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Physiotherapy exercise rehabilitation with tailored exercise adherence support for people with osteoporosis and vertebral fractures: Protocol for a randomised controlled trial – the Osteoporosis Tailored exercise adherence intervention (OPTIN) study.

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Manuscripts

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4 1 Physiotherapy exercise rehabilitation with tailored exercise adherence support for people with
5 osteoporosis and vertebral fractures: Protocol for a randomised controlled trial – the Osteoporosis
6 2 osteoporosis and vertebral fractures: Protocol for a randomised controlled trial – the Osteoporosis
7 3 Tailored exercise adherence intervention (OPTIN) study.

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1 Physical therapy modalities; exercise, osteoporosis, spine, rehabilitation

2 Word count 3967

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1 ABSTRACT

2 **Introduction:** Vertebral fragility fractures affect at least 20% of the older population in the
3 UK. Best practice guidelines recommend the use of exercise to slow the rate of bone loss, to
4 maintain muscle strength and physical function, and to prevent falls and further fractures.
5 However, treatment effects are often small and difficult to sustain and adherence, or the
6 extent to which patients engage in treatment, has been identified as an important issue by
7 many studies. Our hypothesis is that integrating adherence intervention strategies with an
8 exercise intervention will be beneficial. We will compare physiotherapy exercise
9 rehabilitation with adherence support versus physiotherapy exercise rehabilitation alone in
10 terms of effects on (a) physical function, quality of life, and fear of falling and (b) exercise
11 self-efficacy and adherence.

12 **Methods and Analysis:** A multicentre, two-arm, parallel group, superiority randomised
13 controlled trial (RCT) with blinded assessments at baseline (0) and 4, 8, and 12 months, with
14 a nested qualitative study and health economic analysis. 116 participants will be allocated to
15 either (i) out-patient physiotherapy which will include a musculoskeletal assessment and
16 treatment including balance, posture, strength training and low impact weight-bearing
17 exercises over 16 weeks; or (ii) Opt-In intervention. This includes standard physiotherapy as
18 above plus an additional, integrated assessment interview (30mins) and 60 minutes of
19 adherence support spread over the subsequent 16 weeks.

20 **Ethics and Dissemination:** The study protocol was approved by West of Scotland Research
21 Ethics Committee 4 (21/WS/0071). Trial registration number ISRCTN 14465704. The paper is
22 based on Protocol v4.

24 **Strengths and Limitations of this study**

- 25 • The Physiotherapy exercise rehabilitation with tailored exercise adherence support for
26 people with osteoporosis and vertebral fractures (Opt-In) study is a multicentre randomised
27 controlled trial with an embedded qualitative study and economic evaluation.
- 28 • It will recruit from at least six NHS hospitals.
- 29 • The intervention addresses adherence which is an important confounder in many trials of
30 physiotherapy.

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- 1 • The intervention was developed using current research evidence, input from expert
2 clinicians, researchers and patient / public representatives.
 - 3 • Due to the nature of the interventions the physiotherapists delivering the treatments and
4 the participants cannot be blinded.

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1 Introduction

2 Vertebral fragility fractures (VFFs) affect at least 20% of the older population in the UK and present a
3 significant health and economic burden [1, 2]. They are associated with back pain, fatigue, low
4 mood, restrictions in physical function and activities of daily living, and marked, persistent
5 reductions in quality of life (QoL) [1, 2]. Without treatment, progression and functional decline are
6 expected. Conservative treatment for osteoporosis includes bone protective medications and
7 lifestyle adaptations. Guidelines recommend people with osteoporosis keep active and exercise to
8 slow the rate of bone loss, to maintain muscle strength and physical function and to prevent falls
9 and further fractures [3]. Exercise prescription with multi-component exercise programmes that
10 include postural, balance, aerobic weight-bearing and strength exercises are recommended [1-3].

11 Trials evaluating exercise in people with VFFs have reported benefits across a range of outcomes [1,
12 2, 4-10], with a recent Cochrane review concluding there is moderate-quality evidence that exercise
13 improves physical function [1]. However, treatment effects are often small and difficult to sustain
14 [1, 2, 4-10]. For example, in the PROVE trial, significant, clinically relevant benefits to back muscle
15 endurance, balance, walking capacity and physical function following physiotherapy exercise at 4
16 months post-randomisation did not persist at 12 months [2]. Adherence, or the extent to which
17 patients engage in treatment, has been identified as an important issue by many studies [1, 2, 4-6,
18 9]. Partial adherence or non-adherence is associated with worse outcomes and conversely, higher
19 adherence with better outcomes [1, 2, 4-10].

20 Multiple factors affect exercise adherence in older people with chronic health conditions including
21 osteoporosis [11, 12]. These include low exercise self-efficacy, low motivation, depression,
22 insufficient exercise knowledge or skill, physical ability, negative views about treatment and exercise
23 programme design [11,12]. Considering this complexity, interventions to support adherence that
24 recognize personal barriers and facilitators to exercise and that can draw upon multiple adherence
25 techniques are recommended [12, 13].

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2
3 1 Behavioural approaches can include interventions that support exercise through providing additional
4
5 2 monitoring, interventions that aim to alter thinking patterns that contribute to non-adherence and
6
7 3 ones that strengthen behaviours that support adherence [12]. Motivational interviewing is a
8
9 4 collaborative process that explores potential ambivalence, obstacles and facilitators surrounding
10
11 5 behaviour change [6]. There is evidence that additional monitoring, prompts and feedback can
12
13 6 benefit adherence in older adults e.g., via telephone call/ text messages, wearable activity monitors
14
15 7 or by enriching environmental cues [1]. Incorporating exercise into everyday routines can make it
16
17 8 easier to initiate and sustain and creating 'Exercise Action Plans' that specify when, where and how
18
19 9 exercises are undertaken can support this process [1, 13]. Using an intervention mapping approach,
20
21 10 we developed an exercise adherence intervention underpinned theoretically by the COM-B
22
23 11 behaviour change model [14, 15].
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29 12 **Aims**

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32 13 The aims of this study are:

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35 14 • To compare physiotherapy exercise rehabilitation with adherence support with
36
37 15 physiotherapy exercise rehabilitation alone in terms of effects on: (a) physical function,
38
39 16 quality of life, and fear of falling and (b) exercise self-efficacy and adherence.
40
41 17 • To explore patient and physiotherapist views of the intervention and of adhering to exercise.
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43 18 • To understand if physiotherapy exercise rehabilitation with adherence support is cost-
44
45 19 effective.
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49 20 **METHODS AND ANALYSES**

50 51 52 21 Study design

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55 22 A multicentre, two-arm, parallel group, superiority randomised controlled trial (RCT) with blinded
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57 23 assessments at baseline (0) and 4, 8, and 12 months following randomisation, with a nested
58
59 24 qualitative study and health economic analysis. Participants will be allocated to either (i) outpatient
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3 1 physiotherapy which will include a musculoskeletal assessment and 6 treatment sessions over 16
4
5 2 weeks based on the current best practice guidance from the Royal Osteoporosis Society; or (ii) the
6
7 3 Opt-In intervention. This includes outpatient physiotherapy as described above, plus an additional,
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9
10 4 integrated assessment interview (30mins) and 60 minutes of adherence support spread over the
11
12 5 subsequent treatment period of 16 weeks as prescribed by the physiotherapist in collaboration with
13
14 6 the participant. Sessions in both arms can be in-person or virtually via video-call/ telephone as
15
16 7 agreed between participant and therapist (**Figure 1**).

18 19 20 8 Setting

21
22
23 9 At least six National Health Service (NHS) hospitals and their related physiotherapy services.

24 25 26 10 Study Participants

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28
29 11 Adults aged 55 years or over who have a diagnosis of at least one previous osteoporotic vertebral
30
31 12 fracture and back pain.

32 33 34 13 Eligibility

35 36 37 14 Inclusion Criteria

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40 15 Participants may enter the study if they meet ALL the following criteria:

- 41
42
43 16 • Men and women ≥ 55 years: all women must be at least 1 year post-menopausal.
- 44
45
46 17 • One or more VFFs confirmed by radiography, X-Ray, MRI, CT or DEXA scan, people with VFF
47
48 18 of any severity and at any time-point post-fracture are eligible.
- 49
50
51 19 • They must have had an episode of back pain in the previous 12 months.
- 52
53
54 20 • All must be able to walk at least 10 metres independently with or without a walking aid.

55 56 57 21 Exclusion Criteria

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1 Participants may not enter the study if ANY of the following apply:

- 2 • Current conditions that would make participating in physiotherapy or exercise unsafe or
3 confound results. This includes those with significant neurological and psychiatric conditions,
4 severe unstable cardiovascular or pulmonary disease.
- 5 • Bone loss secondary to other metabolic disorders, diseases or medication e.g., rheumatoid
6 arthritis, anorexia, cancer, coeliac disease, steroid use.
- 7 • Individuals whose primary problem is back pain that involves pain radiating into the lower
8 limbs.
- 9 • Vertebroplasty, facet joint injection or physiotherapy within past 12 weeks.

10 Recruitment

11 A member of the patient's direct care team will identify potential participants with VFFs via clinic
12 lists and electronic medical records from relevant metabolic bone clinics, radiology clinics (DEXA),
13 physiotherapy referral lists, and from Rheumatology clinics.

14 Screening and eligibility assessment

15 Potential participants, who respond to an invitation letter will be contacted by telephone to discuss
16 the study further, to check eligibility and to answer any questions. Patients who do not meet the
17 eligibility criteria or who do not wish to participate will receive standard NHS treatment. We will
18 record the age and gender of these patients to assess the generalisability of those recruited.

19 Consent

20 Participants who are eligible and willing to proceed will be approached for informed consent.; they
21 and the researcher will sign and date a consent form. For participants who are recruited to the
22 additional nested qualitative study and interviewed on-line or via telephone, informed consent will

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3 1 be obtained verbally before the interview. The researcher taking consent will read, and fill out, the
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5 2 consent form on behalf of the participant and then sign the form.
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10 11 4 Randomisation 12 13

14 5 Consented participants will be randomised 1:1 using a computer-generated randomisation schedule
15
16 6 prepared by the trial statistician (RK). Individual randomisation will be stratified by recruitment
17
18 7 centre and permuted blocks of varying undisclosed sizes will be used. The randomisation schedule
19
20 8 will be concealed in sequentially numbered, opaque, sealed envelopes for each site. A study
21
22 9 administrator who has no interaction with blinded study staff will manage these envelopes. The
23
24 10 administrator will open the randomisation envelope, and then communicate with the local site who
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26 11 will make the participant aware of their allocated group and refer for physiotherapy; making sure
27
28 12 that participants are allocated to physiotherapists delivering the treatment for their allocated arm.
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32 33 13 Blinding 34 35

36 14 Physiotherapists delivering the interventions and participants will be told the treatment allocation.
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38 15 Initial baseline assessment will occur prior to randomisation and the researcher undertaking
39
40 16 assessments will not be involved in any part of the randomisation procedure to ensure that they are
41
42 17 not able to bias the group allocation. The researcher conducting follow-up measures and the
43
44 18 research team personnel entering data will also not be informed of allocated group and participants
45
46 19 will be asked and reminded not to disclose their treatment group to the researcher at follow-up
47
48 20 appointments.
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52 53 21 Interventions 54 55

56 22 Training and monitoring 57 58 59 60

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3 1 Sessions in both arms can be delivered in-person or virtually via video-call/ telephone as agreed
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5 2 between participant and therapist; to allow flexibility and resilience as COVID restrictions on physical
6
7 3 attendance vary. Treatments were standardised and manualised and the study team provided
8
9 4 training in the multi-component exercise therapy treatments (delivered to all participants) to all
10
11 5 treating physiotherapists. Training in the behavioural adherence support intervention which
12
13 6 comprised assessment and a set of 9 behavioural interventions (the Opt-In toolkit) was delivered
14
15 7 separately to the therapists in the Opt-In arm. Treating physiotherapists will record the delivery and
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17 8 content of each treatment session in adherence logs for each participant. Regular site visits will be
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19 9 carried out to monitor intervention fidelity.
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24 10 Standard Care

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27 11 Participants will be offered a 1-hour physiotherapy assessment and six individual outpatient
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29 12 physiotherapy sessions spread over 16 weeks [2]. The physiotherapy will include a musculoskeletal
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31 13 assessment and treatment including a multi-component, progressed balance, posture, strength
32
33 14 training and low impact weight-bearing exercise [3]. Exercise intensity will be assessed using the 10-
34
35 15 point Rating of Perceived Exertion scale (CR10-RPE), so participants work a moderately hard to hard
36
37 16 (RPE 4-6) intensity. Although current practice may vary, the package agreed as the standard care is
38
39 17 based on consensus, best practice guidelines and successful delivery in the PROVE trial exercise arm
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41 18 [2] and aims to be a credible representation of current best practice treatment across the NHS.
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43 19 Treating therapists will receive prior training on prescription of the exercises [2].
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48 20 Opt -In

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51 21 Participants allocated to Opt-In will receive the standard package described above, plus an
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53 22 additional, integrated assessment interview (30mins) and 60 minutes of adherence support spread
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55 23 over the subsequent treatment period of 16 weeks in an individualised pattern as required by the
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57 24 participant.
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3 1 Participants in the Opt-In arm will complete the Personalized Exercise Questionnaire (PEQ). The PEQ
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5 2 was developed in Canada to support patient-centred exercise prescription for people with
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7 3 osteoporosis and covers topics such as barriers to exercise and goals of treatment [16]. Treating
8
9 4 physiotherapists will have a collaborative discussion with the participant using a motivational
10
11 5 interviewing approach drawing upon PEQ responses and considering goals, motivators, facilitators,
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13 6 and barriers surrounding exercise. It aims to provide physiotherapists with a deeper understanding
14
15 7 of patient motivations and circumstances, to strengthen the therapeutic alliance and the patient's
16
17 8 own motivations for adopting exercise [12]. Using their assessment findings, the questionnaire and
18
19 9 collaborative interview the physiotherapist will assess a participant's exercise capability (C),
20
21 10 opportunity (O) and motivation (M) to carry out exercise behaviour and select an adherence
22
23 11 technique from the Opt-In toolkit in response [14]. Techniques can include education about
24
25 12 osteoporosis and exercises, education about and practice of fall prevention strategies, , Exercise
26
27 13 Action Plans, , a contact telephone call, and self-monitoring and feedback strategies such as,
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29 14 exercise confidence rating scales or using an exercise diary. Techniques are linked to COM-B
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31 15 domains to facilitate physiotherapist decision-making e.g., Education improves capability and
32
33 16 motivation (C, M) and a diagrammatic decision aid was developed to facilitate rapid decision-making
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35 17 during treatment. Each Opt-In arm treating physiotherapist received a toolkit and training by the
36
37 18 study team about techniques and how to use them. Physiotherapists were asked to prescribe at
38
39 19 least 3 adherence techniques from the Opt-In toolkit over 16 weeks but could use more, the exact
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41 20 techniques selected were personalised to the patient as was the pattern and spread of the 60-
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43 21 minute adherence support time. Participants in the intervention arm were given a folder that
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45 22 included their exercises and selected adherence materials e.g., exercise diary, education leaflet,
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47 23 action plan record.

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58 25 Concomitant care
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3 1 Other aspects of health and social care will continue as usual. Analgesia and other medication use
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5 2 will be collected by self-report diary. Additional treatments sourced outside of the trial including
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7 3 contact with general practitioners and other health care professionals will be recorded in self-report
8
9 4 health utilisation diaries in which participants will asked to record their use of health and social care
10
11 5 across the study e.g., GP, nurse, other physio, hospital admissions, home carer visits in standardised
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13 6 study diaries. Diaries will be from 0-4, 4 to 8 and 8 to 12 months [17].
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17 Outcome Measures

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20 8 The primary outcome measure will be the Timed Up and Go (TUG) at 12 months. The TUG is a test of
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22 9 balance, lower limb strength and walking ability with established reliability and validity. It records
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24 10 the time a person takes to stand up from a chair, walk 3 metres at a self-selected speed, turn and
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26 11 walk back and sit down [18].
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30 12 Secondary outcome measures are:
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- 33 13 • QUALEFFO 41: a disease specific measure of health-related quality of life (QoL) applicable to
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35 14 patients with osteoporosis and vertebral fractures. It is a self-administered questionnaire
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37 15 that provides scores on five domains: pain, physical function, social function, general health
38
39 16 perception, mental performance, and a total score. [19].
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46 18 • Timed Loaded Standing (TLS): an assessment of shoulder and back muscle endurance for
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48 19 people with VFF(s). [20].
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55 21 • Thoracic kyphosis angle: measured non-radiographically using a flexicurve ruler, allowing an
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57 22 angle of kyphosis to be calculated which is approximated to radiological measures of
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59 23 kyphosis (Cobb angle) using a standardised formula [21].
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- Back pain: measured with a 10-point Numeric Pain Rating Scale (NPRS): [2].
- Functional Reach (FR) test: a measure of dynamic standing balance developed for older adults. The test has been used in people with VFF and performance is predictive of falls risk [22].
- Six-minute walk (6MW) test: a measure of functional walking capacity and aerobic cardio-respiratory fitness [23].
- Falls Efficacy Scale International (FES-I): a 16 item (3 minute) self-report measure of fear or concern about falling during activities. [24].
- Grip Strength: is the maximum force the hand and forearm muscles can generate measured with an isometric hand dynamometer in kilograms; maximum strength is the mean of three trials (3 seconds each) and measured for both hands [25].
- Self-efficacy for exercise (SEE) scale: a brief (<5 minute) 9-item scale that asks participants to rate how confident they would be that they would engage in exercise on a 10-point scale (not confident to very confident) under different situations e.g., if they were tired. SEE ratings are predictive of exercise behaviour [26].
- Adherence. This will be measured in two ways

- 1
2
3 1 a. Attendance records via clinician completed treatment logs, including a checkbox to log
4
5 2 whether adherence techniques have been prescribed (intervention group only).
6
7
8 3 b. Exercise adherence rating scale (EARS): a brief 6-item scale that asks participants to
9
10 4 describe how they do their recommended exercises on a 5-point scale [27].
11
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14 5 • Falls: documented on the CRF and prospectively using participant completed event diaries.
15
16 6 These will be collected in blocks from 0-4 months, 4 to 8 months, and 8 to 12 months during
17
18 7 the study. Incidence and severity information will be recorded e.g., nature of the fall, its
19
20 8 outcome (no-harm, fracture etc) and any treatment required [2].
21
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23 9
24
25 10 • EQ-5D-5L is a short, generic measure of health related QoL and will be completed to assist
26
27 11 assessment of health economics [28].
28
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30 12
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32
33 13 • Global Rating Change (GRC) scale: a patient's perspective of change based on a 7-point
34
35 14 ordinal scale (much worse, moderately worse, a little worse, no change, a little better,
36
37 15 moderately better, much better) [29].
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43 17 A summary of outcome measures and timepoints is shown in Table 1 (**Table 1**).
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Time Point	Measurement	Enrolment	allocation	Baseline	4 months	8 months	12 months
Screening Log		X					
Eligibility confirmed		x					
Informed Consent		x					
Randomisation			x				
Demographic	Age, gender, weight, ethnicity,			x			
Primary OM	Timed Up & Go			x	x	x	x
Quality of Life	Qualeffo 41			X	X	X	X
Fear Falling	FES-I			X	X	X	X
Back Pain Intensity	NRS-P			X	X	X	X
Back strength / endurance	TLS			X	X	X	X
Walking	6MWT			X	X	X	X
Balance	Functional Reach Test			X	X	X	X
Kyphosis	Flexicurve			X	X	X	X
Exercise Self Efficacy	SEE			X	X	X	X
Exercise adherence	EARS			X	X	X	X
Exercise adherence	Sessions attended				x	x	x

2

3 Table 1: Time Points at which outcomes will be assessed.

4

5 Adverse events

6 Foreseeable adverse events (AE) occurring because of the trial interventions will be recorded.

7 Participants will receive information on potential AEs resulting from the exercises and what they

8 should do if they experience an AE, as would be part of standard NHS procedure. Adverse symptoms

9 in response to treatment and any adverse events will be monitored by clinicians regularly and in line

1
2
3 1 with local departmental procedures and captured on adverse event forms, and via questions on the
4
5 2 CRF.
6
7

8 3 A Serious AE (SAE) is any untoward medical occurrence related to the trial interventions that results
9
10 4 in death, is life-threatening, requires inpatient hospitalisation or prolongation of existing
11
12 5 hospitalisation, or results in persistent or significant disability/incapacity. SAEs are likely to be rare
13
14 6 and are unlikely to occur as a result of the exercise programmes delivered in this study.
15
16

17
18 7 Any reports of SAE will be reported to the trial office within 24 hours of the local research team
19
20 8 becoming aware of the event. They will be reviewed by an independent medically qualified assessor
21
22 9 within 3 days.
23
24

25 26 10 Statistics and analysis

27 28 29 11 Sample Size

30
31
32 12 The primary outcome is the Timed Up & Go (TUG) test. This is the most widely used physical function
33
34 13 measure in RCTs of exercise for people with VFF [4]. The minimal clinically important difference
35
36 14 (MCID) for the TUG has not been established in people with VFF(s), but a MCID of 1.4s is reported for
37
38 15 similar older populations with chronic musculoskeletal disorders [30]. The study requires 104
39
40 16 participants (52 per arm) to be 80% powered to detect a 1.4s difference in TUG score between
41
42 17 groups at a 5% significance level (two-sided) assuming that the standard deviation is 2.5s. Similar
43
44 18 trials have had loss to follow-up rates of 10% at 12 months [2]. To account for this the sample size
45
46 19 has been inflated to 116 participants (58 per arm).
47
48
49

50 51 20 Statistical Analysis

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53
54 21 The study will be reported according to the Consolidated Standards of Reporting Trials (CONSORT)
55
56 22 2010 statement utilising the nonpharmacological and patient-reported outcome extensions [31,32].
57
58 23 Standard descriptive statistics will be used to describe the characteristics of the two groups at
59
60

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2
3 1 baseline. Means and standard deviations (SDs) or medians and interquartile ranges (IQRs) as
4
5 2 appropriate will be used for continuous variables, and numbers and percentages will be used for
6
7 3 binary and categorical variables.
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10 4 Compliance with the intervention will be defined as participating in the extended interview and
11
12 5 prescription of at least 3 adherence support techniques. This will be recorded on treatment logs.
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15 6 Details of the number of physiotherapy sessions attended will also be summarised by treatment
16
17 7 group. The number and proportion of participants who withdraw will be summarised along with
18
19 8 reasons for these. Deaths are not anticipated in this study, but details of any that do occur will also
20
21 9 be summarised by treatment arm.
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25 10 Summary statistics will be presented for all comparative outcomes, and effect estimates will be
26
27 11 reported together with 95% confidence intervals with all tests carried out at a 5% two-sided
28
29 12 significance level.
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32 13 At 12 months post-randomisation the two treatment groups will be compared on the TUG measure
33
34 14 using a multivariate linear regression model adjusting for recruiting centre (stratification factor), age
35
36 15 and baseline TUG score. An unadjusted t-test will also be undertaken. The TUG is also recorded at 4,
37
38 16 and 8 months after randomisation, and an additional analysis utilising all time points, using multi-
39
40 17 level modelling and including a treatment by time interaction if appropriate will be undertaken. For
41
42 18 each of these models, the assumption of approximate normality will be assessed by examining the
43
44 19 residuals. If this assumption is not met the first approach will be to consider a transformation to
45
46 20 achieve normality. If this is not possible, the two groups will be compared using non-parametric
47
48 21 methods (e.g., Mann-Whitney U-test). This analysis will be unadjusted and will consider each time
49
50 22 point separately.
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55 23 Similar analyses will be performed for secondary outcomes which can be considered approximately
56
57 24 continuous (QUALEFFO-41, FES-1, NPRS, TLS, Grip strength, 6MW, FRT, Thoracic kyphosis, SEE and
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1 EARS) at 4-, 8- and 12-months post-randomisation. The appropriateness of the assumption of
2 approximate normality will also be considered and transformation to normality or non-parametric
3 methods used as appropriate. It is not anticipated that the number of falls will be approximately
4 normal, therefore, this will be summarised by treatment group using medians and IQRs and
5 compared using non-parametric methods. The number and proportion of participants experiencing
6 an AE during follow-up will be summarised by treatment group and a logistic regression model
7 adjusted for recruiting centre will be used to compare the rates in the two groups. Severity of AEs
8 will also be summarised by treatment group.

9 In addition, since previous work suggests that change in thoracic kyphosis at follow-up is closely
10 related to baseline values, a subgroup analysis of thoracic kyphosis at follow-up will be completed
11 dependent on whether the participant was kyphotic at baseline [33].

12 All analyses will be performed for the intention to treat (ITT) population. This will include all
13 randomised participants with available data who will be analysed according to their allocated
14 intervention regardless of the treatment they received.

15 In addition, analysis of the primary outcome (TUG at 12 months) will be repeated for the per
16 protocol (PP) population which will include only those participants who received their allocated
17 treatment. Participants with other major protocol deviations (e.g., recruited and later found to be
18 ineligible) will also be excluded from this population.

21 Health Economic Analysis

22 The relative efficiency of the intervention will be assessed by within-trial cost-utility and cost-
23 consequences analyses [34]. The evaluation will take an NHS and personal social services

1 perspective. Resource use for the delivery of Opt-In and at participant level will be combined with
2 unit cost from standard national sources to estimate average total costs. We will estimate the
3 incremental cost per QALY (from EQ-5D-5L) and present the different cost components and multiple
4 benefits of Opt-In in a 'balance sheet' in the cost-consequences analysis.

5 Embedded Qualitative study

6 As part of the main study a nested qualitative study will take place. The qualitative element of this
7 study will involve a subset (12-15) of patients who undertake the Opt-In intervention who will be
8 invited to take part in 4 short (15-20 minute) interviews about their experiences and views about
9 exercise adherence and the adherence intervention at the following time points: i) following
10 assessment ii) during treatment (after 3 sessions), iii) post-treatment (after 4 months), and iv) at 12
11 months. The interviews may occur online via video-call or face-to-face in the person's home or at a
12 local clinic, depending on participant preference. The interviews will be audio recorded and
13 transcribed verbatim. Participants will be given an opportunity to check the interview transcript.

14 Focus groups will be conducted with physiotherapists who undertake the Opt-In intervention, asking
15 them to share their views about promoting exercise adherence and the Opt-In intervention, these
16 will be audio-recorded with a Dictaphone.

17 Purposive sampling will be used to achieve a sample which includes female and male patients,
18 patients of varying activity levels and patients of different ages and disease severity (pain/ number
19 of fractures). These factors may influence the ability to engage with an exercise programme. Since
20 most research regarding adherence in osteoporosis has previously been undertaken with women, it
21 also considered important to capture the views of male patients within the current study and to
22 capture the experiences of people with differing physical activity levels prior to the programme. The
23 quality of a qualitative study is not dependent on its sample size; however, the sample size needs to
24 be sufficiently large to enable relevant data to be obtained, without being so overly large that

1 detailed analysis is subsequently prevented [35]. Information about physiotherapists views of
2 delivering the adherence interventions will also be sought. All those who deliver the adherence
3 techniques will be invited to participate in a focus group.

4 Audio recordings will be listened to, and transcripts read until they become familiar. Data from the
5 interviews with physiotherapists and participants will be analysed separately to understand the
6 perspectives of each group. We will use collaborative methods to ensure a strong voice from PPI
7 members and research rigour. We will use thematic analysis, using the six steps proposed by Braun
8 and Clarke [36].

9 Patient and Public Involvement

10 The study funding application, intervention development and study materials preparation were
11 supported by our patient and public involvement members who will be involved across the course of
12 the study.

13 ETHICS AND DISEMINATION.

14 The study protocol was approved by West of Scotland Research Ethics Committee 4 (Reference
15 21/WS/0071). The University of Oxford is the sponsor. The trial is registered with the International
16 Standard Randomised Controlled Trials database ISRCTN reference number 14465704.

17 The protocol has been reported following the Standard Protocol Items: Recommendations for
18 Interventional Trials (SPIRIT) statement [37]. Results will be published reported following the
19 Consolidated Standards of Reporting Trials (CONSORT) guidelines [38]. The Template for
20 Intervention Description and Replication (TIDieR) statement will be used to report the intervention
21 ensuring replication is possible [39]. Results will be published in a peer reviewed journal with
22 authorship eligibility according to International Committee of Medical Journal Editors (ICJME)
23 criteria. Participants will be asked if they wish to have the results shared with them prior to
24 publication and we will share with those who request this.

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3 1 TRIAL STATUS
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6 2 The first patient was randomised to the trial on 1st September 2021. Recruitment is ongoing.
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9 3 **Contributions of Authors:**
10

11 4 Karen L Barker: Chief Investigator, Conceived and designed the study, was awarded the funding and
12
13 5 had overall responsibility for the study design and delivery and drafted the manuscript. She is the
14
15
16 6 guarantor.

17
18
19 7 Jonathan Room: contributed to study design and provided specific content and edited manuscript.
20
21
22 8 Qualitative lead.
23

24
25 9 Erin Hannink: contributed to study design and provided specific content and edited manuscript
26

27
28 10 Ruth Knight (statistical co-applicant) performed the sample size calculation, prepared randomisation
29
30 11 schedules, planned statistical analysis methods
31

32
33 12 Meredith Newman (Trial Manager), trial design, intervention development, manualisation, training,
34
35 13 supervision, writing and reviewing report.
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37

38
39 14 **Funding**
40

41
42 15 The study is supported by an independent grant from the Chartered Society of Physiotherapy
43
44 16 Charitable Trust (RP/19/01).
45
46

47 17 **Competing Interests**
48

49
50 18 All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf
51
52 19 and declare: no support from any organisation for the submitted work, other than funding
53
54 20 arrangements for the trial described in body of the text; no financial relationships with any
55
56 21 organisations that might have an interest in the submitted work in the previous three years; no
57
58 22 other relationships or activities that could appear to have influenced the submitted work.
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3 1 **Transparency**
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6 2 The lead author (KLB) affirms that the manuscript is an honest, accurate and transparent account of
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8 3 the study being reported.
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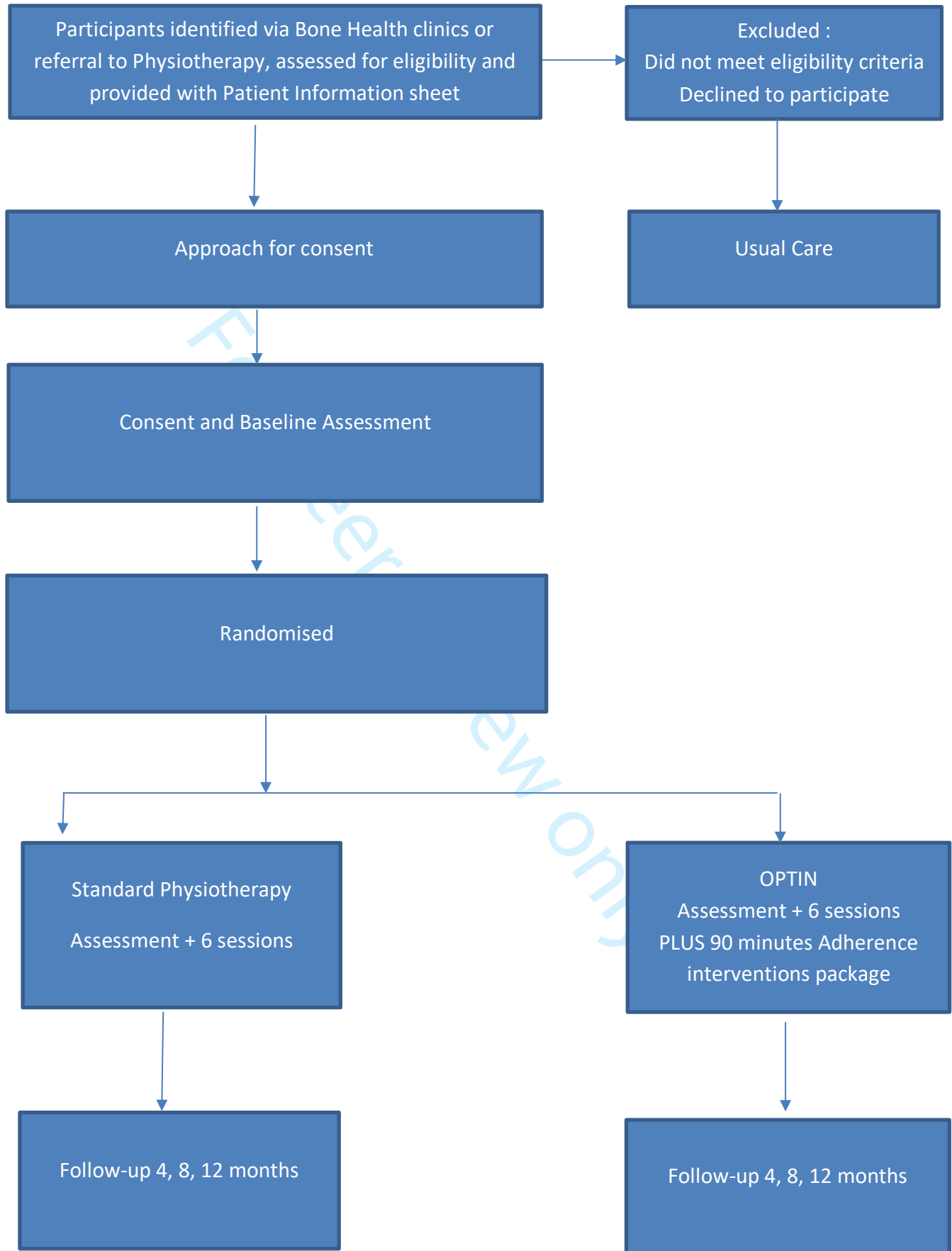
13
14
15 5 **References**
16

- 17 6 1. Gibbs JC, MacIntyre NJ, Ponzano M, et al. Exercise for improving outcomes after
18 7 osteoporotic vertebral fracture. *Cochrane Database Syst Rev*. 2019 Jul 5; 7:
19 8 CD008618. doi: 10.1002/14651858.
- 20
21 9 2. Barker K, Newman M, Stallard N, et al. Physiotherapy Rehabilitation for Osteoporotic
22 10 Vertebral Fracture: A Randomised Controlled Trial and economic evaluation (PROVE
23 11 Trial). *Osteoporos Int*, 2019 Nov 12.
- 24
25 12 3. [https://www.bgs.org.uk/resources/strong-steady-straight-nos-exercise-and-](https://www.bgs.org.uk/resources/strong-steady-straight-nos-exercise-and-osteoporosis-consensus-statement)
26 13 [osteoporosis-consensus-statement](https://www.bgs.org.uk/resources/strong-steady-straight-nos-exercise-and-osteoporosis-consensus-statement).
- 27
28 14 4. Papaioannou A et al. Efficacy of home-based exercise for improving quality of life
29 15 among elderly women with symptomatic osteoporosis-related vertebral fractures.
30 16 *Osteoporos Int* 2003;14: 677–682.
- 31
32 17
33
34 18 5. Gold DT, Shipp KM, Pieper CF, et al. Group treatment improves trunk strength and
35 19 psychological status in older women with vertebral fractures: results of a RCT. *J Am*
36 20 *Geriatr Soc* 2004; 52:1471–1478.
- 37
38 21
39
40 22 6. Bergström I et al. Back extensor training increases muscle strength in
41 23 postmenopausal women with osteoporosis, kyphosis and vertebral fractures. *Adv*
42 24 *Physiother* 2011; 13:110–117.
- 43
44 25
45
46 26 7. Bergland A. et al. Effect of exercise on mobility, balance, and health-related quality
47 27 of life in osteoporotic women with a history of vertebral fracture: a randomized,
48 28 controlled trial. *Osteoporos Int*. 2011; 22: 1863-71.
- 49
50 29 8. Olsen CF, Bergland A. The effect of exercise and education on fear of falling in
51 30 elderly women with osteoporosis and a history of vertebral fracture: results of a
52 31 randomized controlled trial. *Osteoporos Int*. 2014; 2: 2017-25.
- 53
54 32 9. Gibbs JC, McArthur C, Wark J et al. The effect home exercise in older women with
55 33 vertebral fractures: A pilot randomised controlled trial. *Physical Therapy*. 3 Jan 2020
56 34 doi.org/10.1093/ptj/pzz188
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10. Evstigneeva L, Lesnyak O, Bultink IEM et al Effect of a twelve-month physical exercise program of patients with osteoporotic vertebral fractures: a randomised controlled trial. *Osteoporos Int* 2016 27: 2515-24.
11. Room J, Hannink E, Dawes H, et al. What interventions are used to improve exercise adherence in older people and what behavioural techniques are they based on? *BMJ Open*. 2017; 7(12): e019221.
12. Beavious C. Motivational interviewing to improve treatment adherence. *Joint Bone Spine*. 2019 Feb 22: pii: S1297-319X(19)30042-9. doi: 10.1016/j.jbspin.2019.02.005.
13. NICE draft guidance on behaviour change URL: <https://www.nice.org.uk/guidance/ph49/documents/behaviour-change-draft-guidance2>(accessed 11th March 2020).
14. Room J, Boulton M, Dawes H, et al. Development of an exercise adherence intervention for older people. The steps taken designing a complex intervention for the AERO trial. *WCPT 2019: PO-J-09-SUN1*
15. Michie S, van Stralen M, West R. The behaviour change wheel: A new method for characterising and designing behaviour change interventions. *Implementation Science* 2011, 6:42.
16. Rodrigues IB, Jonathan D, Adachi JD, Beattie5 KA, MacDermid JC. Development and validation of a new tool to measure the facilitators, barriers and preferences to exercise in people with osteoporosis. *BMC Musculoskeletal Disorders* 2017 18:540. DOI 10.1186/s12891-017-1914-5.
17. Drummond M, Sculpher M, Torrance G, O'Brien B, Stoddart G. *Methods for the economic evaluation of health care programmes*: Oxford University Press; 2005.
18. Podsiadlo, D. and Richardson, S. (1991). "The timed "Up & Go": a test of basic functional mobility for frail elderly persons." *J Am Geriatr Soc* 39(2): 142-148.
19. International Osteoporosis Foundation Quality of life questionnaires QUALEFFO-41. URL: <https://www.osteoporosis.foundation/health-professionals/research-tools/quality-life-questionnaires> (accessed 30 March 2022).
20. Newman M, Newman R, Hughes T, Vadher K, Barker KL. Is the timed loaded standing test a valid measure of back muscle endurance in people with vertebral osteoporosis? *Osteoporos Int*. 2018; 29:893–905.
21. Greendale GA, Nili NS, Huang MH, Seeger L, Karlamangla AS. The reliability and validity of three non-radiological measures of thoracic kyphosis and their relations to the standing radiological Cobb angle. *Osteoporos Int* 2011; 22:1897–905.
22. Weiner DK, Duncan PW et al. Functional reach: a marker of physical frailty. *J Am Geriatr Soc* 1992; 40(3):203-7.
23. Steffen TM, Hacker TA, Mollinger L. Age- and gender-related test performance in community-dwelling elderly people: Six-Minute Walk Test, Berg Balance Scale, Timed Up and Go Test, and gait speeds. *Phys Ther* 2002;82:128–37.
24. Delbaere K, Close JCT et al. The falls efficacy scale international (FES-I). A comprehensive longitudinal validation study. *Age and Ageing* 2010; 39: 201-16.

- 1
2
3 1 25. Abizanda P, Navarro JL et al. Validity and usefulness of handheld- dynamometry for
4 2 measuring muscle strength in community-dwelling older persons. Arch Gerontol
5 3 Geriatr. 2012; 54(1): 21-7.
6
7 4 26. Resnick B and Jenkins LS. Testing the reliability and validity of the self-efficacy for
8 5 exercise scale. Nurs Res 49 (3): 154-159.
9
10 6 27. Newman-Beinart NA et al. The development and initial psychometric evaluation of a
11 7 measure assessing adherence to prescribed exercise: the Exercise Adherence Rating
12 8 Scale (EARS). Physiotherapy 103 (2017) 180-85.
13
14 9 28. Herdman M, Gudex C, Lloyd A et al. Development and preliminary testing of the new
15 10 five-level version of the EQ-5D-5L (EQ-5D-5L). Qual Life Res 2011; 20 (10): 1727-
16 11 36.28.
17
18 12 29. Kamper SJ, Maher CG, Mackay G. Global rating of change scales: a review of
19 13 strengths and weaknesses and considerations for design. J Man Manip Ther.
20 14 2009;17(3):163-170.
21
22 15 30. Wright A, Cook C, Baxter G, et al. A comparison of 3 methodological approaches to
23 16 defining major clinically important improvements of 4 performance measures in
24 17 patients with hip osteoarthritis. J Orthop Sport Phys. 2011; 41: 319 -27.
25
26 18 31. Schulz KF, Altman DG, Moher D, for the CONSORT Group. CONSORT 2010 Statement:
27 19 updated guidelines for reporting parallel group randomised trials. BMC Trials. 2010;
28 20 11:32.
29
30 21 32. Calvert M, Blazeby J, Altman DG, et al. Reporting of patient-reported outcomes in
31 22 randomised trials: the CONSORT PRO Extension. JAMA. 2013;309(8):814–22.
32
33 23 33. Hannink E, Newman M, Barker KL. Does thoracic kyphosis severity predict response
34 24 to physiotherapy rehabilitation in patients with osteoporotic vertebral fracture? A
35 25 secondary analysis of the PROVE RCT. Physiotherapy Feb 17, 2022,
36
37 26 34. Drummond M, Sculpher M, Torrance G, O'Brien B, Stoddart G. Methods for the
38 27 economic evaluation of health care programmes: Oxford University Press; 2005.
39
40 28 35. Sandelowski, M., Sample size in qualitative research. Research in Nursing and
41 29 Health, 1995. 18(2): p. 179-183.
42
43 30 36. Braun V, Clarke V. What can "thematic analysis" offer health and wellbeing
44 31 researchers? Int J Qual Stud Health Well-being. 2014; 9:26152.
45
46 32 37. Chan A-W, Tetzlaff JM, Gotzsche PC et al. SPIRIT 2013 explanation and elaboration:
47 33 guidance for protocols of clinical trials. BMJ 2013;346: e7586.
48
49 34 38. Schulz KF, Altman DG, Moher D et al. CONSORT 2010 statement: updated guidelines
50 35 for reporting parallel group randomised trials. BMJ 2010;340:c332.
51
52 36 39. Hoffmann TC, Glasziou PP, Boutron I et al. Better reporting of interventions:
53 37 template for intervention description and replication (TIDieR) checklist and guide.
54 38 BMJ 2014; 348:g1687.
55
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Qualitative Interviews n =15-20 participants
Focus group Physiotherapists



SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description
Administrative information		
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym Title Page Lines 1-3
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry Page 3 Line 21
	2b	All items from the World Health Organization Trial Registration Data Set
Protocol version	3	Date and version identifier Page 3 Line 22
Funding	4	Sources and types of financial, material, and other support Page 23 lines 9/10
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors Title page and Page 22/23
	5b	Name and contact information for the trial sponsor Page 19 Line 12
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)
Introduction		
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention P5-6
	6b	Explanation for choice of comparators P6
Objectives	7	Specific objectives or hypotheses P6

1
2 Trial design 8 Description of trial design including type of trial (eg, parallel group,
3 crossover, factorial, single group), allocation ratio, and framework (eg,
4 superiority, equivalence, noninferiority, exploratory) **P6 L22-3**
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8 **Methods: Participants, interventions, and outcomes**
9

10 Study setting 9 Description of study settings (eg, community clinic, academic hospital)
11 and list of countries where data will be collected. Reference to where
12 list of study sites can be obtained **P7 L10**
13

14 Eligibility criteria 10 Inclusion and exclusion criteria for participants. If applicable, eligibility
15 criteria for study centres and individuals who will perform the
16 interventions (eg, surgeons, psychotherapists) **P7-8**
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19 Interventions 11a Interventions for each group with sufficient detail to allow replication,
20 including how and when they will be administered **P10-11**
21

22 11b Criteria for discontinuing or modifying allocated interventions for a
23 given trial participant (eg, drug dose change in response to harms,
24 participant request, or improving/worsening disease) **n/a**
25

26 11c Strategies to improve adherence to intervention protocols, and any
27 procedures for monitoring adherence (eg, drug tablet return,
28 laboratory tests) **p10/11**
29
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31 11d Relevant concomitant care and interventions that are permitted or
32 prohibited during the trial **p12**
33

34 Outcomes 12 Primary, secondary, and other outcomes, including the specific
35 measurement variable (eg, systolic blood pressure), analysis metric
36 (eg, change from baseline, final value, time to event), method of
37 aggregation (eg, median, proportion), and time point for each
38 outcome. Explanation of the clinical relevance of chosen efficacy and
39 harm outcomes is strongly recommended **p12-14**
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42 Participant 13 Time schedule of enrolment, interventions (including any run-ins and
43 timeline washouts), assessments, and visits for participants. A schematic
44 diagram is highly recommended (see Figure) **Table 1**
45

46 Sample size 14 Estimated number of participants needed to achieve study objectives
47 and how it was determined, including clinical and statistical
48 assumptions supporting any sample size calculations **P15**
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51 Recruitment 15 Strategies for achieving adequate participant enrolment to reach
52 target sample size **P8**
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54 **Methods: Assignment of interventions (for controlled trials)**
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56 Allocation:
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2	Sequence	16a	Method of generating the allocation sequence (eg, computer-
3	generation		generated random numbers), and list of any factors for stratification.
4			To reduce predictability of a random sequence, details of any planned
5			restriction (eg, blocking) should be provided in a separate document
6			that is unavailable to those who enrol participants or assign
7			interventions P9
8			
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10	Allocation	16b	Mechanism of implementing the allocation sequence (eg, central
11	concealment		telephone; sequentially numbered, opaque, sealed envelopes),
12	mechanism		describing any steps to conceal the sequence until interventions are
13			assignedp9
14			
15	Implementation	16c	Who will generate the allocation sequence, who will enrol participants,
16			and who will assign participants to interventions P9
17			
18			
19	Blinding	17a	Who will be blinded after assignment to interventions (eg, trial
20	(masking)		participants, care providers, outcome assessors, data analysts), and
21			how P 9
22			
23		17b	If blinded, circumstances under which unblinding is permissible, and
24			procedure for revealing a participant's allocated intervention during
25			the trial n/a
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Methods: Data collection, management, and analysis

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30	Data collection	18a	Plans for assessment and collection of outcome, baseline, and other
31	methods		trial data, including any related processes to promote data quality (eg,
32			duplicate measurements, training of assessors) and a description of
33			study instruments (eg, questionnaires, laboratory tests) along with
34			their reliability and validity, if known. Reference to where data
35			collection forms can be found, if not in the protocolp10
36			
37			
38		18b	Plans to promote participant retention and complete follow-up,
39			including list of any outcome data to be collected for participants who
40			discontinue or deviate from intervention protocols
41			
42	Data	19	Plans for data entry, coding, security, and storage, including any
43	management		related processes to promote data quality (eg, double data entry;
44			range checks for data values). Reference to where details of data
45			management procedures can be found, if not in the protocol
46			
47			
48	Statistical	20a	Statistical methods for analysing primary and secondary outcomes.
49	methods		Reference to where other details of the statistical analysis plan can be
50			found, if not in the protocol P15-6
51			
52		20b	Methods for any additional analyses (eg, subgroup and adjusted
53			analyses) n/a
54			
55		20c	Definition of analysis population relating to protocol non-adherence
56			(eg, as randomised analysis), and any statistical methods to handle
57			missing data (eg, multiple imputation) P15-17
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Methods: Monitoring

Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed n/a
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial n/a
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct P14-15
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor

Ethics and dissemination

Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval P22
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) P 19
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) P8
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable n/a
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site P23
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation n/a

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| Dissemination
policy | 31a | Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions P19 |
| | 31b | Authorship eligibility guidelines and any intended use of professional writers P19 |
| | 31c | Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code |

14 Appendices

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|-------------------------------|----|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Informed consent
materials | 32 | Model consent form and other related documentation given to participants and authorised surrogates |
| Biological
specimens | 33 | Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable |

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*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "[Attribution-NonCommercial-NoDerivs 3.0 Unported](https://creativecommons.org/licenses/by-nc-nd/3.0/)" license.

BMJ Open

Physiotherapy exercise rehabilitation with tailored exercise adherence support for people with osteoporosis and vertebral fractures: Protocol for a randomised controlled trial – the Osteoporosis Tailored exercise adherence intervention (OPTIN) study.

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2022-064637.R1
Article Type:	Protocol
Date Submitted by the Author:	22-Aug-2022
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Primary Subject Heading:	Rheumatology
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4 **1 Physiotherapy exercise rehabilitation with tailored exercise adherence support for people with**
5 **osteoporosis and vertebral fractures: Protocol for a randomised controlled trial – the Osteoporosis**
6 **2 Tailored exercise adherence intervention (OPTIN) study.**
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1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60

Introduction: Vertebral fragility fractures affect at least 20% of the older population in the UK. Best practice guidelines recommend the use of exercise to slow the rate of bone loss, to maintain muscle strength and physical function, and to prevent falls and further fractures. However, treatment effects are often small and difficult to sustain and adherence, or the extent to which patients engage in treatment, has been identified as an important issue by many studies. Our hypothesis is that integrating adherence intervention strategies with an exercise intervention will be beneficial. We will compare physiotherapy exercise rehabilitation with adherence support versus physiotherapy exercise rehabilitation alone in terms of effects on (a) physical function, quality of life, and fear of falling and (b) exercise self-efficacy and adherence.

Methods and Analysis: A multicentre, two-arm, parallel group, superiority randomised controlled trial (RCT) with blinded assessments at baseline (0) and 4, 8, and 12 months, with a nested qualitative study and health economic analysis. 116 participants will be allocated to either (i) out-patient physiotherapy which will include a musculoskeletal assessment and treatment including balance, posture, strength training and low impact weight-bearing exercises over 16 weeks; or (ii) Opt-In intervention. This includes standard physiotherapy as above plus an additional, integrated assessment interview (30mins) and 60 minutes of adherence support spread over the subsequent 16 weeks.

Ethics and Dissemination: The study protocol was approved by West of Scotland Research Ethics Committee 4 (21/WS/0071). Trial registration number ISRCTN 14465704. The paper is based on Protocol v4.

Strengths and Limitations of this study

- The Physiotherapy exercise rehabilitation with tailored exercise adherence support for people with osteoporosis and vertebral fractures (Opt-In) study is a multicentre randomised controlled trial with an embedded qualitative study and economic evaluation.
- It will recruit from at least six NHS hospitals.
- The intervention addresses adherence which is an important confounder in many trials of physiotherapy.
- The intervention was developed using current research evidence, input from expert clinicians, researchers and patient / public representatives.
- Due to the nature of the interventions the physiotherapists delivering the treatments and the participants cannot be blinded.

1 Introduction

2 Vertebral fragility fractures (VFFs) affect at least 20% of the older population in the UK and present a
3 significant health and economic burden [1, 2]. They are associated with back pain, fatigue, low
4 mood, restrictions in physical function and activities of daily living, and marked, persistent
5 reductions in quality of life (QoL) [1, 2]. Without treatment, progression and functional decline are
6 expected. Conservative treatment for osteoporosis includes bone protective medications and
7 lifestyle adaptations. Guidelines recommend people with osteoporosis keep active and exercise to
8 slow the rate of bone loss, to maintain muscle strength and physical function and to prevent falls
9 and further fractures [3,4]. Exercise prescription with multi-component exercise programmes that
10 include postural, balance, aerobic weight-bearing and strength exercises are recommended [1-3].

11 Trials evaluating exercise in people with VFFs have reported benefits across a range of outcomes [1,
12 2, 5-10], with a recent Cochrane review concluding there is moderate-quality evidence that exercise
13 improves physical function [1]. However, treatment effects are often small and difficult to sustain
14 [1, 2, 5-10]. For example, in the PROVE trial, significant, clinically relevant benefits to back muscle
15 endurance, balance, walking capacity and physical function following physiotherapy exercise at 4
16 months post-randomisation did not persist at 12 months [2]. Adherence, or the extent to which
17 patients engage in treatment, has been identified as an important issue by many studies [1, 2, 5-6,
18 9]. Partial adherence or non-adherence is associated with worse outcomes and conversely, higher
19 adherence with better outcomes [1, 2, 5-10].

20 Multiple factors affect exercise adherence in older people with chronic health conditions including
21 osteoporosis [11, 12]. These include low exercise self-efficacy, low motivation, depression,
22 insufficient exercise knowledge or skill, physical ability, negative views about treatment and exercise
23 programme design [11,12]. Considering this complexity, interventions to support adherence that
24 recognize personal barriers and facilitators to exercise and that can draw upon multiple adherence
25 techniques are recommended [12, 13].

1
2
3 1 Behavioural approaches can include interventions that support exercise through providing additional
4
5 2 monitoring, interventions that aim to alter thinking patterns that contribute to non-adherence and
6
7 3 ones that strengthen behaviours that support adherence [12]. Motivational interviewing is a
8
9
10 4 collaborative process that explores potential ambivalence, obstacles and facilitators surrounding
11
12 5 behaviour change [6]. There is evidence that additional monitoring, prompts and feedback can
13
14 6 benefit adherence in older adults e.g., via telephone call/ text messages, wearable activity monitors
15
16 7 or by enriching environmental cues [1]. Incorporating exercise into everyday routines can make it
17
18 8 easier to initiate and sustain and creating 'Exercise Action Plans' that specify when, where and how
19
20 9 exercises are undertaken can support this process [1, 13]. Using an intervention mapping approach,
21
22
23 10 we developed an exercise adherence intervention underpinned theoretically by the Capability,
24
25 11 Opportunity, Motivation - Behaviour (COM-B) behaviour change model [14, 15].
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29 12 **Aims**

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32 13 The aims of this study are:

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35 14 • To compare physiotherapy exercise rehabilitation with adherence support with
36
37 15 physiotherapy exercise rehabilitation alone in terms of effects on: (a) physical function,
38
39 16 quality of life, and fear of falling and (b) exercise self-efficacy and adherence.
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41 17 • To explore patient and physiotherapist views of the intervention and of adhering to exercise.
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44 18 • To understand if physiotherapy exercise rehabilitation with adherence support is cost-
45
46 19 effective.
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49 20 **METHODS AND ANALYSES**

50 51 52 21 Study design

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55 22 A multicentre, two-arm, parallel group, superiority randomised controlled trial (RCT) with blinded
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57 23 assessments at baseline (0) and 4, 8, and 12 months following randomisation, with a nested
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59 24 qualitative study and health economic analysis. Participants will be allocated to either (i) outpatient
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1 physiotherapy which will include a musculoskeletal assessment and 6 treatment sessions over 16
2 weeks based on the current best practice guidance from the Royal Osteoporosis Society; or (ii) the
3 Opt-In intervention. This includes outpatient physiotherapy as described above, plus an additional,
4 integrated assessment interview (30mins) and 60 minutes of adherence support spread over the
5 subsequent treatment period of 16 weeks as prescribed by the physiotherapist in collaboration with
6 the participant. Sessions in both arms can be in-person or virtually via video-call/ telephone as
7 agreed between participant and therapist (**Figure 1**).

8 The trial started recruitment of patients in August 2021 and will continue recruiting until June 2023.

9 Setting

10 At least six National Health Service (NHS) hospitals and their related physiotherapy services.

11 Study Participants

12 Adults aged 55 years or over who have a diagnosis of at least one previous osteoporotic vertebral
13 fracture and back pain.

14 Eligibility

15 Inclusion Criteria

16 Participants may enter the study if they meet ALL the following criteria:

- 17 • Men and women ≥ 55 years: all women must be at least 1 year post-menopausal.
- 18 • One or more VFFs confirmed by radiography, X-Ray, MRI, CT or DEXA scan, people with VFF
19 of any severity and at any time-point post-fracture are eligible.
- 20 • They must have had an episode of back pain in the previous 12 months.
- 21 • All must be able to walk at least 10 metres independently with or without a walking aid.

1 Exclusion Criteria

2 Participants may not enter the study if ANY of the following apply:

- 3 • Current conditions that would make participating in physiotherapy or exercise unsafe or
4 confound results. This includes those with significant neurological and psychiatric conditions,
5 severe unstable cardiovascular or pulmonary disease.
- 6 • Bone loss secondary to other metabolic disorders, diseases or medication e.g., rheumatoid
7 arthritis, anorexia, cancer, coeliac disease, steroid use.
- 8 • Individuals whose primary problem is back pain that involves pain radiating into the lower
9 limbs.
- 10 • Vertebroplasty, facet joint injection or physiotherapy within past 12 weeks.

11 Recruitment

12 A member of the patient's direct care team will identify potential participants with VFFs via clinic
13 lists and electronic medical records from relevant metabolic bone clinics, radiology clinics (DEXA),
14 physiotherapy referral lists, and from Rheumatology clinics.

15 Screening and eligibility assessment

16 Potential participants, who respond to an invitation letter will be contacted by telephone to discuss
17 the study further, to check eligibility and to answer any questions. Patients who do not meet the
18 eligibility criteria or who do not wish to participate will receive standard NHS treatment. We will
19 record the age and gender of these patients to assess the generalisability of those recruited.

20 Consent

21 Participants who are eligible and willing to proceed will be approached for informed consent.; they
22 and the researcher will sign and date a consent form. For participants who are recruited to the

1
2
3 1 additional nested qualitative study and interviewed on-line or via telephone, informed consent will
4
5 2 be obtained verbally before the interview. The researcher taking consent will read, and fill out, the
6
7 3 consent form on behalf of the participant and then sign the form.
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12 13 14 5 Randomisation

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16 6 Consented participants will be randomised 1:1 using a computer-generated randomisation schedule
17
18 7 prepared by the trial statistician (RK). Individual randomisation will be stratified by recruitment
19
20 8 centre and permuted blocks of varying undisclosed sizes will be used. The randomisation schedule
21
22 9 will be concealed in sequentially numbered, opaque, sealed envelopes for each site. A study
23
24 10 administrator who has no interaction with blinded study staff will manage these envelopes. The
25
26 11 administrator will open the randomisation envelope, and then communicate with the local site who
27
28 12 will make the participant aware of their allocated group and refer for physiotherapy; making sure
29
30 13 that participants are allocated to physiotherapists delivering the treatment for their allocated arm.
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34 35 14 Blinding

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38 15 Physiotherapists delivering the interventions and participants will be told the treatment allocation.
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40 16 Initial baseline assessment will occur prior to randomisation and the researcher undertaking
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42 17 assessments will not be involved in any part of the randomisation procedure to ensure that they are
43
44 18 not able to bias the group allocation. The researcher conducting follow-up measures and the
45
46 19 research team personnel entering data will also not be informed of allocated group and participants
47
48 20 will be asked and reminded not to disclose their treatment group to the researcher at follow-up
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50 21 appointments.
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54 55 22 Interventions

56 57 58 23 Training and monitoring

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3 1 Sessions in both arms can be delivered in-person or virtually via video-call/ telephone as agreed
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5 2 between participant and therapist; to allow flexibility and resilience as COVID restrictions on physical
6
7 3 attendance vary. Treatments were standardised and manualised and the study team provided
8
9 4 training in the multi-component exercise therapy treatments (delivered to all participants) to all
10
11 5 treating physiotherapists. Training in the behavioural adherence support intervention which
12
13 6 comprised assessment and a set of 9 behavioural interventions (the Opt-In toolkit) was delivered
14
15 7 separately to the therapists in the Opt-In arm. Treating physiotherapists will record the delivery and
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17 8 content of each treatment session in adherence logs for each participant. Regular site visits will be
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19 9 carried out to monitor intervention fidelity.
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24 10 Standard Care

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27 11 Participants will be offered a 1-hour physiotherapy assessment and six individual outpatient
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29 12 physiotherapy sessions spread over 16 weeks [2]. The physiotherapy will include a musculoskeletal
30
31 13 assessment and treatment including a multi-component, progressed balance, posture, strength
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33 14 training and low impact weight-bearing exercise [3]. Exercise intensity will be assessed using the 10-
34
35 15 point Rating of Perceived Exertion scale (CR10-RPE), so participants work at a moderately hard to
36
37 16 hard (RPE 4-6) intensity. Although current practice may vary, the package agreed as the standard
38
39 17 care is based on consensus, best practice guidelines and successful delivery in the PROVE trial
40
41 18 exercise arm [2] and aims to be a credible representation of current best practice treatment across
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43 19 the NHS. Treating therapists will receive prior training on prescription of the exercises [2].
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48 20 Opt -In

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51 21 Participants allocated to Opt-In will receive the standard package described above, plus an
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53 22 additional, integrated assessment interview (30mins) and 60 minutes of adherence support spread
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55 23 over the subsequent treatment period of 16 weeks in an individualised pattern as required by the
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57 24 participant.
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3 1 Participants in the Opt-In arm will complete the Personalized Exercise Questionnaire (PEQ). The PEQ
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5 2 was developed in Canada to support patient-centred exercise prescription for people with
6
7 3 osteoporosis and covers topics such as barriers to exercise and goals of treatment [16]. Treating
8
9 4 physiotherapists will have a collaborative discussion with the participant using a motivational
10
11 5 interviewing approach drawing upon PEQ responses and considering goals, motivators, facilitators,
12
13 6 and barriers surrounding exercise. It aims to provide physiotherapists with a deeper understanding
14
15 7 of patient motivations and circumstances, to strengthen the therapeutic alliance and the patient's
16
17 8 own motivations for adopting exercise [12]. Using their assessment findings, the questionnaire and
18
19 9 collaborative interview the physiotherapist will assess a participant's exercise capability (C),
20
21 10 opportunity (O) and motivation (M) to carry out exercise behaviour (B) (COM-B) and select an
22
23 11 adherence technique from the Opt-In toolkit in response [14]. Techniques can include education
24
25 12 about osteoporosis and exercises, education about and practice of fall prevention strategies,
26
27 13 Exercise Action Plans, a contact telephone call, and self-monitoring and feedback strategies such as,
28
29 14 exercise confidence rating scales or using an exercise diary. Techniques are linked to COM-B
30
31 15 domains to facilitate physiotherapist decision-making e.g., Education improves capability and
32
33 16 motivation (C, M) and a diagrammatic decision aid was developed to facilitate rapid decision-making
34
35 17 during treatment. Each Opt-In arm treating physiotherapist received a toolkit and training by the
36
37 18 study team about techniques and how to use them. Physiotherapists were asked to prescribe at
38
39 19 least 3 adherence techniques from the Opt-In toolkit over 16 weeks but could use more. The exact
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41 20 techniques selected were personalised to the patient as was the pattern and spread of the 60-
42
43 21 minute adherence support time. Participants in the intervention arm were given a folder that
44
45 22 included their exercises and selected adherence materials e.g., exercise diary, education leaflet,
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47 23 action plan record. Figure 2 summarises the intervention in a logic model.
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25 Concomitant care

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3 1 Other aspects of health and social care will continue as usual. Analgesia and other medication use
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5 2 will be collected by self-report diary. Additional treatments sourced outside of the trial including
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7 3 contact with general practitioners and other health care professionals will be recorded in self-report
8
9 4 health utilisation diaries in which participants will be asked to record their use of health and social care
10
11 5 services across the study e.g., GP, nurse, other physio, hospital admissions, home carer visits in
12
13 6 standardised study diaries. Diaries will be from 0-4, 4 to 8 and 8 to 12 months [17].
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17 Outcome Measures

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20 8 The primary outcome measure will be the Timed Up and Go (TUG) at 12 months. The TUG is a test of
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22 9 balance, lower limb strength and walking ability with established reliability and validity. It records
23
24 10 the time a person takes to stand up from a chair, walk 3 metres at a self-selected speed, turn, walk
25
26 11 back and sit down [18].
27
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30 12 Secondary outcome measures are:

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33 13 • QUALEFFO 41: a disease specific measure of health-related quality of life (QoL) applicable to
34
35 14 patients with osteoporosis and vertebral fractures. It is a self-administered questionnaire
36
37 15 that provides scores on five domains: pain, physical function, social function, general health
38
39 16 perception, mental performance, and a total score. [19].
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46 18 • Timed Loaded Standing (TLS): an assessment of shoulder and back muscle endurance for
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48 19 people with VFF(s). [20].
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52 20
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54
55 21 • Thoracic kyphosis angle: measured non-radiographically using a flexicurve ruler, allowing an
56
57 22 angle of kyphosis to be calculated which is approximated to radiological measures of
58
59 23 kyphosis (Cobb angle) using a standardised formula [21].
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3 1 • Back pain: measured with a 10-point Numeric Pain Rating Scale (NPRS) [22].
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5 2
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8 3 • Functional Reach (FR) test: a measure of dynamic standing balance developed for older
9
10 4 adults. The test has been used in people with VFF and performance is predictive of falls
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12 5 risk [23].
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15 6
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18 7 • Six-minute walk (6MW) test: a measure of functional walking capacity and aerobic cardio-
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20 8 respiratory fitness [24].
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23 9
24 10 • Falls Efficacy Scale International (FES-I): a 16 item (3 minute) self-report measure of fear or
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26 11 concern about falling during activities [25].
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33 13 • Grip Strength: is the maximum force the hand and forearm muscles can generate measured
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35 14 with an isometric hand dynamometer in kilograms; maximum strength is the mean of three
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37 15 trials (3 seconds each) and measured for both hands [26].
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40 16
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43 17 • Self-efficacy for exercise (SEE) scale: a brief (<5 minute) 9-item scale that asks participants to
44
45 18 rate how confident they would be that they would engage in exercise on a 10-point scale
46
47 19 (not confident to very confident) under different situations e.g., if they were tired. SEE
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49 20 ratings are predictive of exercise behaviour [27].
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56 22 • Adherence. This will be measured in two ways:
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3 1 a. Attendance records via clinician completed treatment logs, including a checkbox to log
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5 2 whether adherence techniques have been prescribed (intervention group only).
6
7
8 3 b. Exercise adherence rating scale (EARS): a brief 6-item scale that asks participants to
9
10 4 describe how they do their recommended exercises on a 5-point scale [28].
11
12
13
14 5 • Falls: documented on the CRF and prospectively using participant completed event diaries.
15
16 6 These will be collected in blocks from 0-4 months, 4 to 8 months, and 8 to 12 months during
17
18 7 the study. Incidence and severity formation will be recorded e.g., nature of the fall, its
19
20 8 outcome (no-harm, fracture etc) and any treatment required [2].
21
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23 9
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25 10 • EQ-5D-5L is a short, generic measure of health related QoL and will be completed to assist
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27 11 assessment of health economics [29].
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36 14 A summary of outcome measures and timepoints is shown in Table 1 (**Table 1**).
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A summary of outcome measures and timepoints is shown in Table 1 (**Table 1**).

1

Time Point	Measurement	Enrolment	allocation	Baseline	4 months	8 months	12 months
Screening Log		X					
Eligibility confirmed		x					
Informed Consent		x					
Randomisation			x				
Demographic	Age, gender, weight, ethnicity,			x			
Primary OM	Timed Up & Go			x	x	x	x
Quality of Life	QUALEFFO 41			X	X	X	X
Fear Falling	FES-I			X	X	X	X
Back Pain Intensity	NRS-P			X	X	X	X
Back strength / endurance	TLS			X	X	X	X
Walking	6MWT			X	X	X	X
Balance	Functional Reach Test			X	X	X	X
Kyphosis	Flexicurve			X	X	X	X
Grip Strength	Dynamometer			x	x	x	x
EQ-5D-5L	Health economics			x	x	x	x
Falls	Number of reported falls. Nature; outcome of falls.				x	x	x
Exercise Self Efficacy	SEE			X	X	X	X
Exercise adherence	EARS			X	X	X	X
Exercise adherence	Sessions attended				x	x	x

2

3 Table 1: Time Points at which outcomes will be assessed.

4

5 Adverse events

6 Adverse events (AE) occurring because of the trial interventions will be recorded. Participants will

7 receive information on potential AEs resulting from the exercises and what they should do if they

1
2
3 1 experience an AE, as would be part of standard NHS procedure. Adverse symptoms in response to
4
5 2 treatment and any adverse events will be monitored by clinicians regularly and in line with local
6
7 3 departmental procedures and captured on adverse event forms, and via questions on the CRF.
8
9
10 4 A Serious AE (SAE) is any untoward medical occurrence related to the trial interventions that results
11
12 5 in death, is life-threatening, requires inpatient hospitalisation or prolongation of existing
13
14 6 hospitalisation, or results in persistent or significant disability/incapacity. SAEs are likely to be rare
15
16 7 and are unlikely to occur as a result of the exercise programmes delivered in this study.
17
18
19 8 Any reports of SAE will be reported to the trial office within 24 hours of the local research team
20
21 9 becoming aware of the event. They will be reviewed by an independent medically qualified assessor
22
23 10 within 3 days.
24
25
26
27

28 Statistics and analysis

31 Sample Size

32
33
34 13 The primary outcome is the Timed Up & Go (TUG) test. This is the most widely used physical function
35
36 14 measure in RCTs of exercise for people with VFF [4]. The minimal clinically important difference
37
38 15 (MCID) for the TUG has not been established in people with VFF(s), but a MCID of 1.4s is reported for
39
40 16 similar older populations with chronic musculoskeletal disorders [30]. The study requires 104
41
42 17 participants (52 per arm) to be 80% powered to detect a 1.4s difference in TUG score between
43
44 18 groups at a 5% significance level (two-sided) assuming that the standard deviation is 2.5s. Similar
45
46 19 trials have had loss to follow-up rates of 10% at 12 months [2]. To account for this the sample size
47
48 20 has been inflated to 116 participants (58 per arm).
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53 Statistical Analysis

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56 22 The study will be reported according to the Consolidated Standards of Reporting Trials (CONSORT)
57
58 23 2010 statement utilising the nonpharmacological and patient-reported outcome extensions [31,32].
59
60

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2
3 1 Standard descriptive statistics will be used to describe the characteristics of the two groups at
4
5 2 baseline. Means and standard deviations (SDs) or medians and interquartile ranges (IQRs) as
6
7 3 appropriate will be used for continuous variables, and numbers and percentages will be used for
8
9 4 binary and categorical variables.

10
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12
13 5 Compliance with the intervention will be defined as participating in the extended interview and
14
15 6 prescription of at least 3 adherence support techniques. This will be recorded on treatment logs.
16
17 7 Details of the number of physiotherapy sessions attended will also be summarised by treatment
18
19 8 group. The number and proportion of participants who withdraw will be summarised along with
20
21 9 reasons for these. Deaths are not anticipated in this study, but details of any that do occur will also
22
23 10 be summarised by treatment arm.

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25
26
27 11 Summary statistics will be presented for all comparative outcomes, and effect estimates will be
28
29 12 reported together with 95% confidence intervals with all tests carried out at a 5% two-sided
30
31 13 significance level.

32
33
34
35 14 At 12 months post-randomisation the two treatment groups will be compared on the TUG measure
36
37 15 using a multivariate linear regression model adjusting for recruiting centre (stratification factor), age
38
39 16 and baseline TUG score. An unadjusted t-test will also be undertaken. The TUG is also recorded at 4,
40
41 17 and 8 months after randomisation, and an additional analysis utilising all time points, using multi-
42
43 18 level modelling and including a treatment by time interaction if appropriate will be undertaken. For
44
45 19 each of these models, the assumption of approximate normality will be assessed by examining the
46
47 20 residuals. If this assumption is not met the first approach will be to consider a transformation to
48
49 21 achieve normality. If this is not possible, the two groups will be compared using non-parametric
50
51 22 methods (e.g., Mann-Whitney U-test). This analysis will be unadjusted and will consider each time
52
53 23 point separately.
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3 1 Similar analyses will be performed for secondary outcomes which can be considered approximately
4
5 2 continuous (QUALEFFO-41, FES-1, NPRS, TLS, Grip strength, 6MW, FRT, Thoracic kyphosis, SEE and
6
7 3 EARS) at 4-, 8- and 12-months post-randomisation. The appropriateness of the assumption of
8
9 4 approximate normality will also be considered and transformation to normality or non-parametric
10
11 5 methods used as appropriate. It is not anticipated that the number of falls will be approximately
12
13 6 normal, therefore, this will be summarised by treatment group using medians and IQRs and
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15 7 compared using non-parametric methods. The number and proportion of participants experiencing
16
17 8 an AE during follow-up will be summarised by treatment group and a logistic regression model
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19 9 adjusted for recruiting centre will be used to compare the rates in the two groups. Severity of AEs
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21 10 will also be summarised by treatment group.

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26 11 In addition, since previous work suggests that change in thoracic kyphosis at follow-up is closely
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28 12 related to baseline values, a subgroup analysis of thoracic kyphosis at follow-up will be completed
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30 13 dependent on whether the participant was kyphotic at baseline [33].

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34 14 All analyses will be performed for the intention to treat (ITT) population. This will include all
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36 15 randomised participants with available data who will be analysed according to their allocated
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38 16 intervention regardless of the treatment they received.

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41 17 In addition, analysis of the primary outcome (TUG at 12 months) will be repeated for the per
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43 18 protocol (PP) population which will include only those participants who received their allocated
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45 19 treatment. Participants with other major protocol deviations (e.g., recruited and later found to be
46
47 20 ineligible) will also be excluded from this population.

51 Health Economic Analysis

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54 22 The relative efficiency of the intervention will be assessed by within-trial cost-utility and cost-
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56 23 consequences analyses [34]. The evaluation will take an NHS and personal social services
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58 24 perspective. Resource use for the delivery of Opt-In and at participant level will be combined with
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1 unit cost from standard national sources to estimate average total costs. We will estimate the
2 incremental cost per quality-adjusted life year (QALY) (from EQ-5D-5L) and present the different cost
3 components and multiple benefits of Opt-In in a 'balance sheet' in the cost-consequences analysis.

4 Embedded Qualitative study

5 As part of the main study a nested qualitative study will take place. The qualitative element of this
6 study will involve a subset (12-15) of patients who undertake the Opt-In intervention who will be
7 invited to take part in 4 short (15-20 minute) interviews about their experiences and views about
8 exercise adherence and the adherence intervention at the following time points: i) following
9 assessment ii) during treatment (after 3 sessions), iii) post-treatment (after 4 months), and iv) at 12
10 months. The interviews may occur online via video-call or face-to-face in the person's home or at a
11 local clinic, depending on participant preference. The interviews will be audio recorded and
12 transcribed verbatim. Participants will be given an opportunity to check the interview transcript.
13 Focus groups will be conducted with physiotherapists who undertake the Opt-In intervention, asking
14 them to share their views about promoting exercise adherence and the Opt-In intervention, these
15 will be audio-recorded with a Dictaphone.

16 Purposive sampling will be used to achieve a sample which includes men and women, patients of
17 varying activity levels and patients of different ages and disease severity (pain/ number of fractures).
18 These factors may influence the ability to engage with an exercise programme. Since most research
19 regarding adherence in osteoporosis has previously been undertaken with women, it also
20 considered important to capture the views of men within the current study and to capture the
21 experiences of people with differing physical activity levels prior to the programme. The quality of a
22 qualitative study is not dependent on its sample size; however, the sample size needs to be
23 sufficiently large to enable relevant data to be obtained, without being so overly large that detailed
24 analysis is subsequently prevented [35]. Information about physiotherapists views of delivering the

1 adherence interventions will also be sought. All those who deliver the adherence techniques will be
2 invited to participate in a focus group.

3 Audio recordings will be listened to, and transcripts read until they become familiar. Data from the
4 interviews with physiotherapists and participants will be analysed separately to understand the
5 perspectives of each group. We will use collaborative methods to ensure a strong voice from PPI
6 members and research rigour. We will use thematic analysis, using the six steps proposed by Braun
7 and Clarke [36].

8 Patient and Public Involvement

9 The study funding application, intervention development and study materials preparation were
10 supported by our patient and public involvement members who will be involved across the course of
11 the study.

12 ETHICS AND DISEMINATION.

13 The study protocol was approved by West of Scotland Research Ethics Committee 4 (Reference
14 21/WS/0071). The University of Oxford is the sponsor. The trial is registered with the International
15 Standard Randomised Controlled Trials database ISRCTN reference number 14465704.

16 The protocol has been reported following the Standard Protocol Items: Recommendations for
17 Interventional Trials (SPIRIT) statement [37]. Results will be published reported following the
18 Consolidated Standards of Reporting Trials (CONSORT) guidelines [38]. The Template for
19 Intervention Description and Replication (TIDieR) statement will be used to report the intervention
20 ensuring replication is possible [39]. Results will be published in a peer reviewed journal with
21 authorship eligibility according to International Committee of Medical Journal Editors (ICJME)
22 criteria. Participants will be asked if they wish to have the results shared with them prior to
23 publication and we will share with those who request this. We plan to publish results in an

1 international peer-reviewed journal and at international rehabilitation and bone health focussed
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5 1 international peer-reviewed journal and at international rehabilitation and bone health focussed
6 2 conferences.

3 **Contributions of Authors:**

4 Karen L Barker: Chief Investigator, Conceived and designed the study, was awarded the funding and
5 had overall responsibility for the study design and delivery and drafted the manuscript. She is the
6 guarantor.

7 Jonathan Room: contributed to study design and provided specific content and edited manuscript.
8 Qualitative lead.

9 Erin Hannink: contributed to study design and provided specific content and edited manuscript

10 Ruth Knight (statistical co-applicant) performed the sample size calculation, prepared randomisation
11 schedules, planned statistical analysis methods

12 Meredith Newman (Trial Manager), trial design, intervention development, manualisation, training,
13 supervision, writing and reviewing report.

14 **Funding**

15 The study is supported by an independent grant from the Chartered Society of Physiotherapy
16 Charitable Trust (RP/19/01).

17 **Competing Interests**

18 All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf
19 and declare: no support from any organisation for the submitted work, other than funding
20 arrangements for the trial described in body of the text; no financial relationships with any
21 organisations that might have an interest in the submitted work in the previous three years; no
22 other relationships or activities that could appear to have influenced the submitted work.

1 Transparency

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6 2 The lead author (KLB) affirms that the manuscript is an honest, accurate and transparent account of
7
8 3 the study being reported.
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10 Figure Legends

11 Figure 1: Study Flow Diagram

12 Figure 2: Logic Model for intervention

13 References

- 14 1. Gibbs JC, MacIntyre NJ, Ponzano M, et al. Exercise for improving outcomes after
15 2 osteoporotic vertebral fracture. *Cochrane Database Syst Rev.* 2019 Jul 5; 7:
16 3 CD008618. doi: 10.1002/14651858.
- 17 2. Barker K, Newman M, Stallard N, et al. Physiotherapy Rehabilitation for
18 3 Osteoporotic Vertebral Fracture: A Randomised Controlled Trial and economic
19 4 evaluation (PROVE Trial). *Osteoporos Int*, 2019 Nov 12.
- 20 3. Brooke-Wavell K, Skelton D, Barker KL, Clark EM, de Biase S, Arnold S, Paskins Z,
21 4 Robinson KR, Lewis RM, Tobias JH, Ward KA, Whitney J, Leyland S. Strong, steady
22 5 and straight: UK consensus statement on physical activity and exercise for
23 6 osteoporosis. *Br J Sports Med* 2022 May 16 bjsports-2021-104634.
- 24 4. [https://strwebprdmedia.blob.core.windows.net/media/kuphgv1u/ros-guidance-
25 5 on-managing-symptoms-of-vertebral-fractures-2022.pdf](https://strwebprdmedia.blob.core.windows.net/media/kuphgv1u/ros-guidance-on-managing-symptoms-of-vertebral-fractures-2022.pdf). Accessed 17.08.22
- 26 5. Gold DT, Shipp KM, Pieper CF, et al. Group treatment improves trunk strength and
27 6 psychological status in older women with vertebral fractures: results of a RCT. *J
28 7 Am Geriatr Soc* 2004; 52:1471–1478.
- 29 6. Bergström I et al. Back extensor training increases muscle strength in
30 7 postmenopausal women with osteoporosis, kyphosis and vertebral fractures. *Adv
31 8 Physiother* 2011; 13:110–117.
- 32 7. Bergland A. et al. Effect of exercise on mobility, balance, and health-related
33 8 quality of life in osteoporotic women with a history of vertebral fracture: a
34 9 randomized, controlled trial. *Osteoporos Int.* 2011; 22: 1863-71.

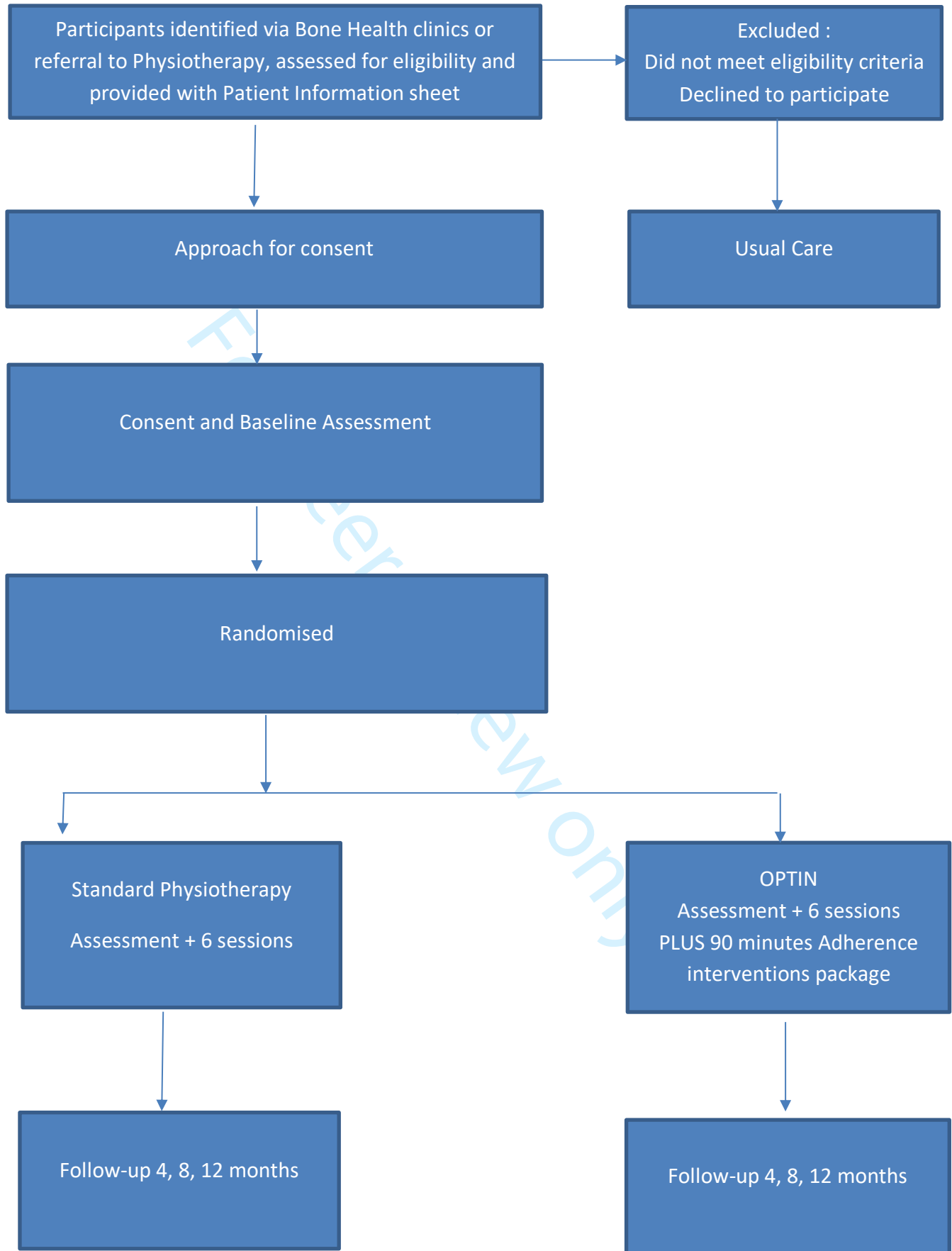
- 1
2
3 1 8. Olsen CF, Bergland A. The effect of exercise and education on fear of falling in
4 2 elderly women with osteoporosis and a history of vertebral fracture: results of a
5 3 randomized controlled trial. *Osteoporos Int*. 2014; 2: 2017-25.
- 6
7 4 9. Gibbs JC, McArthur C, Wark J et al. The effect home exercise in older women with
8 5 vertebral fractures: A pilot randomised controlled trial. *Physical Therapy*. 3 Jan
9 6 2020 doi.org/10.1093/ptj/pzz188
- 10
11 7 10. Evstigneeva L, Lesnyak O, Bultink IEM et al Effect of a twelve-month physical
12 8 exercise program of patients with osteoporotic vertebral fractures: a randomised
13 9 controlled trial. *Osteoporos Int* 2016 27: 2515-24.
- 14
15 10 11. Room J, Hannink E, Dawes H, et al. What interventions are used to improve
16 11 exercise adherence in older people and what behavioural techniques are they
17 12 based on? *BMJ Open*. 2017; 7(12): e019221.
- 18
19 13 12. Beavious C. Motivational interviewing to improve treatment adherence. *Joint*
20 14 *Bone Spine*. 2019 Feb 22: pii: S1297-319X (19)30042-9. doi:
21 15 10.1016/j.jbspin.2019.02.005.
- 22
23 16 13. NICE draft guidance on behaviour change URL:
24 17 [https://www.nice.org.uk/guidance/ph49/documents/behaviour-change-draft-](https://www.nice.org.uk/guidance/ph49/documents/behaviour-change-draft-guidance2)
25 18 [guidance2](https://www.nice.org.uk/guidance/ph49/documents/behaviour-change-draft-guidance2)(accessed 11th March 2020).
- 26
27 19 14. Room J, Boulton M, Dawes H, et al. Development of an exercise adherence
28 20 intervention for older people. The steps taken designing a complex intervention
29 21 for the AERO trial. *WCPT 2019: PO-J-09-SUN1*
- 30
31 22 15. Michie S, van Stralen M, West R. The behaviour change wheel: A new method for
32 23 characterising and designing behaviour change interventions. *Implementation*
33 24 *Science* 2011, 6:42.
- 34
35 25 16. Rodrigues IB, Jonathan D, Adachi JD, Beattie5 KA, MacDermid JC. Development
36 26 and validation of a new tool to measure the facilitators, barriers and preferences
37 27 to exercise in people with osteoporosis. *BMC Musculoskeletal Disorders* 2017
38 28 18:540. DOI 10.1186/s12891-017-1914-5.
- 39
40 29 17. Drummond M, Sculpher M, Torrance G, O'Brien B, Stoddart G. *Methods for the*
41 30 *economic evaluation of health care programmes*: Oxford University Press; 2005.
- 42
43 31 18. Podsiadlo, D. and Richardson, S. (1991). "The timed "Up & Go": a test of basic
44 32 functional mobility for frail elderly persons." *J Am Geriatr Soc* 39(2): 142-148.
- 45
46 33 19. International Osteoporosis Foundation Quality of life questionnaires QUALEFFO-
47 34 41. URL: [https://www.osteoporosis.foundation/health-professionals/research-](https://www.osteoporosis.foundation/health-professionals/research-tools/quality-life-questionnaires)
48 35 [tools/quality-life-questionnaires](https://www.osteoporosis.foundation/health-professionals/research-tools/quality-life-questionnaires) (accessed 30 March 2022).
- 49
50 36 20. Newman M, Newman R, Hughes T, Vadher K, Barker KL. Is the timed loaded
51 37 standing test a valid measure of back muscle endurance in people with vertebral
52 38 osteoporosis? *Osteoporos Int*. 2018; 29:893–905.
- 53
54 39 21. Greendale GA, Nili NS, Huang MH, Seeger L, Karlamangla AS. The reliability and
55 40 validity of three non-radiological measures of thoracic kyphosis and their relations
56 41 to the standing radiological Cobb angle. *Osteoporos Int* 2011; 22:1897–905.

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22. Jensen, M.P. and Karoly, P. (2011). "Self-report scales and procedures for assessing pain in adults", in Turk, D.C. and Melzack, R. (eds). Handbook of pain assessment, 3rd edition. New York, Guilford Press, 19-44.
23. Weiner DK, Duncan PW et al. Functional reach: a marker of physical frailty. *J Am Geriatr Soc* 1992; 40(3):203-7.
24. Steffen TM, Hacker TA, Mollinger L. Age- and gender-related test performance in community-dwelling elderly people: Six-Minute Walk Test, Berg Balance Scale, Timed Up and Go Test, and gait speeds. *Phys Ther* 2002; 82:128-37.
25. Delbaere K, Close JCT et al. The falls efficacy scale international (FES-I). A comprehensive longitudinal validation study. *Age and Ageing* 2010; 39: 201-16.
26. Abizanda P, Navarro JL et al. Validity and usefulness of handheld- dynamometry for measuring muscle strength in community-dwelling older persons. *Arch Gerontol Geriatr*. 2012; 54(1): 21-7.
27. Resnick B and Jenkins LS. Testing the reliability and validity of the self-efficacy for exercise scale. *Nurs Res* 49 (3): 154-159.
28. Newman-Beinart NA et al. The development and initial psychometric evaluation of a measure assessing adherence to prescribed exercise: the Exercise Adherence Rating Scale (EARS). *Physiotherapy* 103 (2017) 180-85.
29. Herdman M, Gudex C, Lloyd A et al. Development and preliminary testing of the new five-level version of the EQ-5D-5L (EQ-5D-5L). *Qual Life Res* 2011; 20 (10): 1727-36.28.
30. Wright A, Cook C, Baxter G, et al. A comparison of 3 methodological approaches to defining major clinically important improvements of 4 performance measures in patients with hip osteoarthritis. *J Orthop Sport Phys*. 2011; 41: 319 -27.
31. Schulz KF, Altman DG, Moher D, for the CONSORT Group. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. *BMC Trials*. 2010; 11:32.
32. Calvert M, Blazeby J, Altman DG, et al. Reporting of patient-reported outcomes in randomized trials: the CONSORT PRO Extension. *JAMA*. 2013;309(8):814-22.
33. Hannink E, Newman M, Barker KL. Does thoracic kyphosis severity predict response to physiotherapy rehabilitation in patients with osteoporotic vertebral fracture? A secondary analysis of the PROVE RCT. *Physiotherapy* Feb 17, 2022,
34. Drummond M, Sculpher M, Torrance G, O'Brien B, Stoddart G. *Methods for the economic evaluation of health care programmes*: Oxford University Press; 2005.
35. Sandelowski, M., *Sample size in qualitative research*. *Research in Nursing and Health*, 1995. 18(2): p. 179-183.
36. Braun V, Clarke V. What can "thematic analysis" offer health and wellbeing researchers? *Int J Qual Stud Health Well-being*. 2014; 9:26152.
37. Chan A-W, Tetzlaff JM, Gotzsche PC et al. SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. *BMJ* 2013;346: e7586.

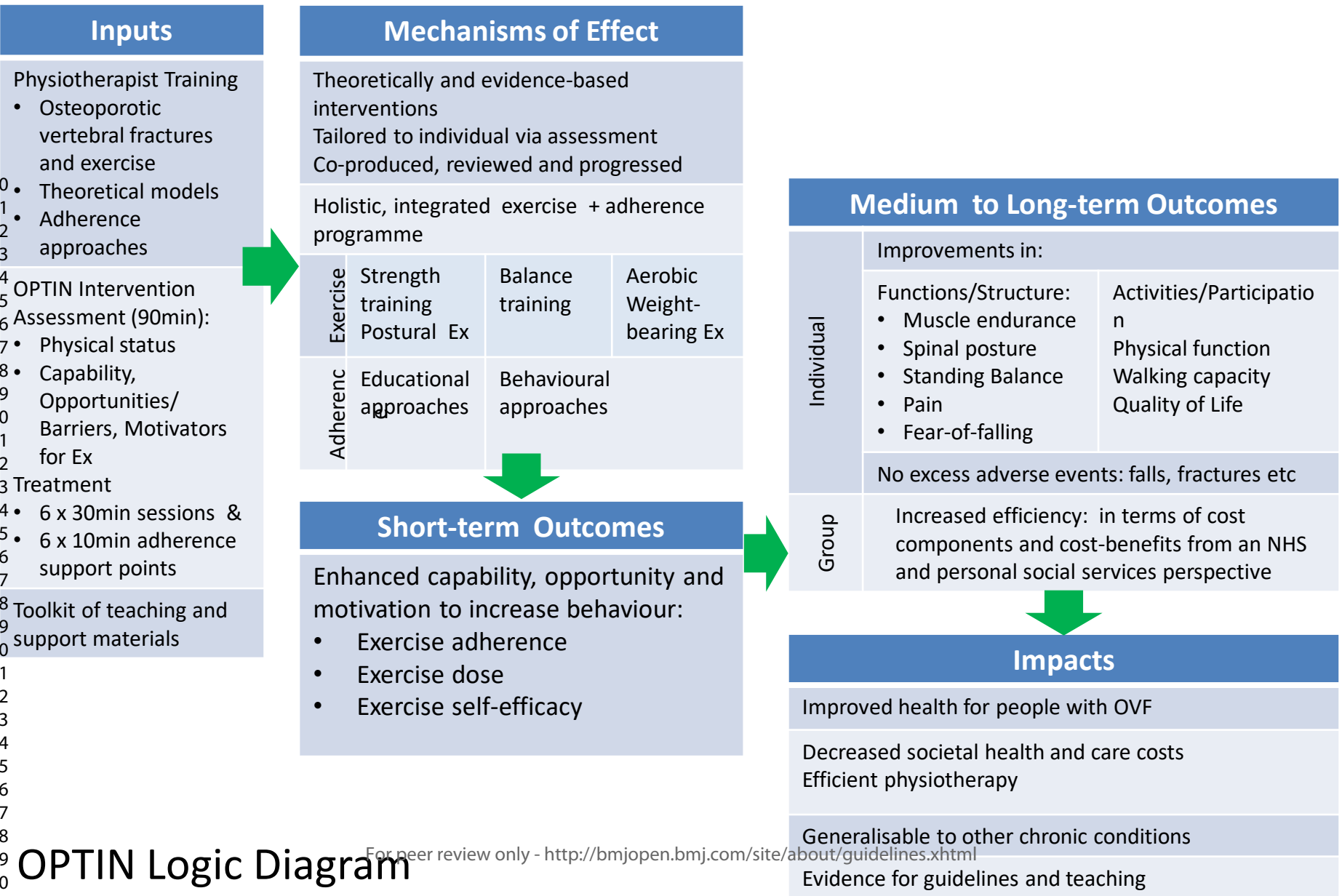
- 1
2
3 1 38. Schulz KF, Altman DG, Moher D et al. CONSORT 2010 statement: updated
4 2 guidelines for reporting parallel group randomised trials. BMJ 2010;340:c332.
5
6 3 39. Hoffmann TC, Glasziou PP, Boutron I et al. Better reporting of interventions:
7 4 template for intervention description and replication (TIDieR) checklist and guide.
8 5 BMJ 2014; 348: g1687.
9
10 6
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For peer review only



Qualitative Interviews n =15-20 participants
Focus group Physiotherapists

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OPTIN Logic Diagram



STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description
Administrative information		
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym Title Page Lines 1-3
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry Page 3 Line 21
	2b	All items from the World Health Organization Trial Registration Data Set
Protocol version	3	Date and version identifier Page 3 Line 22
Funding	4	Sources and types of financial, material, and other support Page 23 lines 9/10
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors Title page and Page 22/23
	5b	Name and contact information for the trial sponsor Page 19 Line 12
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)
Introduction		
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention P5-6
	6b	Explanation for choice of comparators P6
Objectives	7	Specific objectives or hypotheses P6

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Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory) P6 L22-3
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Methods: Participants, interventions, and outcomes

Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained P7 L10
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Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists) P7-8
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Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered P10-11
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	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease) n/a
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	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests) p10/11
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	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial p12
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Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended p12-14
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Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure) Table 1
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Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations P15
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Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size P8
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Methods: Assignment of interventions (for controlled trials)

Allocation:

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2	Sequence	16a	Method of generating the allocation sequence (eg, computer-
3	generation		generated random numbers), and list of any factors for stratification.
4			To reduce predictability of a random sequence, details of any planned
5			restriction (eg, blocking) should be provided in a separate document
6			that is unavailable to those who enrol participants or assign
7			interventions P9
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10	Allocation	16b	Mechanism of implementing the allocation sequence (eg, central
11	concealment		telephone; sequentially numbered, opaque, sealed envelopes),
12	mechanism		describing any steps to conceal the sequence until interventions are
13			assigned p9
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15	Implementation	16c	Who will generate the allocation sequence, who will enrol participants,
16			and who will assign participants to interventions P9
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19	Blinding	17a	Who will be blinded after assignment to interventions (eg, trial
20	(masking)		participants, care providers, outcome assessors, data analysts), and
21			how P 9
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23		17b	If blinded, circumstances under which unblinding is permissible, and
24			procedure for revealing a participant's allocated intervention during
25			the trial n/a
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Methods: Data collection, management, and analysis

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30	Data collection	18a	Plans for assessment and collection of outcome, baseline, and other
31	methods		trial data, including any related processes to promote data quality (eg,
32			duplicate measurements, training of assessors) and a description of
33			study instruments (eg, questionnaires, laboratory tests) along with
34			their reliability and validity, if known. Reference to where data
35			collection forms can be found, if not in the protocol p10
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38		18b	Plans to promote participant retention and complete follow-up,
39			including list of any outcome data to be collected for participants who
40			discontinue or deviate from intervention protocols
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42	Data	19	Plans for data entry, coding, security, and storage, including any
43	management		related processes to promote data quality (eg, double data entry;
44			range checks for data values). Reference to where details of data
45			management procedures can be found, if not in the protocol
46			
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48	Statistical	20a	Statistical methods for analysing primary and secondary outcomes.
49	methods		Reference to where other details of the statistical analysis plan can be
50			found, if not in the protocol P15-6
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52		20b	Methods for any additional analyses (eg, subgroup and adjusted
53			analyses) n/a
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55		20c	Definition of analysis population relating to protocol non-adherence
56			(eg, as randomised analysis), and any statistical methods to handle
57			missing data (eg, multiple imputation) P15-17
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Methods: Monitoring

Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed n/a
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial n/a
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct P14-15
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor

Ethics and dissemination

Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval P22
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) P 19
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) P8
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable n/a
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site P23
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation n/a

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| Dissemination policy | 31a | Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions P19 |
| | 31b | Authorship eligibility guidelines and any intended use of professional writers P19 |
| | 31c | Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code |

14 Appendices

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|----------------------------|----|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Informed consent materials | 32 | Model consent form and other related documentation given to participants and authorised surrogates |
| Biological specimens | 33 | Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable |

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*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "[Attribution-NonCommercial-NoDerivs 3.0 Unported](https://creativecommons.org/licenses/by-nc-nd/3.0/)" license.

BMJ Open

Physiotherapy exercise rehabilitation with tailored exercise adherence support for people with osteoporosis and vertebral fractures: Protocol for a randomised controlled trial – the Osteoporosis Tailored exercise adherence intervention (OPTIN) study.

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2022-064637.R2
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4 1 **Physiotherapy exercise rehabilitation with tailored exercise adherence support for people with**
5 **osteoporosis and vertebral fractures: Protocol for a randomised controlled trial – the Osteoporosis**
6 **2 Tailored exercise adherence intervention (OPTIN) study.**
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1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60

Introduction: Vertebral fragility fractures affect at least 20% of the older population in the UK. Best practice guidelines recommend the use of exercise to slow the rate of bone loss, to maintain muscle strength and physical function, and to prevent falls and further fractures. However, treatment effects are often small and difficult to sustain and adherence, or the extent to which patients engage in treatment, has been identified as an important issue by many studies. Our hypothesis is that integrating adherence intervention strategies with an exercise intervention will be beneficial. We will compare physiotherapy exercise rehabilitation with adherence support versus physiotherapy exercise rehabilitation alone in terms of effects on (a) physical function, quality of life, and fear of falling and (b) exercise self-efficacy and adherence.

Methods and Analysis: A multicentre, two-arm, parallel group, superiority randomised controlled trial (RCT) with blinded assessments at baseline (0) and 4, 8, and 12 months, with a nested qualitative study and health economic analysis. 116 participants will be allocated to either (i) out-patient physiotherapy which will include a musculoskeletal assessment and treatment including balance, posture, strength training and low impact weight-bearing exercises over 16 weeks; or (ii) Opt-In intervention. This includes standard physiotherapy as above plus an additional, integrated assessment interview (30mins) and 60 minutes of adherence support spread over the subsequent 16 weeks.

Ethics and Dissemination: The study protocol was approved by West of Scotland Research Ethics Committee 4 (21/WS/0071). Trial registration number ISRCTN 14465704. The paper is based on Protocol v4.

Strengths and Limitations of this study

- The Physiotherapy exercise rehabilitation with tailored exercise adherence support for people with osteoporosis and vertebral fractures (Opt-In) study is a multicentre randomised controlled trial with an embedded qualitative study and economic evaluation.
- It will recruit from at least six NHS hospitals.
- The intervention addresses adherence which is an important confounder in many trials of physiotherapy.
- The intervention was developed using current research evidence, input from expert clinicians, researchers and patient / public representatives.
- Due to the nature of the interventions the physiotherapists delivering the treatments and the participants cannot be blinded.

1 Introduction

2 Vertebral fragility fractures (VFFs) affect at least 20% of the older population in the UK and present a
3 significant health and economic burden [1, 2]. They are associated with back pain, fatigue, low
4 mood, restrictions in physical function and activities of daily living, and marked, persistent
5 reductions in quality of life (QoL) [1, 2]. Without treatment, progression and functional decline are
6 expected. Conservative treatment for osteoporosis includes bone protective medications and
7 lifestyle adaptations. Guidelines recommend people with osteoporosis keep active and exercise to
8 slow the rate of bone loss, to maintain muscle strength and physical function and to prevent falls
9 and further fractures [3,4]. Exercise prescription with multi-component exercise programmes that
10 include postural, balance, aerobic weight-bearing and strength exercises are recommended [1-3].

11 Trials evaluating exercise in people with VFFs have reported benefits across a range of outcomes [1,
12 2, 5-10], with a recent Cochrane review concluding there is moderate-quality evidence that exercise
13 improves physical function [1]. However, treatment effects are often small and difficult to sustain
14 [1, 2, 5-10]. For example, in the PROVE trial, significant, clinically relevant benefits to back muscle
15 endurance, balance, walking capacity and physical function following physiotherapy exercise at 4
16 months post-randomisation did not persist at 12 months [2]. Adherence, or the extent to which
17 patients engage in treatment, has been identified as an important issue by many studies [1, 2, 5-6,
18 9]. Partial adherence or non-adherence is associated with worse outcomes and conversely, higher
19 adherence with better outcomes [1, 2, 5-10].

20 Multiple factors affect exercise adherence in older people with chronic health conditions including
21 osteoporosis [11, 12]. These include low exercise self-efficacy, low motivation, depression,
22 insufficient exercise knowledge or skill, physical ability, negative views about treatment and exercise
23 programme design [11,12]. Considering this complexity, interventions to support adherence that
24 recognize personal barriers and facilitators to exercise and that can draw upon multiple adherence
25 techniques are recommended [12, 13].

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2
3 1 Behavioural approaches can include interventions that support exercise through providing additional
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5 2 monitoring, interventions that aim to alter thinking patterns that contribute to non-adherence and
6
7 3 ones that strengthen behaviours that support adherence [12]. Motivational interviewing is a
8
9
10 4 collaborative process that explores potential ambivalence, obstacles and facilitators surrounding
11
12 5 behaviour change [6]. There is evidence that additional monitoring, prompts and feedback can
13
14 6 benefit adherence in older adults e.g., via telephone call/ text messages, wearable activity monitors
15
16 7 or by enriching environmental cues [1]. Incorporating exercise into everyday routines can make it
17
18 8 easier to initiate and sustain and creating 'Exercise Action Plans' that specify when, where and how
19
20 9 exercises are undertaken can support this process [1, 13]. Using an intervention mapping approach,
21
22
23 10 we developed an exercise adherence intervention underpinned theoretically by the Capability,
24
25 11 Opportunity, Motivation - Behaviour (COM-B) behaviour change model [14, 15].
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29 12 **Aims**

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32 13 The aims of this study are:

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35 14 • To compare physiotherapy exercise rehabilitation with adherence support with
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37 15 physiotherapy exercise rehabilitation alone in terms of effects on: (a) physical function,
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39 16 quality of life, and fear of falling and (b) exercise self-efficacy and adherence.
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41 17 • To explore patient and physiotherapist views of the intervention and of adhering to exercise.
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44 18 • To understand if physiotherapy exercise rehabilitation with adherence support is cost-
45
46 19 effective.
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49 20 **METHODS AND ANALYSES**

50 51 52 21 Study design

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55 22 A multicentre, two-arm, parallel group, superiority randomised controlled trial (RCT) with blinded
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57 23 assessments at baseline (0) and 4, 8, and 12 months following randomisation, with a nested
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59 24 qualitative study and health economic analysis. Participants will be allocated to either (i) outpatient
60

1 physiotherapy which will include a musculoskeletal assessment and 6 treatment sessions over 16
2 weeks based on the current best practice guidance from the Royal Osteoporosis Society; or (ii) the
3 Opt-In intervention. This includes outpatient physiotherapy as described above, plus an additional,
4 integrated assessment interview (30mins) and 60 minutes of adherence support spread over the
5 subsequent treatment period of 16 weeks as prescribed by the physiotherapist in collaboration with
6 the participant. Sessions in both arms can be in-person or virtually via video-call/ telephone as
7 agreed between participant and therapist (**Figure 1**).

8 The trial started recruitment of patients in August 2021 and will continue recruiting until June 2023.

9 Setting

10 At least six National Health Service (NHS) hospitals and their related physiotherapy services.

11 Study Participants

12 Adults aged 55 years or over who have a diagnosis of at least one previous osteoporotic vertebral
13 fracture and back pain.

14 Eligibility

15 Inclusion Criteria

16 Participants may enter the study if they meet ALL the following criteria:

- 17 • Men and women ≥ 55 years: all women must be at least 1 year post-menopausal.
- 18 • One or more VFFs confirmed by radiography, X-Ray, MRI, CT or DEXA scan, people with VFF
19 of any severity and at any time-point post-fracture are eligible.
- 20 • They must have had an episode of back pain in the previous 12 months.
- 21 • All must be able to walk at least 10 metres independently with or without a walking aid.

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3 1 Exclusion Criteria
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6 2 Participants may not enter the study if ANY of the following apply:
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- 9 3 • Current conditions that would make participating in physiotherapy or exercise unsafe or
10
11 4 confound results. This includes those with significant neurological and psychiatric conditions,
12
13 5 severe unstable cardiovascular or pulmonary disease.
14
15
16 6 • Bone loss secondary to other metabolic disorders, diseases or medication e.g., rheumatoid
17
18 7 arthritis, anorexia, cancer, coeliac disease, steroid use.
19
20
21 8 • Individuals whose primary problem is back pain that involves pain radiating into the lower
22
23 9 limbs.
24
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26 10 • Vertebroplasty, facet joint injection or physiotherapy within past 12 weeks.
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31 11 Recruitment
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33 12 A member of the patient's direct care team will identify potential participants with VFFs via clinic
34
35 13 lists and electronic medical records from relevant metabolic bone clinics, radiology clinics (DEXA),
36
37 14 physiotherapy referral lists, and from Rheumatology clinics.
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39
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41 15 Screening and eligibility assessment
42
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44 16 Potential participants, who respond to an invitation letter will be contacted by telephone to discuss
45
46 17 the study further, to check eligibility and to answer any questions. Patients who do not meet the
47
48 18 eligibility criteria or who do not wish to participate will receive standard NHS treatment. We will
49
50 19 record the age and gender of these patients to assess the generalisability of those recruited.
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54 20 Consent
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57 21 Participants who are eligible and willing to proceed will be approached for informed consent.; they
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59 22 and the researcher will sign and date a consent form. For participants who are recruited to the
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3 1 additional nested qualitative study and interviewed on-line or via telephone, informed consent will
4
5 2 be obtained verbally before the interview. The researcher taking consent will read, and fill out, the
6
7 3 consent form on behalf of the participant and then sign the form [Supplementary file].
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12 13 14 5 Randomisation

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16
17 6 Consented participants will be randomised 1:1 using a computer-generated randomisation schedule
18
19 7 prepared by the trial statistician (RK). Individual randomisation will be stratified by recruitment
20
21 8 centre and permuted blocks of varying undisclosed sizes will be used. The randomisation schedule
22
23 9 will be concealed in sequentially numbered, opaque, sealed envelopes for each site. A study
24
25 10 administrator who has no interaction with blinded study staff will manage these envelopes. The
26
27 11 administrator will open the randomisation envelope, and then communicate with the local site who
28
29 12 will make the participant aware of their allocated group and refer for physiotherapy; making sure
30
31 13 that participants are allocated to physiotherapists delivering the treatment for their allocated arm.
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35 14 Blinding

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38 15 Physiotherapists delivering the interventions and participants will be told the treatment allocation.
39
40 16 Initial baseline assessment will occur prior to randomisation and the researcher undertaking
41
42 17 assessments will not be involved in any part of the randomisation procedure to ensure that they are
43
44 18 not able to bias the group allocation. The researcher conducting follow-up measures and the
45
46 19 research team personnel entering data will also not be informed of allocated group and participants
47
48 20 will be asked and reminded not to disclose their treatment group to the researcher at follow-up
49
50 21 appointments.
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52
53

54 55 22 Interventions

56 57 58 23 Training and monitoring 59 60

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3 1 Sessions in both arms can be delivered in-person or virtually via video-call/ telephone as agreed
4
5 2 between participant and therapist; to allow flexibility and resilience as COVID restrictions on physical
6
7 3 attendance vary. Treatments were standardised and manualised and the study team provided
8
9 4 training in the multi-component exercise therapy treatments (delivered to all participants) to all
10
11 5 treating physiotherapists. Training in the behavioural adherence support intervention which
12
13 6 comprised assessment and a set of 9 behavioural interventions (the Opt-In toolkit) was delivered
14
15 7 separately to the therapists in the Opt-In arm. Treating physiotherapists will record the delivery and
16
17 8 content of each treatment session in adherence logs for each participant. Regular site visits will be
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19 9 carried out to monitor intervention fidelity.
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24 10 Standard Care

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27 11 Participants will be offered a 1-hour physiotherapy assessment and six individual outpatient
28
29 12 physiotherapy sessions spread over 16 weeks [2]. The physiotherapy will include a musculoskeletal
30
31 13 assessment and treatment including a multi-component, progressed balance, posture, strength
32
33 14 training and low impact weight-bearing exercise [3]. Exercise intensity will be assessed using the 10-
34
35 15 point Rating of Perceived Exertion scale (CR10-RPE), so participants work at a moderately hard to
36
37 16 hard (RPE 4-6) intensity. Although current practice may vary, the package agreed as the standard
38
39 17 care is based on consensus, best practice guidelines and successful delivery in the PROVE trial
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41 18 exercise arm [2] and aims to be a credible representation of current best practice treatment across
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43 19 the NHS. Treating therapists will receive prior training on prescription of the exercises [2].
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48 20 Opt -In

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51 21 Participants allocated to Opt-In will receive the standard package described above, plus an
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53 22 additional, integrated assessment interview (30mins) and 60 minutes of adherence support spread
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55 23 over the subsequent treatment period of 16 weeks in an individualised pattern as required by the
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57 24 participant.
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3 1 Participants in the Opt-In arm will complete the Personalized Exercise Questionnaire (PEQ). The PEQ
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5 2 was developed in Canada to support patient-centred exercise prescription for people with
6
7 3 osteoporosis and covers topics such as barriers to exercise and goals of treatment [16]. Treating
8
9 4 physiotherapists will have a collaborative discussion with the participant using a motivational
10
11 5 interviewing approach drawing upon PEQ responses and considering goals, motivators, facilitators,
12
13 6 and barriers surrounding exercise. It aims to provide physiotherapists with a deeper understanding
14
15 7 of patient motivations and circumstances, to strengthen the therapeutic alliance and the patient's
16
17 8 own motivations for adopting exercise [12]. Using their assessment findings, the questionnaire and
18
19 9 collaborative interview the physiotherapist will assess a participant's exercise capability (C),
20
21 10 opportunity (O) and motivation (M) to carry out exercise behaviour (B) (COM-B) and select an
22
23 11 adherence technique from the Opt-In toolkit in response [14]. Techniques can include education
24
25 12 about osteoporosis and exercises, education about and practice of fall prevention strategies,
26
27 13 Exercise Action Plans, a contact telephone call, and self-monitoring and feedback strategies such as,
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29 14 exercise confidence rating scales or using an exercise diary. Techniques are linked to COM-B
30
31 15 domains to facilitate physiotherapist decision-making e.g., Education improves capability and
32
33 16 motivation (C, M) and a diagrammatic decision aid was developed to facilitate rapid decision-making
34
35 17 during treatment. Each Opt-In arm treating physiotherapist received a toolkit and training by the
36
37 18 study team about techniques and how to use them. Physiotherapists were asked to prescribe at
38
39 19 least 3 adherence techniques from the Opt-In toolkit over 16 weeks but could use more. The exact
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41 20 techniques selected were personalised to the patient as was the pattern and spread of the 60-
42
43 21 minute adherence support time. Participants in the intervention arm were given a folder that
44
45 22 included their exercises and selected adherence materials e.g., exercise diary, education leaflet,
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47 23 action plan record. Figure 2 summarises the intervention in a logic model.
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25 Concomitant care

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3 1 Other aspects of health and social care will continue as usual. Analgesia and other medication use
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5 2 will be collected by self-report diary. Additional treatments sourced outside of the trial including
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7 3 contact with general practitioners and other health care professionals will be recorded in self-report
8
9 4 health utilisation diaries in which participants will asked to record their use of health and social care
10
11 5 services across the study e.g., GP, nurse, other physio, hospital admissions, home carer visits in
12
13 6 standardised study diaries. Diaries will be from 0-4, 4 to 8 and 8 to 12 months [17].
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17 Outcome Measures

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20 8 The primary outcome measure will be the Timed Up and Go (TUG) at 12 months. The TUG is a test of
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22 9 balance, lower limb strength and walking ability with established reliability and validity. It records
23
24 10 the time a person takes to stand up from a chair, walk 3 metres at a self-selected speed, turn, walk
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26 11 back and sit down [18].
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30 12 Secondary outcome measures are:

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33 13 • QUALEFFO 41: a disease specific measure of health-related quality of life (QoL) applicable to
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35 14 patients with osteoporosis and vertebral fractures. It is a self-administered questionnaire
36
37 15 that provides scores on five domains: pain, physical function, social function, general health
38
39 16 perception, mental performance, and a total score. [19].
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46 18 • Timed Loaded Standing (TLS): an assessment of shoulder and back muscle endurance for
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48 19 people with VFF(s). [20].
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55 21 • Thoracic kyphosis angle: measured non-radiographically using a flexicurve ruler, allowing an
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57 22 angle of kyphosis to be calculated which is approximated to radiological measures of
58
59 23 kyphosis (Cobb angle) using a standardised formula [21].
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3 1 • Back pain: measured with a 10-point Numeric Pain Rating Scale (NPRS) [22].
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8 3 • Functional Reach (FR) test: a measure of dynamic standing balance developed for older
9
10 4 adults. The test has been used in people with VFF and performance is predictive of falls
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12 5 risk [23].
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18 7 • Six-minute walk (6MW) test: a measure of functional walking capacity and aerobic cardio-
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20 8 respiratory fitness [24].
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23 9
24 10 • Falls Efficacy Scale International (FES-I): a 16 item (3 minute) self-report measure of fear or
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26 11 concern about falling during activities [25].
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33 13 • Grip Strength: is the maximum force the hand and forearm muscles can generate measured
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35 14 with an isometric hand dynamometer in kilograms; maximum strength is the mean of three
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37 15 trials (3 seconds each) and measured for both hands [26].
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40 16
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43 17 • Self-efficacy for exercise (SEE) scale: a brief (<5 minute) 9-item scale that asks participants to
44
45 18 rate how confident they would be that they would engage in exercise on a 10-point scale
46
47 19 (not confident to very confident) under different situations e.g., if they were tired. SEE
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49 20 ratings are predictive of exercise behaviour [27].
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56 22 • Adherence. This will be measured in two ways:
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3 1 a. Attendance records via clinician completed treatment logs, including a checkbox to log
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5 2 whether adherence techniques have been prescribed (intervention group only).
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7
8 3 b. Exercise adherence rating scale (EARS): a brief 6-item scale that asks participants to
9
10 4 describe how they do their recommended exercises on a 5-point scale [28].
11
12
13
14 5 • Falls: documented on the CRF and prospectively using participant completed event diaries.
15
16 6 These will be collected in blocks from 0-4 months, 4 to 8 months, and 8 to 12 months during
17
18 7 the study. Incidence and severity formation will be recorded e.g., nature of the fall, its
19
20 8 outcome (no-harm, fracture etc) and any treatment required [2].
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23 9
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25 10 • EQ-5D-5L is a short, generic measure of health related QoL and will be completed to assist
26
27 11 assessment of health economics [29].
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36 14 A summary of outcome measures and timepoints is shown in Table 1 (**Table 1**).
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A summary of outcome measures and timepoints is shown in Table 1 (**Table 1**).

1

Time Point	Measurement	Enrolment	allocation	Baseline	4 months	8 months	12 months
Screening Log		X					
Eligibility confirmed		x					
Informed Consent		x					
Randomisation			x				
Demographic	Age, gender, weight, ethnicity,			x			
Primary OM	Timed Up & Go			x	x	x	x
Quality of Life	QUALEFFO 41			X	X	X	X
Fear Falling	FES-I			X	X	X	X
Back Pain Intensity	NRS-P			X	X	X	X
Back strength / endurance	TLS			X	X	X	X
Walking	6MWT			X	X	X	X
Balance	Functional Reach Test			X	X	X	X
Kyphosis	Flexicurve			X	X	X	X
Grip Strength	Dynamometer			x	x	x	x
EQ-5D-5L	Health economics			x	x	x	x
Falls	Number of reported falls. Nature; outcome of falls.				x	x	x
Exercise Self Efficacy	SEE			X	X	X	X
Exercise adherence	EARS			X	X	X	X
Exercise adherence	Sessions attended				x	x	x

2

3 Table 1: Time Points at which outcomes will be assessed.

4

5 Adverse events

6 Adverse events (AE) occurring because of the trial interventions will be recorded. Participants will

7 receive information on potential AEs resulting from the exercises and what they should do if they

1
2
3 1 experience an AE, as would be part of standard NHS procedure. Adverse symptoms in response to
4
5 2 treatment and any adverse events will be monitored by clinicians regularly and in line with local
6
7 3 departmental procedures and captured on adverse event forms, and via questions on the CRF.
8
9
10 4 A Serious AE (SAE) is any untoward medical occurrence related to the trial interventions that results
11
12 5 in death, is life-threatening, requires inpatient hospitalisation or prolongation of existing
13
14 6 hospitalisation, or results in persistent or significant disability/incapacity. SAEs are likely to be rare
15
16 7 and are unlikely to occur as a result of the exercise programmes delivered in this study.
17
18
19 8 Any reports of SAE will be reported to the trial office within 24 hours of the local research team
20
21 9 becoming aware of the event. They will be reviewed by an independent medically qualified assessor
22
23 10 within 3 days.
24
25
26
27

28 Statistics and analysis

31 Sample Size

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33
34 13 The primary outcome is the Timed Up & Go (TUG) test. This is the most widely used physical function
35
36 14 measure in RCTs of exercise for people with VFF [4]. The minimal clinically important difference
37
38 15 (MCID) for the TUG has not been established in people with VFF(s), but a MCID of 1.4s is reported for
39
40 16 similar older populations with chronic musculoskeletal disorders [30]. The study requires 104
41
42 17 participants (52 per arm) to be 80% powered to detect a 1.4s difference in TUG score between
43
44 18 groups at a 5% significance level (two-sided) assuming that the standard deviation is 2.5s. Similar
45
46 19 trials have had loss to follow-up rates of 10% at 12 months [2]. To account for this the sample size
47
48 20 has been inflated to 116 participants (58 per arm).
49
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53 Statistical Analysis

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55
56 22 The study will be reported according to the Consolidated Standards of Reporting Trials (CONSORT)
57
58 23 2010 statement utilising the nonpharmacological and patient-reported outcome extensions [31,32].
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3 1 Standard descriptive statistics will be used to describe the characteristics of the two groups at
4
5 2 baseline. Means and standard deviations (SDs) or medians and interquartile ranges (IQRs) as
6
7 3 appropriate will be used for continuous variables, and numbers and percentages will be used for
8
9 4 binary and categorical variables.

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12
13 5 Compliance with the intervention will be defined as participating in the extended interview and
14
15 6 prescription of at least 3 adherence support techniques. This will be recorded on treatment logs.
16
17 7 Details of the number of physiotherapy sessions attended will also be summarised by treatment
18
19 8 group. The number and proportion of participants who withdraw will be summarised along with
20
21 9 reasons for these. Deaths are not anticipated in this study, but details of any that do occur will also
22
23 10 be summarised by treatment arm.

24
25
26
27 11 Summary statistics will be presented for all comparative outcomes, and effect estimates will be
28
29 12 reported together with 95% confidence intervals with all tests carried out at a 5% two-sided
30
31 13 significance level.

32
33
34
35 14 At 12 months post-randomisation the two treatment groups will be compared on the TUG measure
36
37 15 using a multivariate linear regression model adjusting for recruiting centre (stratification factor), age
38
39 16 and baseline TUG score. An unadjusted t-test will also be undertaken. The TUG is also recorded at 4,
40
41 17 and 8 months after randomisation, and an additional analysis utilising all time points, using multi-
42
43 18 level modelling and including a treatment by time interaction if appropriate will be undertaken. For
44
45 19 each of these models, the assumption of approximate normality will be assessed by examining the
46
47 20 residuals. If this assumption is not met the first approach will be to consider a transformation to
48
49 21 achieve normality. If this is not possible, the two groups will be compared using non-parametric
50
51 22 methods (e.g., Mann-Whitney U-test). This analysis will be unadjusted and will consider each time
52
53 23 point separately.
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3 1 Similar analyses will be performed for secondary outcomes which can be considered approximately
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5 2 continuous (QUALEFFO-41, FES-1, NPRS, TLS, Grip strength, 6MW, FRT, Thoracic kyphosis, SEE and
6
7 3 EARS) at 4-, 8- and 12-months post-randomisation. The appropriateness of the assumption of
8
9 4 approximate normality will also be considered and transformation to normality or non-parametric
10
11 5 methods used as appropriate. It is not anticipated that the number of falls will be approximately
12
13 6 normal, therefore, this will be summarised by treatment group using medians and IQRs and
14
15 7 compared using non-parametric methods. The number and proportion of participants experiencing
16
17 8 an AE during follow-up will be summarised by treatment group and a logistic regression model
18
19 9 adjusted for recruiting centre will be used to compare the rates in the two groups. Severity of AEs
20
21 10 will also be summarised by treatment group.

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26 11 In addition, since previous work suggests that change in thoracic kyphosis at follow-up is closely
27
28 12 related to baseline values, a subgroup analysis of thoracic kyphosis at follow-up will be completed
29
30 13 dependent on whether the participant was kyphotic at baseline [33].

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34 14 All analyses will be performed for the intention to treat (ITT) population. This will include all
35
36 15 randomised participants with available data who will be analysed according to their allocated
37
38 16 intervention regardless of the treatment they received.

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41 17 In addition, analysis of the primary outcome (TUG at 12 months) will be repeated for the per
42
43 18 protocol (PP) population which will include only those participants who received their allocated
44
45 19 treatment. Participants with other major protocol deviations (e.g., recruited and later found to be
46
47 20 ineligible) will also be excluded from this population.

21 Health Economic Analysis

22
23 22 The relative efficiency of the intervention will be assessed by within-trial cost-utility and cost-
24
25 23 consequences analyses [34]. The evaluation will take an NHS and personal social services
26
27 24 perspective. Resource use for the delivery of Opt-In and at participant level will be combined with
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1 unit cost from standard national sources to estimate average total costs. We will estimate the
2 incremental cost per quality-adjusted life year (QALY) (from EQ-5D-5L) and present the different cost
3 components and multiple benefits of Opt-In in a 'balance sheet' in the cost-consequences analysis.

4 Embedded Qualitative study

5 As part of the main study a nested qualitative study will take place. The qualitative element of this
6 study will involve a subset (12-15) of patients who undertake the Opt-In intervention who will be
7 invited to take part in 4 short (15-20 minute) interviews about their experiences and views about
8 exercise adherence and the adherence intervention at the following time points: i) following
9 assessment ii) during treatment (after 3 sessions), iii) post-treatment (after 4 months), and iv) at 12
10 months. The interviews may occur online via video-call or face-to-face in the person's home or at a
11 local clinic, depending on participant preference. The interviews will be audio recorded and
12 transcribed verbatim. Participants will be given an opportunity to check the interview transcript.
13 Focus groups will be conducted with physiotherapists who undertake the Opt-In intervention, asking
14 them to share their views about promoting exercise adherence and the Opt-In intervention, these
15 will be audio-recorded with a Dictaphone.

16 Purposive sampling will be used to achieve a sample which includes men and women, patients of
17 varying activity levels and patients of different ages and disease severity (pain/ number of fractures).
18 These factors may influence the ability to engage with an exercise programme. Since most research
19 regarding adherence in osteoporosis has previously been undertaken with women, it also
20 considered important to capture the views of men within the current study and to capture the
21 experiences of people with differing physical activity levels prior to the programme. The quality of a
22 qualitative study is not dependent on its sample size; however, the sample size needs to be
23 sufficiently large to enable relevant data to be obtained, without being so overly large that detailed
24 analysis is subsequently prevented [35]. Information about physiotherapists views of delivering the

1 adherence interventions will also be sought. All those who deliver the adherence techniques will be
2 invited to participate in a focus group.

3 Audio recordings will be listened to, and transcripts read until they become familiar. Data from the
4 interviews with physiotherapists and participants will be analysed separately to understand the
5 perspectives of each group. We will use collaborative methods to ensure a strong voice from PPI
6 members and research rigour. We will use thematic analysis, using the six steps proposed by Braun
7 and Clarke [36].

8 Patient and Public Involvement

9 The study funding application, intervention development and study materials preparation were
10 supported by our patient and public involvement members who will be involved across the course of
11 the study.

12 ETHICS AND DISEMINATION.

13 The study protocol was approved by West of Scotland Research Ethics Committee 4 (Reference
14 21/WS/0071). The University of Oxford is the sponsor. The trial is registered with the International
15 Standard Randomised Controlled Trials database ISRCTN reference number 14465704.

16 The protocol has been reported following the Standard Protocol Items: Recommendations for
17 Interventional Trials (SPIRIT) statement [37]. Results will be published reported following the
18 Consolidated Standards of Reporting Trials (CONSORT) guidelines [38]. The Template for
19 Intervention Description and Replication (TIDieR) statement will be used to report the intervention
20 ensuring replication is possible [39]. Results will be published in a peer reviewed journal with
21 authorship eligibility according to International Committee of Medical Journal Editors (ICJME)
22 criteria. Participants will be asked if they wish to have the results shared with them prior to
23 publication and we will share with those who request this. We plan to publish results in an

1 international peer-reviewed journal and at international rehabilitation and bone health focussed
2
3
4
5 1 international peer-reviewed journal and at international rehabilitation and bone health focussed
6 conferences.
7

8 **Contributions of Authors:**

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11 4 Karen L Barker: Chief Investigator, Conceived and designed the study, was awarded the funding and
12 had overall responsibility for the study design and delivery and drafted the manuscript. She is the
13 guarantor.
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19 7 Jonathan Room: contributed to study design and provided specific content and edited manuscript.
20
21 8 Qualitative lead.
22

23
24 9 Erin Hannink: contributed to study design and provided specific content and edited manuscript
25

26
27 10 Ruth Knight (statistical co-applicant) performed the sample size calculation, prepared randomisation
28 schedules, planned statistical analysis methods
29

30
31
32 12 Meredith Newman (Trial Manager), trial design, intervention development, manualisation, training,
33 supervision, writing and reviewing report.
34
35
36

37 **Funding**

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39
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41 15 The study is supported by an independent grant from the Chartered Society of Physiotherapy
42 Charitable Trust (RP/19/01).
43
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46 **Competing Interests**

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48
49 18 All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf
50 and declare: no support from any organisation for the submitted work, other than funding
51 arrangements for the trial described in body of the text; no financial relationships with any
52 organisations that might have an interest in the submitted work in the previous three years; no
53 other relationships or activities that could appear to have influenced the submitted work.
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1 Transparency

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6 2 The lead author (KLB) affirms that the manuscript is an honest, accurate and transparent account of
7
8 3 the study being reported.
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10 11 4 Figure Legends

12 13 14 5 Figure 1: Study Flow Diagram

15 16 17 6 Figure 2: Logic Model for intervention

18 19 20 7 References

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22
23 8 1. Gibbs JC, MacIntyre NJ, Ponzano M, et al. Exercise for improving outcomes after
24 9 osteoporotic vertebral fracture. *Cochrane Database Syst Rev.* 2019 Jul 5; 7:
25 10 CD008618. doi: 10.1002/14651858.
- 26
27 11 2. Barker K, Newman M, Stallard N, et al. Physiotherapy Rehabilitation for
28 12 Osteoporotic Vertebral Fracture: A Randomised Controlled Trial and economic
29 13 evaluation (PROVE Trial). *Osteoporos Int*, 2019 Nov 12.
- 30
31 14 3. Brooke-Wavell K, Skelton D, Barker KL, Clark EM, de Biase S, Arnold S, Paskins Z,
32 15 Robinson KR, Lewis RM, Tobias JH, Ward KA, Whitney J, Leyland S. Strong, steady
33 16 and straight: UK consensus statement on physical activity and exercise for
34 17 osteoporosis. *Br J Sports Med* 2022 May 16 bjsports-2021-104634.
- 35
36 18 4. [https://strwebprdmedia.blob.core.windows.net/media/kuphgv1u/ros-guidance-](https://strwebprdmedia.blob.core.windows.net/media/kuphgv1u/ros-guidance-on-managing-symptoms-of-vertebral-fractures-2022.pdf)
37 19 [on-managing-symptoms-of-vertebral-fractures-2022.pdf](https://strwebprdmedia.blob.core.windows.net/media/kuphgv1u/ros-guidance-on-managing-symptoms-of-vertebral-fractures-2022.pdf). Accessed 17.08.22
- 38
39
40 20
- 41 21 5. Gold DT, Shipp KM, Pieper CF, et al. Group treatment improves trunk strength and
42 22 psychological status in older women with vertebral fractures: results of a RCT. *J*
43 23 *Am Geriatr Soc* 2004; 52:1471–1478.
- 44
45 24
- 46
47 25 6. Bergström I et al. Back extensor training increases muscle strength in
48 26 postmenopausal women with osteoporosis, kyphosis and vertebral fractures. *Adv*
49 27 *Physiother* 2011; 13:110–117.
- 50
51 28
- 52 29 7. Bergland A. et al. Effect of exercise on mobility, balance, and health-related
53 30 quality of life in osteoporotic women with a history of vertebral fracture: a
54 31 randomized, controlled trial. *Osteoporos Int.* 2011; 22: 1863-71.
- 55
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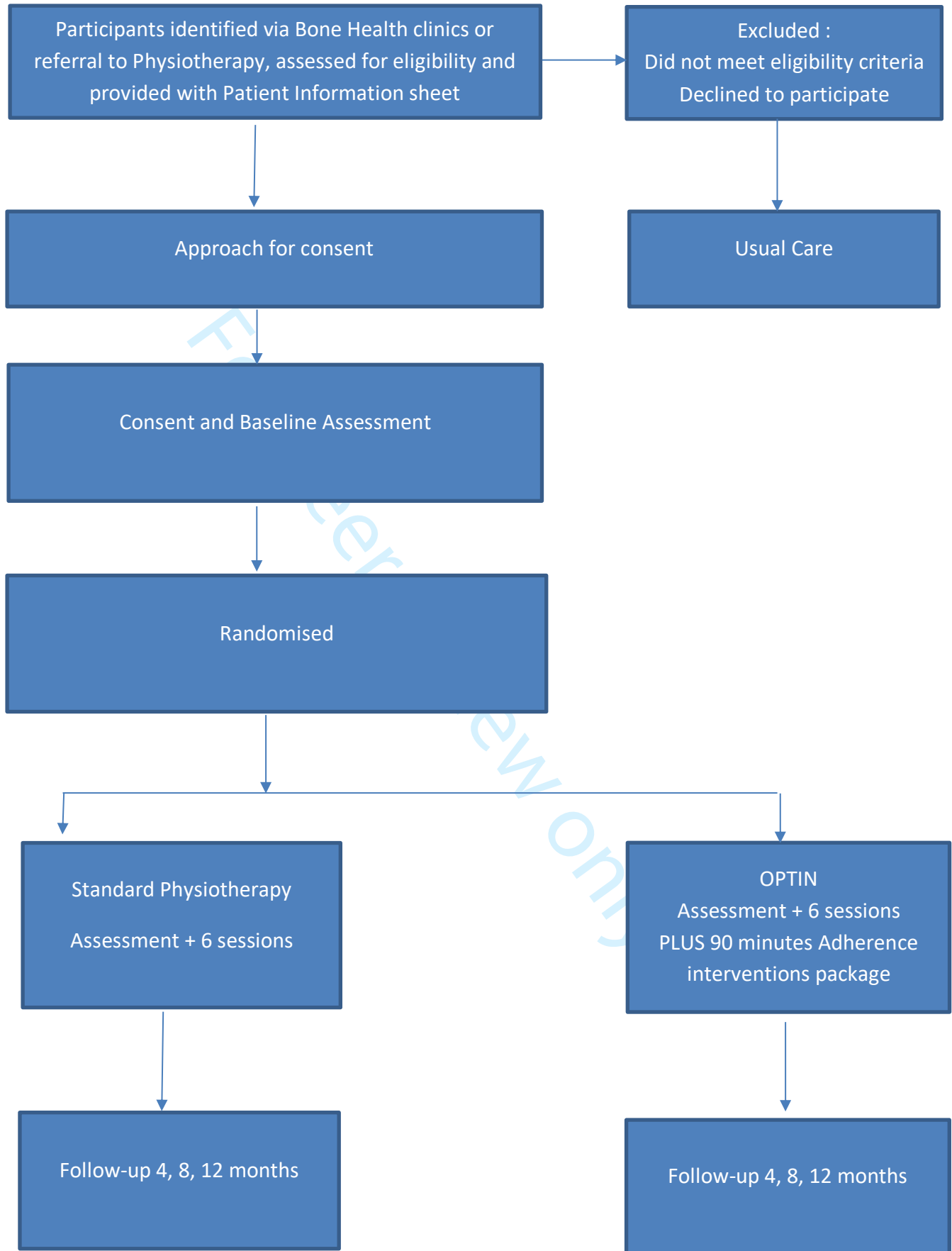
- 1
2
3 1 8. Olsen CF, Bergland A. The effect of exercise and education on fear of falling in
4 2 elderly women with osteoporosis and a history of vertebral fracture: results of a
5 3 randomized controlled trial. *Osteoporos Int*. 2014; 2: 2017-25.
- 6
7 4 9. Gibbs JC, McArthur C, Wark J et al. The effect home exercise in older women with
8 5 vertebral fractures: A pilot randomised controlled trial. *Physical Therapy*. 3 Jan
9 6 2020 doi.org/10.1093/ptj/pzz188
- 10
11 7 10. Evstigneeva L, Lesnyak O, Bultink IEM et al Effect of a twelve-month physical
12 8 exercise program of patients with osteoporotic vertebral fractures: a randomised
13 9 controlled trial. *Osteoporos Int* 2016 27: 2515-24.
- 14
15 10 11. Room J, Hannink E, Dawes H, et al. What interventions are used to improve
16 11 exercise adherence in older people and what behavioural techniques are they
17 12 based on? *BMJ Open*. 2017; 7(12): e019221.
- 18
19 13 12. Beavious C. Motivational interviewing to improve treatment adherence. *Joint*
20 14 *Bone Spine*. 2019 Feb 22: pii: S1297-319X (19)30042-9. doi:
21 15 10.1016/j.jbspin.2019.02.005.
- 22
23 16 13. NICE draft guidance on behaviour change URL:
24 17 [https://www.nice.org.uk/guidance/ph49/documents/behaviour-change-draft-](https://www.nice.org.uk/guidance/ph49/documents/behaviour-change-draft-guidance2)
25 18 [guidance2](https://www.nice.org.uk/guidance/ph49/documents/behaviour-change-draft-guidance2)(accessed 11th March 2020).
- 26
27 19 14. Room J, Boulton M, Dawes H, et al. Development of an exercise adherence
28 20 intervention for older people. The steps taken designing a complex intervention
29 21 for the AERO trial. *WCPT 2019: PO-J-09-SUN1*
- 30
31 22 15. Michie S, van Stralen M, West R. The behaviour change wheel: A new method for
32 23 characterising and designing behaviour change interventions. *Implementation*
33 24 *Science* 2011, 6:42.
- 34
35 25 16. Rodrigues IB, Jonathan D, Adachi JD, Beattie5 KA, MacDermid JC. Development
36 26 and validation of a new tool to measure the facilitators, barriers and preferences
37 27 to exercise in people with osteoporosis. *BMC Musculoskeletal Disorders* 2017
38 28 18:540. DOI 10.1186/s12891-017-1914-5.
- 39
40 29 17. Drummond M, Sculpher M, Torrance G, O'Brien B, Stoddart G. *Methods for the*
41 30 *economic evaluation of health care programmes*: Oxford University Press; 2005.
- 42
43 31 18. Podsiadlo, D. and Richardson, S. (1991). "The timed "Up & Go": a test of basic
44 32 functional mobility for frail elderly persons." *J Am Geriatr Soc* 39(2): 142-148.
- 45
46 33 19. International Osteoporosis Foundation Quality of life questionnaires QUALEFFO-
47 34 41. URL: [https://www.osteoporosis.foundation/health-professionals/research-](https://www.osteoporosis.foundation/health-professionals/research-tools/quality-life-questionnaires)
48 35 [tools/quality-life-questionnaires](https://www.osteoporosis.foundation/health-professionals/research-tools/quality-life-questionnaires) (accessed 30 March 2022).
- 49
50 36 20. Newman M, Newman R, Hughes T, Vadher K, Barker KL. Is the timed loaded
51 37 standing test a valid measure of back muscle endurance in people with vertebral
52 38 osteoporosis? *Osteoporos Int*. 2018; 29:893–905.
- 53
54 39 21. Greendale GA, Nili NS, Huang MH, Seeger L, Karlamangla AS. The reliability and
55 40 validity of three non-radiological measures of thoracic kyphosis and their relations
56 41 to the standing radiological Cobb angle. *Osteoporos Int* 2011; 22:1897–905.

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22. Jensen, M.P. and Karoly, P. (2011). "Self-report scales and procedures for assessing pain in adults", in Turk, D.C. and Melzack, R. (eds). Handbook of pain assessment, 3rd edition. New York, Guilford Press, 19-44.
23. Weiner DK, Duncan PW et al. Functional reach: a marker of physical frailty. *J Am Geriatr Soc* 1992; 40(3):203-7.
24. Steffen TM, Hacker TA, Mollinger L. Age- and gender-related test performance in community-dwelling elderly people: Six-Minute Walk Test, Berg Balance Scale, Timed Up and Go Test, and gait speeds. *Phys Ther* 2002; 82:128-37.
25. Delbaere K, Close JCT et al. The falls efficacy scale international (FES-I). A comprehensive longitudinal validation study. *Age and Ageing* 2010; 39: 201-16.
26. Abizanda P, Navarro JL et al. Validity and usefulness of handheld- dynamometry for measuring muscle strength in community-dwelling older persons. *Arch Gerontol Geriatr*. 2012; 54(1): 21-7.
27. Resnick B and Jenkins LS. Testing the reliability and validity of the self-efficacy for exercise scale. *Nurs Res* 49 (3): 154-159.
28. Newman-Beinart NA et al. The development and initial psychometric evaluation of a measure assessing adherence to prescribed exercise: the Exercise Adherence Rating Scale (EARS). *Physiotherapy* 103 (2017) 180-85.
29. Herdman M, Gudex C, Lloyd A et al. Development and preliminary testing of the new five-level version of the EQ-5D-5L (EQ-5D-5L). *Qual Life Res* 2011; 20 (10): 1727-36.28.
30. Wright A, Cook C, Baxter G, et al. A comparison of 3 methodological approaches to defining major clinically important improvements of 4 performance measures in patients with hip osteoarthritis. *J Orthop Sport Phys*. 2011; 41: 319 -27.
31. Schulz KF, Altman DG, Moher D, for the CONSORT Group. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. *BMC Trials*. 2010; 11:32.
32. Calvert M, Blazeby J, Altman DG, et al. Reporting of patient-reported outcomes in randomized trials: the CONSORT PRO Extension. *JAMA*. 2013;309(8):814-22.
33. Hannink E, Newman M, Barker KL. Does thoracic kyphosis severity predict response to physiotherapy rehabilitation in patients with osteoporotic vertebral fracture? A secondary analysis of the PROVE RCT. *Physiotherapy* Feb 17, 2022,
34. Drummond M, Sculpher M, Torrance G, O'Brien B, Stoddart G. *Methods for the economic evaluation of health care programmes*: Oxford University Press; 2005.
35. Sandelowski, M., *Sample size in qualitative research*. *Research in Nursing and Health*, 1995. 18(2): p. 179-183.
36. Braun V, Clarke V. What can "thematic analysis" offer health and wellbeing researchers? *Int J Qual Stud Health Well-being*. 2014; 9:26152.
37. Chan A-W, Tetzlaff JM, Gotzsche PC et al. SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. *BMJ* 2013;346: e7586.

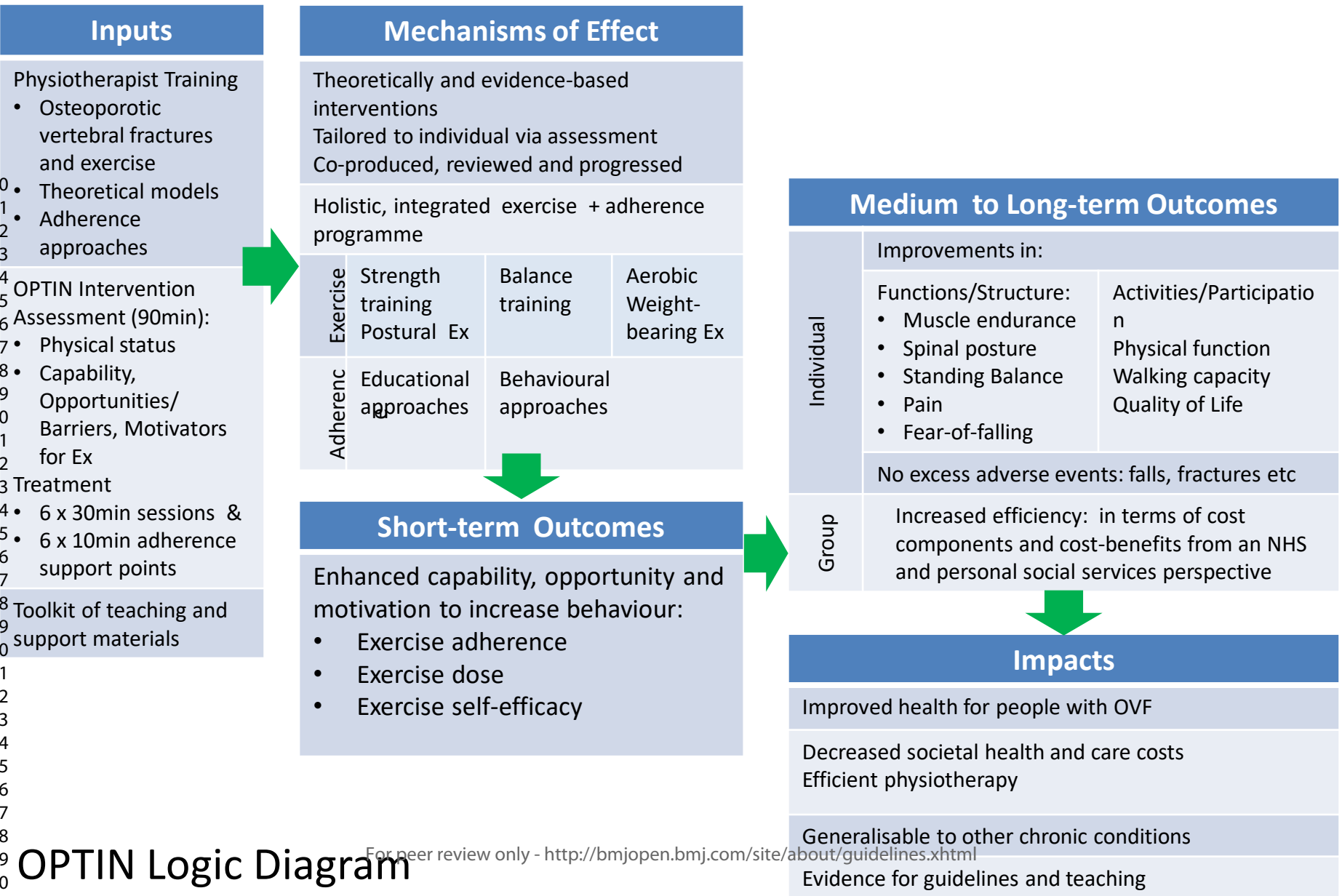
- 1
2
3 1 38. Schulz KF, Altman DG, Moher D et al. CONSORT 2010 statement: updated
4 2 guidelines for reporting parallel group randomised trials. BMJ 2010;340:c332.
5
6 3 39. Hoffmann TC, Glasziou PP, Boutron I et al. Better reporting of interventions:
7 4 template for intervention description and replication (TIDieR) checklist and guide.
8 5 BMJ 2014; 348: g1687.
9
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For peer review only



Qualitative Interviews n =15-20 participants
Focus group Physiotherapists

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OPTIN Logic Diagram



TRUST LOGO (if applicable), or a placeholder, 'local logo/letterhead'



Chief Investigator: Professor Karen Barker

Principal Investigator: <<PI name here>>

<<Local hospital address here>>

<i>Study code</i>	<i>Site code</i>	<i>Participant number</i>
O P T		

CONSENT FORM – Main study

OsteoPorosis Tailored exercise adherence INtervention (Opt-In)

*If you agree,
please initial each
box*

1. I confirm that I have read the information sheet dated..... (version.....) for this study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.	
3. I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals from University of Oxford, from regulatory authorities and from the NHS Trust(s), where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	
4. I agree to my General Practitioner being informed of my participation in the study.	
5. I understand I may be contacted for the option to participate in qualitative interview or focus group related to the study.	
6. I agree to take part in this study.	

Name of Participant	Date	Signature
Name of Person taking Consent	Date	Signature

**1 copy for participant; 1 copy for local researcher site file; 1 (original) to be kept in medical notes (if participant is a patient).*

Consent Form – Main study	v1.0 / 21MAY2021
OsteoPorosis Tailored exercise adherence INtervention (Opt-In)	IRAS Project number: 287716
Chief Investigator: Professor Karen Barker	REC Reference number: 21/WS/0071

For peer review only - <http://bmjopen.bmj.com/site/about/guidelines.xhtml>



STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description
Administrative information		
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym Title Page Lines 1-3
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry Page 3 Line 21
	2b	All items from the World Health Organization Trial Registration Data Set
Protocol version	3	Date and version identifier Page 3 Line 22
Funding	4	Sources and types of financial, material, and other support Page 23 lines 9/10
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors Title page and Page 22/23
	5b	Name and contact information for the trial sponsor Page 19 Line 12
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)
Introduction		
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention P5-6
	6b	Explanation for choice of comparators P6
Objectives	7	Specific objectives or hypotheses P6

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2 Trial design 8 Description of trial design including type of trial (eg, parallel group,
3 crossover, factorial, single group), allocation ratio, and framework (eg,
4 superiority, equivalence, noninferiority, exploratory) P6 L22-3
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8 **Methods: Participants, interventions, and outcomes**

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10 Study setting 9 Description of study settings (eg, community clinic, academic hospital)
11 and list of countries where data will be collected. Reference to where
12 list of study sites can be obtained P7 L10
13

14 Eligibility criteria 10 Inclusion and exclusion criteria for participants. If applicable, eligibility
15 criteria for study centres and individuals who will perform the
16 interventions (eg, surgeons, psychotherapists) P7-8
17
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19 Interventions 11a Interventions for each group with sufficient detail to allow replication,
20 including how and when they will be administered P10-11
21

22 11b Criteria for discontinuing or modifying allocated interventions for a
23 given trial participant (eg, drug dose change in response to harms,
24 participant request, or improving/worsening disease) n/a
25

26 11c Strategies to improve adherence to intervention protocols, and any
27 procedures for monitoring adherence (eg, drug tablet return,
28 laboratory tests) p10/11
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31 11d Relevant concomitant care and interventions that are permitted or
32 prohibited during the trial p12
33

34 Outcomes 12 Primary, secondary, and other outcomes, including the specific
35 measurement variable (eg, systolic blood pressure), analysis metric
36 (eg, change from baseline, final value, time to event), method of
37 aggregation (eg, median, proportion), and time point for each
38 outcome. Explanation of the clinical relevance of chosen efficacy and
39 harm outcomes is strongly recommended p12-14
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42 Participant 13 Time schedule of enrolment, interventions (including any run-ins and
43 timeline washouts), assessments, and visits for participants. A schematic
44 diagram is highly recommended (see Figure) Table 1
45

46 Sample size 14 Estimated number of participants needed to achieve study objectives
47 and how it was determined, including clinical and statistical
48 assumptions supporting any sample size calculations P15
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51 Recruitment 15 Strategies for achieving adequate participant enrolment to reach
52 target sample size P8
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54 **Methods: Assignment of interventions (for controlled trials)**

55 Allocation:
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2	Sequence	16a	Method of generating the allocation sequence (eg, computer-
3	generation		generated random numbers), and list of any factors for stratification.
4			To reduce predictability of a random sequence, details of any planned
5			restriction (eg, blocking) should be provided in a separate document
6			that is unavailable to those who enrol participants or assign
7			interventions P9
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10	Allocation	16b	Mechanism of implementing the allocation sequence (eg, central
11	concealment		telephone; sequentially numbered, opaque, sealed envelopes),
12	mechanism		describing any steps to conceal the sequence until interventions are
13			assignedp9
14			
15	Implementation	16c	Who will generate the allocation sequence, who will enrol participants,
16			and who will assign participants to interventions P9
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19	Blinding	17a	Who will be blinded after assignment to interventions (eg, trial
20	(masking)		participants, care providers, outcome assessors, data analysts), and
21			how P 9
22			
23		17b	If blinded, circumstances under which unblinding is permissible, and
24			procedure for revealing a participant's allocated intervention during
25			the trial n/a
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Methods: Data collection, management, and analysis

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30	Data collection	18a	Plans for assessment and collection of outcome, baseline, and other
31	methods		trial data, including any related processes to promote data quality (eg,
32			duplicate measurements, training of assessors) and a description of
33			study instruments (eg, questionnaires, laboratory tests) along with
34			their reliability and validity, if known. Reference to where data
35			collection forms can be found, if not in the protocolp10
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38		18b	Plans to promote participant retention and complete follow-up,
39			including list of any outcome data to be collected for participants who
40			discontinue or deviate from intervention protocols
41			
42	Data	19	Plans for data entry, coding, security, and storage, including any
43	management		related processes to promote data quality (eg, double data entry;
44			range checks for data values). Reference to where details of data
45			management procedures can be found, if not in the protocol
46			
47			
48	Statistical	20a	Statistical methods for analysing primary and secondary outcomes.
49	methods		Reference to where other details of the statistical analysis plan can be
50			found, if not in the protocol P15-6
51			
52		20b	Methods for any additional analyses (eg, subgroup and adjusted
53			analyses) n/a
54			
55		20c	Definition of analysis population relating to protocol non-adherence
56			(eg, as randomised analysis), and any statistical methods to handle
57			missing data (eg, multiple imputation) P15-17
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Methods: Monitoring

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24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60	Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct P14-15
	Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor

Ethics and dissemination

26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60	Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval P22
	Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) P 19
	Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) P8
		26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable n/a
	Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial
	Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site P23
	Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators
	Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation n/a

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| Dissemination
policy | 31a | Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions P19 |
| | 31b | Authorship eligibility guidelines and any intended use of professional writers P19 |
| | 31c | Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code |

14 Appendices

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|-------------------------------|----|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Informed consent
materials | 32 | Model consent form and other related documentation given to participants and authorised surrogates |
| Biological
specimens | 33 | Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable |

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*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "[Attribution-NonCommercial-NoDerivs 3.0 Unported](https://creativecommons.org/licenses/by-nc-nd/3.0/)" license.