

# INPLASY PROTOCOL

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## Ankylosing spondylitis disease activity and serum vitamin D levels: a systematic review and meta-analysis

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None declared.

**Review question / Objective:** Through a meta-analysis of case-control studies and cross-sectional research on AS, we examined the relationship between blood vitamin D levels and disease activity in order to establish the rationale for using VD as a therapeutic adjunctive treatment for AS.

**Condition being studied:** The clinical symptoms of ankylosing spondylitis (AS), a chronic inflammatory rheumatic illness, include inflammatory back pain, ossification of the spinal ligaments, osteophytes, thoracolumbar kyphosis, and pathologic fractures.

**Information sources:** The database of PubMed, the Cochrane Library, EMBASE, and the Chinese National Knowledge Infrastructure (CNKI).

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 07 September 2022 and was last updated on 07 September 2022 (registration number INPLASY202290030).

### INTRODUCTION

**Review question / Objective:** Through a meta-analysis of case-control studies and cross-sectional research on AS, we examined the relationship between blood vitamin D levels and disease activity in order to establish the rationale for using VD

as a therapeutic adjunctive treatment for AS.

**Rationale:** It has not been established previously that serum Vitamin D (VD) levels and important monitoring indicators of disease activity in patients with ankylosing spondylitis (AS) correlate. The Bath Ankylosing Spondylitis Disease Activity

Index (BASDAI), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) are the three major monitoring indices of AS disease activity, and we expect to establish their link with serum VD levels through this meta-analysis.

**Condition being studied:** The clinical symptoms of ankylosing spondylitis (AS), a chronic inflammatory rheumatic illness, include inflammatory back pain, ossification of the spinal ligaments, osteophytes, thoracolumbar kyphosis, and pathologic fractures.

## METHODS

**Search strategy:** Two of our authors (CML and CYH) conducted a literature search of PubMed, the Cochrane Library, EMBASE, and the Chinese National Knowledge Infrastructure (CNKI) to include, and all studies on the relationship between VD and AS were included to the extent possible in accordance with the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. The literature search was performed by a random combination of the following search terms: "vitamin D" or "vitamin D levels" or "25-hydroxyvitamin D" or "25-hydroxyvitamin D levels" or "25 (OH) D" or "25 (OH) D levels" and "ankylosing spondylitis" or "ankylosing spondyloarthritis" or "Bechterew's disease", with a time frame limited to August 2022 after the database was created.

**Participant or population:** Adult patients with ankylosing spondylitis/Ankylosing spondylitis patients.

**Intervention:** None.

**Comparator:** Healthy adults.

**Study designs to be included:** Published case-control studies, cohort studies, and cross-sectional studies.

**Eligibility criteria:** Exclusion criteria: (1) the type of literature was a review, systematic evaluation, meta-analysis, case report,

animal study, in vitro study and editorial article, (2) the control group population was not healthy, (3) patients and controls were taking VD supplements, and (4) 25 (OH) D levels were missing in patients or controls.

**Information sources:** The database of PubMed, the Cochrane Library, EMBASE, and the Chinese National Knowledge Infrastructure (CNKI).

**Main outcome(s):** Serum vitamin D (VD) levels, correlation between vitamin D levels and Ankylosing Spondylitis Disease Activity Index (BASDAI).

**Additional outcome(s):** Erythrocyte sedimentation rate (ESR), C-reactive protein level (CRP), as well as correlation between serum VD level and ESR, CRP.

**Data management:** Excel is used for data aggregation and classification, while Review Manager is used for data statistics and analysis.

**Quality assessment / Risk of bias analysis:** Cross-sectional studies were evaluated using the Agency for Healthcare Research and Quality (AHRQ), whereas cohort and case-control studies were evaluated using the Newcastle-Ottawa-Scale (NOS). Finally, for statistical analysis, we chose case-control studies with NOS scores  $\geq 7$  or cross-sectional studies with AHRQ ratings  $\geq 4$ .

**Strategy of data synthesis:** Applying Review Manager software version 5.4 for data analysis, all extracted data were examined. Using mean differences (MD) and 95% confidence intervals, serum 25 (OH) D, ESR, and CRP levels, as well as correlations between serum VD levels and important markers of AS disease activity, were examined between AS patients and controls (CI). A fixed-effects model was utilized when homogeneity was poor ( $I^2 \leq 50\%$ ). A random-effects model was applied otherwise. When  $P \leq 0.05$ , differences were deemed statistically significant. To determine the effect of each individual study on the overall meta-analysis, sensitivity analyses were carried out by

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excluding each study individually one at a time.

**Subgroup analysis:** For the correlation of serum 25(OH)D levels and serum VD with BASDAI, we performed a subgroup analysis by dividing the study into Asia, Europe and Africa, according to the continent where the article study was completed.

**Sensitivity analysis:** To determine the effect of each individual study on the overall meta-analysis, sensitivity analyses were carried out by excluding each study individually one at a time.

**Language restriction:** None.

**Country(ies) involved:** China, Guizhou University of Traditional Chinese Medicine.

**Keywords:** Ankylosing spondylitis, disease activity, vitamin D.

**Contributions of each author:**

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