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Efficacy of Low-magnitude High-frequency Vibration (LMHFV) on Musculoskeletal Health of Subjects on Wheelchair: A Study Protocol for A Single-blinded Randomized Controlled Study

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3 1 **Efficacy of Low-magnitude High-frequency Vibration (LMHFV) on Musculoskeletal Health**
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5 2 **of Subjects on Wheelchair: A Study Protocol for A Single-blinded Randomized Controlled**
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7 3 **Study**
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1 **ABSTRACT**

2 **Introduction**

3 Low-magnitude high-frequency vibration (LMHFV) is a non-invasive biophysical intervention
4 providing whole-body mechanical stimulation shown to benefit muscle strength, postural control,
5 balancing ability, new bone formation, spinal bone mineral density (BMD), and blood circulation.
6 Current LMHFV treatment requires elderlies to stand upright on the platform 20min/day, making
7 it difficult for those with a poor musculoskeletal ability who cannot stand for long periods.
8 Therefore, the vibration platform is modified to treat disabled patients at sitting position, which
9 efficacy of LMHFV on this group of elderlies will be verified. It is hypothesized that the new
10 design of LMHFV is beneficial to wheelchair users in terms of vertebral BMD, muscle health and
11 musculoskeletal functions.

12 **Methods and analysis**

13 This is a single-blinded randomized controlled trial that investigates the effect of LMHFV on
14 vertebral BMD, muscle health, balancing and functional ability in wheelchair users.

15 Healthy elderlies aged 65 years or above, with walking difficulties and using a wheelchair are
16 eligible. Recruited subjects will be randomized to either LMHFV or control group. The primary
17 outcome is to assess lumbar spine BMD by dual-energy X-ray absorptiometry (DXA) that is
18 clinically recommended for osteoporosis diagnosis. All primary and secondary outcome
19 assessments will be performed at baseline and 6 months post-treatment. Two-way repeated
20 measures ANOVA will be used to compare measured outcomes between two groups at different
21 time points.

22 **Ethics and dissemination**

1 The study protocol was approved by the Clinical Research Ethics Committee of the Chinese
2 University of Hong Kong (Ref. no 2019.087-T). Results will be disseminated through peer-
3 reviewed publications, conferences, and workshops.

4 **Trial registration number**

5 ClinicalTrials.gov, NCT04180267.

6 **Keywords**

7 Osteoporosis, Vibration Therapy, Wheelchair users, Vertebral BMD, LMHFV

11 **Strengths and limitations of this study**

- 12 • This is the first study that investigates the efficacy of LMHFV on wheelchair users, hence
13 data generated will be with high clinical translation values.
- 14 • This trial cannot be double-blinded since blinding subjects for the LMHFV treatment is not
15 feasible.
- 16 • The vibration signals can be easily felt and placebo is rare in vibration studies.

1 INTRODUCTION

2 Ageing is an emerging socio-economic problem in Hong Kong. The ageing population at 65 or
3 above increased continuously from 0.46 million (8.2%) to 1.27 million (17.9%) from 1988 to 2018
4¹. The prevalence of osteoporosis also increases due to the escalating ageing population².
5 Osteoporosis is an age-induced disorder with progressive loss of bone that leads to deterioration
6 of bone microarchitecture and hence low BMD. It increases the risk of fragility fracture known to
7 be associated with increased morbidity and mortality³.
8 Elderly people with disability or mobility impairments due to trauma, chronic illnesses or over-
9 weight may avoid walking and rely on wheelchairs for most daily activities. Many studies showed
10 that wheelchair users had greater bone loss compared to walkers^{4 5}. Physical activity is one of the
11 recommended approaches for preventing osteoporosis. However, some elderly people may be
12 restricted from exercise training because they are not physically fit to perform the intensive
13 exercise⁶, leading to a vicious cycle of musculoskeletal deterioration.
14 Low-magnitude high-frequency vibration (LMHFV) is a promising intervention proposed as an
15 alternative to physical exercise⁷ for treating osteoporosis. It is a non-invasive biophysical
16 intervention that provides systemic vertical vibrations at 20 - 90Hz at amplitude of less than 1.0g
17 (g = gravitational acceleration)⁸. Previous studies demonstrated that LMHFV treatment could
18 enhance muscle strength⁹, postural control¹⁰, balancing ability^{6 11 12}, new bone formation¹³⁻¹⁵,
19 spinal BMD⁶, and blood circulation⁶.
20 There were some studies reporting the effect of whole-body vibration treatment on wheelchair
21 users with spinal cord injury. They showed that whole-body vibration treatment could increase
22 upper limb performance during propulsion of the wheelchairs in terms of average speed and time

1 of displacement and blood flow to paralyzed muscles in the lower limbs¹⁶⁻¹⁸. However, there is a
2 lack of evidence for the effect of LMHFV on elderly people with poor walking and standing ability
3 (such as subjects on wheelchair), which is a missing gap of our knowledge.

4 In this study, we hypothesize that LMHFV would enhance the musculoskeletal health of the elderly
5 people with walking difficulties and relying on wheelchairs for daily mobility, in terms of vertebral
6 bone quality and muscle performance. The objective is to investigate the effects of LMHFV on
7 vertebral BMD, muscle performance and balancing ability in disabled elderly subjects. The
8 vibration platform will be modified to suit the disabled patients for treatment at sitting position.
9 The results of this study would broaden the indications of vibration platform to benefit more people
10 in the community, which have a good potential of translation.

12 **METHODS AND ANALYSIS**

13 *Study design*

14 This is a single-blinded randomized controlled trial to study the effects of LMHFV on vertebral
15 BMD and muscle performance of disabled elderly. This is a two-year study, in which the recruited
16 wheelchair users will receive a 6-month LMHFV treatment.

17 *Study participants*

18 Subjects will be recruited from the specialist outpatient clinic or orthopaedic wards of the Prince
19 of Wales Hospital (PWH) of the Chinese University of Hong Kong, or community centers or
20 elderly homes. Subjects will be recruited based on the inclusion and exclusion criteria. All

1 recruited subjects will be requested by an investigator to give a written consent and will perform
2 the following assessments at the PWH.

3 *Inclusion criteria*

4 Inclusion criteria are listed as follows:

- 5 1. Subjects of both genders aged ≥ 65 years.
- 6 2. Subjects with walking difficulties, especially those who usually walk indoor but use
7 wheelchairs outdoor.
- 8 3. Subjects with good general health conditions.

9 *Exclusion criteria*

10 Exclusion criteria are as follows:

- 11 1. Subjects cannot stand and walk independently.
- 12 2. Subjects who had vibration treatment before.
- 13 3. Subjects with malignancy.
- 14 4. Subjects with acute fractures or severe osteoarthritis¹⁹.
- 15 5. Subjects with cardiovascular concern such as with pace-maker in-situ.
- 16 6. Subjects with chronic inflammatory conditions known to affect muscle metabolism such as
17 rheumatoid arthritis.
- 18 7. Subjects with high frequency of physical activities, such as subjects who participated in regular
19 exercise five times a week or more.

20 *Randomization and grouping*

1 After baseline assessment, eligible subjects will be randomized by sealed-envelope drawing of
2 computer-generated random numbers. The random number list is kept strictly confidential and the
3 researchers will not have access to the list. They will be randomized into either one of two groups:
4 LMHFV or control group.

5 *Assessments*

6 Two groups of subjects will be subjected to the same assessments: [1] demographic data collection;
7 [2] BMD measurement at the spine (primary outcome) and hip; [3] handgrip strength; [4]
8 quadriceps strength; [5] balancing ability test, [6] quality of life (QoL); and [6] adverse event
9 reporting, if any. The compliance of the subjects in LMHFV group will be recorded in a SD card
10 in the machine; meanwhile the subjects will be given a calendar to self-record the usage for
11 counter-checking. A flow diagram of the whole trial is shown in Figure 1.

12 *Interventions*

13 After baseline visit, regular phone reminders will be used to remind subjects to complete their
14 LMHFV interventions and about the date of their end-point assessments. Contacts will be
15 provided for any queries during the study.

16 LMHFV is a non-invasive biophysical intervention providing whole-body vibration signals for
17 mechanical stimulation. Subjects are required to sit upright on the vibration platform (V-Health
18 Limited, Hong Kong) providing a frequency 35 Hz, 0.3× gravitational acceleration at peak-to-peak
19 displacement of less than 0.1 mm for 20 min/day. Treatment will be given for at least 3 days/week.
20 In this study, the design of vibration platforms is modified for wheelchair users. A chair and a
21 supporting footrest are fixed on the platform (Figure 2). Subjects are instructed to sit on the chair
22 and rest their feet on the footrest for 20 min/day. The research staff will instruct safety precautions

1 and operative procedures. Each patient in the control group will remain in their habitual life style
2 without vibration treatment.

3 *Blinding*

4 Investigators, outcome assessors and the statistician will be blinded to the grouping allocation that
5 is performed by one independent staff and kept confidential from team members. Outcome
6 assessments will be performed by a central technician at the Bone Quality and Health Centre of
7 the Chinese University of Hong Kong, who has obtained International Society for Clinical
8 Densitometry (ISCD) certificate and is independent from this project. All subjects will be
9 reminded not to disclose their grouping to the assessors. However, blinding the subjects for the
10 LMHFV treatment is not feasible because the vibration signals can be easily felt and placebo is
11 rare in vibration studies^{6 11}.

12 *Primary outcome measures*

13 All primary and secondary outcome assessments for the two groups will be performed at baseline
14 and 6 months post-treatment.

15 The primary outcome of this study is vertebral BMD. BMD will be assessed by standard DXA
16 (Delphi W, Hologic, Waltham, MA, USA) which is a gold standard assessment for osteoporosis
17 recommended by World Health Organization (WHO). Spine and hip are the two standard sites for
18 the diagnosis of osteoporosis and both will be measured. The only ethical concern is the additional
19 DXA assessments, which emits a low-dose radiation at 10 microSv, roughly equivalent to 1 day
20 exposure to natural background radiation. In our institute, the short-term precision error of areal
21 BMD (aBMD) by DXA was 2.07% at the femoral neck and 1.35%²⁰ at the lumbar spine.

22 *Secondary outcome measures*

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3 1 Secondary outcomes include muscle strength assessment, balancing ability and quality of life
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5 2 (QoL).
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8 3 Handgrip strength and quadriceps strength will be assessed. Handgrip strength will be measured
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10 4 by dynamometer (5030JI, JAMAR, USA) on dominant hand of each subject. Participants will be
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12 5 instructed to hold the device with the arm at right angle and elbow to the side of the body. The
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14 6 maximum effort will be taken from 3 trials²¹. Quadriceps strength will be measured by instructing
15
16 7 the subjects to perform an active extension of the knee joint at a sitting position with both feet free
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18 8 from the ground, and the hip and knee joint flexed at 90°. The peak forces of the knee extension
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20 9 will be measured by a dynamometer attached at the malleoli level and repeated thrice in each lower
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22 10 limb with the maximum force taken for analysis⁶.
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27 11 To assess the balancing ability, modified functional reach test²² and postural stability test will be
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29 12 performed. Modified functional reach test is a simple test for fall risk assessment²³. It measures
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31 13 the maximal distance that the subject can reach when the subjects sits on a bench with their hip,
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33 14 knees, and ankles positioned at 90° of flexion, with feet positioned flat on the floor. A level
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35 15 yardstick will be mounted on the wall at the height of each subject's acromion of the non-paretic
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37 16 side, while sitting on bench with no back or arm rests. Subjects are required to lean as far as
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39 17 possible in each direction without rotating or touching the wall. The furthest position of the fifth
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41 18 finger will be marked on the yardstick. If the subject cannot raise the paretic arm, the distance
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43 19 covered by the acromion during leaning will be used¹⁹. Postural stability test measures subjects'
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45 20 ability to maintain their center of balance. Center of pressure (COP) is the average point at which
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47 21 the body concentrates. COP can be tested by Biodex Balance System (Biodex Medical Systems,
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49 22 Inc, NY, USA). Subjects are required to sit on the platform without support from feet and keep
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1 arms folded across chest. Thighs need to be kept parallel, with 75% of their length supported on
2 the platform²⁴.

3 To assess the health-related quality of life, validated Chinese version of the 36-item Short-Form
4 Health Survey (SF-36) will be used for quantitative evaluation of the subjects' physical and mental
5 component summary. Subjects with higher scores indicate a general better quality of life^{6 25}.

6 *Recruitment Strategy*

7 Subjects will be recruited for this RCT through two approaches: 1) Promotional and educational
8 talks at community centres; 2) Collaboration with social workers from each collaborating
9 community centre.

10 Before recruitment, they will be informed of the potential benefits and risks of the interventions in
11 this study. They will then be required to fill out an informed consent and can withdraw from this
12 study without any condition.

13 *Sample size calculation*

14 Vertebral BMD is used as the primary outcome in this study. Our previous bedrest study²⁶ showed
15 that vibration could reduce the loss of bone mineral density at various skeletal sites by 5-10%. The
16 total sample size is estimated to be 70 subjects using two-way repeated measures ANOVA with
17 power at 0.8 and alpha of 0.05. With consideration of around 15% dropout, the sample size is
18 increased to n=80.

19 *Data analysis*

1 Two-way repeated measures ANOVA will be used for comparing the measured outcomes between
2 two groups at different time points. SPSS version 25.0 (IBM, NY, USA) will be used to perform
3 analysis and significance level is set at $p < 0.05$.

4 *Data monitoring*

5 All investigators will be responsible for record keeping. Only principle and co-investigators,
6 authorized research personnel and Ethical Committee can access to the personal data during and
7 after the study. All data collection will be performed with strict adherence to the professional
8 standards of confidentiality. Any personal information, including subjects' name, address, phone
9 number etc., will be removed from all records. Important documents will be retained for at least 3
10 years after the completion of the study for final report and inspection.

11 *Data Statement*

12 Data and resources will be shared with other eligible investigators through academically
13 established means. The protocol and datasets used or analysed in this study will be available from
14 the corresponding author upon reasonable request. Researchers who provide a methodologically
15 sound proposal may access data to achieve aims in the approved proposal.

16 *Patient and public involvement*

17 Patients and the public were not involved in the design or planning of the study. Members of the
18 public are involved in the recruitment of participants or conduct of the study. We will report test
19 results to participants in plain language after their end-point assessments are completed. Results
20 will be available to the public and patients in the forms of educational talks and booklets or flyers
21 and published in open access peer-reviewed journals.

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3 1 *Ethics and dissemination*
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6 2 The study protocol has been approved by the Clinical Research Ethics Committee of the Chinese
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8 3 University of Hong Kong (Ref. no 2019.087-T). Trial results will be published in peer-reviewed
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10 4 journals and disseminated at relevant conferences and to the public via educational talks and
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12 5 booklets or flyers.
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19 7 **DISCUSSION**
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22 8 To our knowledge, this is the first study to investigate the efficacy of low-magnitude high-
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24 9 frequency vibration therapy (LMHFV) on wheelchair users. As the worldwide ageing population
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26 10 escalates, the number of people with mobility impairment or disability would also increase²⁷.
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28 11 These people would inevitably be relying on wheelchair to assist their daily living²⁸. Wheelchair-
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30 12 bound elderlies usually have limited physical activity and is therefore associated to lower BMD²⁹
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32 13 and ability to control body position, and thus have an increased risk of fall and osteoporotic
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34 14 fractures. A study from Grant Medical Center in the United States investigated 30 wheelchair-
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36 15 bound subjects who fell from wheelchair over a 5 years period³⁰. The report showed that elderlies
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38 16 who were older than 65 years of age with higher fall risk were associated with lack of physical
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40 17 activity and poor nutrition, leading to a decrease in muscle mass and strength. As most
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42 18 osteoporotic fractures are caused by combination of poor balance, falls, and deteriorating bone
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44 19 strength. Therefore, LMHFV is the proposed strategy to target musculoskeletal deterioration in
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46 20 wheelchair users for the prevention of more detrimental consequences.
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52 21 LMHFV has previously been reported to have positive effects on reducing fall and fracture risks,
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54 22 enhancing muscle strength and improving balancing ability in healthy community-dwelling older
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1 people^{6 31}. Supported with this evidence, it is therefore hypothesized that LMHFV would provide
2 positive effects on the musculoskeletal health and physical performance in terms of BMD, muscle
3 strength, balancing ability on elderlies with disability or mobility impairments who rely on
4 wheelchairs for locomotion.

5 Vibration is a good treatment modality that is easy to implement for physically challenged patients,
6 like wheelchair users. However, there is a scarce of literature reporting its effect on this group of
7 patients who are most desperately in need of the treatment. There have been a few reports on the
8 application of vibration treatment on wheelchair users with spinal cord injury (SCI). Menéndez's
9 study reported in 2016 investigated the acute effect of whole-body vibration¹⁸. Ten patients with
10 SCI were recruited and treated with various treatment schemes including the whole-body vibration
11 (WBV). Patients were instructed to sit on wheelchairs with their feet rested on the vibration
12 platform (Galileo Home, Galileo, Novotec, Germany, 10 Hz, 5 mm peak-to-peak). Their results
13 have shown an enhancement to the mean blood velocity (MBV) and peak blood velocity (PBV)
14 by approximately 25% at 7 minutes after a 1-minute vibration treatment. A separate study in 2016,
15 also by Menéndez's group, investigated the long-term combined treatment effect of WBV and
16 electromyostimulatin (ES) in SCI patients. Seventeen subjects with SCI were randomized into
17 treatment group and control group for 12 weeks. Patients in treatment group received 30 sections
18 of 10-minute WBV and ES stimulation over a 12-week period¹⁷. The treatment group was reported
19 to show increased resting arterial diameter, increased blood flow, and increased muscle thickness
20 at the gastrocnemius after 12 weeks of treatment. Although these studies employed a side-
21 alternating vibration (instead of vertical-oscillating vibration) only to the lower limbs, these results
22 suggested that mechanical stimulation in the form of vibration could provide benefits to blood flow
23 that is associated with better performance-related outcomes in paralyzed skeletal muscles.

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3 1 Therefore, suggesting that the proposed LMHFV treatment, providing a vertical oscillating
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5 2 stimulation (Figure 1B) to the whole-body would be beneficial to the target group of patients.
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8 3 Findings of the current clinical trial would generate valuable data that is of high clinical translation
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10 4 values for wider application of vibration therapy in the community; and to generate clinical
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12 5 evidence that is not restricted to the healthy and mobile older people, but also to the group of
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14 6 patients with mobility impairments and high risk of further musculoskeletal function deterioration.
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17 7 **TRIAL STATUS**

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20 8 This trial is in process of planning subject recruitment.
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44
45 18 this study.
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49 19 **AUTHOR CONTRIBUTIONS**

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52 20 All the authors designed the study and composed the manuscript. All authors read and approved
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54 21 the final manuscript.
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1 **ETHICS APPROVAL**

2 The study protocol was approved by the Clinical Research Ethics Committee of the Chinese
3 University of Hong Kong (Ref. no 2019.087-T) and conformed to the Declaration of Helsinki.
4 Results will be disseminated through peer-reviewed publications, conferences and workshops.

5 **CONSENT FOR PUBLICATION**

6 Not applicable.

7 **COMPETING INTERESTS**

8 The authors declare no conflict of interest.

9 **ABBREVIATIONS**

- 10 Low-magnitude high-frequency vibration (LMHFV)
11 Bone mineral density (BMD)
12 Areal BMD (aBMD)
13 X-ray absorptiometry (DXA)
14 Quality of life (QoL)
15 International Society for Clinical Densitometry (ISCD)
16 World Health Organization (WHO)
17 Center of pressure (COP)
18 36-item Short-Form Health Survey (SF-36)
19 Spinal cord injury (SCI)
20 Whole-body vibration (WBV)
21 Mean blood velocity (MBV)
22 Peak blood velocity (PBV)
23 Electromyostimulatin (ES)

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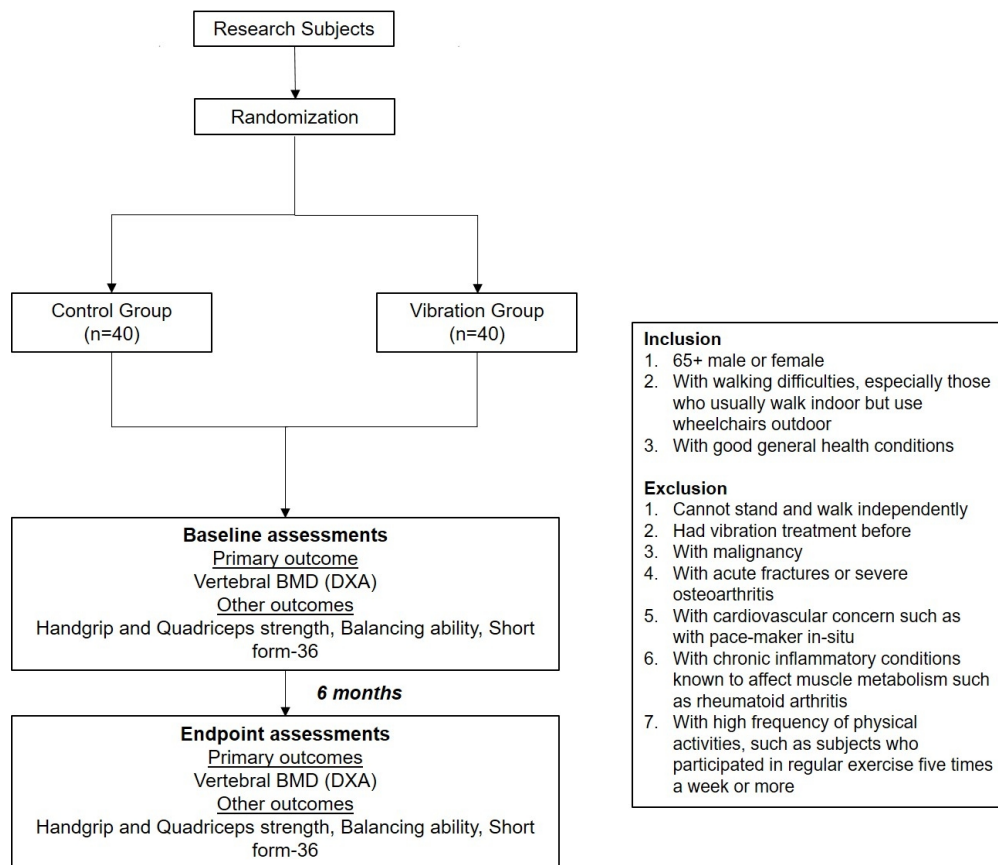
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3 **1 FIGURE LEGEND**
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6 **2 Figure 1** Flow diagram showing the grouping and assessments in this study.
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9 **3 Figure 2** A vertical-oscillating vibration platform modified to provide a seating place for the
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12 4 research subject to receive the 20 min/day treatment. This representative vibration platform is
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14 5 installed in a community centre situated in a public housing estate with 6692 units/families in the
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16 6 Shatin district of Hong Kong.
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22 8 Word count: 2862
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35 Flow diagram showing the grouping and assessments in this study.

36 109x96mm (300 x 300 DPI)



A vertical-oscillating vibration platform modified to provide a seating place for the research subject to receive the 20 min/day treatment. This representative vibration platform is installed in a community centre situated in a public housing estate with 6692 units/families in the Shatin district of Hong Kong.

48x67mm (300 x 300 DPI)

低幅高頻振動治療

對使用輪椅，行動不便的老年人在骨骼肌肉健康上的影響的研究

Efficacy of Low-magnitude High-frequency Vibration (LMHFV) on musculoskeletal health of subjects on wheelchair, a randomized controlled study

參加者同意書

Consent Form

我在此聲明：

I declare that:

1. 本人已閱讀及明白這份參與研究同意書，並且已經獲得提問的權利。我已經被知會我可能遇到的風險和得益。我所提出的問題已得到滿意的解答。

I confirm that I have read and understood the information sheet for the above study and have had the opportunity to ask questions. I have been told about the risks and benefits and I have had my questions answered to my satisfaction.

2. 我明白我的參與完全出於自願並且可以在任何時候退出，而無需任何理由。我的決定不會影響我所受到的醫療服務和法律權利。如果我決定退出這項研究，我同意之前收集到的資料可繼續被使用。

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. If I decide to withdraw from this study, I agree that the information collected about me up to the point when I withdraw may continue to be processed.

3. 我明白機構審查委員會、倫理委員會或監察機構的成員可能會查閱我的醫療紀錄，我同意授權有關人員查閱我的記錄。

I understand that sections of any of my medical notes may be looked at by responsible individuals from regulatory authorities where it is relevant to my taking part in research. I give permission for these individuals to have access to my records.

4. 我同意參與這項研究。

I agree to take part in the above study.

5. 簽署這同意書並不表示我放棄任何權利。

I do not waive any liability rights by signing this form.

6. 我的簽署表示我已得到這檔的副本。我會保留這副本直至我參與完結為止。

My signature indicates that a copy of this form has been given to me and I will keep it until the end of my participation in the study.

參與者的簽署 (Signature)

參與者姓名 (Name of participant)

簽署日期 (Date)

研究者/代表簽署
(Signature of investigator or delegate)

研究者/代表姓名
(Name of investigator or delegate)

簽署日期 (Date)

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

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Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, Hróbjartsson A, Mann H, Dickersin K, Berlin J, Doré C, Parulekar W, Summerskill W, Groves T, Schulz K, Sox H, Rockhold FW, Rennie D, Moher D. SPIRIT 2013 Statement: Defining standard protocol items for clinical trials. *Ann Intern Med.* 2013;158(3):200-207

			Page
	Reporting Item		Number
Administrative information			
Title	#1 Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym		1

1	Trial registration	#2a	Trial identifier and registry name. If not yet registered,	3
2			name of intended registry	
3				
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6	Trial registration:	#2b	All items from the World Health Organization Trial	See this
7	data set		Registration Data Set	checklist
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12	Protocol version	#3	Date and version identifier	n/a
13				
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15	Funding	#4	Sources and types of financial, material, and other	14
16			support	
17				
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20	Roles and	#5a	Names, affiliations, and roles of protocol contributors	n/a
21	responsibilities:			
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23	contributorship			
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28	Roles and	#5b	Name and contact information for the trial sponsor	n/a
29	responsibilities:			
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31	sponsor contact			
32	information			
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38	Roles and	#5c	Role of study sponsor and funders, if any, in study	n/a
39	responsibilities:		design; collection, management, analysis, and	
40			interpretation of data; writing of the report; and the	
41	sponsor and funder		decision to submit the report for publication, including	
42			whether they will have ultimate authority over any of	
43			these activities	
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52	Roles and	#5d	Composition, roles, and responsibilities of the	n/a
53	responsibilities:		coordinating centre, steering committee, endpoint	
54			adjudication committee, data management team, and	
55	committees			
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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	4-5
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	4
Objectives	#7	Specific objectives or hypotheses	5
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, non-inferiority, exploratory)	4-5
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	5

1	Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If	6
2				
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4			applicable, eligibility criteria for study centres and	
5				
6			individuals who will perform the interventions (eg,	
7				
8			surgeons, psychotherapists)	
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11	Interventions:	#11a	Interventions for each group with sufficient detail to allow	7-8
12				
13	description		replication, including how and when they will be	
14				
15				
16			administered	
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19	Interventions:	#11b	Criteria for discontinuing or modifying allocated	n/a
20				
21	modifications		interventions for a given trial participant (eg, drug dose	
22				
23			change in response to harms, participant request, or	
24				
25			improving / worsening disease)	
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29	Interventions:	#11c	Strategies to improve adherence to intervention	7
30				
31	adherence		protocols, and any procedures for monitoring adherence	
32				
33			(eg, drug tablet return; laboratory tests)	
34				
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36	Interventions:	#11d	Relevant concomitant care and interventions that are	n/a
37				
38	concomitant care		permitted or prohibited during the trial	
39				
40				
41				
42	Outcomes	#12	Primary, secondary, and other outcomes, including the	8-10
43				
44			specific measurement variable (eg, systolic blood	
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46			pressure), analysis metric (eg, change from baseline,	
47				
48			final value, time to event), method of aggregation (eg,	
49				
50			median, proportion), and time point for each outcome.	
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53			Explanation of the clinical relevance of chosen efficacy	
54				
55			and harm outcomes is strongly recommended	
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1	Participant timeline	#13	Time schedule of enrolment, interventions (including any	5-7;
2			run-ins and washouts), assessments, and visits for	Figure 2
3			participants. A schematic diagram is highly	
4			recommended (see Figure)	
5				
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11	Sample size	#14	Estimated number of participants needed to achieve	10
12			study objectives and how it was determined, including	
13			clinical and statistical assumptions supporting any	
14			sample size calculations	
15				
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21	Recruitment	#15	Strategies for achieving adequate participant enrolment	10
22			to reach target sample size	
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26	Methods:			
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28	Assignment of			
29	interventions (for			
30	controlled trials)			
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36	Allocation: sequence	#16a	Method of generating the allocation sequence (eg,	7
37	generation		computer-generated random numbers), and list of any	
38			factors for stratification. To reduce predictability of a	
39			random sequence, details of any planned restriction (eg,	
40			blocking) should be provided in a separate document	
41			that is unavailable to those who enrol participants or	
42			assign interventions	
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53	Allocation	#16b	Mechanism of implementing the allocation sequence (eg,	7
54	concealment		central telephone; sequentially numbered, opaque,	
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58	mechanism			
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sealed envelopes), describing any steps to conceal the sequence until interventions are assigned

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6	Allocation:	#16c	Who will generate the allocation sequence, who will
7			
8	implementation		enrol participants, and who will assign participants to
9			interventions
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13	Blinding (masking)	#17a	Who will be blinded after assignment to interventions
14			
15			(eg, trial participants, care providers, outcome
16			assessors, data analysts), and how
17			
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21	Blinding (masking):	#17b	If blinded, circumstances under which unblinding is
22			
23	emergency		permissible, and procedure for revealing a participant's
24			allocated intervention during the trial
25	unblinding		
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29	Methods: Data		
30			
31	collection,		
32			
33	management, and		
34			
35	analysis		
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38	Data collection plan	#18a	Plans for assessment and collection of outcome,
39			
40			baseline, and other trial data, including any related
41			processes to promote data quality (eg, duplicate
42			measurements, training of assessors) and a description
43			of study instruments (eg, questionnaires, laboratory
44			tests) along with their reliability and validity, if known.
45			
46			Reference to where data collection forms can be found,
47			
48			if not in the protocol
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1	Data collection plan:	#18b	Plans to promote participant retention and complete	7
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3	retention		follow-up, including list of any outcome data to be	
4			collected for participants who discontinue or deviate from	
5			intervention protocols	
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11	Data management	#19	Plans for data entry, coding, security, and storage,	11
12			including any related processes to promote data quality	
13			(eg, double data entry; range checks for data values).	
14			Reference to where details of data management	
15			procedures can be found, if not in the protocol	
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23	Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary	10-11
24			outcomes. Reference to where other details of the	
25			statistical analysis plan can be found, if not in the	
26			protocol	
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33	Statistics: additional	#20b	Methods for any additional analyses (eg, subgroup and	n/a
34	analyses		adjusted analyses)	
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39	Statistics: analysis	#20c	Definition of analysis population relating to protocol non-	n/a
40	population and		adherence (eg, as randomised analysis), and any	
41	missing data		statistical methods to handle missing data (eg, multiple	
42			imputation)	
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48	Methods: Monitoring			
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51	Data monitoring:	#21a	Composition of data monitoring committee (DMC);	See
52	formal committee		summary of its role and reporting structure; statement of	comment
53			whether it is independent from the sponsor and	
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1 competing interests; and reference to where further
 2 details about its charter can be found, if not in the
 3 protocol. Alternatively, an explanation of why a DMC is
 4 not needed
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10 *(DMC is unlikely to have the opportunity to make a*
 11 *difference in this short term study where patient follow up*
 12 *is only 6 months and this study has minimal patient risk)*
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21 Data monitoring: 22 interim analysis	#21b	Description of any interim analyses and stopping 23 guidelines, including who will have access to these 24 interim results and make the final decision to terminate 25 the trial	n/a
31 Harms	#22	Plans for collecting, assessing, reporting, and managing 32 solicited and spontaneously reported adverse events 33 and other unintended effects of trial interventions or trial 34 conduct	10
41 Auditing	#23	Frequency and procedures for auditing trial conduct, if 42 any, and whether the process will be independent from 43 investigators and the sponsor	n/a
48 Ethics and 49 dissemination			
54 Research ethics 55 approval	#24	Plans for seeking research ethics committee / 56 institutional review board (REC / IRB) approval	15

1 2 3 4 5 6 7 8 9 10 11 12	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)	n/a
13 14 15 16 17 18 19 20	Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	6
21 22 23 24 25 26 27 28	Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	n/a
29 30 31 32 33 34 35 36 37 38	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	11
39 40 41 42 43	Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	15
44 45 46 47 48 49 50	Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	11
51 52 53 54 55 56 57 58 59 60	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

1 Dissemination policy: [#31a](#) Plans for investigators and sponsor to communicate trial 12
 2 trial results results to participants, healthcare professionals, the
 3 public, and other relevant groups (eg, via publication,
 4 reporting in results databases, or other data sharing
 5 arrangements), including any publication restrictions
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13 Dissemination policy: [#31b](#) Authorship eligibility guidelines and any intended use of n/a
 14 authorship professional writers
 15
 16
 17

18 Dissemination policy: [#31c](#) Plans, if any, for granting public access to the full n/a
 19 reproducible protocol, participant-level dataset, and statistical code
 20 research
 21
 22
 23
 24
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26 Appendices

27
 28
 29 Informed consent [#32](#) Model consent form and other related documentation See
 30 materials given to participants and authorised surrogates uploaded
 31 document
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36 Biological specimens [#33](#) Plans for collection, laboratory evaluation, and storage of n/a
 37 biological specimens for genetic or molecular analysis in
 38 the current trial and for future use in ancillary studies, if
 39 applicable
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46 None The SPIRIT checklist is distributed under the terms of the Creative Commons Attribution
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 48 tool made by the [EQUATOR Network](#) in collaboration with [Penelope.ai](#)
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BMJ Open

Efficacy of Low-magnitude High-frequency Vibration (LMHFV) on Musculoskeletal Health of Participants on Wheelchair: A Study Protocol for A Single-blinded Randomized Controlled Study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2020-038578.R1
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Complete List of Authors:	Chow, Simon Kwoon Ho; Chinese University of Hong Kong, Ho, Chung Yan; Chinese University of Hong Kong Wong, Hiu Wun; Chinese University of Hong Kong Chim, Yu Ning; Chinese University of Hong Kong, Wong, Ronald Wong Man-Yeung ; Chinese University of Hong Kong Cheung, Wing Hoi; Chinese University of Hong Kong,
Primary Subject Heading:	Rehabilitation medicine
Secondary Subject Heading:	Geriatric medicine
Keywords:	Musculoskeletal disorders < ORTHOPAEDIC & TRAUMA SURGERY, GERIATRIC MEDICINE, Bone diseases < ORTHOPAEDIC & TRAUMA SURGERY

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3 1 **Efficacy of Low-magnitude High-frequency Vibration (LMHFV) on Musculoskeletal**
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5 2 **Health of Participants on Wheelchair: A Study Protocol for A Single-blinded Randomized**
6
7 3 **Controlled Study**
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10 4 Simon Kwoon-Ho Chow ^{1,2}, Chung Yan Ho ¹, Hiu Wun Wong¹, Yu Ning Chim¹, Ronald Man
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12 5 Yeung Wong ¹, Wing Hoi Cheung ^{1,2}
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21

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1 **ABSTRACT**

2 **Background**

3 Osteoporosis is an age-related disease with progressive loss of bone, leading to fragile bone. It is
4 one of the major health issues in older adults and causes medical, social and economic impacts
5 globally. Patients with osteoporosis have high risk of osteoporotic fractures. Low-magnitude
6 high-frequency vibration (LMHFV) is a non-invasive biophysical intervention providing whole-
7 body mechanical stimulation. Previous studies showed that LMHFV is beneficial to **muscle**
8 **strength, postural control, balancing ability, new bone formation, spinal bone mineral density**
9 **(BMD), and blood circulation.** During the LMHFV treatment, older adults need to stand upright
10 on the platform for 20min/day. However, some physically weak elderlies with poor
11 musculoskeletal ability cannot stand for a long period. Therefore, the design of vibration
12 platform is modified for the disabled patients to treat at sitting position and the efficacy of
13 LMHFV on this group of elderlies will be verified. It is hypothesized that new design of
14 LMHFV is beneficial to wheelchair users in terms of vertebral BMD, muscle health and
15 musculoskeletal functions.

16 **Methods**

17 This study is a single-blinded randomized controlled trial to investigate the effect of LMHFV on
18 vertebral BMD, muscle health, balancing ability and functional ability in wheelchair users
19 (mainly on wheelchair for outdoor activities).

20 Healthy elderlies aged 65 years or above, with walking difficulties and using wheelchair are
21 eligible. Exclusion criteria are those: [1] cannot stand and walk independently, [2] have vibration
22 treatment before, [3] with malignancy, [4] with acute fractures or severe osteoarthritis, [5] with

1 cardiovascular concern such as with pace-maker in-situ, [6] with chronic inflammatory
2 conditions known to affect muscle metabolism such as rheumatoid arthritis, and [7] with high
3 frequency of physical activities, such as participants who participated in regular exercise five
4 times a week or more.

5 Recruited participants will be randomized to either LMHFV or control group. Participant
6 assigned to LMHFV group will receive LMHFV (35Hz, 0.3g, 20min/day, at least 3 times/week)
7 for 6 months. The primary outcome is BMD at the lumbar spine to be assessed by dual-energy
8 X-ray absorptiometry (DXA) that is clinically recommended for the diagnosis of osteoporosis.
9 All primary and secondary outcome assessments for all groups will be performed in the
10 investigators' institute at baseline and 6 months post-treatment.

11 **Discussion**

12 This study aims to investigate the effects of LMHFV on wheelchair users. The findings of this
13 study will help to confirm the efficacy of LMHFV on vertebral BMD, muscle health, balancing
14 ability and functional outcomes in wheelchair using elderlies. LMHFV therapy is an
15 intervention strategy that is easy to implement at the community healthcare level or individually
16 at home that has previously been proven to reduce fall risk and muscle strength at the lower limb.
17 The ultimate goal is to improve their bone and muscle quality of wheelchair users, as well as
18 enhancing their quality of life.

19 **Article summary**

20 **Strengths and limitations of this study**

- 21 • This is the first study that investigates the efficacy of LMHFV on wheelchair users, hence
22 data generated will be with high clinical translation values.

- 1 • This trial cannot be double-blinded since blinding subjects for the LMHFV treatment is
2 not feasible.
- 3 • The vibration signals can be easily felt and placebo is rare in vibration studies.

4 **Trial registration**

5 ClinicalTrials.gov NCT04180267. Registered on Nov 26th, 2019.

6 **Keywords**

7 Osteoporosis, Vibration Therapy, Wheelchair users, Vertebral BMD, LMHFV

8 **BACKGROUND**

9 Ageing is an emerging socio-economic problem in Hong Kong. The ageing population at 65 or
10 above increased continuously from 0.46 million (8.2%) to 1.27 million (17.9%) from 1988 to
11 2018 ¹. The prevalence of osteoporosis also increases due to the escalating ageing population ².
12 Osteoporosis is an age-induced disorder with progressive loss of bone that leads to deterioration
13 of bone microarchitecture and hence low BMD. It increases the risk of fragility fracture known
14 to be associated with increased morbidity and mortality ³.
15 Older adults with disability or mobility impairments due to trauma, chronic illnesses or over-
16 weight may avoid walking and rely on wheelchairs for most daily activities. Many studies
17 showed that wheelchair users had greater bone loss compared to walkers ^{4,5}. Physical activity is
18 one of the recommended approaches for preventing osteoporosis. However, some older adults
19 may be restricted from exercise training because they are not physically fit to perform the
20 intensive exercise ⁶, leading to a vicious cycle of musculoskeletal deterioration.

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3 1 Low-magnitude high-frequency vibration (LMHFV) is a promising intervention proposed as an
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5 2 alternative to physical exercise⁷ for treating osteoporosis. It is a non-invasive biophysical
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7 3 intervention that provides systemic vertical vibrations at 20 - 90Hz at amplitude of less than 1.0g
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9 4 (g = gravitational acceleration)⁸. Previous studies demonstrated that LMHFV treatment could
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11 5 enhance muscle strength⁶, postural control⁹, balancing ability^{6 10 11}, new bone formation¹²⁻¹⁴,
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13 6 spinal BMD⁶, and blood circulation⁶.

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17 7 There were some studies reporting the effect of whole-body vibration treatment on wheelchair
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19 8 users with spinal cord injury. They showed that whole-body vibration treatment could increase
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21 9 upper limb performance during propulsion of the wheelchairs in terms of average speed, time of
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23 10 displacement and blood flow to paralyzed muscles in the lower limbs¹⁵⁻¹⁷. However, there is a
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25 11 lack of evidence for the effect of LMHFV on older adults with poor walking and standing ability
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27 12 (such as non-paralyzed wheelchair users), which is a missing gap of our knowledge.

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32 13 In this study, we hypothesize that LMHFV would enhance the musculoskeletal health of the
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34 14 older adults with walking difficulties and relying on wheelchairs for daily mobility, in terms of
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36 15 vertebral bone quality and muscle performance. The objective is to investigate the effects of
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38 16 LMHFV on vertebral BMD, muscle performance and balancing ability in disabled older
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40 17 participants. The vibration platform will be modified to suit the disabled patients for treatment at
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42 18 sitting position. The results of this study would broaden the indications of vibration platform to
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44 19 benefit more people in the community, which have a good potential of translation.
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51 **METHODS**

52 *Study design*

1 This is a single-blinded randomized controlled trial to study the effects of LMHV on vertebral
2 BMD and muscle performance of disabled older adults (Figure 1). This is a two-year study, in
3 which the recruited wheelchair users will receive a 6-month LMHFV treatment. The study
4 protocol was approved by the Clinical Research Ethics Committee of the Chinese University of
5 Hong Kong (Ref. no 2019.087-T), with expected start date of January 1 of 2020 and end date of
6 October 1 of 2021.

7 *Study participants*

8 Participants will be recruited from the specialist outpatient clinic or orthopaedic wards of the
9 Prince of Wales Hospital (PWH) of the Chinese University of Hong Kong, or community centers
10 or elderly homes. Participants will be recruited based on the inclusion and exclusion criteria. All
11 recruited participants will be requested to give a written consent and will perform the following
12 assessments at the PWH.

13 *Inclusion criteria*

14 Inclusion criteria are listed as follows:

- 15 1. Participants of both genders aged ≥ 65 years.
- 16 2. Participants with walking difficulties, especially those who usually walk indoor but use
17 wheelchairs outdoor.
- 18 3. Participants with good general health conditions.

19 *Exclusion criteria*

20 Exclusion criteria are as follows:

- 21 1. Participants cannot stand and walk independently.

- 1 2. Participants who had vibration treatment before.
- 2 3. Participants with malignancy.
- 3 4. Participants with acute fractures or severe osteoarthritis ¹⁸.
- 4 5. Participants with cardiovascular concern such as with pace-maker in-situ.
- 5 6. Participants with chronic inflammatory conditions known to affect muscle metabolism such
- 6 as rheumatoid arthritis.
- 7 7. Participants with high frequency of physical activities, such as participants who participated
- 8 in regular exercise five times a week or more.

9 *Randomization and Grouping*

10 After eligibility screening, recruited participants will be randomized by sealed-envelope drawing
11 of computer-generated random numbers. The random number list is kept strictly confidential and
12 the researchers will not have access to the list. Research participants will be randomized into
13 either one of two groups: LMHFV or control group.

14 *Assessments*

15 Two groups of participants will be subjected to the same assessments: [1] demographic data
16 collection; [2] BMD measurement at the spine (primary outcome) and hip; [3] balancing ability
17 test, [4] quality of life (QoL); and [5] adverse event reporting, if any. Compliance of the
18 participants in LMHFV group will be recorded in an SD card in the treatment device while the
19 participants will also be given a treatment calendar to self-record the usage for cross-validation.
20 Adverse or fall events are recorded by a calendar provided to each participant who will be
21 instructed to record the date and details of each event as previously reported ⁶.

22 *Interventions*

1 LMHFV is a non-invasive biophysical intervention providing whole-body vibration signals for
2 mechanical stimulation. No known side effects are associated with this treatment except when a
3 small risk of falling during the transfer of participants from the wheelchair to the treatment
4 device. As the benefits discussed above including muscle strength⁶, postural control⁹, balancing
5 ability^{6 10 11}, and blood circulation⁶ may benefit wheelchair users' musculoskeletal health, risks
6 of falling could be minimized with the help of the on-site researchers.

7 Participants are required to sit upright on the vibration platform (V-Health Limited, Hong Kong)
8 providing a frequency 35 Hz, 0.3× gravitational acceleration at peak-to-peak displacement of less
9 than 0.1 mm for 20 min/day. Treatment will be given for at least 3 days/week. In this study, the
10 design of vibration platforms is modified for wheelchair users. A chair and a supporting footrest
11 are fixed on the platform (Figure 2). Participants are instructed to sit on the chair and rest their
12 feet on the footrest for 20 min/day. The research staff will instruct safety precautions and
13 operative procedures. Each patient in the control group are instructed to maintain their habitual
14 lifestyle without vibration treatment nor specific instructions given to take on additional physical
15 exercise. Physical activities will be monitored via questionnaires.

16 *Blinding*

17 Investigators, outcome assessors and the statistician will be blinded to the grouping allocation
18 that is performed by one independent staff and kept confidential from team members. Outcome
19 assessments will be performed by a central technician at the Bone Quality and Health Centre of
20 the Chinese University of Hong Kong, who has obtained International Society for Clinical
21 Densitometry (ISCD) certificate and is independent from this project. All participants will be
22 reminded not to disclose their grouping to the assessors. However, blinding the participants for

1 the LMHFV treatment is not feasible because the vibration signals can be easily felt and placebo
2 is rare in vibration studies ^{6 10}.

3 *Primary outcome measures*

4 All primary and secondary outcome assessments for the two groups will be performed at baseline
5 and 6 months post-treatment.

6 The primary outcome of this study is vertebral BMD. BMD will be assessed by standard DXA
7 (Delphi W, Hologic, Waltham, MA, USA) which is a gold standard assessment for osteoporosis
8 recommended by World Health Organization (WHO). Spine and hip are the two standard sites
9 for the diagnosis of osteoporosis and both will be measured. In our institute, the short-term
10 precision error of areal BMD (aBMD) by DXA was 2.07% at the femoral neck and 1.35% ¹⁹ at
11 the lumbar spine.

12 *Secondary outcome measures*

13 Secondary outcomes include muscle strength assessment, balancing ability and quality of life
14 (QoL).

15 Handgrip strength and quadriceps strength will be assessed. Handgrip strength will be measured
16 by dynamometer (5030JI, JAMAR, USA) on dominant hand of each participant. Participants will
17 be instructed to hold the device with the arm at right angle and elbow to the side of the body. The
18 maximum effort will be taken from 3 trials ²⁰. Quadriceps strength will be measured by
19 instructing the participants to perform an active extension of the knee joint at a sitting position
20 with both feet free from the ground, and the hip and knee joint flexed at 90°. The peak forces of
21 the knee extension will be measured by a dynamometer attached at the malleoli level and
22 repeated thrice in each lower limb with the maximum force taken for analysis⁶.

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3 1 To assess the balancing ability, modified functional reach test ²¹ and postural stability test will be
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5 2 performed. Modified functional reach test is a simple test for fall risk assessment ²². It measures
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7 3 the maximal distance that the participant can reach when the participant sits on a bench with their
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9 4 hip, knees, and ankles positioned at 90° of flexion, with feet positioned flat on the floor. A level
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11 5 yardstick will be mounted on the wall at the height of each participant's acromion of the non-
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13 6 paretic side, while sitting on bench with no back or arm rests. Participants are required to lean as
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15 7 far as possible in each direction without rotating or touching the wall. The furthest position of the
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17 8 fifth finger will be marked on the yardstick. If the participant cannot raise the paretic arm, the
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19 9 distance covered by the acromion during leaning will be used ¹⁸. Postural stability test measures
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21 10 participants' ability to maintain their center of balance. Center of pressure (COP) is the average
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23 11 point at which the body concentrates. COP can be tested by Biodex Balance System (Biodex
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25 12 Medical Systems, Inc, NY, USA). Participants are required to sit on the platform without support
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27 13 from feet and keep arms folded across chest. Thighs need to be kept parallel, with 75% of their
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29 14 length supported on the platform²³.

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33 15 To assess the health-related quality of life, validated Chinese version of the 36-item Short-Form
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35 16 Health Survey (SF-36) will be used for quantitative evaluation of the participants' physical and
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37 17 mental component summary. Participants with higher scores indicate a general better quality of
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39 18 life^{6 24}.

39 *Sample size calculation*

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43 20 Vertebral BMD is used as the primary outcome in this study. Our previous bedrest study
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45 21 ²⁵ showed that vibration could reduce the loss of bone mineral density at various skeletal sites by
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47 22 5-10%. The total sample size is estimated to be 80 participants using two-way repeated measures

1 ANOVA with power at 0.8 and alpha of 0.05. With consideration of around 15% dropout, the
2 sample size is increased to n=80.

3 *Data Analysis*

4 Data in this study will be analysed according to the intention-to-treat principle followed by per-
5 protocol analysis. Missing data will be handled using last-observation-carried-forward approach.
6 Normality tests will be performed to determine the normal distribution of data. Two-way
7 repeated measures ANOVA will be used for comparing the measured outcomes between two
8 groups at different time points; chi-square tests are used to compare proportions for categorical
9 variables. Non-parametric tests will be employed if normality assumption is violated. Additional
10 sub-group analysis be explored and stratified by gender, BMI, and age. SPSS version 25.0
11 (IBM, NY, USA) will be used to perform analysis and significance level is set at $p < 0.05$.

12 *Data monitoring*

13 All investigators will be responsible for record keeping. Only principle and co-investigators,
14 authorized research personnel and Ethical Committee can access to the personal data during and
15 after the study. All data collection will be performed with strict adherence to the professional
16 standards of confidentiality. Any personal information, including participants' name, address,
17 phone number etc, will be removed from all records. Important documents will be retained for at
18 least 3 years after the completion of the study for final report and inspection.

19 *Data Statement*

20 Data and resources will be shared with other eligible investigators through academically
21 established means. The protocol and datasets used or analysed in this study will be available

1 from the corresponding author upon reasonable request. Researchers who provide a
2 methodologically sound proposal may access data to achieve aims in the approved proposal.

3 *Patient and public involvement*

4 Patients and the public were not involved in the design or planning of the study. Members of the
5 public are involved in the recruitment of participants or conduct of the study. We will report test
6 results to participants in plain language after their end-point assessments are completed. Results
7 will be available to the public and patients in the forms of educational talks and booklets or
8 flyers and published in open access peer-reviewed journals.

9 *Ethics and dissemination*

10 LMHFV is a non-invasive intervention and reported to have no serious adverse effect⁶. The only
11 ethical concern is the additional DXA assessments, which emits a low-dose radiation at 10
12 microSv, roughly equivalent to 1 day exposure to natural background radiation.

14 **DISCUSSION**

15 To our knowledge, this is the first study to investigate the efficacy of low-magnitude high-
16 frequency vibration therapy (LMHFV) on wheelchair users. As the worldwide ageing
17 population escalates, the number of people with mobility impairment or disability would also
18 increase²⁶. These people would inevitably be relying on wheelchair to assist their daily living²⁷.
19 Wheelchair-bound elderly usually have limited physical activity and is therefore associated to
20 lower BMD²⁸ and ability to control body position, and thus have an increased risk of fall and
21 osteoporotic fractures. A study from Grant Medical Center in the United States investigated 30

1 wheelchair-bound participants who fell from wheelchair over a 5 years period²⁹. The report
2 showed that elderlies who were older than 65 years of age with higher fall risk were associated
3 with lack of physical activity and poor nutrition, leading to a decrease in muscle mass and
4 strength. As most osteoporotic fractures are caused by combination of poor balance, falls, and
5 deteriorating bone strength. Therefore, LMHFV is the proposed strategy to target
6 musculoskeletal deterioration in wheelchair users for the prevention of more detrimental
7 consequences.

8 LMHFV has previously been reported to have positive effects on reducing fall and fracture risks,
9 enhancing muscle strength and improving balancing ability in healthy community-dwelling older
10 people^{6 30}. Supported with this evidence, it is therefore hypothesized that LMHFV would
11 provide positive effects on the musculoskeletal health and physical performance in terms of
12 BMD, muscle strength, balancing ability on elderlies with disability or mobility impairments
13 who rely on wheelchairs for locomotion.

14 Vibration is a good treatment modality that is easy to implement for physically challenged
15 patients, like wheelchair users. However, there is a scarce of literature reporting its effect on this
16 group of patients who are most desperately in need of the treatment. There have been a few
17 reports on the application of vibration treatment on wheelchair users with spinal cord injury
18 (SCI). Menéndez's study reported in 2016 investigated the acute effect of whole-body vibration
19¹⁷. Ten patients with SCI were recruited and treated with various treatment schemes including the
20 whole-body vibration (WBV). Patients were instructed to sit on wheelchairs with their feet rested
21 on the vibration platform (Galileo Home, Galileo, Novotec, Germany, 10 Hz, 5 mm peak-to-
22 peak). Their results have shown an enhancement to the mean blood velocity (MBV) and peak
23 blood velocity (PBV) by approximately 25% at 7 minutes after a 1-minute vibration treatment. A

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3 1 separate study in 2016, also by Menéndez's group, investigated the long-term combined
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5 2 treatment effect of WBV and electromyostimulatin (ES) in SCI patients. Seventeen participants
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7 3 with SCI were randomized into treatment group and control group for 12 weeks. Patients in
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9 4 treatment group received 30 sections of 10-minute WBV and ES stimulation over a 12-week
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11 5 period ¹⁶. The treatment group was reported to show increased resting arterial diameter,
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13 6 increased blood flow, and increased muscle thickness at the gastrocnemius after 12 weeks of
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15 7 treatment. Although these studies employed a side-alternating vibration (instead of vertical-
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17 8 oscillating vibration) only to the lower limbs, these results suggested that mechanical stimulation
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19 9 in the form of vibration could provide benefits to blood flow that is associated with better
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21 10 performance-related outcomes in paralyzed skeletal muscles. Therefore, suggesting that the
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23 11 proposed LMHFV treatment, providing a vertical oscillating stimulation (Figure 1) to the whole-
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25 12 body would be beneficial to the target group of patients.

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31 13 Findings of the current clinical trial would generate valuable data that is of high clinical
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33 14 translation values for wider application of vibration therapy in the community; and to generate
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35 15 clinical evidence that is not restricted to the healthy and mobile older people, but also to the
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37 16 group of patients with mobility impairments and high risk of further musculoskeletal function
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39 17 deterioration. Although the study only investigates the a treatment period of 6-months due to
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41 18 limited research resources, a longer or sustained use of the vibration treatment may be observed
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43 19 as suggested by our previous study that beneficial effects on healthy older adults are maintained
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45 20 even after 12-months of treatment cessation ³⁰.

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53 22 **DECLARATION**

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3 1 Acknowledgements: This study was supported by Project Impact Enhancement Fund (Ref:
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5 2 PIEF/U3/01) and Evidence-Based Orthopaedics Clinical Education and Research Program
6
7 3 (EBO) of the Chinese University of Hong Kong; V-health Limited for lending and modifications
8
9 4 the vibration platforms used for this study. The authors declare no conflict of interest.
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13 **TRAIL STATUS**

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16 6 This trial is in process of planning participant recruitment.
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19 **ACKNOWLEDGEMENTS**

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23
24 9 Health Centre of the Department of Orthopaedics and Traumatology, Faculty of Medicine, The
25
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28 11 their participation in this study.
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35 13 This study was supported by Project Impact Enhancement Fund (Ref: PIEF/U3/01) and
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37 14 Evidence-Based Orthopaedics Clinical Education and Research Program (EBO) of the Chinese
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39 15 University of Hong Kong; V-health Limited for lending and modifications the vibration
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41 16 platforms used for this study.
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45 **AUTHOR CONTRIBUTIONS**

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48 18 SKHC, YNC, RMYW, WHC conceptualized the study; SKHC, YNC, CYH drafted the
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50 19 manuscript; CYH, HWW execute the research project and data collection. All authors reviewed
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52 20 and approved the final manuscript.
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55 **ETHICS APPROVAL**

1 The study protocol was approved by the Clinical Research Ethics Committee of the Chinese
2 University of Hong Kong (Ref. no 2019.087-T) and conformed to the Declaration of Helsinki.
3 Results will be disseminated through peer-reviewed publications, conferences and workshops.

4 **CONSENT FOR PUBLICATION**

5 Not applicable.

6 **ABBREVIATIONS**

7 Low-magnitude high-frequency vibration (LMHFV)
8 Bone mineral density (BMD)
9 Areal BMD (aBMD)
10 X-ray absorptiometry (DXA)
11 Quality of life (QoL)
12 International Society for Clinical Densitometry (ISCD)
13 World Health Organization (WHO)
14 Center of pressure (COP)
15 36-item Short-Form Health Survey (SF-36)
16 Spinal cord injury (SCI)
17 Whole-body vibration (WBV)
18 Mean blood velocity (MBV)
19 Peak blood velocity (PBV)
20 Electromyostimulatin (ES)

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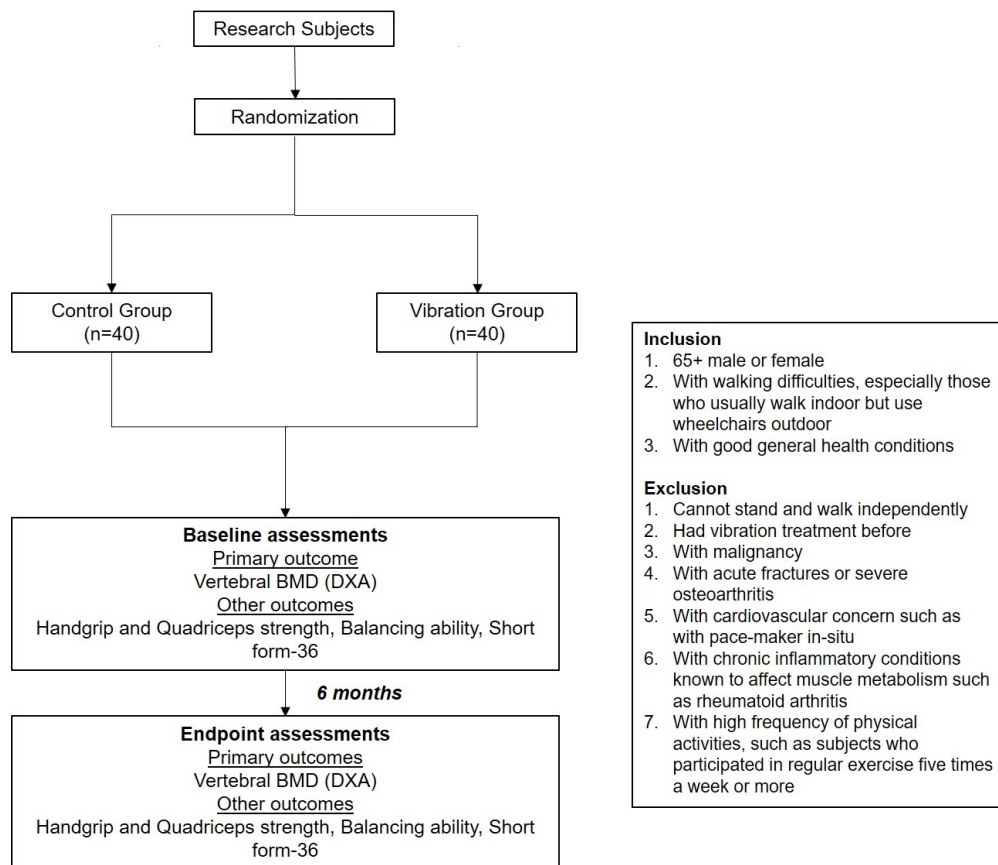
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15
16 10 **FIGURE LEGEND**

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18
19 11 **Figure 1** Flow diagram showing the grouping and assessments in this study.

20
21
22 12 **Figure 2** A vertical-oscillating vibration platform modified to provide a seating place for the
23
24 13 research participant to receive the 20 min/day treatment. This representative vibration platform
25
26 14 is installed in a community centre situated in a public housing estate with 6692 units/families in
27
28 15 the Shatin district of Hong Kong.



35 Flow diagram showing the grouping and assessments in this study.

36 109x96mm (300 x 300 DPI)



A vertical-oscillating vibration platform modified to provide a seating place for the research subject to receive the 20 min/day treatment. This representative vibration platform is installed in a community centre situated in a public housing estate with 6692 units/families in the Shatin district of Hong Kong.

48x67mm (300 x 300 DPI)

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRIT reporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, Hróbjartsson A, Mann H, Dickersin K, Berlin J, Doré C, Parulekar W, Summerskill W, Groves T, Schulz K, Sox H, Rockhold FW, Rennie D, Moher D. SPIRIT 2013 Statement: Defining standard protocol items for clinical trials. *Ann Intern Med.* 2013;158(3):200-207

			Page
	Reporting Item		Number
Administrative information			
Title	#1 Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym		1

1 2 3 4 5	Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	3
6 7 8 9 10	Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	See this checklist
11 12 13	Protocol version	#3	Date and version identifier	n/a
14 15 16 17 18 19	Funding	#4	Sources and types of financial, material, and other support	14
20 21 22 23 24 25 26 27	Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	n/a
28 29 30 31 32 33 34 35 36 37	Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	n/a
38 39 40 41 42 43 44 45 46 47 48 49 50 51	Roles and responsibilities: sponsor and funder	#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	n/a
52 53 54 55 56 57 58 59 60	Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and	n/a

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

Background and rationale: choice of comparators [#6b](#) Explanation for choice of comparators

Objectives [#7](#) Specific objectives or hypotheses

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, non-inferiority, exploratory)

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

1	Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If	6
2				
3				
4			applicable, eligibility criteria for study centres and	
5				
6			individuals who will perform the interventions (eg,	
7				
8			surgeons, psychotherapists)	
9				
10				
11	Interventions:	#11a	Interventions for each group with sufficient detail to allow	7-8
12				
13	description		replication, including how and when they will be	
14				
15				
16			administered	
17				
18				
19	Interventions:	#11b	Criteria for discontinuing or modifying allocated	n/a
20				
21	modifications		interventions for a given trial participant (eg, drug dose	
22				
23			change in response to harms, participant request, or	
24				
25			improving / worsening disease)	
26				
27				
28				
29	Interventions:	#11c	Strategies to improve adherence to intervention	7
30				
31	adherence		protocols, and any procedures for monitoring adherence	
32				
33			(eg, drug tablet return; laboratory tests)	
34				
35				
36	Interventions:	#11d	Relevant concomitant care and interventions that are	n/a
37				
38	concomitant care		permitted or prohibited during the trial	
39				
40				
41				
42	Outcomes	#12	Primary, secondary, and other outcomes, including the	8-10
43				
44			specific measurement variable (eg, systolic blood	
45				
46			pressure), analysis metric (eg, change from baseline,	
47				
48			final value, time to event), method of aggregation (eg,	
49				
50			median, proportion), and time point for each outcome.	
51				
52				
53			Explanation of the clinical relevance of chosen efficacy	
54				
55			and harm outcomes is strongly recommended	
56				
57				
58				
59				
60				

1	Participant timeline	#13	Time schedule of enrolment, interventions (including any	5-7;
2			run-ins and washouts), assessments, and visits for	Figure 2
3			participants. A schematic diagram is highly	
4			recommended (see Figure)	
5				
6				
7				
8				
9				
10				
11	Sample size	#14	Estimated number of participants needed to achieve	10
12			study objectives and how it was determined, including	
13			clinical and statistical assumptions supporting any	
14			sample size calculations	
15				
16				
17				
18				
19				
20				
21	Recruitment	#15	Strategies for achieving adequate participant enrolment	10
22			to reach target sample size	
23				
24				
25				
26	Methods:			
27				
28	Assignment of			
29	interventions (for			
30	controlled trials)			
31				
32				
33				
34				
35				
36	Allocation: sequence	#16a	Method of generating the allocation sequence (eg,	7
37	generation		computer-generated random numbers), and list of any	
38			factors for stratification. To reduce predictability of a	
39			random sequence, details of any planned restriction (eg,	
40			blocking) should be provided in a separate document	
41			that is unavailable to those who enrol participants or	
42			assign interventions	
43				
44				
45				
46				
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52				
53	Allocation	#16b	Mechanism of implementing the allocation sequence (eg,	7
54	concealment		central telephone; sequentially numbered, opaque,	
55				
56				
57				
58	mechanism			
59				
60				

sealed envelopes), describing any steps to conceal the sequence until interventions are assigned

1			
2			
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5			
6	Allocation:	#16c	Who will generate the allocation sequence, who will
7			
8	implementation		enrol participants, and who will assign participants to
9			interventions
10			
11			
12			
13	Blinding (masking)	#17a	Who will be blinded after assignment to interventions
14			
15			(eg, trial participants, care providers, outcome
16			assessors, data analysts), and how
17			
18			
19			
20			
21	Blinding (masking):	#17b	If blinded, circumstances under which unblinding is
22			
23	emergency		permissible, and procedure for revealing a participant's
24			allocated intervention during the trial
25	unblinding		
26			
27			
28			
29	Methods: Data		
30			
31	collection,		
32			
33	management, and		
34			
35	analysis		
36			
37			
38			
39	Data collection plan	#18a	Plans for assessment and collection of outcome,
40			
41			baseline, and other trial data, including any related
42			processes to promote data quality (eg, duplicate
43			measurements, training of assessors) and a description
44			of study instruments (eg, questionnaires, laboratory
45			tests) along with their reliability and validity, if known.
46			
47			Reference to where data collection forms can be found,
48			
49			if not in the protocol
50			
51			
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1	Data collection plan:	#18b	Plans to promote participant retention and complete	7
2				
3	retention		follow-up, including list of any outcome data to be	
4			collected for participants who discontinue or deviate from	
5			intervention protocols	
6				
7				
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9				
10				
11	Data management	#19	Plans for data entry, coding, security, and storage,	11
12			including any related processes to promote data quality	
13			(eg, double data entry; range checks for data values).	
14			Reference to where details of data management	
15			procedures can be found, if not in the protocol	
16				
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22				
23	Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary	10-11
24			outcomes. Reference to where other details of the	
25			statistical analysis plan can be found, if not in the	
26			protocol	
27				
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31				
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33	Statistics: additional	#20b	Methods for any additional analyses (eg, subgroup and	n/a
34	analyses		adjusted analyses)	
35				
36				
37				
38	Statistics: analysis	#20c	Definition of analysis population relating to protocol non-	n/a
39	population and		adherence (eg, as randomised analysis), and any	
40	missing data		statistical methods to handle missing data (eg, multiple	
41			imputation)	
42				
43				
44				
45				
46				
47				
48	Methods: Monitoring			
49				
50				
51	Data monitoring:	#21a	Composition of data monitoring committee (DMC);	See
52	formal committee		summary of its role and reporting structure; statement of	comment
53			whether it is independent from the sponsor and	
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1 competing interests; and reference to where further
 2 details about its charter can be found, if not in the
 3 protocol. Alternatively, an explanation of why a DMC is
 4 not needed
 5
 6
 7
 8
 9

10 *(DMC is unlikely to have the opportunity to make a*
 11 *difference in this short term study where patient follow up*
 12 *is only 6 months and this study has minimal patient risk)*
 13
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21 Data monitoring: 22 interim analysis	#21b	23 Description of any interim analyses and stopping 24 guidelines, including who will have access to these 25 interim results and make the final decision to terminate 26 the trial	n/a
31 Harms	#22	32 Plans for collecting, assessing, reporting, and managing 33 solicited and spontaneously reported adverse events 34 and other unintended effects of trial interventions or trial 35 conduct	10
41 Auditing	#23	42 Frequency and procedures for auditing trial conduct, if 43 any, and whether the process will be independent from 44 investigators and the sponsor	n/a
48 Ethics and 49 dissemination			
54 Research ethics 55 approval	#24	56 Plans for seeking research ethics committee / 57 institutional review board (REC / IRB) approval	15

1	Protocol	#25	Plans for communicating important protocol	n/a
2				
3	amendments		modifications (eg, changes to eligibility criteria,	
4			outcomes, analyses) to relevant parties (eg,	
5			investigators, REC / IRBs, trial participants, trial	
6			registries, journals, regulators)	
7				
8				
9				
10				
11				
12				
13	Consent or assent	#26a	Who will obtain informed consent or assent from	6
14			potential trial participants or authorised surrogates, and	
15			how (see Item 32)	
16				
17				
18				
19				
20				
21	Consent or assent:	#26b	Additional consent provisions for collection and use of	n/a
22	ancillary studies		participant data and biological specimens in ancillary	
23			studies, if applicable	
24				
25				
26				
27				
28	Confidentiality	#27	How personal information about potential and enrolled	11
29			participants will be collected, shared, and maintained in	
30			order to protect confidentiality before, during, and after	
31			the trial	
32				
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38	Declaration of	#28	Financial and other competing interests for principal	15
39	interests		investigators for the overall trial and each study site	
40				
41				
42				
43				
44	Data access	#29	Statement of who will have access to the final trial	11
45			dataset, and disclosure of contractual agreements that	
46			limit such access for investigators	
47				
48				
49				
50				
51	Ancillary and post	#30	Provisions, if any, for ancillary and post-trial care, and for	n/a
52	trial care		compensation to those who suffer harm from trial	
53			participation	
54				
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1 Dissemination policy: [#31a](#) Plans for investigators and sponsor to communicate trial 12
 2 trial results results to participants, healthcare professionals, the
 3 public, and other relevant groups (eg, via publication,
 4 reporting in results databases, or other data sharing
 5 arrangements), including any publication restrictions
 6
 7
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13 Dissemination policy: [#31b](#) Authorship eligibility guidelines and any intended use of n/a
 14 authorship professional writers
 15
 16
 17

18 Dissemination policy: [#31c](#) Plans, if any, for granting public access to the full n/a
 19 reproducible protocol, participant-level dataset, and statistical code
 20 research
 21
 22
 23
 24
 25

26 Appendices

27
 28
 29 Informed consent [#32](#) Model consent form and other related documentation See
 30 materials given to participants and authorised surrogates uploaded
 31 document
 32
 33
 34
 35

36 Biological specimens [#33](#) Plans for collection, laboratory evaluation, and storage of n/a
 37 biological specimens for genetic or molecular analysis in
 38 the current trial and for future use in ancillary studies, if
 39 applicable
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 45

46 None The SPIRIT checklist is distributed under the terms of the Creative Commons Attribution
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 48 tool made by the [EQUATOR Network](#) in collaboration with [Penelope.ai](#)
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