Systematic Reviews

PROTOCOL

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Impact of multicomponent physical exercise and high-intensity interval training on osteoporosis in postmenopausal women: protocol for a systematic review and network meta-analysis of randomized controlled trials

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Abstract

Background Osteoporosis is a progressive degenerative bone condition leading to increased fracture risk. Therefore, osteoporosis acknowledges around 200 million cases, with about 70% of the cases occurring in postmenopausal women. Medicaments are often suggested to treat osteoporotic conditions, but physical exercise also plays an essential role. The current literature highlights multicomponent training (MCT) and high-intensity and high-impact exercises as physical exercise interventions that positively affect postmenopausal women's bone health. Furthermore, there is prior evidence of systematic reviews about the positive effects of both methods on the bone health of this population. Despite this prior evidence, no systematic reviews with metanalytic methods compare the effectiveness of the two interventions.

Methods and analysis.

The study will follow the guidelines of PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) and was registered at the International Prospective Register of Systematic Reviews (PROSPERO) under the registration number (CRD42024604930). This systematic review and meta-analysis will include only randomized controlled clinical trials (RCTs), which have verified the effects of one or both physical exercise methods on postmenopausal women's bone mineral density (BMD). The systematic search will be implemented at eight electronic databases, namely PubMed/MEDLINE, Web of Science (WoS), EBSCO, Cochrane Central Register of Controlled Trials (CENTRAL), Scopus, CINAHL, and SPORTDiscus, which will be used to retrieve the data of interest. The RCTs' risk of bias (RoB) will be assessed with the RoB 2 Cochrane tool, and between-study heterogeneity will be checked through the analysis of Half-Cauchy distribution. Additionally, a network meta-analysis will be applied to compare the between-studies dose–response on the patients' bone health. The final database search was completed on January 18, 2025.

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Discussion In this study, we hope to find consistent results about the effects of MCT and HIIT in postmenopausal women with osteoporosis. Therefore, we also expect to observe between-intervention effects after the network meta-analysis approaches. A Bayesian network meta-analysis will be conducted using Markov Chain Monte Carlo simulations. Exercise dose will be modeled in METs-min/week to explore dose–response relationships. The deviance information criterion (DIC) will be used to compare model fit. Confidence in the results will be evaluated using the CINeMA framework. This way, this study will significantly impact this field of knowledge.

Ethics and dissemination.

The design of this review protocol did not involve patients.

Systematic review registration: PROSPERO CRD42024604930.

Introduction

Osteoporosis is a condition defined by decreased bone density and degradation of bone microarchitecture, leading to increased fragility and susceptibility to fractures. The disease can affect various regions of the skeleton, being diagnosed and classified according to the degree of bone loss and history of previous fractures [1]. With an estimated global prevalence of 200 million cases, osteoporosis constitutes a significant public health problem, with considerable economic repercussions [2, 3]. Approximately 70% of cases occur in women in the postmenopausal phase [1, 4].

Osteoporosis is a widely prevalent condition and is expected to increase in the coming years. It is estimated that about 30% of women in Europe and the USA have osteoporosis, and at least 40% of these women will suffer one or more fractures related to the disease in their lifetime. The consequences of this condition include a significant reduction in quality of life, compromising functional capacity, independence, and mobility. Additionally, osteoporosis represents a significant risk to life, as one in every three people dies within 12 months after a hip fracture [5].

The primary treatment for osteoporosis usually includes medications aimed at increasing BMD. However, exercises play an essential role in reducing other risk factors associated with falls and fractures, such as muscle weakness, loss of balance, and decreased functional capacity. In order for exercises to provide these benefits, it is crucial that they are correctly prescribed and that the patient maintains proper adherence to the program [5]. Regular physical activity can help minimize bone loss and reduce the frequency of falls and fractures [6].

Although there are studies investigating the benefits of physical exercise for osteoporosis [7, 8], there is a scarcity of specific research on the effects of MCT and HIIT in treating osteoporosis in postmenopausal women. A comprehensive search in the literature revealed only two systematic reviews with this.

type of intervention in the studied population. The first one analyzed the effects of HIIT on bone health, but presented limitations, such as consulting a restricted number of databases and the absence of meta-analyses [9]. The second review focused on MCT, but used mixed samples of middle-aged and older women, without conducting subgroup analyses by the participants' age [10]. Therefore, there is a clear need for studies that include complementary analyses and more robust search strategies, overcoming the limitations of previous works. In face of the limitations identified in previous studies, the need for more in-depth research using broader search strategies and complementary analyses is evident. Future investigations should focus on the role of MCT and HIIT in preventing fractures and improving bone health in postmenopausal women with osteoporosis. Furthermore, despite the importance of diagnostic methods such as dual-energy X-ray absorptiometry (DXA) and tools such as fracture risk assessment (FRAX), few studies analyze these parameters together in the context of physical exercise [9, 10]. Therefore, more research is essential to clarify the effects of these interventions and provide a solid scientific basis for treatment and prevention strategies in postmenopausal women with osteoporosis.

Methods

Study registration

The protocol of this study followed the guidelines of PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) [11]. The study protocol was prior registered at the International prospective register of systematic reviews (PROSPERO) under the registration number CRD42024604930.

Eligible criteria for study selection

Types of studies

RCTs reviewed by peers and published in English language will be included in the search, since most of the relevant literature is published in that language, thus ensuring greater scope and reliability for the study. Although the inclusion will be restricted to studies published in English, we acknowledge the potential for language bias. This decision was based on practical

considerations, such as the team's linguistic expertise and the predominance of high-quality evidence published in English in international peer-reviewed journals. Nonetheless, the limitations imposed by language restrictions—particularly the risk of omitting relevant studies published in other languages—will be addressed in the discussion and considered during the interpretation of findings, as emphasized by Moher et al. [12], Sterne et al. [13], Jackson and Kuriyama [14], and Busse et al. [15].

Grey literature was excluded, as the studies included in the academic repository could still not be peer-reviewed articles. A wide collection of peer-reviewed studies is already available. The exclusion of grey literature was motivated by the aim to focus on peer-reviewed studies, which typically undergo more rigorous methodological scrutiny. However, we recognize that this approach may increase the risk of publication bias and potentially overestimate effect sizes. This limitation will be critically discussed in the final interpretation of results. The impact of excluding non-peer-reviewed sources has been well documented in previous methodological research [16–20], reinforcing the need for transparency in this decision.

Types of participants

The eligible participants will be postmenopausal women, defined as those who have experienced the permanent cessation of menstruation for at least 12 consecutive months. Although inclusion is based on menopausal status rather than chronological age, it is expected that most participants will be 45 years or older, as consistent with epidemiological norms for postmenopausal onset. Participants must also present a bone mineral density (BMD) *T*-score of less than or equal to −2.5 to be considered eligible. The inclusion criteria will be strictly limited to females, focusing exclusively on postmenopausal women. Studies that include both men and women will be excluded. However, there will be no restrictions regarding ethnicity, severity of symptoms, or disease duration.

Types of interventions and comparators

We will include treatments in which osteoporosis has been diagnosed based on BMD measured only with gold standard equipment, i.e., DXA [21]. The study compares the effects of two types of exercise interventions—high-intensity interval training (HIIT) and multicomponent training (MCT)—on this condition [22, 23]. Interventions must have a duration of at least 8 months. HIIT sessions are characterized by alternating short bouts of high-intensity exercise, performed at ≥ 80% of maximum heart rate (HRmax) or ≥ 90% of VO_2max, with recovery periods consisting of rest or light activity (typically ≤ 50% of HRmax). Common work-to-rest ratios range from 1:1 to 2:1, although variations such as 1:2 are also acceptable if the intensity thresholds are met. The total duration of each HIIT session typically ranges from 15 to 30 min, and training frequency is commonly two to three sessions per week. Eligible HIIT modalities include running, cycling, circuit training, or similar structured formats that allow for controlled intensity intervals [24]. In contrast, multicomponent training (MCT) refers to exercise programs that incorporate at least two or more exercise modalities within the same program, such as aerobic training (≤ 70% VO_2max), resistance training (at 60–80% of 1RM), balance, and/or flexibility exercises. These components may be delivered within the same session or spread across a weekly schedule. Interventions must report sufficient detail on the training structure to allow classification into either MCT or HIIT categories [24].

Studies implementing mixed interventions that combine both HIIT and MCT within a single experimental group will be excluded, unless outcome data are presented separately for each component. Only studies that allow independent assessment of HIIT and MCT effects will be eligible for inclusion in the network meta-analysis.

Types of outcome measures

The primary outcome of interest will be the mean differences in bone mineral density (BMD). The secondary outcome will focus on physical fitness, assessed through validated functional tests commonly used in postmenopausal women. These may include the Short Physical Performance Battery (SPPB) [25], the Senior Fitness Test [26], 6-min walk test (6MWT), chair stand test, and handgrip strength, among others. To ensure comparability across studies using different tests, we will calculate standardized mean differences (SMDs) for each outcome domain. When necessary, we will classify and group outcomes by physical fitness domains (e.g., muscle strength, balance, aerobic capacity, flexibility), and convert raw scores to common units or *z*-scores, following methods recommended in the Cochrane Handbook [27]. This approach will allow for a meaningful synthesis of the functional fitness outcomes across different trials.

Search strategies for the identification of studies

Electronic searches

The systematic search was conducted across seven electronic databases, and the final search was completed on January 18, 2025, ensuring that the most recent and relevant studies were included. The following electronic databases were searched: PubMed/MEDLINE, Web of Science (WoS), EBSCO, Cochrane Central Register of Controlled Trials (CENTRAL), Scopus, CINAHL, and SPORTDiscus. In the Scopus database, subject area filters were revised to minimize the risk of excluding

relevant trials published in multidisciplinary or overlapping fields. Therefore, only non-relevant fields (e.g., Veterinary, Mathematics, Chemical Engineering) were excluded, while multidisciplinary and health-related categories were retained. This adjustment aimed to ensure a comprehensive and unbiased search across all potentially relevant domains. Specific search strategies validated for identifying randomized controlled trials (RCTs), such as those recommended in the Cochrane Handbook, were used as references to construct the queries. These strategies included Medical Subject Headings (MeSH) and equivalent terms, which were adapted and enriched for each database to ensure comprehensiveness. Detailed search strategies are presented in Fig. 1. Filters were minimized to avoid the exclusion of relevant studies, focusing only on essential criteria, such as publication type (RCTs) and language (English), as outlined in Table 1.

Data collection and analysis

Study selections

The potentially relevant articles will be evaluated for eligibility through screening of titles and abstracts, and

PubMed/MEDLINE

#1 Women [MeSH terms]
#2 Woman
#3 "Women's Groups"
#4 "Women Groups"
#5 "Women's Group"
#6 "Women, Working"
#7 "Older Women"
#8 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7
#9 Exercise [MeSH terms]
#10 "Physical Exercise"
#11 "Multicomponent training"
#12 "Multicomponent physical exercise"
#13 MCT
#14 MCPE
#15 "High-Intensity Interval Training [MeSH terms]
#16 "High Intensity Interval Training"
#17 "High-Intensity Intermittent Exercise"
18 "Sprint Interval Training"
#19 HIIT
#20 #9 OR #10 OR #11 OR #12 OR#13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19
#21 "Physical Functional Performance [MeSH terms]
#22 "Functional Performance"
#23 "Physical Performance"
#24 "Physical Fitness"
#25 "Gait Analysis" [MeSH terms]
#26 "Gait Analyses"
#27 "Cardiorespiratory Fitness" [MeSH terms]
#28 "Body Composition" [MeSH terms]
#29 Osteoporosis [MeSH terms]
#30 "Age-Related Osteoporosis" [MeSH terms]
#31 "Age-Related Osteoporoses"
#32 "Age Related Osteoporosis"
#33 "Age-Related Bone Loss"
#34 "Age-Related Bone Losses"
#35 "Senile Osteoporoses"
#36 "Senile Osteoporosis"
#37 "Post-Traumatic Osteoporoses"
#38 "Post-Traumatic Osteoporosis"
#39 "Osteoporosis, Postmenopausal" [MeSH terms]
#40 "Post-Menopausal Osteoporoses"
#41 "Post-Menopausal Osteoporosis"
#42 "Postmenopausal Osteoporoses"
#43 "Perimenopausal Bone Loss"
#44 "Postmenopausal Bone Losses"
#45 "Perimenopausal Bone Losses"
#46 "Bone Diseases, Metabolic" [MeSH terms]
#47 "Metabolic Bone Diseases"
#48 "Metabolic Bone Disease"
#49 Osteopenia
#50 "Low Bone Density"
#51 "Low Bone Densities"
#52 "Low Bone Mineral Density"
#53 #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR 45 OR #46 OR #47 OR #48 OR #50 OR #51 OR #52
#53 #8 AND #20 AND #52

Cochrane

#1 MeSH descriptor: [Women] explode all trees
#2 (Women OR Woman OR "Women's Groups" OR "Women Groups" OR "Women's Group" OR "Women, Working" OR "Older Women") (Word variations have been searched)
#3 #1 OR #2
#4 (Exercise) (Word variations have been searched)
#5 (Exercise OR "Physical Exercise" OR "Multicomponent training" OR "Multicomponent physical exercise" OR MCT OR MCPE) (Word variations have been searched)
#6 MeSH descriptor: [High-Intensity Interval Training] explode all trees
#7 ("High-Intensity Interval Training" OR "High Intensity Interval Training" OR "High-Intensity Intermittent Exercise" OR "Sprint Interval Training" OR HIIT) (Word variations have been searched)
#8 #4 OR #5 OR #6 OR #7
#9 MeSH descriptor: [Physical Functional Performance] explode all trees
#10 ("Physical Functional Performance" OR "Physical Performance" OR "Physical Fitness") (Word variations have been searched)
#11 MeSH descriptor: [Gait Analysis] explode all trees
#12 ("Gait Analysis" OR "Gait Analyses") (Word variations have been searched)
#13 MeSH descriptor: [Cardiorespiratory Fitness] explode all trees
#14 ("Cardiorespiratory Fitness") (Word variations have been searched)
#15 MeSH descriptor: [Body Composition] explode all trees
#16 ("Body Composition") (Word variations have been searched)
#17 MeSH descriptor: [Osteoporosis] explode all trees
#18 (Osteoporosis OR "Age-Related Osteoporosis" OR "Age-Related Osteoporoses" OR "Age Related Osteoporosis" OR "Age-Related Bone Loss" OR "Age-Related Bone Losses" OR "Senile Osteoporoses" OR "Senile Osteoporosis" OR "Post-Traumatic Osteoporoses" OR "Post-Traumatic Osteoporosis") (Word variations have been searched)
#19 MeSH descriptor: [Osteoporosis, Postmenopausal] explode all trees
#20 ("Osteoporosis, Postmenopausal" OR "Post-Menopausal Osteoporoses" OR "Post-Menopausal Osteoporosis" OR "Postmenopausal Osteoporoses" OR "Perimenopausal Bone Loss" OR "Postmenopausal Bone Losses" OR "Perimenopausal Bone Losses") (Word variations have been searched)
#21 MeSH descriptor: [Bone Diseases, Metabolic] explode all trees
#22 ("Bone Diseases, Metabolic" OR "Metabolic Bone Diseases" OR "Metabolic Bone Disease" OR "Osteopenia" OR "Osteopenias" OR "Low Bone Density" OR "Low Bone Densities" OR "Low Bone Mineral Density") (Word variations have been searched)
#23 #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22
#24 #3 AND #8 AND #23

Fig. 1 Search strategies PubMed and Cochrane

Table 1 Matching filters in each database

Database	Filters
PubMed/MEDLINE	- Data: 2014–2024 - Article Type: RCT - Species: Humans - Language: English - Other: Exclude preprints; MEDLINE
Web of Science (WoS)	- Year of publication: 2014–2025 - Document Types: Article - Languages: English - Document Types Exclude: Early Access or Proceeding Paper or Retracted Publication or Book Chapters or Data Paper - Exclude – Sustainable Development Goals: 02 Zero Hunger or 04 Quality Education or 11 Sustainable Cities And Communities
EBSCO	- Search modes: Search for all the search terms I have indicated - Apply related words - Apply equivalent subjects - Restrict results: Full Text; Available References; Scientific Journals (Peer Reviewed) - Publication date: 2014–2024 - Publication type: Article - Language: English - Full Text PDF
Cochrane	- Publication date: 01/01/2014 a 31/12/2024
Scopus	- Publication date: 2014–2025 - Subjects Area (Excluded): Veterinary; Mathematics; Chemical Engineering; Dentistry; Earth and Planetary Sciences - Document Type: Article - Language: English - Keyword: Randomized Clinical Trial (RCT)
CINAHL	- Full text - Available references - Publication date: January 2014–December 2024 - Reviewed by experts - Publication type: Journal Article - Language: English - Expanders: Apply related words; Apply equivalent subjects - Search mode: Find all my search terms
SPORTDiscus	- Full text - Available references - Publication date: January 2014–December 2024 - Reviewed by experts - Document type: Article - Language: English

subsequently selected after a full-text review based on previously defined inclusion and exclusion criteria. The literature search and selection process will be initially conducted by two reviewers and then verified by a third author. Any disagreement will be resolved through discussion among the three authors. All studies will be managed and stored using Rayyan, an online platform tool for systematic review and meta-analysis (https://www.rayyan.ai/) [28] The reasons for excluding studies will be recorded and presented in a PRISMA flowchart.

Data extraction and management

The relevant data from each study, including year of publication, sample size, participants' characteristics (e.g., age and T-score), and training modalities (type of exercise, frequency, and duration), will be extracted using a standardized and previously established Microsoft® Excel spreadsheet. Two reviewers will conduct the extraction process independently, and any discrepancies will be resolved through discussion or consultation with a third reviewer. All extracted data will be managed and analyzed in R Studio. Additional data will also be collected, such as intervention details, primary and secondary outcomes, and study design. Where necessary, data transformations will be performed, including unit conversions, normalization, calculation of means or standard deviations, and effect sizes of treatments to ensure consistency across the study comparison.

Effect sizes for continuous outcomes will be calculated as mean differences (MD) when outcomes are measured

using the same scale across studies (e.g., BMD in g/cm^2), or standardized mean differences (SMD) when different instruments or scales are used (e.g., functional fitness tests). Where studies report pre- and post-intervention means and standard deviations, we will compute change scores and their corresponding standard deviations, using appropriate formulas recommended in the Cochrane Handbook. When only baseline and follow-up values are available without change scores, and standard deviations of the change are not reported, we will impute these using a correlation coefficient derived from similar studies or from those that report both values. If needed, we will convert reported effect sizes (e.g., confidence intervals, standard errors) into standard deviations using validated methods. All effect size calculations will be performed in R Studio using appropriate meta-analytic packages.

A sensitivity analysis will be conducted to evaluate the robustness of the results, accounting for factors such as sample size, high risk of bias 2 (RoB 2), missing data, and the analytical models used. Studies with low methodological quality after assessment will be excluded to maintain the reliability and validity of the findings.

Calibration exercises for study selection and data extraction

Before the formal study selection and data extraction processes, calibration exercises will be conducted to ensure consistency and accuracy among the reviewers. Two independent reviewers will screen a pilot set of 10 randomly selected articles, evaluating them against the inclusion and exclusion criteria. Discrepancies will be discussed and resolved in consultation with a third reviewer to refine the application of the criteria. Similarly, for data extraction, the same reviewers will independently extract data from five studies using a standardized extraction form. Any disagreements will be resolved through discussion or consultation with a third reviewer. These exercises will ensure that all reviewers are aligned and reduce variability in decision-making during the review process.

Assessment of RoB and quality

The Cochrane Collaboration tool for assessing RoB 2 will be used to evaluate the RoB for randomized clinical trials [29]. It contains five bias domains: bias due to the randomization process, deviation from intended intervention, missing outcome data, measurement of outcomes, selection of the reported result, and "overall risk of bias" judgment [30].

Studies with low methodological quality will be excluded based on the results of the risk of bias assessment using the Cochrane Risk of Bias Tool 2.0 (RoB 2.0). Low methodological quality will be defined as studies rated as "high risk of bias" in two or more of the five domains assessed by RoB 2.0, including bias arising from the randomization process, bias due to deviations from intended interventions, bias due to missing outcome data, bias in measurement of the outcome, and bias in selection of the reported result. Additionally, studies that lack essential methodological details required to make an informed judgment, even after contacting the authors for clarification, will also be classified as low quality. Consistent concerns about methodological integrity, such as unclear allocation concealment, incomplete outcome data, or selective outcome reporting, will further support the classification of low quality.

Managing missing data

In case of missing, inadequate, or confusing data, we will contact the corresponding author to request the essential information. If it is not possible to obtain this information, only the accessible data will be used in the analysis, with the limitations duly discussed.

Assessment of heterogeneity

The between-studies heterogeneity (T2) assessment will be performed in R, programming language, where the Half-Cauchy distribution will be used [31].

The Half-Cauchy distribution was chosen as a prior for between-study variance in the Bayesian framework [32, 33], as it provides a weakly informative yet robust prior, particularly suitable for modeling uncertainty in variance parameters. Compared to traditional heterogeneity estimates such as I^2 or τ^2, the Half-Cauchy prior accommodates extreme values more effectively and reduces the risk of over-shrinking the between-study variance, which can occur with more restrictive priors. This approach has been recommended in Bayesian meta-analytic methods [34–36], especially when the number of included studies is relatively small or when true heterogeneity is expected. While I^2 is commonly used in frequentist analyses, the Half-Cauchy prior provides a more flexible and principled alternative for variance estimation in Bayesian models [36].

In Bayesian meta-analysis, the tau (τ) value represents the standard deviation of the true effect sizes across studies and is used as a measure of between-study heterogeneity [37]. Higher values of τ indicate greater heterogeneity, meaning that the true effects vary more substantially between studies [37]. Although no universal thresholds apply due to dependence on the outcome scale, values of τ below 0.1 are often interpreted as low heterogeneity, between 0.1 and 0.3 as moderate, and above 0.3 as high, depending on the context [37]. This continuous metric provides an alternative to I^2

commonly used in frequentist approaches and allows for a more nuanced understanding of heterogeneity within the Bayesian framework [37].

This statistical text is adequate for this network meta-analysis because it considers positive means variances and their respective standard errors in the pre-post comparisons in the target randomized controlled trials. The Half-Cauchy test works addressing very high values for the tails into the distributions; thus, adding high rigor levels to consider variances in the extremes of the distributions and estimating the studies with high variability in the posterior expectation as significantly heterogeneous at a 95% confidence interval [38]. As outputs, the tau heterogeneity scores, the *p*-value of heterogeneity probabilities, and the corresponding confidence interval will be exposed [31].

Data synthesis

To analyze the pre-post differences between studies' doses of the two different types of exercise, a Network meta-analysis will be performed considering the variables "study" "time of intervention (duration)" the exercise "dose" defined by the resulting in METs-min/week, predefined by Ainsworth and colleagues [39], "pre-post mean differences" "standard errors of the differences" and "effect sizes of the differences" where between-studies measurements are not consistent [31].

To standardize comparisons across interventions of varying intensity and structure, METs-min/week will be used as a continuous variable to quantify the exercise dose. This energy expenditure metric allows different exercise types (e.g., HIIT, MCT) to be integrated into a single analytical framework, enhancing comparability and enabling dose–response analysis. The use of METs-min/week follows the Compendium of Physical Activities [39], which provides standardized MET values for a wide range of activities and has been widely adopted in physical activity research.

To control for differences in intervention duration, studies will be grouped into duration-based subgroups (e.g., 8–10, 10–12, 12–14 weeks) to allow for fair comparisons across similar timeframes. The Bayesian model will be informed by prior probabilities derived from the sample's observed means and standard deviations, which will serve as reference distributions for posterior inference [31].

The Bayesian network meta-analysis will be conducted using Markov Chain Monte Carlo Simulation (MCMCS), a method that approximates posterior parameter distributions via iterative sampling [40]. Model fit will be evaluated through the Deviance Information Criterion (DIC), which penalizes model complexity while rewarding goodness of fit; lower DIC values indicate more optimal models [33]. This will determine whether a fixed-effect or random-effect model is best suited for the data.

Trace and density plots will be generated to assess convergence and mixing of MCMC chains [41]. Additionally, the Potential Scale Reduction Factor (PSRF) will be computed via the Gelman–Rubin statistic, with values between 1.00 and 1.05 indicating adequate chain convergence and sampling efficiency [42].

A network plot will be developed to visualize the relationships between the control group and varying doses of the exercise methods. Furthermore, comparisons of post–prior probabilities will be visualized through random forests and bar plots, ranking the importance of each intervention and dose combination [31].

Confidence in network meta-analysis estimates

To enhance the interpretability and trustworthiness of the findings, we will apply the CINeMA (Confidence in Network Meta-Analysis) framework to evaluate the certainty of evidence for each treatment comparison in the network. CINeMA is based on the GRADE approach and assesses confidence across six key domains: within-study bias, reporting bias, indirectness, imprecision, heterogeneity, and incoherence. This assessment will be performed using the CINeMA web application (https://cinema.ispm.unibe.ch/) as recommended by Nikolakopoulou et al. [43] and Salanti et al. [44]. The results will be presented alongside the primary outcomes to provide a transparent and structured evaluation of the network estimates.

Subgroup analysis and sensitive analysis

We will perform predefined subgroup analyses to explore the influence of specific study characteristics on treatment effects. Subgroups will include participant age (e.g., 45–60 vs. > 60 years), sample size (small vs. large trials), and overall risk of bias. We hypothesize that younger postmenopausal women may respond more favorably to HIIT due to higher tolerance for intense physical effort, while older women may benefit more from MCT, which typically involves moderate intensity and better functional integration. Additionally, we expect that studies classified as low risk of bias will present smaller and more conservative effect sizes compared to those with higher risk of bias.

A sensitivity analysis will be performed using leave-one-out cross-validation. In this method, each study will be iteratively excluded, and the meta-analysis will be rerun to evaluate the impact of that study on the overall results. This strategy will allow us to identify influential studies whose inclusion may disproportionately affect the findings. If the exclusion of a specific study significantly

reduces the T^2 or τ values, it may be removed from the final model to enhance the robustness and stability of the results [45].

Patient and public involvement

The design of this review protocol did not involve patients.

Discussion

In this systematic review and network meta-analysis, we will evaluate the effects of MCT and HIIT on BMD and functional fitness of postmenopausal women with osteoporosis. Physical exercise is widely recognized as one of the main non-pharmacological interventions for individuals with osteoporosis [46]. However, so far, we have not found systematic reviews that compare the efficacy of these two physical exercise training methodologies in this specific context. Therefore, we have developed this protocol to systematically review and meta-analyze, with a Bayesian approach, the effectiveness of MCT and HIIT in women with osteoporosis, following the guidelines of the Cochrane Manual V.5.2.0, with the aim of providing solid evidence and more precise guidance for clinical practice [27]. We hope to find robust findings about the benefits of the two physical exercise methods for postmenopausal women with osteoporosis.

The systematic review and network meta-analysis are expected to be completed by September 2025, including final data synthesis, interpretation, and manuscript submission.

Limitations of the planned review

This protocol presents a comprehensive and methodologically rigorous plan for conducting a systematic review and Bayesian network meta-analysis. Nonetheless, several limitations must be acknowledged. First, the inclusion of only English-language studies may introduce language bias and limit the comprehensiveness of the evidence base. Second, the exclusion of grey literature may increase the risk of publication bias by omitting relevant but unpublished or non-peer-reviewed data. Third, substantial heterogeneity may be present across studies due to variations in intervention design, exercise protocols, and outcome measurement tools. Fourth, despite efforts to standardize physical fitness outcomes, differences in the type and administration of functional tests may limit comparability. Finally, missing or incomplete data in some studies may impact the accuracy of effect estimates, although strategies such as author contact and imputation will be used to mitigate this issue.

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Author contribution
AMM: conception, design of the study, and data collection.
AS: data collection and manuscript writing.
SE: data collection, manuscript writing, and interpretation.
PF, TB, DM: critical review and approval of the final manuscript.
All authors read and approved the final version of the manuscript.

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Data availability
The data used and analyzed during this study are available with the corresponding author upon reasonable request. All data supporting the findings of this study have been organized to ensure access, respecting privacy and confidentiality guidelines.

Declarations

Ethics approval and consent to participate
This study did not involve human participants, human data, human tissue, animals, or plants. Therefore, the need for ethical approval and consent to participate does not apply to this study. Ethics statement: Not applicable.

Consent for publication
This manuscript does not include individual data of people (such as details, images or videos). Therefore, publication consent is not applicable.

Competing interests
The authors declare that they have no competing financial or non-financial interests related to the content of this article.

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References

1. LeBoff MS, Greenspan SL, Insogna KL, Lewiecki EM, Saag KG, Singer AJ, et al. The clinician's guide to prevention and treatment of osteoporosis. Osteoporos Int J Establ Result Coop Eur Found Osteoporos Natl Osteoporos Found USA. 2022Oct;33(10):2049–102.
2. Pierini FS, Brom M, Scolnik M, Scaglioni V, Rosa JE, Soriano ER. Osteoporotic fractures in rheumatoid arthritis patients in Argentina: a matched retrospective cohort study. Adv Rheumatol Lond Engl. 2021Apr 7;61(1):21.
3. Wright NC, Looker AC, Saag KG, Curtis JR, Delzell ES, Randall S, et al. The recent prevalence of osteoporosis and low bone mass in the United States based on bone mineral density at the femoral neck or lumbar spine. J Bone Miner Res Off J Am Soc Bone Miner Res. 2014Nov;29(11):2520–6.
4. Radominski SC, Bernardo W, de Paula AP, Albergaria B, Moreira C, Fernandes CE, et al. Diretrizes brasileiras para o diagnóstico e tratamento

da osteoporose em mulheres na pós-menopausa. Rev Bras Reumatol. 2017Jan;1(57):452–66.
5. Daly RM, Via JD, Duckham RL, Fraser SF, Helge EW. Exercise for the prevention of osteoporosis in postmenopausal women: an evidence-based guide to the optimal prescription. Braz J Phys Ther. 2018Nov 22;23(2):170.
6. Bragonzoni L, Barone G, Benvenuti F, Canal V, Ripamonti C, Marini S, et al. A randomized clinical trial to evaluate the efficacy and safety of the ACTLIFE exercise program for women with post-menopausal osteoporosis: study protocol. Int J Environ Res Public Health [Internet]. 2020;17(3). Available from: https://www.cochranelibrary.com/central/doi/https://doi.org/10.1002/central/CN-02086329/full
7. Pinheiro MB, Oliveira J, Bauman A, Fairhall N, Kwok W, Sherrington C. Evidence on physical activity and osteoporosis prevention for people aged 65+ years: a systematic review to inform the WHO guidelines on physical activity and sedentary behaviour. Int J Behav Nutr Phys Act. 2020Nov 26;17(1):150.
8. Schapira D. Physical exercise in the prevention and treatment of osteoporosis: a review. J R Soc Med. 1988Aug;81(8):461.
9. Manaye S, Cheran K, Murthy C, Bornemann EA, Kamma HK, Alabbas M, et al. The role of high-intensity and high-impact exercises in improving bone health in postmenopausal women: a systematic review. Cureus. 2023Feb 5;15(2): e34644.
10. Linhares DG, Borba-Pinheiro CJ, de Castro JBP, dos Santos AOB, dos Santos LL, Cordeiro L de S, et al. Effects of multicomponent exercise training on the health of older women with osteoporosis: a systematic review and meta-analysis. Int J Environ Res Public Health. 2022 Oct 30;19(21):14195.
11. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. PLOS Med. 2021Mar 29;18(3): e1003583.
12. Moher D, Pham B, Lawson ML, Klassen TP. The inclusion of reports of randomised trials published in languages other than English in systematic reviews. Health Technol Assess Winch Engl. 2003;7(41):1–90.
13. Sterne JAC, Egger M, Smith GD. Investigating and dealing with publication and other biases in meta-analysis. 2001 Jul 14 [cited 2025 May 16]; Available from: https://www.bmj.com/content/323/7304/101
14. Jackson JL, Kuriyama A. How often do systematic reviews exclude articles not published in English? J Gen Intern Med. 2019Aug 1;34(8):1388–9.
15. Busse JW, Bruno P, Malik K, Connell G, Torrance D, Ngo T, et al. An efficient strategy allowed English-speaking reviewers to identify foreign-language articles eligible for a systematic review. J Clin Epidemiol. 2014May;67(5):547–53.
16. Mahood Q, Van Eerd D, Irvin E. Searching for grey literature for systematic reviews: challenges and benefits. Res Synth Methods. 2014;5(3):221–34.
17. Conn VS, Valentine JC, Cooper HM, Rantz MJ. Grey Literature in Meta-Analyses. Nurs Res. 2003Aug;52(4):256.
18. Kamei F, Pinto G, Wiese I, Ribeiro M, Soares S. What evidence we would miss if we do not use grey literature? In: Proceedings of the 15th ACM / IEEE International Symposium on Empirical Software Engineering and Measurement (ESEM) [Internet]. New York, NY, USA: Association for Computing Machinery; 2021 [cited 2025 May 16]. p. 1–11. (ESEM '21). Available from: https://doi.org/10.1145/3475716.3475777
19. Blackhall K. Finding studies for inclusion in systematic reviews of interventions for injury prevention – the importance of grey and unpublished literature. Inj Prev. 2007Oct 1;13(5):359–359.
20. Paez A. Gray literature: an important resource in systematic reviews. J Evid-Based Med. 2017;10(3):233–40.
21. Krugh M, Langaker MD. Dual-Energy X-Ray Absorptiometry. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [cited 2024 Oct 29]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK519042/
22. Batacan RB, Duncan MJ, Dalbo VJ, Tucker PS, Fenning AS. Effects of high-intensity interval training on cardiometabolic health: a systematic review and meta-analysis of intervention studies. Br J Sports Med. 2017Mar 1;51(6):494–503.
23. Labata-Lezaun N, González-Rueda V, Llurda-Almuzara L, López-de-Celis C, Rodríguez-Sanz J, Bosch J, et al. Effectiveness of multicomponent training on physical performance in older adults: a systematic review and meta-analysis. Arch Gerontol Geriatr. 2023Jan;104: 104838.
24. ACSM_CMS [Internet]. [cited 2024 Dec 17]. ACSM Blog. Available from: https://www.acsm.org/blog-detail
25. de Fátima Ribeiro Silva C, Ohara DG, Matos AP, Pinto ACPN, Pegorari MS. Short physical performance battery as a measure of physical performance and mortality predictor in older adults: a comprehensive literature review. Int J Environ Res Public Health. 2021 Oct 10;18(20):10612.
26. Mason RC, Horvat M, Nocera J. The effects of exercise on the physical fitness of high and moderate-low functioning older adult women. J Aging Res. 2016;2016:8309284.
27. Higgins J, Thomas J. Cochrane Handbook for Systematic Reviews of Interventions [Internet]. 2022 [cited 2023 Jul 20]. Available from: https://training.cochrane.org/handbook/current
28. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan—a web and mobile app for systematic reviews. Syst Rev. 2016Dec 5;5(1):210.
29. Higgins JPT, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011Oct;18(343): d5928.
30. Nejadghaderi SA, Balibegloo M, Rezaei N. The Cochrane risk of bias assessment tool 2 (RoB 2) versus the original RoB: a perspective on the pros and cons. Health Sci Rep. 2024Jun 3;7(6): e2165.
31. Shim SR, Kim SJ, Lee J, Rücker G. Network meta-analysis: application and practice using R software. Epidemiol Health. 2019Jan;1(41): e2019013.
32. Gelman A. Prior distributions for variance parameters in hierarchical models (comment on article by Browne and Draper). Bayesian Anal. 2006Sep;1(3):515–34.
33. Spiegelhalter DJ, Best NG, Carlin BP, Van Der Linde A. Bayesian measures of model complexity and fit. J R Stat Soc Ser B Stat Methodol. 2002;64(4):583–639.
34. Ilmawan M. Navigating heterogeneity in meta-analysis: methods for identification and management. Deka Med. 2024Aug;13(1): e269.
35. Xu L, Pan L, Xiang L, Zheng B, Sun X, Li J, et al. A Bayesian network meta-analysis of non-pharmacological interventions for neonatal pain management: a clinical effectiveness comparison. Front Pediatr [Internet]. 2025 Apr 25 [cited 2025 May 16];13. Available from: https://www.frontiersin.org/journals/pediatrics/articles/https://doi.org/10.3389/fped.2025.1547308/full
36. Viechtbauer W, López-López J. Location-scale models for meta-analysis. Res Synth Methods. 2022Apr;1:13.
37. Harrer M, Cuijpers P, Furukawa TA, Ebert DD. Chapter 13 Bayesian Meta-Analysis | Doing Meta-Analysis in R [Internet]. [cited 2025 May 16]. Available from: https://bookdown.org/MathiasHarrer/ng_Meta_Analysis_in_R/bayesian-ma.html
38. Gelman A, Carlin JB, Stern HS, Dunson DB, Vehtari A, Rubin DB. Bayesian Data Analysis. 3rd ed. New York: Chapman and Hall/CRC; 2015. p. 675.
39. Ainsworth BE, Haskell WL, Herrmann SD, Meckes N, Bassett DR, Tudor-Locke C, et al. 2011 Compendium of Physical Activities: a second update of codes and MET values. Med Sci Sports Exerc. 2011Aug;43(8):1575–81.
40. Raices Cruz I, Lindström J, Troffaes MCM, Sahlin U. Iterative importance sampling with Markov chain Monte Carlo sampling in robust Bayesian analysis. Comput Stat Data Anal. 2022Dec;1(176): 107558.
41. Lim D, Chen MH, Ibrahim JG, Kim S, Shah AK, Lin J. metapack: An R Package for Bayesian Meta-Analysis and Network Meta-Analysis with a Unified Formula Interface. R J. 2022Dec 19;14(3):142.
42. Brooks SP, Gelman A. General methods for monitoring convergence of iterative simulations. J Comput Graph Stat. 1998Dec 1;7(4):434–55.
43. Nikolakopoulou A, Higgins JPT, Papakonstantinou T, Chaimani A, Del Giovane C, Egger M, et al. CINeMA: An approach for assessing confidence in the results of a network meta-analysis. PLoS Med. 2020Apr;17(4): e1003082.
44. Papakonstantinou T, Nikolakopoulou A, Higgins JPT, Egger M, Salanti G. CINeMA: Software for semiautomated assessment of the confidence in the results of network meta-analysis. Campbell Syst Rev. 2020Mar;16(1): e1080.
45. Viechtbauer W, Cheung MWL. Outlier and influence diagnostics for meta-analysis. Res Synth Methods. 2010Apr;1(2):112–25.
46. Zhang L, Zheng YL, Wang R, Wang XQ, Zhang H. Exercise for osteoporosis: A literature review of pathology and mechanism. Front Immunol. 2022Sep;9(13):1005665.

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