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The CHILL BONES (combining high-intensity impact loading and lifting with mind-body exercise for optimisation of nervous system and skeletal health) trial: protocol for a parallel-group, semi-randomised controlled trial

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ABSTRACT

Introduction Animal studies suggest that elevated sympathetic nervous system (SNS) activity can accelerate bone loss. However, this area has not been well researched in humans. High-intensity Resistance and Impact Training (HiRIT) is recognised as an effective treatment for osteoporosis and osteopenia. Alternate forms of exercise such as mind-body exercise may be used to modulate sympathetic activity, which could have an additive benefit for skeletal adaptation when used in conjunction with HiRIT. The aim of this study is to investigate whether the combination of mind-body exercise (Tai Chi) and HiRIT can be used to concurrently modulate SNS activity and improve skeletal health.

Methods and analysis The CHILL BONES trial is a semi-randomised controlled trial where consenting adults over 60 years, who have low bone mass (total hip, femoral neck and/or lumbar spine T-score <−1.0) will be randomly allocated to participate in 8 months of twice-weekly Tai Chi, HiRIT or combined (Tai Chi+HiRIT) exercise. If participants are unwilling or unable to undertake exercise, they may opt into a non-exercising control group. The primary outcome will be total hip areal bone mineral density (BMD) measured using dual-energy X-ray absorptiometry. Secondary outcomes include femoral neck BMD, lumbar spine BMD, resting and reflexive skin sympathetic nerve activity and heart rate variability. Outcomes will be measured at baseline and post-intervention (8 months). Both intention-to-treat and per-protocol analyses will be undertaken.

Ethics and dissemination Ethical approval was granted by the Griffith University Human Research Ethics Committee (GUHREC; GU Ref No: 2023/448). Trial findings will be disseminated to participants via a plain-language summary upon completion. Results will be formally reported through peer-reviewed journals and conference presentations.

Trial registration number ACTRN12623001209684; Australian New Zealand Clinical Trials Registry.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The use of an existing community-based Tai Chi intervention enhances study feasibility; however, it may also limit standardisation and generalisability of the program.
⇒ A comprehensive suite of outcome measures for bone health and cardiovascular autonomic function ensures robust data collection.
⇒ Non-invasive techniques for the estimation of sympathetic nervous system activity minimise participant burden; however, they provide an estimate and not a direct measure of neural activity.
⇒ A non-randomised, self-selected control group of participants unwilling or unable to exercise was selected for ethical reasons, but this may introduce selection bias.

BACKGROUND AND RATIONALE

Osteoporosis is a common, age-related skeletal disorder that affects approximately 3.8% of the Australian population.[1] The condition is characterised by low bone mass and microarchitectural deterioration, which increases susceptibility to minimal trauma fracture (eg, fall-related fracture).[2] In older populations, fracture is strongly associated with increased healthcare utilisation, morbidity and premature mortality.[3] The costs associated with fracture management are substantial, exceeding $2 billion annually within Australia.[4] To mitigate the future economic and societal burden of fracture, cost-effective strategies that target bone-related and fall-related indices of fracture risk are required.

Exercise is a safe and cost-effective non-pharmacological intervention that can simultaneously improve bone density and reduce falls, thereby reducing primary risk

factors for fracture.[5] However, not all forms of exercise are equally beneficial for bone. High-intensity Resistance and Impact Training (HiRIT) is most effective for stimulating osteogenesis, particularly, in older adults with low bone mass.[6] When performed twice-weekly for 8 months, HiRIT induced favourable changes in femoral neck geometry and lumbar spine bone mineral density (BMD)—both of which are important determinants of bone strength.[5 7] The osteogenic benefits of HiRIT contrast with lower-intensity forms of exercise (i.e., Pilates or low-load resistance training), which have limited to no effect on bone.[5 8] HiRIT efficacy can be attributed to the application of mechanical loads (achieved through impact loading and 80%–85% of 1 repetition maximum resistance exercise), which induce high strains within bone and provide an effective stimulus for adaptation.[7 9]

The benefits of HiRIT for fracture prevention are not constrained to the skeletal system. HiRIT also improves muscle strength, which induces favourable changes in fall-related indices of fracture risk such as functional balance and mobility.[7 8]

Tai Chi, a 'mind-body' exercise, is an alternate form of exercise, capable of achieving clinically meaningful reductions in risk of falling (30%) and fall incidence (20%) in community-dwelling older adults.[10 11] Unlike HiRIT, the physical component of Tai Chi involves multidirectional, whole-body movement sequences, which require constant adjustment of centre of mass. As such, balance may be enhanced through different mechanisms than that of HiRIT, namely improved neuromuscular control and dual-task performance.[12 13] Therefore, improvements in balance achieved through Tai Chi may complement muscle strength and skeletal benefits of HiRIT. As such, the combination of these exercise modalities may be an optimal exercise intervention for fracture prevention.

As a weight-bearing, minimal impact form of exercise, Tai Chi is likely incapable of producing sufficient strain for skeletal adaptation.[6] However, some lower-quality studies report an attenuation of the age-associated decline in bone mass following long-term (>9 months) Tai Chi practice.[14–17] In the absence of a direct mechanical stimulus, these results may be explained by the indirect effects of the autonomic nervous system.[18 19] Indeed, Tai Chi practice reduces the low frequency component of heart rate variability (HRV), which reflects an indirect estimate of activity within the sympathetic branch of the autonomic nervous system (ANS).[20–22] Since elevated sympathetic nervous system activity is proposed to have a negative influence on bone metabolism, lowering such activity through Tai Chi may attenuate bone loss. As such, concurrent practice of Tai Chi and HiRIT may foster greater skeletal adaptation, beyond what can be achieved through HiRIT alone.[20 22] Coupled with the known benefits for balance, this novel exercise combination could reduce the risk of fracture to a greater extent than either exercise alone.[10]

METHODS

Study aims

The primary objective of the CHILL BONES trial is to determine whether an 8-month combined mind-body and osteogenic exercise intervention (Tai Chi+HiRIT) is a more effective exercise therapy for improving skeletal health (primary outcome total hip areal BMD) and reducing fracture risk in older adults with low bone mass than Tai Chi or HiRIT alone. The study also provides a unique opportunity to explore whether the skeletal outcomes of the combined intervention are mediated by modulation of the sympathetic nervous system. It is hypothesised that the combined exercise therapy will improve primary and secondary outcomes to a greater extent than either exercise alone (HiRIT or Tai Chi) or the control.

Study design and setting

This study is a four-arm parallel-group, semi-randomised controlled trial, with three randomised intervention arms (Tai Chi, HiRIT and Tai Chi+HiRIT) and a self-selected, non-exercising control arm. All measurements (baseline and follow-up) will be undertaken in the Bone Densitometry Research Laboratory, Griffith University, Gold Coast, Australia.

Patient and Public Involvement

The design, conduct or reporting plans for this research do not involve patients or the public.

Recruitment and eligibility criteria

Proposed participant flow and eligibility criteria for the trial can be found within the Consolidated Standards of Reporting Trials diagram (figure 1). We plan to recruit community-dwelling adults over the age of 60 years, who are independently ambulant and in good general health. Recruitment will occur on a rolling basis and will be targeted towards Gold Coast senior community groups, clubs and events. Word of mouth, flyers, presentations, promotional products and social media will be used to attract potential participants. Potential volunteers will be screened from initial contact with the primary investigator via phone interview or online form. Once preliminary eligibility is established and informed consent is obtained, participants will undergo a baseline assessment, which includes further eligibility screening via dual-energy X-ray absorptiometry (DXA) and ECG for entry into the intervention arms (prior to randomisation). Those with low bone mass (total hip (TH), femoral neck (FN) and/or lumbar spine (LS) areal bone mineral density (BMD T-score <−1.0)) will be included. Following allocation, participation in the trial will be discontinued where: (1) consent is withdrawn, (2) there is delayed disclosure of exclusion criteria, (3) the participant commences medication or is diagnosed with a condition known to influence bone metabolism, (4) an injury or medical event sustained throughout the trial renders the participant unable to continue, (5) the participant commences

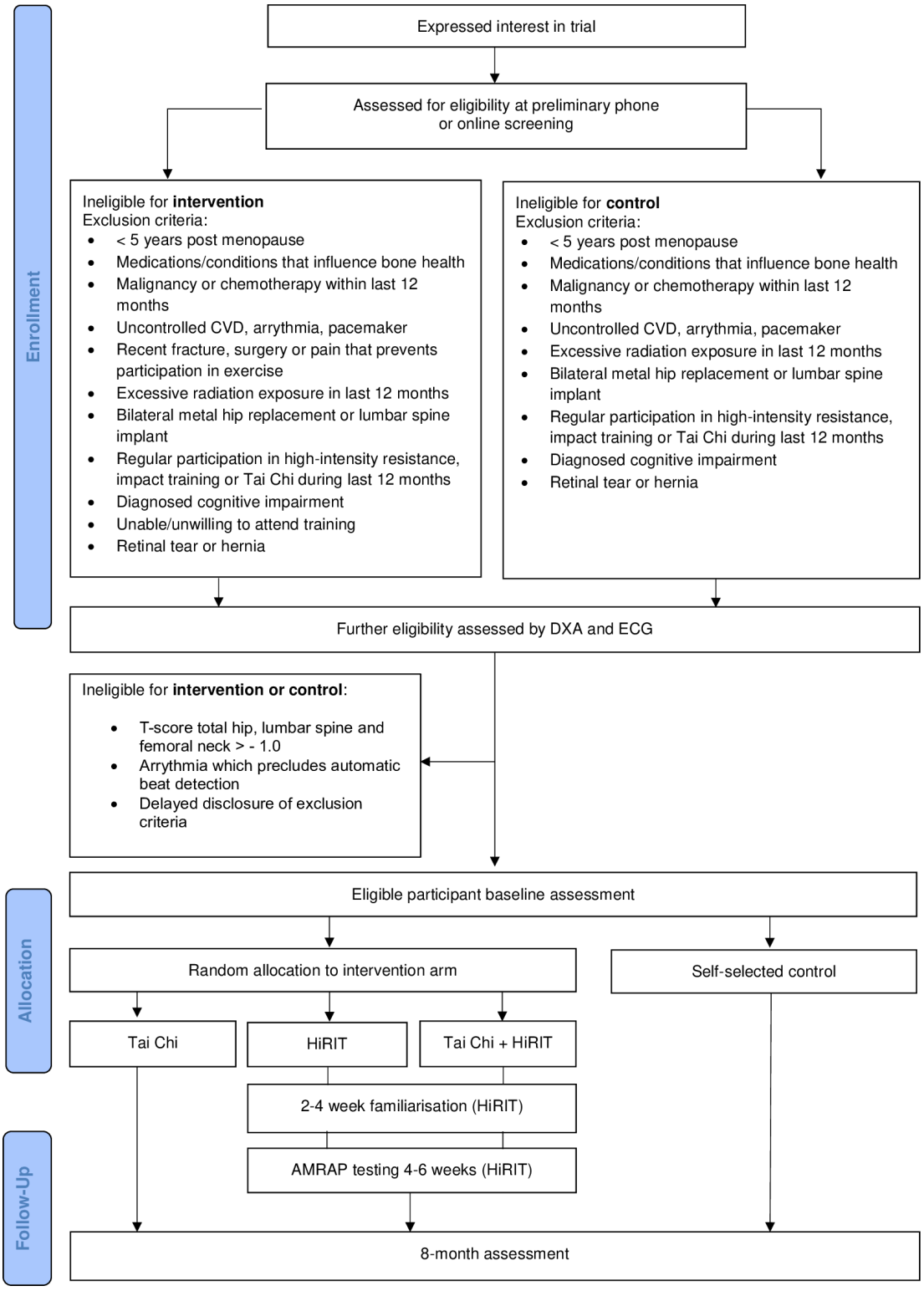

Figure 1 CONSORT diagram of proposed participant flow. CONSORT, Consolidated Standards of Reporting Trials.

exercise external to the trial that is consistent with what is being examined within the trial, (5) the participant ceases the intervention for >3 consecutive weeks and (6) general practitioner or other medical professional advises against participation in the trial. We plan to recruit 10–15 participants to the study each month, over a 14-month period spanning from October 2023 through to December 2024. A log of all contact with potential participants will be maintained by the investigator. Participants will be offered a $30 gift card as reimbursement for their time and travel.

Randomisation and allocation

Eligible participants who opt into an exercise intervention option will be randomly allocated to one of three

intervention arms: Tai Chi, HiRIT and combined (Tai Chi+HiRIT) in a 1:1:1 ratio. Randomisation occurs in blocks of six, with stratification by sex. The allocation sequence was generated by freely available software (www.jerrydallal.com; accessed on 8 July 2023). An external source prepared the allocations in sealed envelopes to maintain blinding of the lead investigator and participant until completion of baseline testing. Allocations are revealed once informed consent is obtained for the exercise intervention, and criteria for the exercise safety screening questionnaire are satisfied. All participants, including those who self-select the control group, will be instructed to maintain their usual lifestyle activities throughout the intervention period. A self-selected, non-randomised control group is more appropriate than a randomised control group for this study, as it may be considered unethical to completely restrict exercise from an older population with low bone mass.

Interventions

High-intensity resistance and impact training (HiRIT)

Participants allocated to HiRIT will complete two 30-min sessions each week, on non-consecutive days, for a period of 8 months—the minimum period required to detect changes in bone mass via densitometry. All HiRIT training sessions will be performed on the university campus, in groups of 4–6 participants, and will be supervised by the investigator to minimise potential risks associated with rolling entry into interventions (new participants frequently joining existing participants).

Participants will complete a known effective progressive resistance training program based on the LIFTMOR protocol, which consists of five sets of five repetitions of three weighted exercises (deadlift, back squat, overhead press) and one impact exercise (jumping chin-up).[9] The first 2–4 weeks will serve as a familiarisation period, whereby participants will learn how to perform the techniques correctly to avoid injury. During this period, participants will perform the weighted exercises with low load or body weight and will use soft-legged landings or heel drops for the impact exercise. Following familiarisation, the load will be gradually increased until participants are lifting 80%–85% of one repetition max (1RM) for each weighted exercise. For the impact exercise, participants will progress to a stiff-legged landing.

Intensity of weighted exercise will be assessed every 4–6 weeks using the 'As Many Repetitions As Possible' (AMRAP) method to individualise progression. Participants will be asked to perform as many repetitions as possible on the second set of the exercise (to allow for preparation on the first set) while under constant supervision. Weight and maximum number of repetitions performed with consistent technique will be entered into an online calculator (https://strengthlevel.com/one-rep-max-calculator). Once 1RM is calculated, 80%–85% of this weight will be assigned as the new load for the exercise. The AMRAP approach was adopted to reduce risk of injury associated with 1RM testing in older populations with low bone mass.[23]

Tai Chi

Participants allocated to the Tai Chi group will undertake a 60-min supervised class, once per week at local parklands (through an existing Active and Healthy initiative) and a 30-min video-based program at home, throughout the intervention period. The class will be led by a Tai Chi master, who has over 40 years of teaching experience. The instructor will remain consistent for both modes of delivery. For the first 2–4 weeks, participants will learn the 18 foundational movements of Tai Chi Qigong Shibashi. Exercise progression will be achieved through the introduction of more complex, multidirectional movements and a narrower base of support. To accommodate variable experience levels (due to rolling recruitment), a demonstration of each movement and possible progressions will be provided each session. Participants will be encouraged to self-select a progression that suits their ability, once they master the basic set. Each month, new participants will meet to perform one video-based session on campus, under the supervision of the lead investigator for quality assurance purposes.

Combined (Tai Chi + HiRIT)

Those allocated to the combined intervention will complete two 30-min HiRIT sessions in addition to two Tai Chi sessions (60-min community-based plus 30-min home-based), each week over the intervention period. Tai Chi will be performed following the completion of the HiRIT sessions, essentially back-to-back, allowing for travel.

Control

Participants who opt into the non-randomised control group will be encouraged to maintain their usual lifestyle activities (ie, physical activity and dietary pattern) across the intervention period.

Measurement timing

Assessment of primary and secondary outcomes will occur at baseline (T0) and following the 8-month intervention period (T1), with the exception of safety and adherence. Adherence and adverse events including falls, fracture and musculoskeletal injury will be monitored throughout the intervention period by the investigator and through participant self-reporting in training diaries. The safety and adherence profiles of each intervention will be assessed at the end of the 8-month training period. All other outcomes will be assessed by a single investigator who is not blind to allocation. The investigator, testing equipment, procedures and facilities will remain consistent for both measurement time-points.

Outcomes

Primary outcome

The primary outcome is 8-month TH areal BMD (Norland Elite, Swissray, Edison, NJ, USA) due to its

clinical relevance to hip fracture. All outcomes, including secondary outcomes, are summarised in table 1 (online supplemental table 1).

Secondary outcomes

Anthropometrics and body composition

Participant height will be measured to the nearest 0.1 cm using a wall-mounted stadiometer (Model 216; Seca, Hamburg, Germany). Weight will be measured to the nearest 0.1 kg using a mechanical beam scale (Model 700; Seca, Hamburg, Germany). Body Mass Index (BMI) will be calculated as weight/height^2 (kg/m^2). Whole body (WB) DXA scans (Norland Elite, Swissray, Edison, NJ, USA) will be used to determine lean muscle mass, fat mass and percentage body fat using standard procedures.

Bone-related risk factors for fractures

Lumbar spine and femoral neck areal BMD

LS and FN areal BMD will be obtained using DXA (Norland Elite, Swissray, Edison, NJ, USA).

Geometric and volumetric indices of bone strength

Peripheral quantitative computed tomography (pQCT) will be used to examine left tibial geometry and strength (pQCT, XCT-3000, Stratec Medizintechnik, Pforzheim, Germany). A standard four-slice protocol will be used to acquire images at 4%, 14%, 38% and 66% of tibial length from the distal tibial endplate. Analyses will be performed by the same technician using host software (version 6.20, Stratec Medizintechnik, Pforzheim, Germany). Volumetric BMD (vBMD, mg/cm^3), cortical thickness (mm) and polar strength-strain index (pSSI, mm^3) will be determined at the 38% site.[24] Trabecular vBMD will be derived from the 4% site. Where the left lower limb is unable to be scanned due to the presence of metalware, the right lower limb will be examined.

Fall-related risk factors for fracture

Muscle quantity and quality

Muscle quality will be evaluated using pQCT and DXA. Calf muscle cross-sectional area (CSA, cm^2) and density (mg/cm^3) (determined by pQCT at the 66% tibial site).[25] Additionally, appendicular skeletal muscle mass (ASM) will be calculated as the sum of lean mass (g) within the extremities, obtained from WB DXA. ASM will be adjusted for body size using ASM/h^2.[26]

Functional performance

Dynamic balance will be assessed using the Functional Gait Assessment (FGA). The FGA is a 10-item assessment, with a cut-off score of 22/30 predictive of falls in community-dwelling older adults (sensitivity=100%, specificity=78%).[27]

Gait speed and functional mobility will be assessed with the Timed Up and Go test. The protocol for this test can be found in Shumway-Cook *et al*.[28] A cut-off value of >13.5 s is predictive of falls in older adults (sensitivity=80%, specificity=100%).[28] The Five Times Sit to Stand test will be used as a functional measure of lower extremity strength. Participants will be instructed to stand upright from a chair without using their arms and return to the seated position for five repetitions. Time to complete the task will be recorded, as a correlate of leg extension strength in older adults.[29]

Dominant hand grip strength will be used to estimate upper extremity strength. A hand-held dynamometer (JAMAR, Hatfield, PA, USA) will be used, while participants are seated in an upright position with their elbow flexed to 90 degrees, and wrist in neutral position, supported on a table. Participants will be instructed to squeeze the dynamometer with maximum effort. The average of three trials will be compared with cut-off values for low grip strength, which correlates with sarcopenia (<27 kg males, <16 kg females).[26]

Indices of autonomic nervous system (ANS) activity

Tonic and reflexive responses from the ANS will be evaluated through non-invasive measurements, including HRV, skin sympathetic nerve activity (SKNA) and beat-to-beat arterial blood pressure. Participants will be assessed between the hours of 8–11 am following an overnight fast and abstinence from caffeinated beverages, strenuous exercise and alcohol. Room temperature and humidity will be maintained at 22 degrees and 57%, respectively, as environmental conditions may influence ANS activity. All measurements will be performed in a supine position to control for the effects of posture on cardiovascular function.

A 10-min baseline recording (tonic response) will be taken following the completion of the DXA scans to ensure participants are in a resting state. They will then complete gated breathing (5 min) at a frequency of 0.2 Hz (12 breaths per minute) to control for respiratory sinus arrythmia. To assess the reflexive responses of the ANS, participants will complete 2–3 trials of the Deep Breathing Test (1 min per test, 6 breaths per minute) and Valsalva manoeuvre (10–15 s per test, 40 mm Hg pressure) using the FinaPres Nova Guided Autonomic Testing suite (Finapres Medical Systems, Enschede, The Netherlands) (figure 2). There will be at least 2 min of recovery between tests. Participants will be instructed to avoid talking and moving during data acquisition to reduce movement artefact. All measurement signals will be acquired simultaneously and continuously for a period of approximately 40 min using LabChart 8 Pro software coupled with a Powerlab35 Series data acquisition system (ADInstruments, Sydney, Australia), with event markers placed in accordance with the testing periods outlined in figure 2.

Heart rate variability will be acquired with disposable Ag-AgCl surface electrodes (Medi-Trace, Kendall, North Ryde, Australia) from lead II via an Octal Bio Amp sampling at 10 kHz (ADInstruments, Sydney, Australia). Channel settings will be adjusted for humans (QRS width 0.08 s and minimum peak height to 2 SD) to optimise R-wave detection. Frequency-domain and time-domain outcomes (see table 1—online supplemental file 1) will be

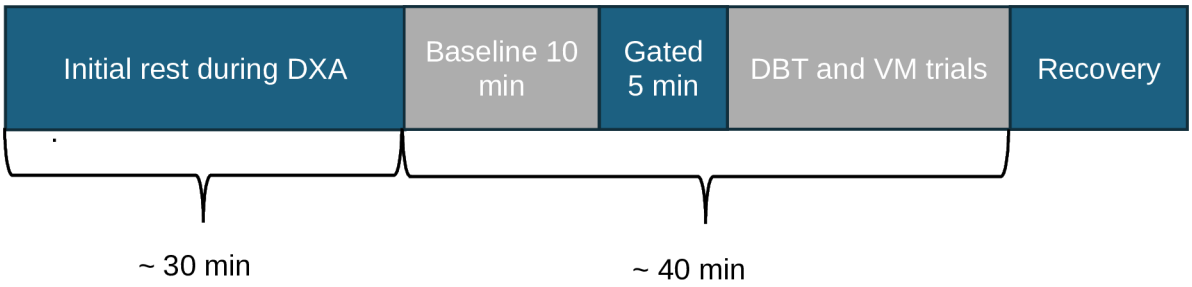

Figure 2 Timeline of autonomic activity measurements.

derived from R-R intervals using the HRV analysis module in LabChart 8 (ADInstruments, Sydney, Australia).

Skin sympathetic nerve activity will be acquired from ECG lead I, using the protocol published by Kusayama *et al*.[30] SKNA burst analysis will be undertaken using JMP software (JMP Version 17.2, SAS Institute Inc, Cary, North Carolina, USA).

Beat-to-beat blood pressure will be measured continuously via a finger cuff using the NOVA System (Finapres Medical Systems, Enschede, The Netherlands). The finger cuff will be attached to the middle phalanx of the middle finger of the left hand. An arm cuff, which is used for calibration, will be attached to the left upper limb, except in cases where previous breast surgery precludes blood pressure measurement. In these cases, the right limb will be used instead. A height correction unit will be attached to the finger cuff and at a site that is level with the heart to compensate for height differences between the finger cuff and the heart.

Participant reported outcomes

Fear of falling will be assessed using the Falls Efficacy Scale International—a 16-item questionnaire including functional activities that challenge balance.[31 32] Participants will be asked to rate their concern for falling across a variety of scenarios which would pose a challenge to their balance.

Health-related quality of life will be measured using the AQoL-8D, which is comprised of 8 dimensions within physical and psychosocial domains. Each item has 4–6 response levels, with higher scores indicative of poorer QoL. It has been validated for use in the Australian population. Psychometric scoring will be performed using a freely available 'unweighted' SPSS algorithm (https://www.monash.edu/business/che/aqol/using-aqol/scoring).[33]

The Patient Health Questionnaire-9 will also be used within the study as a reliable and valid measure of depression symptom severity.[34] Participants will complete the questionnaires on their own via an online form.

Lifestyle Behaviours

Daily average dietary calcium intake will be estimated using the Auscal questionnaire, which has been validated for the Australian diet. [35] Questionnaire data will be analysed using Foodworks nutritional analysis software (Version 10, Xyris Software, Brisbane, Australia).

Bone-relevant physical activity participation across the lifespan will be quantified using the bone-specific physical activity questionnaire (BPAQ).[36] An analysis will be performed using a customised calculator available online (http://www.fithdysign.com/BPAQ/).

Adherence and monitoring

Following HiRIT and Tai Chi training sessions, participants will rate their muscle soreness on a 10-point visual analogue scale in their training diaries. HiRIT participants will also report the weight lifted, as well as repetitions and sets completed for each of the resistance exercises. Weight lifted and AMRAP results will also be recorded by the primary investigator. All participants, including those in the control group, will report any changes to their lifestyle behaviours including diet, physical activity, medical conditions, and medications within their diaries across the 8-month intervention period. Adverse events or effects (eg, injury, fall, fracture) will also be recorded in the diary. Adherence will be monitored through attendance records and training diaries. Completion of 64 training sessions for Tai Chi and HiRIT (128 for combined intervention) over the 8-month intervention period will be regarded as 100% adherence.

Data Management

All participants will be allocated a unique identifier to ensure data remains de-identified for analysis and publication. Paper records will be stored within a secure filing cabinet while electronic data will be stored on password-protected computers. Digital back-ups will be uploaded to the Griffith University Research Repository for a minimum of 15 years, in accordance with the Australian Code for the Responsible Conduct of Research. Test results such as blood pressure, heart rhythm and DXA results may be shared with a participant's general practitioner, where the participant has directly requested a copy of the results from the primary investigator. Participants will be provided with a summary of their test results via email after each testing session. All participants will be given the opportunity to discuss their results with the investigator, once they receive their results summary. All participant data will remain de-identified (coded) to maintain confidentiality. There will be no interim analyses available prior to trial completion. All data collection and the analysis of the final trial dataset will be undertaken by the primary investigator for consistency.

Power analysis

Sample size was calculated based on previous data from a similar study, which examined BMD in post-menopausal women who participated in a resistance and impact training intervention.[37] The minimum sample size required to detect a mean difference in TH BMD of 0.004 g/cm^2 with an SD of 0.012 g/cm^2 at 80% power and alpha of 0.05 for a repeated measures analysis of variance (ANOVA) with four groups (between factor) and two measurement time-points (within factor) is 142 (n=36 per group). Accounting for a potential attrition rate of 20% which has been derived from similar trials, the minimum number required for each group will be n=42.[38]

In the absence of a priori data, a conservative effect size estimate of 0.2 was used to power our secondary analyses (indices of autonomic activity) and subgroup analyses (sex, presence/absence of beta blocker). A total sample size of n=76 (across the four groups) is required to sufficiently power these analyses, which falls within our planned sample size.

Data analysis

Statistical analyses

Statistical analyses will be performed using RStudio (Posit, Boston, Massachusetts, USA). Normality of the distribution of continuous variables will be assessed using the Kolmogorov-Smirnov test. Descriptive statistics will be generated for baseline participant characteristics for each group and will be presented as mean±SD for continuous data or n (%) for categorical data.

A one-way ANOVA will determine whether there are any pre-intervention (T0) between-group differences in normally distributed continuous variables. A non-parametric equivalent (Kruskal-Wallis test) will be used where continuous data are not normally distributed. χ^2 analyses will be performed to detect between-group differences in baseline categorical variables. Any variables found to be significantly different between groups at the pre-intervention time-point will serve as covariates. Analysis of covariance (ANCOVA) will be performed to examine the treatment effect of group, using baseline and follow-up data. All analyses will be adjusted for raw baseline data. Covariates including age, BMI and adherence will also be included in the adjusted analyses, with the addition of calcium intake and bone-relevant physical activity participation for musculoskeletal outcomes. Both adjusted and unadjusted analyses will be examined. Bonferroni correction will be employed for post hoc pairwise comparisons to determine the treatment group with the greatest improvement in outcomes. Intention-to-treat and per-protocol analyses will be carried out to reduce attrition bias. Participants with greater than 70% adherence will be included in the per-protocol analyses. Missing follow-up data secondary to study withdrawal will be accounted for using mean value imputation, for each variable, within their respective intervention groups. Further per-protocol exploratory subgroup analyses will be performed to investigate whether sex influences the treatment effect for bone-related outcomes. Adverse events/effects and change in quality of life will also be investigated in a separate per-protocol univariate analysis.

Associations between autonomic and skeletal outcomes pre-intervention and post-intervention will be analysed using correlation analyses. Separate subgroup analyses will be undertaken based on sex. Backwards-stepwise regression analysis will then be performed with the inclusion of any autonomic variable found to be significantly associated with a skeletal outcome to explore the contribution of the autonomic variable to skeletal health. Statistical significance will be set to $p<0.05$.

Ethics and dissemination

Full ethical approval for this study has been granted by the GUHREC (Ref No: 2023/448) and all aspects of the study will be undertaken in accordance with the Declaration of Helsinki. We do not anticipate any protocol amendments. Written informed consent will be obtained from each participant by the primary investigator, prior to baseline data collection and determination of further eligibility for exercise (see online supplemental file 2). As Tai Chi is known to be a very low-risk activity and previous trials of the HiRIT intervention (LIFTMOR and LIFTMOR-M) have reported minimal adverse events, early termination of the trial is highly unlikely.[5 7 9] As such, a Data Safety Monitoring Committee was not assembled. Nevertheless, multiple strategies will be implemented to minimise the risk of adverse events including (1) small group sizes, (2) supervision by a physiotherapist, (3) regular strength testing, (4) gradual loading with training exposure and (5) low-load familiarisation at commencement of intervention to allow for acclimation. While the community-based Tai Chi intervention is delivered to a larger group (approximately 20–30 people), participants will be encouraged to self-select the version of each Tai sequence that best suits their ability, so as to minimise risk of injury. Safety will be monitored through observation of supervised classes and participant reporting of injury and illnesses through training diaries. Should a serious adverse event/effect arise, it will be reported immediately to the approving GUHREC in compliance with the University Code for the Responsible Conduct of Research and the Australian Code for the Responsible Conduct of Research (NHMRC). Non-serious adverse events will be included in an annual report. Injured participants will be referred to their general practitioner and/or a qualified physiotherapist external to the trial as required. At the completion of the intervention, overall study findings will be relayed in plain language to participants via email. The findings of the study will be disseminated via scientific conference presentation and reported in scientific journals.

DISCUSSION

To our knowledge, the CHILL BONES trial will be the first to examine the efficacy of a novel, combined exercise

therapy for the optimisation of skeletal health and reduction of fracture risk in older adults with low bone mass. By incorporating indices of autonomic activity as secondary outcomes, we are able to determine whether associations exist between skeletal health and peripheral sympathetic nervous system activity, which could be leveraged within a combined exercise intervention to enhance the effectiveness of osteogenic exercise.

The outcomes of this study may have important clinical implications pertaining to exercise prescription for the management of age-related bone loss and prevention of fracture, in addition to broadening our understanding of the interaction between autonomic nervous system activity and skeletal health in humans. Importantly, we use cost-effective, community-based exercise groups within the trial, which could be easily adopted by public health services to prevent fracture on a population-based scale.

Limitations

This study has several limitations. First, the use of a non-randomised control group may introduce selection bias. However, it may be considered unethical to restrict exercise from a population who could benefit from it. A self-selected control group is also likely to reduce drop out from the control condition. Second, non-invasive measurements of ANS activity are only capable of providing an estimate of autonomic activity, based upon output from the end-organ in which it is measuring (ie, heart, skin). By using largely cardiac-derived outcomes as a surrogate for whole body autonomic outflow, direct causality cannot be established, and inferences must be made about the state of the parasympathetic and sympathetic nervous systems. Direct measurement (ie, microneurography, plasma catecholamines) may be more accurate; however, they were not considered appropriate for this study population, in light of potential risks associated with these invasive measures (ie, infection, bleeding). Third, the primary investigator will not be blind to group allocation at follow-up. A consistent investigator at both measurement time-points, however, will improve measurement reliability. Finally, our somewhat strict exclusion criteria and time commitment of the combined intervention may have biased our sample to a degree, thereby, limiting the generalisability of results to the broader older population. Excluding conditions influencing bone and the autonomic system was necessary; however, it served to enhance the ability to detect changes in outcomes related to the interventions.

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Contributors All authors made substantial contribution to the study conceptualisation, design and participated in reviewing and editing this article. The article was written by JC, BW and BB. JC is the guarantor.

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Competing interests Belinda Beck is the Director of The Bone Clinic. All other authors have no competing interests to declare.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data sharing not applicable as no datasets generated and/or analysed for this study.

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REFERENCES

1 Australian Institute of Health and Welfare. Osteoporosis and minimal trauma fractures. Australian Institute of Health and Welfare; 2024.
2 Kanis JA, McCloskey EV, Johansson H, *et al*. A reference standard for the description of osteoporosis. *Bone* 2008;42:467–75.
3 Cosman F, de Beur SJ, LeBoff MS, *et al*. Clinician's Guide to Prevention and Treatment of Osteoporosis. *Osteoporos Int* 2014;25:2359–81.
4 Tatangelo G, Watts J, Lim K, *et al*. The Cost of Osteoporosis, Osteopenia, and Associated Fractures in Australia in 2017. *J Bone Miner Res* 2019;34:616–25.
5 Watson SL, Weeks BK, Weis LJ, *et al*. High-Intensity Resistance and Impact Training Improves Bone Mineral Density and Physical Function in Postmenopausal Women With Osteopenia and Osteoporosis: The LIFTMOR Randomized Controlled Trial. *J Bone Miner Res* 2018;33:211–20.
6 Beck BR, Daly RM, Singh MAF, *et al*. Exercise and Sports Science Australia (ESSA) position statement on exercise prescription for the prevention and management of osteoporosis. *J Sci Med Sport* 2017;20:438–45.
7 Harding AT, Weeks BK, Lambert C, *et al*. Effects of supervised high-intensity resistance and impact training or machine-based isometric training on regional bone geometry and strength in middle-aged and older men with low bone mass: The LIFTMOR-M semi-randomised controlled trial. *Bone* 2020;136:S8756-3282(20)30142-3.
8 Kistler-Fischbacher M, Weeks BK, Beck BR. The effect of exercise intensity on bone in postmenopausal women (part 1): A systematic review. *Bone* 2021;143:S8756-3282(20)30476-2.
9 Watson SL, Weeks BK, Weis LJ, *et al*. Heavy resistance training is safe and improves bone, function, and stature in postmenopausal women with low to very low bone mass: novel early findings from the LIFTMOR trial. *Osteoporos Int* 2015;26:2889–94.
10 Chen W, Li M, Li H, *et al*. Tai Chi for fall prevention and balance improvement in older adults: a systematic review and meta-analysis of randomized controlled trials. *Front Public Health* 2023;11.
11 Sherrington C, Fairhall NJ, Wallbank GK, *et al*. Exercise for preventing falls in older people living in the community. *Cochrane Database Syst Rev* 2019;1:CD012424.
12 Li F, Harmer P, Fisher KJ, *et al*. Tai Chi and fall reductions in older adults: a randomized controlled trial. *J Gerontol A Biol Sci Med Sci* 2005;60:187–94.

13 Tousignant M, Corriveau H, Roy P-M, *et al*. Efficacy of supervised Tai Chi exercises versus conventional physical therapy exercises in fall prevention for frail older adults: a randomized controlled trial. *Disabil Rehabil* 2013;35:1429–35.
14 Chan K, Qin L, Lau M, *et al*. A randomized, prospective study of the effects of Tai Chi Chun exercise on bone mineral density in postmenopausal women. *Arch Phys Med Rehabil* 2004;85:717–22.
15 Qin L, Choy W, Leung K, *et al*. Beneficial effects of regular Tai Chi exercise on musculoskeletal system. *J Bone Miner Metab* 2005;23:186–90.
16 Wayne PM, Kiel DP, Buring JE, *et al*. Impact of Tai Chi exercise on multiple fracture-related risk factors in post-menopausal osteopenic women: a pilot pragmatic, randomized trial. *BMC Complement Altern Med* 2012;12:7.
17 Woo J, Hong A, Lau E, *et al*. A randomised controlled trial of Tai Chi and resistance exercise on bone health, muscle strength and balance in community-living elderly people. *Age Ageing* 2007;36:262–8.
18 Elefteriou F. Impact of the Autonomic Nervous System on the Skeleton. *Physiol Rev* 2018;98:1083–112.
19 Farr JN, Charkoudian N, Barnes JN, *et al*. Relationship of sympathetic activity to bone microstructure, turnover, and plasma osteopontin levels in women. *J Clin Endocrinol Metab* 2012;97:4219–27.
20 Audette JF, Jin YS, Newcomer R, *et al*. Tai Chi versus brisk walking in elderly women. *Age Ageing* 2006;35:388–93.
21 Liu J, Xie H, Liu M, *et al*. The Effects of Tai Chi on Heart Rate Variability in Older Chinese Individuals with Depression. *IJERPH* 2018;15:2771.
22 Zhou Y, Wang Q, Larkey L, *et al*. Tai Chi Effects on Heart Rate Variability: A Systematic Review and Meta-Analysis. *J Integr Complement Med* 2024;30:121–32.
23 Brzycki M. Strength Testing—Predicting a One-Rep Max from Reps-to-Fatigue. *Journal of Physical Education, Recreation & Dance* 1993;64:88–90.
24 Sheu Y, Zmuda JM, Boudreau RM, *et al*. Bone strength measured by peripheral quantitative computed tomography and the risk of nonvertebral fractures: the osteoporotic fractures in men (MrOS) study. *J Bone Miner Res* 2011;26:63–71.
25 Cesari M, Leeuwenburgh C, Lauretani F, *et al*. Frailty syndrome and skeletal muscle: results from the Invecchiare in Chianti study. *Am J Clin Nutr* 2006;83:1142–8.
26 Cruz-Jentoft AJ, Bahat G, Bauer J, *et al*. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing* 2019;48:16–31.
27 Wrisley DM, Kumar NA. Functional gait assessment: concurrent, discriminative, and predictive validity in community-dwelling older adults. *Phys Ther* 2010;90:761–73.
28 Shumway-Cook A, Brauer S, Woollacott M. Predicting the probability for falls in community-dwelling older adults using the Timed Up & Go Test. *Phys Ther* 2000;80:896–903.
29 Bohannon RW, Bubela DJ, Magasi SR, *et al*. Sit-to-stand test: Performance and determinants across the age-span. *Isokinet Exerc Sci* 2010;18:235–40.
30 Kusayama T, Wong J, Liu X, *et al*. Simultaneous noninvasive recording of electrocardiogram and skin sympathetic nerve activity (neuECG). *Nat Protoc* 2020;15:1853–77.
31 Yardley L, Beyer N, Hauer K, *et al*. Development and initial validation of the Falls Efficacy Scale-International (FES-I). *Age Ageing* 2005;34:614–9.
32 Delbaere K, Close JCT, Mikolaizak AS, *et al*. The Falls Efficacy Scale International (FES-I). A comprehensive longitudinal validation study. *Age Ageing* 2010;39:210–6.
33 Richardson J, Iezzi A, Khan MA, *et al*. Validity and reliability of the Assessment of Quality of Life (AQoL)-8D multi-attribute utility instrument. *Patient* 2014;7:85–96.
34 Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med* 2001;16:606–13.
35 Beck B, Weeks B, Norling T. A novel australian calcium-specific diet questionnaire: validity and reliability. In: *Osteoporosis International*. SPRINGER LONDON LTD 236 GRAYS INN RD, 6TH FLOOR LONDON WC1X 8HL, ENGLAND, 2011: S626–7.
36 Weeks BK, Beck BR. The BPAQ: a bone-specific physical activity assessment instrument. *Osteoporos Int* 2008;19:1567–77.
37 Bolton KL, Egerton T, Wark J, *et al*. Effects of exercise on bone density and falls risk factors in post-menopausal women with osteopenia: a randomised controlled trial. *J Sci Med Sport* 2012;15:102–9.
38 Kelley GA, Kelley KS. Dropouts and compliance in exercise interventions targeting bone mineral density in adults: a meta-analysis of randomized controlled trials. *J Osteoporos* 2013;2013:250423.