (least deprived), usual care ERS and Co-PARS were ranked respectively: 20th and 21st (income), 20th and 21st (employment), 22nd and 24th (Education) and 10th and 11th (living environment).

Co-produced PA referral scheme (Co-PARS – centre A)

Participants received the same 12-week subsidised access to a fitness centre as usual care plus a series of one-to-one behaviour change consultations (60-minute induction followed by 30-minute consultations at weeks 4, 8, 12 and 18). A log book was provided for each participant to set action

plans, log progress and facilitate consultation discussions. Consultations were delivered by exercise referral practitioners in an autonomy supportive counselling style, drawing on the principles of self-determination theory [28]. This additional support aimed to encourage habitual opportunities to increase PA as well as activities available at the fitness centre. A full descripion of the theoretical underpinning and behaviour change intervention components is available elsewhere [23].

Prior to the pilot of Co-PARS [26] practitioners received training in self-determination theory-based communication strategies led by a sport and exercise psychologist (last author [PMW]), involving a workshop, one-to-one sessions and follow-up group meetings. Following the pilot, a further series of group meetings involving exercise referral practitioners and the research team were held to develop aspects of delivery that required refinement (as outlined in the introduction). Full details of the training are available from p.m.watson@ljmu.ac.uk).

No-treatment control (NTC). Participants received a lifestyle advice booklet only (offered to all study arms at baseline data collection), based on national guidance for PA, nutrition, smoking cessation and alcohol consumption.

[INSERT FIGURE 1 SOMEWHERE HERE]

Outcome measures

Primary outcome*: Cardio-respiratory fitness (CRF).* Maximal oxygen consumption (VO_2max^{-2}) was estimated via the sub-maximal Astrand-Rhyming cycle ergometer protocol [29]. The protocol is a single-stage cycling test designed to elicit a steady-state heart rate over a period of ~6 minutes.

Accelerometer-derived PA. Tri-axial ActiGraph GT3x accelerometers (ActiGraph, Pensacola, FL, USA) measured PA for 7 days, which have been validated in a comparable population [30]. Raw triaxial acceleration values were converted into an omnidirectional measure of acceleration, referred to as Euclidian norm minus one [31]. Minimum wear time was 10 hours per day and 3 days per week including one weekend day [32]. The R package GGIR [31] facilitated extraction of user-defined

acceleration thresholds: 5.9 to 69.1 mg for light-intensity PA [33], 69.1 to 258.7 mg as moderate and >258.7 mg as vigorous-intensity PA [34].

Vascular health. Our previous work has demonstrated carotid artery reactivity (CAR) may be a promising outcome variable to assess in PA interventions for at-risk populations [35]. Further, endothelial function may provide prognostic value beyond that of traditional risk factors [36] with an increase of 1% in brachial artery flow-mediated dilation (FMD) associated with a 12-15% lower risk of CV events [33,34]. FMD and CAR were measured using ultrasound techniques [35]. Both techniques measure vascular endothelial function and have independently predicted future risk of cardiovascular events in humans [36,37]. Blood pressure was measured in the supine position using an automated blood pressure device (Omron Healthcare UK Limited, Milton Keynes, UK).

Anthropometric measures. Since obesity is a critical risk factor for poor health and cardiovascular disease, anthropometric variables were measured to investigate potential intervention effects on body mass. Waist-to-height ratio is a stronger predictor of early health risk than Body Mass Index (BMI) alone [38], therefore we collected both BMI (mass in kg / stature in m^2) and waist-to-height ratio (waist circumference / stature).

Mental wellbeing. As PA is known to enhance mental wellbeing [39] and clinical populations are more susceptible to mental ill-health [40], it was important to identify whether Co-PARS led to any changes in mental health (positive or negative). Mental wellbeing was measured using the 14-item Warwick-Edinburgh Mental Well-being Scale (WEMWBS; [41], which asks participants to rate their psychological wellbeing (e.g. "I've been feeling cheerful") over the previous 2 weeks (measured on a likert scale of 1 (none of the time) to 5 (all of the time)).

Fitness centre engagement (Co-PARS and usual care only). The number of occasions participants attended the fitness centre between baseline and 12 weeks (weekly attendance) and 12 weeks to 6 months (monthly attendance) was obtained from computerised attendance records. When measuring intervention engagement it was deemed inappropriate to calculate the mean number of

sessions per week, since this could exaggerate the engagement of individuals who attended with high frequency in the early weeks then dropped out (when compared with individuals who attended moderately but consistently for the full 12 weeks). Therefore a formula was used to calculate a percentage for '12-week engagement' (based on the recommended bi-weekly attendance):

$$\left(\frac{((n1*0.5) + (n2) + (n3*1.2))}{12} \right) * 100$$

n1 = number of weeks in which participant attends once only
n2 = number of weeks in which participant attends twice
n3 = number of weeks in which participant attends three or more times

This formula took into account both *frequency* and *consistency* of attendance to yield a percentage score that ranged from 0% (no attendance) to 120% (attendance of three or more times per week for the whole 12 weeks).

Monthly attendance post-12 weeks was calculated as a mean attendance across months 4 to 6, therefore did not take consistency of attendance into account.

Behaviour change consultation attendance (Co-PARS only). The number of consultations offered and attended were measured by exercise referral practitioners at induction, 4, 8, 12, and 18 weeks.

Sample size

Sample size was determined to detect a meaningful difference in CRF at 12 weeks based on our pilot results [26]. To detect a difference of 2 $ml.kg^{-1}min^{-1}$ between Co-PARS and usual care, 42 participants were required per arm (f= .25, *p*= .05, power = .80). To detect a difference of 3.2 $ml.kg^{-1}min^{-1}$ between the intervention arms and the no-treatment control, 17 participants were required for the no-treatment control (f= .5, *p*= .05, power = .80). Thus, a total sample of 101 participants were required.

Statistical analyses

An intention-to-treat approach was used assuming no change in non-respondents (last observation carried forward) to produce a conservative estimate of intervention effects. Delta changes (Δ) from

pre- to post-intervention were calculated for each group and entered as the dependent variable in repeated measures linear mixed model analyses. A random intercept model was used with fixed effects for study arm (Co-PARS, usual care ERS, no-treatment control) and time (baseline-to-week-12 change, week-12-to-6-month change, and baseline-to-6-month change) and participants included as random effects. Least squared difference (LSD) was used for post hoc testing. Testing for baseline differences to identify covariates was avoided, as this method has been demonstrated to inflate bias, instead pre-intervention was entered into the model as a covariate. Furthermore, all linear mixed model analyses were repeated with age and employment as covariates as a comparison to the results presented in this study (with baseline score as a covariate) due to their known prognostic value. Using age and employment as covariates resulted in no change in inferences presented in this study. One-way ANOVAs were used to compare baseline values between intervention arms. Fitness centre engagement was determined as described above. Behaviour change consultation attendance is presented descriptively. For non-normally distributed data, median and interquartile range is presented and within group median change was calculated via Wilcoxon signed-rank tests.

RESULTS

Participants. 68 participants provided baseline data, 56 of whom provided 12-week data, and 58 of whom provided 6-month data (figure 2).

Baseline characteristics (table 1). No significant differences were noted between arms for age, sex, ethnicity, BMI, referral reason, or accelerometer-derived PA levels (p>.05). Full-time employment status (p=.001) and CRF (p=.015) were significantly higher in the control compared to usual care and Co-PARS. Smoking status was significantly higher in usual care compared to Co-PARS and control (p=.010). Mental wellbeing was significantly lower in Co-PARS compared to control (p=.023).

[INSERT FIGURE 2 SOMEWHERE HERE]

Table 1. Baseline characteristics presented as Mean ± SD or % (n) of group.

	Co-produced PA referral (*n*=33)	Usual care ERS (*n*=19)	No-treatment control (*n*=16)	Between arm *p*-value
Age (years)	57 ± 12	53 ± 16	48 ± 15	*p*=.319
Female (% of sample)	58 (19)	47 (9)	56 (9)	*p*=.774
White British (% of sample)	82 (27)	95 (18)	75 (12)	*p*=.132
Full-time employment (% of sample)	18 (6)	26 (5)	62 (10)	*p*=.001
Never smoked (% of sample)	73 (24)	37 (7)	81 (13)	*p*=.002
Body mass index (kg/m^2)	31 ± 7	33 ± 6	29 ± 6	*p*=.226
Systolic blood pressure (mmHg)	131 ± 11	138 ± 18	123 ± 12	*p*=.010
Primary referral reason / health concern (control)				*p*=.132
Cardiometabolic (% of sample)	67 (22)	43 (8)	62 (10)	-
Cancer (% of sample)	6 (2)	5 (1)	6 (1)	-
Mental Health (% of sample)	18 (6)	26 (5)	19 (3)	-
Musculoskeletal (% of sample)	9 (3)	26 (5)	13 (2)	-
Comorbidity (% of sample)	85 (28)	100 (19)	81 (13)	*p*=.166
Meeting the PA guidelines (% of sample)*	73 (22)	71 (10)	93 (13)	*p*=.223

P-values represent between arm baseline effects. There was no between arm effect for referral reason, thus no between arm *p*-values are provided for referral reason sub groups.
*Chief Medical Officers' 2019 physical activity guidelines: 150 minutes of moderate-intensity physical activity per week.

Baseline-to-12-Week effects

Raw outcome values are presented for baseline, week 12, and 6 months in Table 2. There was a significant effect for study arm in baseline-to-12-week change in CRF (*p*=.002). Post hoc testing

revealed a significantly higher CRF change in Co-PARS (2.4) compared to the ERS (0.3; p=.021) and control (-0.6; p=.001), but no difference between the ERS and control (p=.314). A significant effect for study arm was found in change in FMD% (p=.002), with FMD% change significantly higher in Co-PARS (2.4) compared to control (-1.1; p=.001) but not the ERS (0.8; p=.099). The change in FMD% was not significantly different between the ERS and control (p=.71). No statistically significant study arm effects were noted for changes in CAR%, blood pressure, resting heart rate, anthropometric measures, PA or WEMWBS at 12 weeks (p>.05).

Baseline-to-6-month effects

No statistically significant study arm effects were noted for change in WEMWBS or PA at 6 months (p>.05).

Fitness centre engagement (Co-PARS and usual care ERS) and consultation attendance (Co-PARS only).

Table 3 reports the participant fitness centre engagement data for the Co-PARS and usual care ERS. Although not statistically significant, Co-PARS engagement was 9% higher, participants attended the fitness centre on average 3 times more per month, and 23% more participants were attending the fitness centre beyond 6-months follow-up compared to usual care. Co-PARS behaviour change consultation attendance is reported in Table 4.

Table 2. Cardiometabolic health outcomes and PA levels at baseline, 12 weeks, 6 months, and between arm baseline-to 12-week or 6-month effect. All variables are presented as Mean ± SD.

	Co-PARS			Usual Care ERS			No-Treatment Control			
	Baseline	***Week 12***	**6 Month**	**Baseline**	**Week 12**	**6 Month**	**Baseline**	**Week 12**	**6 Month**	**Between arm effect *p*-value[(a)]**
					Fitness (n=56)					
CRF $_{ml.kg.^{-1}min^{-1}}$	22.2±7	24.6±7	-	23.3±6.6	23.6±7	-	29.6±9.2	28.9±8.7	-	*p*=.002
					Physical Activity					
GT3x *(n= 61)* $_{Mins.day}$										
Light intensity	90±52	98±64	107±75	98±36	93±31	158±145	90±37	101±33	*86*±40	*p*=.332
Moderate intensity	44±32	42±29	42±33	43±28	43±30	55±55	60±31	65±24	*54*±21	*p*=.260
Vigorous intensity	1±3	1±2	1±2	1±2	1±1	1±2	2±4	2±3	*3*±8	*p*=.108
					Vascular Ultrasound (n=64)					
CAR%	1.7±2.7	2.8±2.2	-	2.7±1.8	3.9±2.8	-	2.5±2.7	1.7±2.7	-	*p*=.073
CAR Baseline $_{cm}$	0.69±0.07	0.69±0.06	-	0.69±0.08	0.7±0.09	-	0.65±0.07	0.64±0.06	-	*p*=.130
FMD%	4.4±2.3	6.8±2.7	-	4.2±2	5±2.1	-	6.2±2.1	5.2±2.8	-	*p*=.002
FMD Baseline $_{cm}$	0.39±0.07	0.38±0.06	-	0.39±0.09	0.41 0.08	-	0.38±0.08	0.37±0.06	-	*p*=.728
					Cardiometabolic (n=68)					
BMI $_{kg.m2}$	31±7	30±7	-	33±6	32±6	-	29±6	29±6	-	*p*=.323
WHR	62±9	61±10	-	64±8	63±8	-	56±9	56±9	-	*p*=.261
SBP $_{mmHg}$	131±11	127±12	-	138±18	132±15	-	123±12	118±13	-	*p*=.937
DBP $_{mmHg}$	73±7	71±8	-	73±9	71±11	-	72±11	68±10	-	*p*=.584
RHR $_{bpm}$	70±10	65±10		70±12	68±11		66±12	63±9		*p*=.540
					Mental Wellbeing (*n*=68)					
WEMWBS	46±9	*51±10*	*48±10*	49±10	52±11	*50±13*	53±9	56±9	*53±10*	*p*=.796

Co-PARS, Co-produced PA referral scheme**; ERS,** Exercise referral scheme**; CRF**, Cardiorespiratory Fitness; **GT3x**, Accelerometer; **CAR**, Carotid artery reactivity; **FMD**, Flow-mediated dilation; **BMI**, Body Mass Index; **WHR**, Waist-to-Height ratio; **SBP**, Systolic blood pressure; **DBP**, Diastolic blood pressure; **RHR**, Resting heart rate, **WEMWBS,** Warwick-Edinburgh Mental Wellbeing Scale

[a] *F*-statistic for between arm baseline-to-6-month change or baseline-to-week 12 change if variable not collected at 6 months.

Missing data was due to inability to complete the CRF test (*n*=12), inability to complete the vascular ultrasound protocols (*n*=4), and insufficient accelerometer wear time or non-return (*n*=7).

Table 3. Fitness centre engagement.

	Co-PARS (*n*=33)	Usual Care (*n*=19)	Between centre difference
% Engagement[a] (Mean ± SD)	42±29	33±27	*p*=.267
Number of fitness centre visits (per person per month) week 12 to 6 months (Med, IQR)	3(0-14)	0 (0-1)	*p*=.072
% of baseline sample who attended fitness centre at least once beyond 6 months (% of sample, n)	39 (13)	16 (3)	*p*=.101

[a]Based on the formula (((n1*0.5)+(n2)+(n3*1.2))/12) * 100; n1=number of weeks in which participant attends once only; n2=number of weeks in which participant attends twice; n3=number of weeks in which participant attends three or more times. [a]**Engagement**;.based on a recommended attendance of twice weekly, a formula was used to calculate a percentage for "12-week engagement", which took into account both frequency and consistency of attendance (see methods).

Table 4. Co-PARS behaviour change consultation attendance (based on baseline sample of 33 participants).

Consultation	% Booked (n)	% Attended (n)
Induction	91(30)	93(28)
Week 4	82(27)	78(21)
Week 8	67(22)	91(20)
Week 12	64(21)	81(17)
Week 18	55(18)	50(9)

DISCUSSION

This was the first study to investigate the effectiveness of a theoretically-grounded, co-produced PA referral scheme (Co-PARS) compared to a usual care ERS and no treatment. Despite challenges in recruitment that meant the study was statistically underpowered, the findings demonstrated significant and clinically meaningful improvements in CRF and vascular health in Co-PARS compared to the usual care and no treatment. No statistically significant effects were noted for accelerometer-derived PA levels or mental wellbeing at 12-weeks or 6-months.

The effect of usual care ERSs compared to theoretically-grounded interventions on CRF has not been previously explored. We observed a significant increase in CRF in Co-PARS compared to usual care and a no-treatment control. According to values reported by Clausen *et al*. [42] both Co-PARS (22 ml.kg.$^{-1}$min^{-1}) and usual care (23 ml.kg.$^{-1}$min^{-1}) participants were below the lower limit of 'healthy' (27.7 ml.kg.$^{-1}$min^{-1}) for baseline CRF [43]. As low CRF is associated with a substantially elevated risk of all-cause mortality [43], the magnitude of change demonstrated in Co-PARS (2.4 ml.kg.$^{-1}$min^{-1}) may be clinically meaningful. For example, in at-risk populations, relatively small magnitudes (≤1 ml.kg.$^{-1}$min^{-1}) have been shown to significantly reduce clustered cardiometabolic risk [44]. Thus, Co-PARS was effective at improving CRF in individuals with low CRF by a clinically meaningful amount.

Promising improvements in vascular health were also noted in the Co-PARS group, with brachial artery FMD significantly improved compared to usual care and control arms. Although CAR was not statistically different between arms, both Co-PARS and usual care demonstrated a potentially meaningful within-arm improvement compared with no treatment, which exhibited a deterioration in vascular health. Such improvements in vascular measures may have prognostic implications. For example, a 1% increase in FMD has been suggested to reduce the future risk of CVD events by 13% [36].

Despite low baseline CRF, a substantial percentage of Co-PARS (73%) and usual care (71%) participants were meeting the Department of Health [45] guidelines of 150 minutes of moderate-intensity PA per

week. We observed a similar finding in our pilot [26] and subsequently raised the question as to the use of PA guidelines to assess eligibility for ERSs (NICE, 2014), as it appears from our data that individuals classified as "physically active" can still be very unfit and therefore can benefit from ERSs in terms of improved fitness and cardiometabolic health. A further discrepancy was noted in the lack of change in PA levels in Co-PARS, despite improved CRF. It is possible measurement issues contributed to this discrepancy. Accelerometers can measure certain types of PA such as walking, running, and stair climbing [46]. They may not, however, sufficiently identify activities typical of an ERS delivered within a fitness centre environment (e.g. cycling, resistance training, circuits, swimming). Given Co-PARS had higher (albeit non-significant) fitness centre engagement compared to usual care, it is possible PA changes occurred that were not detected by the accelerometry data. Consideration therefore needs to be given to the appropriateness of accelerometers to measure PA in ERSs. Alternative methods such as heart-rate monitors combined with self-report data may be worthy of consideration, although further work would be required to develop standardized data collection and analysis protocols (taking into account the limitations of each of these methods if used in isolation [47]). Researchers are therefore urged to consider CRF as a primary outcome in ERSs until appropriate alternative methods of measuring PA behaviour are developed. Ultimately, it is not clear why the increase in fitness occurred without a corresponding change in PA and further research is required to elucidate the relationship between PA and fitness in this population.

In addition to physiological health outcomes, we found baseline mental wellbeing to be below the national average (score of 50) in both Co-PARS (46) and usual care (49), but not the control (53) [48]. Despite no significant between-group effect for mental wellbeing, within-group changes at 12 weeks were deemed clinically meaningful for Co-PARS (5) and usual care (3) but not in the no treatment control. It is notable that the post-intervention magnitude of change observed in mental wellbeing for Co-PARS (5) was larger than that observed in a meta-analysis encompassing >23,000 participants across 13 different ERSs (3), which were comparable in nature to the usual care ERS in this study [49].

From the 6-month data it appeared the scheme was not effective at promoting *sustained* PA behaviour change or mental wellbeing improvements. It must be noted, however, that the wellbeing levels were still higher than baseline and even small magnitudes of change (1-3) may be meaningful in clinical populations [50]. As discussed earlier, it may be that measuring PA using the methods described in this study prevented the identification of activities typical of a fitness centre environment. This notion is supported by the post-week-12 attendance data, which highlighted Co-PARS participants were regularly attending the fitness centre whereas the usual care participants were not. Challenges of maintaining sustained health outcomes post-ERSs have been highlighted elsewhere [3]. And whilst a recent systematic review reported longer length schemes (>20 weeks) may be more effective than shorter schemes [8], the four long ERSs (20-26 weeks) collected pre-post data only. Thus we do not know if longer length ERSs result in enhanced health outcomes *post intervention* compared with shorter schemes. To determine if longer length schemes are indeed more effective, longer-term follow-up data collection is required, ideally at 6 and 12 months post intervention [51].

Through a phased approach we have assessed the effectiveness of Co-PARS resulting from several years of co-production. Whilst the effects of co-production are difficult to isolate, a comparison of results at different stages of intervention refinement suggests the phased development approach had some positive effects. Unpublished engagement data from centre A in 2014-2015 (when the centre was running a usual care ERS) shows that engagement improved after the introduction of Co-PARS (42% vs 28% in 2014-2015), whereas engagement reduced in the usual care centre over the same period (32% vs 37% in 2014-2015). Furthermore, consultation attendance for Co-PARS in the current study was substantially higher than in our previous pilot (54% attended induction plus ≥3 behaviour change consultations, vs 9% in the pilot [26]), which may have been a reflection of refinements made to the intervention after the pilot (e.g. improved focus on holistic PA, improved monitoring procedures, improved continuity of instructors). These improvements in engagement highlight the importance of allowing time for complex interventions to develop [52], and are particularly promising given the effectiveness of ERSs are highly dependent on participant adherence [5,21]. Furthermore,

this study has demonstrated how investing in the "bottom-up" development of an intervention can lead to an effective and sustainable model. We therefore support the arguments of Rutter and colleagues [53] in that a shift in thinking is needed, instead of asking whether an intervention works to fix a problem, researchers should aim to identify if and how it contributes to reshaping a system in a favourable way. As such, we propose the co-production and implementation process may be as important as the scheme content itself.

Methodological considerations

This is the first known study to investigate the effectiveness of a co-produced PA referral scheme (Co-PARS) in comparison to usual care and a no-treatment control. Our novel approach addresses an important gap in the sport and exercise medicine literature [54], in that we employed rigorous laboratory-based instruments to measure health outcomes that can be achieved through an ecologically valid, "real-world" intervention. We observed a very high retention at 6-month follow up, which may be due in part to the fact many of the participants were retired (and therefore may have more available time). It is possible also that the high retention was facilitated by the co-production process, which involved ongoing relationships between the research and delivery teams (and therefore helped with the logistics of returning accelerometers for the co-PARS and usual care groups). Whilst this paper highlights many strengths of co-production, we do not wish to present co-production as a panacea [19] and it is important potential challenges and costs are considered prior to undertaking such an approach [21,22].

We must acknowledge some limitations of the study. Whilst there is a need for high-quality RCTs of theoretically informed approaches to PA behaviour change [3], several pragmatic reasons meant an RCT approach was not appropriate for the present study. Firstly, it was important participants could choose the most convenient fitness centre. Secondly, it was important we continued work with the same fitness centre and staff (following co-production [23] and pilot [26] phases) in order to develop the intervention to the point where it was deemed to have a worthwhile effect [52]. A pragmatic

research approach was therefore deemed most appropriate to evaluate Co-PARS with high ecological validity. Pragmatic constraints (e.g. fitness centre refurbishments, staff illness) did however mean the required sample size was not achieved, thus inferences of effectiveness need to be taken with caution. This is particularly true for the PA data, where the relatively high variability (compared with CRF) may have contributed to the lack of change observed in PA in this study. It is recommended future work considers pragmatic risks and contingencies when planning recruitment and plans sufficient time to cope with recruitment delays. For pragmatic reasons, not all outcomes were collected at 6-months follow-up and further research is needed to collect long-term, objective health data following PA referral schemes. Finally, it must be noted that while the trial registration appears to be retrospective (April 6th 2018), the initial submission was several months prior to this (January 11th 2018). Final sign-off was delayed due to capacity issues within the research team.

CONCLUSION

A co-produced, theoretically-grounded PA referral scheme (Co-PARS) led to improved CRF and vascular health in at-risk individuals when compared to usual care and no treatment. In addition, clinically meaningful improvements in vascular health and mental wellbeing were observed at 12-weeks in both Co-PARS and usual care, but not the no treatment control group. Of note, PA remained unchanged at 12-weeks and 6-months follow-up. Adopting a phased approach has enabled multi-stakeholder input and ongoing intervention refinement, resulting in an intervention that showed promising effects on engagement and clinically meaningful improvements to participant health.

Figure Legends

Figure 1. 'PaT Plot' describing intervention arm components.[55]

Figure 2. Participant flow diagram within the three study arms (March 2018-January 2019).

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Pragmatic evaluation of a co-produced physical activity referral scheme: A quasi-experimental study

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Contributorship Statement

BJRB contributed to the study design, data collection, data analysis, and preparation of the final document. PMW, DHJT, and RCM contributed to the study design, data analysis, and preparation of the final document. MC contributed to the data collection and approved the final version. LEFG, FG, DC, PW, and GW intellectually contributed to this paper and approved the final version.

Objectives. UK exercise referral schemes (ERSs) have been criticised for focusing too much on exercise prescription and not enough on sustainable physical activity (PA) behaviour change. Previously, a theoretically-grounded intervention (Co-PARS) was co-produced to support long-term PA behaviour change in individuals with health conditions. The purpose of this study was to investigate the effectiveness of Co-PARS compared to a usual care ERS and no treatment for increasing cardiorespiratory fitness.

Design. A three-arm quasi-experimental trial.

Setting. Two leisure centres providing a) Co-PARS, b) usual exercise referral care, and one no-treatment control.

Participants. 68 adults with lifestyle-related health conditions (e.g. cardiovascular, diabetes, depression) were recruited to Co-PARS, usual care, or no treatment.

Intervention. 16-weeks of physical activity behaviour change support delivered at 4, 8, 12, and 18 weeks, in addition to the usual care 12-week leisure centre access.

Outcome measures. Cardiorespiratory fitness, vascular health, PA, and mental wellbeing were measured at baseline, 12 weeks, and 6 months (PA and mental wellbeing only). Fitness centre engagement (Co-PARS and usual care) and behaviour change consultation attendance (Co-PARS) were assessed. Following an intention-to-treat approach, repeated-measures linear mixed models were used to explore intervention effects.

Results. Significant improvements in cardiorespiratory fitness (p=.002) and vascular health (p=.002) were found in Co-PARS compared to usual care and no-treatment at 12 weeks. No significant changes in PA or wellbeing at 12 weeks or 6 months were noted. Intervention engagement was higher in Co-PARS than usual care, though this was not statistically significant.

Conclusion. A co-produced PA behaviour change intervention led to promising improvements in cardiorespiratory and vascular health at 12 weeks, despite no effect for PA levels at 12 weeks or 6 months.

Trial registration: ClinicalTrials.gov: NCT03490747

Keywords: Cardiovascular Health; Self-Determination Theory; Exercise Referral; Behaviour Change Intervention; Translational Research.

Strengths and limitations of the study

- This study advances the literature on exercise referral effectiveness by pragmatically evaluating a co-produced physical activity referral intervention, which was underpinned by multiple stakeholders and behaviour change theory.
- The study documents the third phase of a novel and iterative approach which co-produced, piloted, and then evaluated (this study) a physical activity referral intervention that was deemed feasible to implement in practice.
- Objective and subjective measures provide insight into the potential effects for patient health.
- It is not possible to directly attribute intervention effects to the phased co-production approach, although supported by the Medical Research Council.
- A larger sample size is needed to substantiate findings.

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Competing interests

The authors declare that they have no competing interests.

Authors' contributions

BJRB contributed to the study design, data collection, data analysis, and preparation of the final document. PMW, DHJT, and RCM contributed to the study design, data analysis, and preparation of the final document. MC contributed to the data collection and approved the final version. LEFG, FG, DC, PW, and GW intellectually contributed to this paper and approved the final version.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Word count

~3000

Ethics approval and consent to participate

Full written consent was obtained from participants and the study was approved by NHS Research Ethics Committee (REC: 18/NW/0039 - Project: 238547).

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INTRODUCTION

Physical inactivity is the fourth leading cause of death worldwide and costs the UK an estimated £7.4 billion annually, including £0.9 billion to the NHS alone[1]. Exercise referral schemes (ERSs) provide a promising framework to facilitate physical activity (PA) behaviour change in at-risk populations. Typically, UK ERSs consist of a referral from a healthcare professional to a 12-16-week tailored exercise programme provided by a qualified practitioner.

There is inconsistent evidence as to the effectiveness of ERSs on PA behaviour, mental well-being, quality of life, and physical health outcomes [2–4]. More recently, however, promising effects of ERSs have been demonstrated in Wales [5], Sweden [6], and Spain [7] and a systematic review identified promising effects of UK ERSs on self-reported PA and cardiovascular health markers [8]. Prior and colleagues [9] demonstrated that for every 11 participants referred to a 24-week ERS, 1 participant went on to report achieving ≥90 min/week of PA at 12-months. For perspective, it is estimated that 67-167 patients (categorised as ≤10% cardiovascular disease (CVD) risk) need to receive statin treatment for 5 years to prevent one major vascular event [10]. Whilst we are not suggesting PA behaviour change is a comparable outcome to a serious clinical event, it is notable that replacing 30 minutes of TV viewing time with PA across the UK population, could reduce premature mortality by 5-15%, depending on activity intensity [11]. The majority of studies evaluating ERSs, however, have drawn on self-reported PA data and future studies employing device-based measures are needed to substantiate these observations.

Despite recent promise for the effectiveness of ERSs [7–9,12], substantial heterogeneity exists in both design and delivery [13,14], reflecting varying assumptions on how best to promote health behaviour change [15,16]. This limits potential scalability of 'successful' ERSs. Traditionally, ERSs have focussed on short-term exercise prescription without appropriate evidence of effectiveness or underpinning of

behaviour change theory [17]. A recent attempt to integrate behaviour change theory into an ERS [18] however, showed no advantage over a standard ERS at 12 weeks or 6 months. The authors noted considerable implementation challenges when training staff, such as work-related demands that may have reduced the importance of the theory-based training. It is plausible that delivery staff asked to implement interventions designed by academics may lack ownership and feel less motivated/competent. One potential way to promote ownership and engagement might be to adopt a co-production approach, as a means of co-creating value across the public sector [19–21]. Though not a panacea, the involvement of practitioners, managers and service-users in co-production has potential to improve intervention relevance, fidelity, and effectiveness [22].

Previously, a theoretically-grounded PA referral scheme (Co-PARS) was co-produced by academics, policy-makers, practitioners, and service-users [23] in Liverpool, UK, with a focus on supporting sustainable PA behaviour change. Liverpool is the 3rd most deprived local authority in England and has the 2nd highest proportion of Lower Super Output Areas (LSOAs) in the most deprived 10% nationally [24]. Interventional work with at-risk patients is therefore critical and is aligned with the concept of proportionate universalism [25]. Underpinned by self-determination theory [24], the co-produced intervention differed from usual ERS care in its focus on PA behaviour change (rather than exercise prescription), and inclusion of frequent one-to-one consultations with exercise referral practitioners (compared to usual care which included formal contact at induction only). A pilot of Co-PARS [26] showed clinically meaningful improvements in cardiorespiratory fitness (CRF) and PA, although as we did not include a usual care control, it was unknown whether these effects were due to the fact participants were taking part in an ERS or due to the unique elements of Co-PARS. Furthermore, despite having very low CRF (<27.7 $ml.kg^{-1}.min^{-1}$) [26] we found 64% of the baseline pilot sample were meeting the PA guidelines [27] of at least 150 minutes moderate-intensity PA per week (measured objectively via accelerometry). This suggested CRF may be a more appropriate primary outcome measure than PA for this low-fit population (whilst changing PA behaviour was the focus of the intervention, a target health outcome of this behaviour change was improved CRF). The pilot also

allowed the opportunity to investigate delivery processes, and we noted several areas that required refinement in preparation for a controlled trial. These refinements included, increasing the number of behaviour change consultations from four to five; enhanced focus on daily PA opportunities (rather than focussing on activities offered at the fitness centre); adapting staff timetables to promote consistency of care and to allow participant one-to-one consultations to take place in a private room; and reducing practitioner paperwork. Building on our previous pilot work, the aim of the current study was to investigate the effectiveness of Co-PARS compared to a usual care ERS and a no-treatment control on change in cardiorespiratory fitness (CRF) at 12 weeks and PA and wellbeing at 6 months.

METHODS

Study Design

A three-arm quasi-experimental trial involving: 1. Co-PARS (delivered at fitness centre A); 2. usual care ERS (delivered at fitness centre B); and 3. no-treatment control. This paper reports trial outcomes (CRF, vascular health, PA, mental wellbeing) measured at baseline, 12 weeks, and 6 months (PA and mental wellbeing only). Additional data were collected to investigate psychosocial processes of change, intervention fidelity and cost-effectiveness; due to space limitations they are not considered in the present manuscript, but findings can be obtained on request from p.m.watson@ljmu.ac.uk. Full written consent was obtained from participants and the study was approved by NHS Research Ethics Committee (REC: 18/NW/0039 - Project: 238547) and registered on ClinicalTrials.gov (NCT03490747).

Patient and Public Involvement

The intervention was previously co-produced, piloted, and adapted with substantial service user input [23,26].

Participants and Recruitment

Inclusion criteria were the same for all three conditions (Co-PARS, usual care, no-treatment). Participants were eligible if aged ≥18 years with a health-related risk factor (e.g. hypertension, hyperglycaemia, obesity) and/or health condition (e.g. diabetes, cardiovascular disease, depression)

that may be alleviated by increasing PA levels. Participants with uncontrolled health conditions, severe psychological or neurological conditions were excluded. Participants for the Co-PARS and usual care arms were recruited from fitness centre A (Co-PARS) and fitness centre B (usual care) respectively (where they had been referred for exercise by a health professional). Reception staff at both centres provided study information and gained consent to pass participant details to the researcher. Participants for the no-treatment control were recruited via posters, electronic invitations, and email communications primarily at the university site. Participants were not eligible for the no-treatment control if they were currently attending an exercise referral scheme. Interested participants for all groups were sent an information sheet and baseline data collection was arranged.

Study Arms

Intervention arm components are presented in Figure 1.

Usual care exercise referral scheme (ERS – centre B). Usual care followed a standard ERS model of 12-week subsidised access to a fitness centre (swimming, gym, group classes). Participants met an exercise referral practitioner for an initial, 1-hour induction (week 1) during which a 12-week exercise programme was provided for the participant. Any further contact with a practitioner was informal and opportunistic. This system was already in place and was considered usual care for the local area. Centre B was chosen as a comparison centre due to its similarity in referral numbers and socio-economic make-up of the local population to centre A (where Co-PARS was being delivered). For example, based on areas within Liverpool ranked from 1 (most deprived) to 30 (least deprived), usual care ERS and Co-PARS were ranked respectively: 20th and 21st (income), 20th and 21st (employment), 22nd and 24th (Education) and 10th and 11th (living environment).

Co-produced PA referral scheme (Co-PARS – centre A)

Participants received the same 12-week subsidised access to a fitness centre as usual care plus a series of one-to-one behaviour change consultations (60-minute induction followed by 30-minute consultations at weeks 4, 8, 12 and 18). A log book was provided for each participant to set action

plans, log progress and facilitate consultation discussions. Consultations were delivered by exercise referral practitioners in an autonomy supportive counselling style, drawing on the principles of self-determination theory [28]. This additional support aimed to encourage habitual opportunities to increase PA as well as activities available at the fitness centre. A full descripion of the theoretical underpinning and behaviour change intervention components is available elsewhere [23].

Prior to the pilot of Co-PARS [26] practitioners received training in self-determination theory-based communication strategies led by a sport and exercise psychologist (last author [PMW]), involving a workshop, one-to-one sessions and follow-up group meetings. Following the pilot, a further series of group meetings involving exercise referral practitioners and the research team were held to develop aspects of delivery that required refinement (as outlined in the introduction). Full details of the training are available from p.m.watson@ljmu.ac.uk).

No-treatment control (NTC). Participants received a lifestyle advice booklet only (offered to all study arms at baseline data collection), based on national guidance for PA, nutrition, smoking cessation and alcohol consumption.

[INSERT FIGURE 1 SOMEWHERE HERE]

Outcome measures

Primary outcome*: Cardio-respiratory fitness (CRF).* Maximal oxygen consumption (VO_2max^{-2}) was estimated via the sub-maximal Astrand-Rhyming cycle ergometer protocol [29]. The protocol is a single-stage cycling test designed to elicit a steady-state heart rate over a period of ~6 minutes.

Accelerometer-derived PA. Tri-axial ActiGraph GT3x accelerometers (ActiGraph, Pensacola, FL, USA) measured PA for 7 days, which have been validated in a comparable population [30]. Raw triaxial acceleration values were converted into an omnidirectional measure of acceleration, referred to as Euclidian norm minus one [31]. Minimum wear time was 10 hours per day and 3 days per week including one weekend day [32]. The R package GGIR [31] facilitated extraction of user-defined

acceleration thresholds: 5.9 to 69.1 mg for light-intensity PA [33], 69.1 to 258.7 mg as moderate and >258.7 mg as vigorous-intensity PA [34].

Vascular health. Our previous work has demonstrated carotid artery reactivity (CAR) may be a promising outcome variable to assess in PA interventions for at-risk populations [35]. Further, endothelial function may provide prognostic value beyond that of traditional risk factors [36] with an increase of 1% in brachial artery flow-mediated dilation (FMD) associated with a 12-15% lower risk of CV events [33,34]. FMD and CAR were measured using ultrasound techniques [35]. Both techniques measure vascular endothelial function and have independently predicted future risk of cardiovascular events in humans [36,37]. Blood pressure was measured in the supine position using an automated blood pressure device (Omron Healthcare UK Limited, Milton Keynes, UK).

Anthropometric measures. Since obesity is a critical risk factor for poor health and cardiovascular disease, anthropometric variables were measured to investigate potential intervention effects on body mass. Waist-to-height ratio is a stronger predictor of early health risk than Body Mass Index (BMI) alone [38], therefore we collected both BMI (mass in kg / stature in m^2) and waist-to-height ratio (waist circumference / stature).

Mental wellbeing. As PA is known to enhance mental wellbeing [39] and clinical populations are more susceptible to mental ill-health [40], it was important to identify whether Co-PARS led to any changes in mental health (positive or negative). Mental wellbeing was measured using the 14-item Warwick-Edinburgh Mental Well-being Scale (WEMWBS; [41], which asks participants to rate their psychological wellbeing (e.g. "I've been feeling cheerful") over the previous 2 weeks (measured on a likert scale of 1 (none of the time) to 5 (all of the time)).

Fitness centre engagement (Co-PARS and usual care only). The number of occasions participants attended the fitness centre between baseline and 12 weeks (weekly attendance) and 12 weeks to 6 months (monthly attendance) was obtained from computerised attendance records. When measuring intervention engagement it was deemed inappropriate to calculate the mean number of

sessions per week, since this could exaggerate the engagement of individuals who attended with high frequency in the early weeks then dropped out (when compared with individuals who attended moderately but consistently for the full 12 weeks). Therefore a formula was used to calculate a percentage for '12-week engagement' (based on the recommended bi-weekly attendance):

$$\left(\frac{((n1*0.5) + (n2) + (n3*1.2))}{12}\right) * 100$$

n1 = number of weeks in which participant attends once only
n2 = number of weeks in which participant attends twice
n3 = number of weeks in which participant attends three or more times

This formula took into account both *frequency* and *consistency* of attendance to yield a percentage score that ranged from 0% (no attendance) to 120% (attendance of three or more times per week for the whole 12 weeks).

Monthly attendance post-12 weeks was calculated as a mean attendance across months 4 to 6, therefore did not take consistency of attendance into account.

Behaviour change consultation attendance (Co-PARS only). The number of consultations offered and attended were measured by exercise referral practitioners at induction, 4, 8, 12, and 18 weeks.

Sample size

Sample size was determined to detect a meaningful difference in CRF at 12 weeks based on our pilot results [26]. To detect a difference of 2 $ml.kg^{-1}min^{-1}$ between Co-PARS and usual care, 42 participants were required per arm (f= .25, *p*= .05, power = .80). To detect a difference of 3.2 $ml.kg^{-1}min^{-1}$ between the intervention arms and the no-treatment control, 17 participants were required for the no-treatment control (f= .5, *p*= .05, power = .80). Thus, a total sample of 101 participants were required.

Statistical analyses

An intention-to-treat approach was used assuming no change in non-respondents (last observation carried forward) to produce a conservative estimate of intervention effects. Delta changes (Δ) from

pre- to post-intervention were calculated for each group and entered as the dependent variable in repeated measures linear mixed model analyses. A random intercept model was used with fixed effects for study arm (Co-PARS, usual care ERS, no-treatment control) and time (baseline-to-week-12 change, week-12-to-6-month change, and baseline-to-6-month change) and participants included as random effects. Least squared difference (LSD) was used for post hoc testing. Testing for baseline differences to identify covariates was avoided, as this method has been demonstrated to inflate bias, instead pre-intervention was entered into the model as a covariate. Furthermore, all linear mixed model analyses were repeated with age and employment as covariates as a comparison to the results presented in this study (with baseline score as a covariate) due to their known prognostic value. Using age and employment as covariates resulted in no change in inferences presented in this study. One-way ANOVAs were used to compare baseline values between intervention arms. Fitness centre engagement was determined as described above. Behaviour change consultation attendance is presented descriptively. For non-normally distributed data, median and interquartile range is presented and within group median change was calculated via Wilcoxon signed-rank tests.

RESULTS

Participants. 68 participants provided baseline data, 56 of whom provided 12-week data, and 58 of whom provided 6-month data (figure 2).

Baseline characteristics (table 1). No significant differences were noted between arms for age, sex, ethnicity, BMI, referral reason, or accelerometer-derived PA levels (p>.05). Full-time employment status (p=.001) and CRF (p=.015) were significantly higher in the control compared to usual care and Co-PARS. Smoking status was significantly higher in usual care compared to Co-PARS and control (p=.010). Mental wellbeing was significantly lower in Co-PARS compared to control (p=.023).

[INSERT FIGURE 2 SOMEWHERE HERE]

Table 1. Baseline characteristics presented as Mean ± SD or % (n) of group.

	Co-produced PA referral (*n*=33)	Usual care ERS (*n*=19)	No-treatment control (*n*=16)	Between arm *p*-value
Age (years)	57 ± 12	53 ± 16	48 ± 15	*p*=.319
Female (% of sample)	58 (19)	47 (9)	56 (9)	*p*=.774
White British (% of sample)	82 (27)	95 (18)	75 (12)	*p*=.132
Full-time employment (% of sample)	18 (6)	26 (5)	62 (10)	*p*=.001
Never smoked (% of sample)	73 (24)	37 (7)	81 (13)	*p*=.002
Body mass index (kg/m^2)	31 ± 7	33 ± 6	29 ± 6	*p*=.226
Systolic blood pressure (mmHg)	131 ± 11	138 ± 18	123 ± 12	*p*=.010
Primary referral reason / health concern (control)				*p*=.132
Cardiometabolic (% of sample)	67 (22)	43 (8)	62 (10)	-
Cancer (% of sample)	6 (2)	5 (1)	6 (1)	-
Mental Health (% of sample)	18 (6)	26 (5)	19 (3)	-
Musculoskeletal (% of sample)	9 (3)	26 (5)	13 (2)	-
Comorbidity (% of sample)	85 (28)	100 (19)	81 (13)	*p*=.166
Meeting the PA guidelines (% of sample)*	73 (22)	71 (10)	93 (13)	*p*=.223

P-values represent between arm baseline effects. There was no between arm effect for referral reason, thus no between arm *p*-values are provided for referral reason sub groups.
*Chief Medical Officers' 2019 physical activity guidelines: 150 minutes of moderate-intensity physical activity per week.

Baseline-to-12-Week effects

Raw outcome values are presented for baseline, week 12, and 6 months in Table 2. There was a significant effect for study arm in baseline-to-12-week change in CRF (*p*=.002). Post hoc testing

revealed a significantly higher CRF change in Co-PARS (2.4) compared to the ERS (0.3; p=.021) and control (-0.6; p=.001), but no difference between the ERS and control (p=.314). A significant effect for study arm was found in change in FMD% (p=.002), with FMD% change significantly higher in Co-PARS (2.4) compared to control (-1.1; p=.001) but not the ERS (0.8; p=.099). The change in FMD% was not significantly different between the ERS and control (p=.71). No statistically significant study arm effects were noted for changes in CAR%, blood pressure, resting heart rate, anthropometric measures, PA or WEMWBS at 12 weeks (p>.05).

Baseline-to-6-month effects

No statistically significant study arm effects were noted for change in WEMWBS or PA at 6 months (p>.05).

Fitness centre engagement (Co-PARS and usual care ERS) and consultation attendance (Co-PARS only).

Table 3 reports the participant fitness centre engagement data for the Co-PARS and usual care ERS. Although not statistically significant, Co-PARS engagement was 9% higher, participants attended the fitness centre on average 3 times more per month, and 23% more participants were attending the fitness centre beyond 6-months follow-up compared to usual care. Co-PARS behaviour change consultation attendance is reported in Table 4.

Table 2. Cardiometabolic health outcomes and PA levels at baseline, 12 weeks, 6 months, and between arm baseline-to 12-week or 6-month effect. All variables are presented as Mean ± SD.

	Co-PARS			Usual Care ERS			No-Treatment Control			
	Baseline	***Week 12***	**6 Month**	**Baseline**	**Week 12**	**6 Month**	**Baseline**	**Week 12**	**6 Month**	**Between arm effect *p*-value[a]**
					Fitness (n=56)					
CRF $_{ml.kg.^{-1}min^{-1}}$	22.2±7	24.6±7	-	23.3±6.6	23.6±7	-	29.6±9.2	28.9±8.7	-	*p*=.002
					Physical Activity					
GT3x *(n= 61)* $_{Mins.day}$										
Light intensity	90±52	98±64	107±75	98±36	93±31	158±145	90±37	101±33	*86*±40	*p*=.332
Moderate intensity	44±32	42±29	42±33	43±28	43±30	55±55	60±31	65±24	*54*±21	*p*=.260
Vigorous intensity	1±3	1±2	1±2	1±2	1±1	1±2	2±4	2±3	*3*±8	*p*=.108
					Vascular Ultrasound (n=64)					
CAR%	1.7±2.7	2.8±2.2	-	2.7±1.8	3.9±2.8	-	2.5±2.7	1.7±2.7	-	*p*=.073
CAR Baseline $_{cm}$	0.69±0.07	0.69±0.06	-	0.69±0.08	0.7±0.09	-	0.65±0.07	0.64±0.06	-	*p*=.130
FMD%	4.4±2.3	6.8±2.7	-	4.2±2	5±2.1	-	6.2±2.1	5.2±2.8	-	*p*=.002
FMD Baseline $_{cm}$	0.39±0.07	0.38±0.06	-	0.39±0.09	0.41 0.08	-	0.38±0.08	0.37±0.06	-	*p*=.728
					Cardiometabolic (n=68)					
BMI $_{kg.m2}$	31±7	30±7	-	33±6	32±6	-	29±6	29±6	-	*p*=.323
WHR	62±9	61±10	-	64±8	63±8	-	56±9	56±9	-	*p*=.261
SBP $_{mmHg}$	131±11	127±12	-	138±18	132±15	-	123±12	118±13	-	*p*=.937
DBP $_{mmHg}$	73±7	71±8	-	73±9	71±11	-	72±11	68±10	-	*p*=.584
RHR $_{bpm}$	70±10	65±10		70±12	68±11		66±12	63±9		*p*=.540
					Mental Wellbeing (*n*=68)					
WEMWBS	46±9	*51±10*	*48±10*	49±10	52±11	*50±13*	53±9	56±9	*53±10*	*p*=.796

Co-PARS, Co-produced PA referral scheme**; ERS,** Exercise referral scheme**; CRF**, Cardiorespiratory Fitness; **GT3x**, Accelerometer; **CAR**, Carotid artery reactivity; **FMD**, Flow-mediated dilation; **BMI**, Body Mass Index; **WHR**, Waist-to-Height ratio; **SBP**, Systolic blood pressure; **DBP**, Diastolic blood pressure; **RHR**, Resting heart rate, **WEMWBS,** Warwick-Edinburgh Mental Wellbeing Scale

[a] *F*-statistic for between arm baseline-to-6-month change or baseline-to-week 12 change if variable not collected at 6 months.

Missing data was due to inability to complete the CRF test (*n*=12), inability to complete the vascular ultrasound protocols (*n*=4), and insufficient accelerometer wear time or non-return (*n*=7).

Table 3. Fitness centre engagement.

	Co-PARS (*n*=33)	Usual Care (*n*=19)	Between centre difference
% Engagement[a] (Mean ± SD)	42±29	33±27	*p*=.267
Number of fitness centre visits (per person per month) week 12 to 6 months (Med, IQR)	3(0-14)	0 (0-1)	*p*=.072
% of baseline sample who attended fitness centre at least once beyond 6 months (% of sample, n)	39 (13)	16 (3)	*p*=.101

[a]Based on the formula (((n1*0.5)+(n2)+(n3*1.2))/12) * 100; n1=number of weeks in which participant attends once only; n2=number of weeks in which participant attends twice; n3=number of weeks in which participant attends three or more times. [a]**Engagement**;.based on a recommended attendance of twice weekly, a formula was used to calculate a percentage for "12-week engagement", which took into account both frequency and consistency of attendance (see methods).

Table 4. Co-PARS behaviour change consultation attendance (based on baseline sample of 33 participants).

Consultation	% Booked (n)	% Attended (n)
Induction	91(30)	93(28)
Week 4	82(27)	78(21)
Week 8	67(22)	91(20)
Week 12	64(21)	81(17)
Week 18	55(18)	50(9)

DISCUSSION

This was the first study to investigate the effectiveness of a theoretically-grounded, co-produced PA referral scheme (Co-PARS) compared to a usual care ERS and no treatment. Despite challenges in recruitment that meant the study was statistically underpowered, the findings demonstrated significant and clinically meaningful improvements in CRF and vascular health in Co-PARS compared to the usual care and no treatment. No statistically significant effects were noted for accelerometer-derived PA levels or mental wellbeing at 12-weeks or 6-months.

The effect of usual care ERSs compared to theoretically-grounded interventions on CRF has not been previously explored. We observed a significant increase in CRF in Co-PARS compared to usual care and a no-treatment control. According to values reported by Clausen *et al*. [42] both Co-PARS (22 ml.kg.$^{-1}$min^{-1}) and usual care (23 ml.kg.$^{-1}$min^{-1}) participants were below the lower limit of 'healthy' (27.7 ml.kg.$^{-1}$min^{-1}) for baseline CRF [43]. As low CRF is associated with a substantially elevated risk of all-cause mortality [43], the magnitude of change demonstrated in Co-PARS (2.4 ml.kg.$^{-1}$min^{-1}) may be clinically meaningful. For example, in at-risk populations, relatively small magnitudes (≤1 ml.kg.$^{-1}$min^{-1}) have been shown to significantly reduce clustered cardiometabolic risk [44]. Thus, Co-PARS was effective at improving CRF in individuals with low CRF by a clinically meaningful amount.

Promising improvements in vascular health were also noted in the Co-PARS group, with brachial artery FMD significantly improved compared to usual care and control arms. Although CAR was not statistically different between arms, both Co-PARS and usual care demonstrated a potentially meaningful within-arm improvement compared with no treatment, which exhibited a deterioration in vascular health. Such improvements in vascular measures may have prognostic implications. For example, a 1% increase in FMD has been suggested to reduce the future risk of CVD events by 13% [36].

Despite low baseline CRF, a substantial percentage of Co-PARS (73%) and usual care (71%) participants were meeting the Department of Health [45] guidelines of 150 minutes of moderate-intensity PA per

week. We observed a similar finding in our pilot [26] and subsequently raised the question as to the use of PA guidelines to assess eligibility for ERSs (NICE, 2014), as it appears from our data that individuals classified as "physically active" can still be very unfit and therefore can benefit from ERSs in terms of improved fitness and cardiometabolic health. A further discrepancy was noted in the lack of change in PA levels in Co-PARS, despite improved CRF. It is possible measurement issues contributed to this discrepancy. Accelerometers can measure certain types of PA such as walking, running, and stair climbing [46]. They may not, however, sufficiently identify activities typical of an ERS delivered within a fitness centre environment (e.g. cycling, resistance training, circuits, swimming). Given Co-PARS had higher (albeit non-significant) fitness centre engagement compared to usual care, it is possible PA changes occurred that were not detected by the accelerometry data. Consideration therefore needs to be given to the appropriateness of accelerometers to measure PA in ERSs. Alternative methods such as heart-rate monitors combined with self-report data may be worthy of consideration, although further work would be required to develop standardized data collection and analysis protocols (taking into account the limitations of each of these methods if used in isolation [47]). Researchers are therefore urged to consider CRF as a primary outcome in ERSs until appropriate alternative methods of measuring PA behaviour are developed. Ultimately, it is not clear why the increase in fitness occurred without a corresponding change in PA and further research is required to elucidate the relationship between PA and fitness in this population.

In addition to physiological health outcomes, we found baseline mental wellbeing to be below the national average (score of 50) in both Co-PARS (46) and usual care (49), but not the control (53) [48]. Despite no significant between-group effect for mental wellbeing, within-group changes at 12 weeks were deemed clinically meaningful for Co-PARS (5) and usual care (3) but not in the no treatment control. It is notable that the post-intervention magnitude of change observed in mental wellbeing for Co-PARS (5) was larger than that observed in a meta-analysis encompassing >23,000 participants across 13 different ERSs (3), which were comparable in nature to the usual care ERS in this study [49].

From the 6-month data it appeared the scheme was not effective at promoting *sustained* PA behaviour change or mental wellbeing improvements. It must be noted, however, that the wellbeing levels were still higher than baseline and even small magnitudes of change (1-3) may be meaningful in clinical populations [50]. As discussed earlier, it may be that measuring PA using the methods described in this study prevented the identification of activities typical of a fitness centre environment. This notion is supported by the post-week-12 attendance data, which highlighted Co-PARS participants were regularly attending the fitness centre whereas the usual care participants were not. Challenges of maintaining sustained health outcomes post-ERSs have been highlighted elsewhere [3]. And whilst a recent systematic review reported longer length schemes (>20 weeks) may be more effective than shorter schemes [8], the four long ERSs (20-26 weeks) collected pre-post data only. Thus we do not know if longer length ERSs result in enhanced health outcomes *post intervention* compared with shorter schemes. To determine if longer length schemes are indeed more effective, longer-term follow-up data collection is required, ideally at 6 and 12 months post intervention [51].

Through a phased approach we have assessed the effectiveness of Co-PARS resulting from several years of co-production. Whilst the effects of co-production are difficult to isolate, a comparison of results at different stages of intervention refinement suggests the phased development approach had some positive effects. Unpublished engagement data from centre A in 2014-2015 (when the centre was running a usual care ERS) shows that engagement improved after the introduction of Co-PARS (42% vs 28% in 2014-2015), whereas engagement reduced in the usual care centre over the same period (32% vs 37% in 2014-2015). Furthermore, consultation attendance for Co-PARS in the current study was substantially higher than in our previous pilot (54% attended induction plus ≥3 behaviour change consultations, vs 9% in the pilot [26]), which may have been a reflection of refinements made to the intervention after the pilot (e.g. improved focus on holistic PA, improved monitoring procedures, improved continuity of instructors). These improvements in engagement highlight the importance of allowing time for complex interventions to develop [52], and are particularly promising given the effectiveness of ERSs are highly dependent on participant adherence [5,21]. Furthermore,

this study has demonstrated how investing in the "bottom-up" development of an intervention can lead to an effective and sustainable model. We therefore support the arguments of Rutter and colleagues [53] in that a shift in thinking is needed, instead of asking whether an intervention works to fix a problem, researchers should aim to identify if and how it contributes to reshaping a system in a favourable way. As such, we propose the co-production and implementation process may be as important as the scheme content itself.

Methodological considerations

This is the first known study to investigate the effectiveness of a co-produced PA referral scheme (Co-PARS) in comparison to usual care and a no-treatment control. Our novel approach addresses an important gap in the sport and exercise medicine literature [54], in that we employed rigorous laboratory-based instruments to measure health outcomes that can be achieved through an ecologically valid, "real-world" intervention. We observed a very high retention at 6-month follow up, which may be due in part to the fact many of the participants were retired (and therefore may have more available time). It is possible also that the high retention was facilitated by the co-production process, which involved ongoing relationships between the research and delivery teams (and therefore helped with the logistics of returning accelerometers for the co-PARS and usual care groups). Whilst this paper highlights many strengths of co-production, we do not wish to present co-production as a panacea [19] and it is important potential challenges and costs are considered prior to undertaking such an approach [21,22].

We must acknowledge some limitations of the study. Whilst there is a need for high-quality RCTs of theoretically informed approaches to PA behaviour change [3], several pragmatic reasons meant an RCT approach was not appropriate for the present study. Firstly, it was important participants could choose the most convenient fitness centre. Secondly, it was important we continued work with the same fitness centre and staff (following co-production [23] and pilot [26] phases) in order to develop the intervention to the point where it was deemed to have a worthwhile effect [52]. A pragmatic

research approach was therefore deemed most appropriate to evaluate Co-PARS with high ecological validity. Pragmatic constraints (e.g. fitness centre refurbishments, staff illness) did however mean the required sample size was not achieved, thus inferences of effectiveness need to be taken with caution. This is particularly true for the PA data, where the relatively high variability (compared with CRF) may have contributed to the lack of change observed in PA in this study. It is recommended future work considers pragmatic risks and contingencies when planning recruitment and plans sufficient time to cope with recruitment delays. For pragmatic reasons, not all outcomes were collected at 6-months follow-up and further research is needed to collect long-term, objective health data following PA referral schemes. Finally, it must be noted that while the trial registration appears to be retrospective (April 6th 2018), the initial submission was several months prior to this (January 11th 2018). Final sign-off was delayed due to capacity issues within the research team.

CONCLUSION

A co-produced, theoretically-grounded PA referral scheme (Co-PARS) led to improved CRF and vascular health in at-risk individuals when compared to usual care and no treatment. In addition, clinically meaningful improvements in vascular health and mental wellbeing were observed at 12-weeks in both Co-PARS and usual care, but not the no treatment control group. Of note, PA remained unchanged at 12-weeks and 6-months follow-up. Adopting a phased approach has enabled multi-stakeholder input and ongoing intervention refinement, resulting in an intervention that showed promising effects on engagement and clinically meaningful improvements to participant health.

Figure Legends

Figure 1. 'PaT Plot' describing intervention arm components.[55]

Figure 2. Participant flow diagram within the three study arms (March 2018-January 2019).

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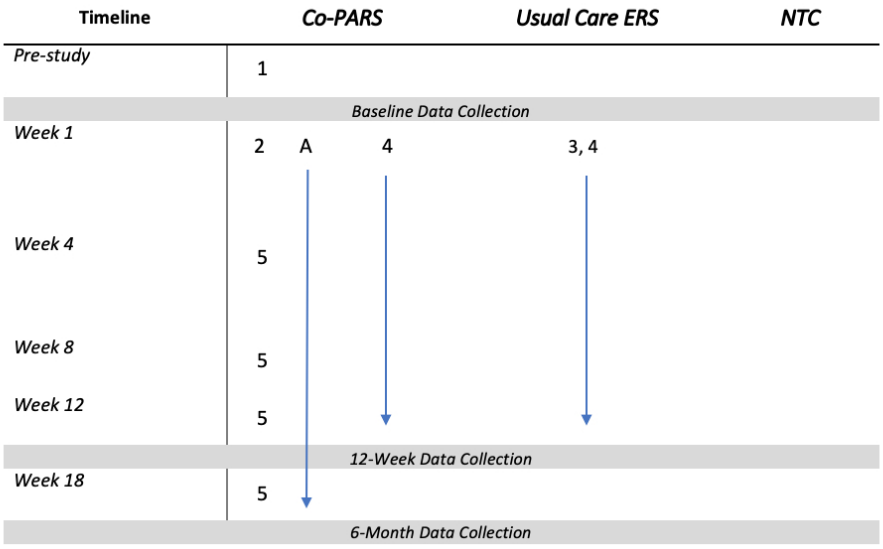
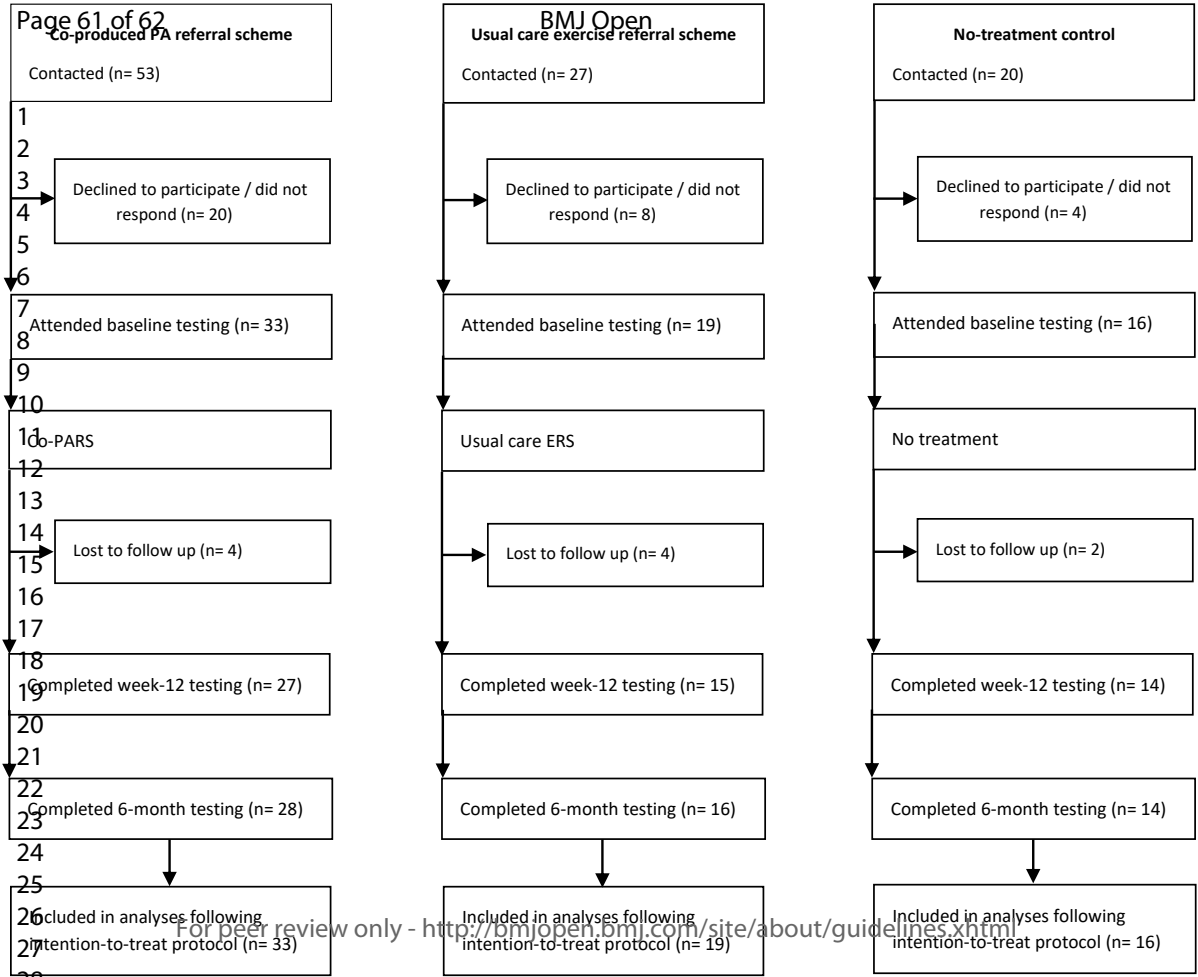


Baseline and 12-week measures – *Cardiorespiratory Fitness (CRF), Warwick Edinburgh Mental Wellbeing Scale (WEMWBS), Accelerometer Derived PA, Body Mass Index (BMI), Waist-To-Height Ratio, Blood Pressure, Flow-Mediated Dilation (FMD), Carotid Artery Reactivity (CAR).*

6-month measures – *WEMWBS and accelerometer derived PA.*

1	Training delivered to Exercise Referral Practitioners in PA behaviour change by a trained HCPC-registered Psychologist [PMW]. Training included: 1. Needs analysis (observation of current practices); 2. Education (Full day workshop); 3. Behaviour change support (one-to-one sessions over 4 weeks); 4. Ongoing support as required.
2	1-hour induction underpinned by Self-Determination Theory [28] to foster participant autonomy, competence, and relatedness. The focus was on getting to know the participant, discussing participant goals and agreeing a programme of activities tailored to their needs. Participant self-report PA logbook was provided.
3	Usual care exercise referral induction focussed on prescribing an individualised 12-week exercise programme appropriate for the specific health condition.
4	12-week subsidised access to a fitness centre (swimming pool, gymnasium, group classes etc.).
5	30-minute behaviour change consultation focussed on fostering participant autonomy, competence, and relatedness with the aim of enhancing long-term PA behaviour change. Included review of participant self-report PA logbook, discussion of progress towards goals and revision of action plans as appropriate. During the week 8, week 12 and week 18 consultations, participants were supported to make plans for continuing PA after the subsidised 12-week fitness centre access finished.
A	Participant self-report PA logbook. An A5 booklet in which participants could write down their action plans and record the PA they engaged in (for 18 weeks). There was space for participants to record how they were feeling and any challenges they were facing. The logbook also provided information about PA benefits, guidelines and testimonials from previous participants.
Numbers (1-5) represent intervention activities. Letters (A) represent an intervention tool.	

Figure 1. PaT Plot' describing intervention arm components.



TREND Statement Checklist

Paper Section/Topic	Item No.	Descriptor	Reported? ✓	Reported? Pg #
TITLE and ABSTRACT				
Title and Abstract	1	• Information on how units were allocated to interventions	✓	1,2
		• Structured abstract recommended	✓	2
		• Information on target population or study sample	✓	2
INTRODUCTION				
Background	2	• Scientific background and explanation of rationale	✓	4-5
		• Theories used in designing behavioral interventions	✓	6
METHODS				
Participants	3	• Eligibility criteria for participants, including criteria at different levels in recruitment/sampling plan (e.g., cities, clinics, subjects)	✓	5-6
		• Method of recruitment (e.g., referral, self-selection), including the sampling method if a systematic sampling plan was implemented	✓	5-6
		• Recruitment setting	✓	6,7
		• Settings and locations where the data were collected	✓	5-6
Interventions	4	• Details of the interventions intended for each study condition and how and when they were actually administered, specifically including:	✓	6-8
		○ Content: what was given?	✓	6-8
		○ Delivery method: how was the content given?	✓	6-8
		○ Unit of delivery: how were subjects grouped during delivery?	✓	6-8
		○ Deliverer: who delivered the intervention?	✓	6-8
		○ Setting: where was the intervention delivered?	✓	6-8
		○ Exposure quantity and duration: how many sessions or episodes or events were intended to be delivered? How long were they intended to last?	✓	6-8
		○ Time span: how long was it intended to take to deliver the intervention to each unit?	✓	6-8
		○ Activities to increase compliance or adherence (e.g., incentives)		N/A
Objectives	5	• Specific objectives and hypotheses	✓	5
Outcomes	6	• Clearly defined primary and secondary outcome measures	✓	7-8
		• Methods used to collect data and any methods used to enhance the quality of measurements	✓	7-8
		• Information on validated instruments such as psychometric and biometric properties		N/A
Sample size	7	• How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules	✓	8
Assignment method	8	• Unit of assignment (the unit being assigned to study condition, e.g., individual, group, community)		N/A
		• Method used to assign units to study conditions, including details of any restriction (e.g., blocking, stratification, minimization)		N/A
		• Inclusion of aspects employed to help minimize potential bias induced due to non-randomization (e.g., matching)		N/A
Blinding (masking)	9	• Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to study condition assignment; if so, statement regarding how the blinding was accomplished and how it was assessed		N/A
Unit of Analysis	10	• Description of the smallest unit that is being analysed to assess intervention effects (e.g., individual, group, or community)	✓	8-9
		• If the unit of analysis differs from the unit of assignment, the analytical method used to account for this (e.g., adjusting the standard error estimates by the design effect or using multilevel analysis)		N/A
Statistical methods	11	• Statistical methods used to compare study groups for primary methods outcome(s), including complex methods for correlated data	✓	8-9
		• Statistical methods used for additional analyses, such as subgroup analyses and adjusted analysis	✓	8-9
		• Methods for imputing missing data, if used		N/A

TREND Statement Checklist

		• Statistical software or programs used	✓	8-9
RESULTS				
Participant flow	12	• Flow of participants through each stage of the study: enrollment, assignment, allocation and intervention exposure, follow-up, analysis (a diagram is strongly recommended)	✓	9
		○ Enrollment: the numbers of participants screened for eligibility, found to be eligible or not eligible, declined to be enrolled, and enrolled in the study	✓	9
		○ Assignment: the numbers of participants assigned to a study condition	✓	9
		○ Allocation and intervention exposure: the number of participants assigned to each study condition and the number of participants who received each intervention	✓	9
		○ Follow-up: the number of participants who completed the follow-up or did not complete the follow-up (i.e., lost to follow-up), by study condition	✓	9
		○ Analysis: the number of participants included in or excluded from the main analysis, by study condition	✓	9
		• Description of protocol deviations from study as planned, along with reasons		N/A
Recruitment	13	• Dates defining the periods of recruitment and follow-up	✓	9
Baseline data	14	• Baseline demographic and clinical characteristics of participants in each study condition	✓	10
		• Baseline characteristics for each study condition relevant to specific disease prevention research	✓	10
		• Baseline comparisons of those lost to follow-up and those retained, overall and by study condition		N/A
		• Comparison between study population at baseline and target population of interest		N/A
Baseline equivalence	15	• Data on study group equivalence at baseline and statistical methods used to control for baseline differences		N/A
Numbers analyzed	16	• Number of participants (denominator) included in each analysis for each study condition, particularly when the denominators change for different outcomes; statement of the results in absolute numbers when feasible	✓	10-13
		• Indication of whether the analysis strategy was “intention to treat” or, if not, description of how non-compliers were treated in the analyses	✓	8-9
Outcomes and estimation	17	• For each primary and secondary outcome, a summary of results for each estimation study condition, and the estimated effect size and a confidence interval to indicate the precision	✓	10
		• Inclusion of null and negative findings	✓	10
		• Inclusion of results from testing pre-specified causal pathways through which the intervention was intended to operate, if any		N/A
Ancillary analyses	18	• Summary of other analyses performed, including subgroup or restricted analyses, indicating which are pre-specified or exploratory		N/A
Adverse events	19	• Summary of all important adverse events or unintended effects in each study condition (including summary measures, effect size estimates, and confidence intervals)	✓	10
DISCUSSION				
Interpretation	20	• Interpretation of the results, taking into account study hypotheses, sources of potential bias, imprecision of measures, multiplicative analyses, and other limitations or weaknesses of the study	✓	14-17
		• Discussion of results taking into account the mechanism by which the intervention was intended to work (causal pathways) or alternative mechanisms or explanations	✓	14-17
		• Discussion of the success of and barriers to implementing the intervention, fidelity of implementation	✓	14-17
		• Discussion of research, programmatic, or policy implications	✓	14-17
Generalizability	21	• Generalizability (external validity) of the trial findings, taking into account the study population, the characteristics of the intervention, length of follow-up, incentives, compliance rates, specific sites/settings involved in the study, and other contextual issues	✓	14-17
Overall evidence	22	• General interpretation of the results in the context of current evidence and current theory	✓	14-17

From: Des Jarlais, D. C., Lyles, C., Crepaz, N., & the Trend Group (2004). Improving the reporting quality of nonrandomized evaluations of behavioral and public health interventions: The TREND statement. *American Journal of Public Health*, 94, 361-366. For more information, visit: http://www.cdc.gov/trendstatement/