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# Can vertebral osteoporosis accelerate lumbar disc degeneration? A systematic review and meta-analysis from animal studies

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**ADMINISTRATIVE INFORMATION**

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**Conflicts of interest -** None declared.

**INPLASY registration number:** INPLASY202370099

**Amendments -** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 24 July 2023 and was last updated on 24 July 2023.

## INTRODUCTION

**Review question / Objective** The effect of vertebral osteoporosis on disc degeneration remains controversial. The aim of this study was to systematically evaluate related animal studies to shed more light on the effect of vertebral osteoporosis on disc degeneration and to promote the resolution of the controversy.

**Condition being studied** Blood supply from the vertebral body and endplates is the primary source of nutrients to the intervertebral discs, and alterations in the structure of the vertebral body and endplates after osteoporosis may have an effect on the nutrient supply to the discs. However, there is no consensus on exactly what this effect is and whether vertebral bone loss is a protective or destructive factor for the disc. Some studies have suggested that vertebral bone loss is a protective factor for the intervertebral disc, favoring the penetration of nutrients into the disc and cushioning mechanical stress. Other studies have suggested that vertebral bone loss is a destructive factor for the intervertebral disc, and that the abnormal bone remodeling of the endplate triggered by bone loss accelerates endplate calcification and hinders nutrient penetration. This debate remains unresolved until now.

## METHODS

**Participant or population** Animals with osteoporosis caused by human intervention.

**Intervention** Ovariectomy.

**Comparator** Sham surgery.

**Study designs to be included** Animal studies to investigate the effect of vertebral osteoporosis or decreased bone density on intervertebral discs.

**Eligibility criteria** Studies meeting the following criteria will be included: (1) Animal studies

exploring the effects of vertebral osteoporosis or reduced bone density on the intervertebral disc. There is no restriction on country or language, and there is no restriction on the type of animal, the type of modeling, the type of intervention, the duration of observation, or the imaging method. (2) Studies in which vertebral osteoporosis and disc degeneration were comprehensively assessed and for which complete assessment data were available. Studies were excluded based on the following criteria: (1) Studies that assessed cervical or caudal disc degeneration. (2) Studies that lacked key outcome metrics to determine the success of modeling. (3) Studies that lacked histologic and molecular biological evidence to support them. (4) Imaging and biomechanical studies. (5) Reviews, letters to the editor, studies that have been retracted, and studies with plagiarized data and images.

**Information sources** We performed a literature search in PubMed, Cochrane Library, and Embase databases with the search terms osteoporosis, bone mineral density, disc degeneration, endplate degeneration, and animal studies up to February 1, 2023.

**Main outcome(s)** DHI, histological score, number of endplate osteoblasts, number of endplate osteoclasts, type I collagen, type II collagen, aggrecan, ADAMTS-4, MMP-1 , MMP-3, MMP-13, disc volume.

**Quality assessment / Risk of bias analysis** The quality of the included animal studies was evaluated using the CAMARADES checklist. The scale includes the following: calculation of sample size, generation of randomized sequences, blinded assessment of results, appropriate animal models, application of rational anesthetic drugs, compliance with animal protection laws, publication of papers after peer review, and declaration of potential conflicts of interest.

**Strategy of data synthesis** We performed statistical analysis of data extracted from each study using STATA software (version 15.1). Continuous variables were reported as mean difference (MD) and 95% confidence interval (CI), while dichotomous variables were reported as odds ratio (OR) and 95% CI. Statistical heterogeneity was judged according to the I2 statistic. The greater the I2, the greater the heterogeneity. If there was heterogeneity in this study (I2≥50%), a randomeffects model was used; otherwise, a fixed-effects model (I2 <50%) was used.

**Subgroup analysis** Subgroups were analyzed according to animal species and different forms of data presentation.

**Sensitivity analysis** Sensitivity analysis was carried out on all evaluation indicators by removing the literature one by one.

**Country(ies) involved** China.

**Keywords** animal studies; disc degeneration; meta-analysis; osteoporosis.

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