INPLASY PROTOCOL

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Review Stage at time of this submission: **Preliminary searches.**

Conflicts of interest:
None declared.

Pharmacological and non-pharmacological interventions for osteoporosis: a protocol for an overview with an evidence map and a network meta-analysis of trials

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Review question / Objective: **To map the methodological quality and reporting quality of published systemayic reviews or meta analyses of interventions for osteoporosis . Meanwhile, a network meta analysis of trials identified from published meta analyses will be conducted to summarize and compare the efficacy and safety evidence.**
Condition being studied: **Osteoporosis is a common bone disease with a high prevalence in the world . It could increase the risk of fracture because of bone mass reduction. This disease caused lager economic and health burden.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 05 May 2021 and was last updated on 19 May 2021 (registration number INPLASY202150022).

INTRODUCTION

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METHODS

Search strategy: #1 OR "Osteoporosis"[Mesh], "Osteoporosis, Postmenopausal"[Mesh], osteoporosis [Title/ Abstract], osteoporosis [Title/ Abstract] Abstract], "bone loss"[Title/ Abstract], "bone losses"[Title/Abstract] #2 /OR : "Systematic Review"[Publication Type], "Systematic Reviews as topic"[Mesh] Mesh], "Network Meta "Network Meta—Analysis"[Mesh] Analysis"[Mesh], , "Meta"Meta--analysis"[Publication Type]analysis" [Publication Type], , "Meta" Meta--analysis as analysis as topic"[Mesh]topic"[Mesh], , "systematic review"[Title/ Abstract]"systematic review"[Title/ Abstract], , "meta"meta--analysis"[Title/ Abstract]analysis"[Title/Abstract] #3 #1 AND #2 #3 #1 AND #2.

Participant or population: Patients were diagnosed with osteoporosis. There are no age, gender, or race.

Intervention: All available pharmacological and nonpharmacological treatments including drugs, herbal medicine, acupuncture, etc.

Comparator: Placebo, no treatment, or any available pharma cological and nonpharmacological treatments.

Study designs to be included: Systema reviews or meta analyses of interventions for osteoporosis published in English or Chinese.

Eligibility criteria: We will exclude protocols, narrative reviews, confere nce abstracts, preclinical studies.

Information sources: PubMed, Cochrane library, Embase, CNKI and CBM will be systematically searched from inception to May 2021 for published s ystema reviews or meta analyses of interventions for osteoporosis.

Main outcome(s): Effective rate, bone mineral density, pain improvement.

Additional outcome(s): Level of serum calcium, quality of life, adverse events.

Data management: Two independent reviewers will screen records and extract key data from included systematic review and trials . Any disagreements will be resolved through discussion when possible. The key data will include: first author, publication year, country of corresponding author, journal, sample size, settings of trials, characteristics of patient (e.g., age , gender, types of osteoporosis), interventions and comparisons, outcomes of interest.

Quality assessment / Risk of bias analysis: 1) The quality of systematic reviews : Two reviewers will independently apply the AMSTAR 2 and PRISMA 2020 to assess each included meta analysis, and any disagreements will be resolved by consensus. 2 Risk of bias in randomized controlled trials : T he risk of bias in randomized controlled trials will be assessed using the Cochrane risk of bias tool. A trial will be considered as low quality if random sequence generation or allocation concealment , or blinding was evaluated as a high risk of bias, regardless of the risk of other domains, otherwise it will be considered as high quality. 3) Strength of Evidence: The GRADE method will be used to assess the strength of evidence regarding each primary outcome.

Strategy of data synthesis: The results of methodological and reporting quality of included systematic reviews will be presented as number and percentage. Meanwhile, the evidence mapping method will be used to visualize the methodological and reporting quality. The Markov Chain Monte Car lo method will be used to perform the Bayesian network meta analyses statistical analyses will be conducted using WinBUGS 1.4.3 (MRC Biostatistics Unit, Cambridge, UK) and gemtc package in R 4.0.2 (R Core Team, Vienna, Austria) Austria). Three Markov chains with 1 00 000 iterations after an initial burn in of 40 000 will be used in the analyses The inconsistency between direct and indirect estimates will be checked

using the node splitting method. The relative efficacy of different interventions will be ranked using s urface under the cumulative ranking area Stata 16.0 (StataCorp, College Station, software will be used to make the network plots of network meta analyses and complete conventional meta analys e s s tatistical heterogeneity across trials will be assessed using I 2 statistics; I 2 5 0 will be considered as considerable heterogeneity . Odds ratio (OR) and s tandard mean difference (SMD) with their 95% credible intervals (CI will be used to present t he binary and continuous outcomes , respectively . In conventional meta analys es, subgroup analyses will be conducted based several variable , they including age of patients, anatomic sites of osteoporosis, reasons of osteoporosis, duration of follow up, and quality of trials Meanwhile, s ensitivity analysis will be performed by exclud ing the trials with small sample sizes N 6 0)0). Publication bias will be examined using funnel plots and Egger's test. Two sided P value 0.05 will be regarded as statistically significant.

Subgroup analysis: In conventional meta-analyses, subgroup analyses will be conducted based several variable , they including age of patients , anatomic sites of osteoporosis, reasons of osteoporosis, duration of follow up, and quality of trials.

Sensitivity analysis: In conventional meta analyse es, sensitivity analysis will be performed by excluding the trials with small sample sizes (N 6 0).

Language: English.

Country(ies) involved: Mainland China.

Other relevant information: None.

Keywords: osteoporosis, network meta analysis, overview, systematic review, AMSTAR 2.

Dissemination plans: The results of this study will submit to a peer reviewed journal for publication.

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