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ADMINISTRATIVE INFORMATION**Support** - The authors received no financial support for this research.**Review Stage at time of this submission** - Preliminary searches.**Conflicts of interest** - The authors declare that they have no relevant or material financial interests that relate to the research described in this paper.**INPLASY registration number:** INPLASY202630107**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 29 March 2026 and was last updated on 29 March 2026.**INTRODUCTION**

Review question / Objective The aim of this systemic review is to assess data regarding anti-resorptive therapy and osteonecrotic jaw (ONJ) in prostate cancer patients with bone metastasis and analyze the incidence of ONJ in such patients. The meta-analysis aims to investigate the relationship between different anti-resorptive medicines and the osteonecrosis jaw occurrence.

Rationale Prostate cancer is the most common type of cancer in men, a large proportion of advanced prostate cancer patients develop bone metastases, and they survive many years with it. Thus, they frequently receive antiresorptive therapy for a long period to prevent skeletal-related events. Osteonecrosis of the jaw is a serious complication associated with long-term antiresorptive therapy. With the introduction of different anti-resorptive medications over time, their effect on the

occurrence of osteonecrosis was always considered as a significant clinical concern and has been continuously investigated and closely monitored. Moreover, other risk factors can also influence the occurrence of ONJ, and dentists are the first healthcare providers able to identify those risk factors and play a major role in preventing and early detection of ONJ.

Condition being studied Medication-related osteonecrosis of the jaw (MRONJ) is a complication associated with antiresorptive therapy, characterized by exposed necrotic bone in the maxillofacial region persisting for more than eight weeks. It can be asymptomatic, painful, with swelling or purulent discharge, and it is unresponsive to surgical or medical treatment.

METHODS

Search strategy A comprehensive literature search will be conducted in PubMed, the

Cochrane Library, BioMed Central, and Google Scholar. The search strategy will include a combination of keywords and Boolean operators. An example of a search strategy is as follows: (“Osteonecrosis of the jaw” OR “Medication-related osteonecrosis of the jaw” OR “ MRONJ” OR “ONJ”) AND (“ Bisphosphonates” OR “Zoledronic acid” OR “Denosumab” OR “ Antiresorptive medications” OR “ Bone modifying agents”) AND (“Prostate cancer” OR “Prostate neoplasm”) AND (“Bone metastasis” OR “ Bone metastases” OR “Skeletal metastasis”).

Participant or population Prostate cancer with bone metastasis patients enrolled in studies to find the effect and outcome of anti-resorptive medicines will be eligible for this review, with no exclusion based on ethnicity or age.

Intervention Bisphosphonate and Denosumab anti-resorptive medications. They have been proven to improve the quality of life and reduce the incidence of skeletal-related events. However, it is important to be aware of their complications. Their long-term use can lead to osteonecrosis of the jaw (ONJ) which can be hard to treat and lead to painful events.

Comparator The meta-analysis aims to investigate the relationship between anti-resorptive medicines and osteonecrosis jaw occurrence. The analysis will be applied to study the effect of Bisphosphonate and Denosumab drugs on the development of ONJ.

Study designs to be included Empirical studies with quantitative methods.

Eligibility criteria The inclusion criteria will have articles conducted to study the development of ONJ in prostate cancer patients with bone metastasis lesions from inception until the present time. Articles should mention the total number of prostate patients during the study and the number of patients developing osteonecrotic jaw (ONJ).

Information sources PubMed, Cochrane Library, Biomed, and Google Scholar. Manual searches will also be conducted in the reference lists of the included articles.

Main outcome(s) The incidence of ONJ in patients receiving anti-resorptive medicines and the different effect of Bisphosphonate and Denosumab on the occurrence of ONJ.

Data management All records identified through the search strategy will be imported into Rayyan

software to facilitate the screening process. Three reviewers will independently evaluate the articles. Data found in articles conducted to study the development of ONJ in prostate cancer patients with bone metastasis lesions will be extracted and documented.

Quality assessment / Risk of bias analysis The quality of the included studies will be assessed independently by two reviewers using Newcastle-Ottawa scale. This scale evaluates studies based on three domains: Selection, Comparability, and Outcome/Exposure assessment. Disagreements will be resolved through discussion with the third reviewer.

Strategy of data synthesis This systematic review and meta-analysis will be conducted and reported in accordance with the PRISMA guidelines. To carry out the synthesis and analysis of the information collected, a data sheet will be implemented to organize and categorize the data in a systematic manner. An I2 statistical calculation, chi-squared, and tau-squared τ^2 values will be carried out to detect the heterogeneity of the studies. The data in the meta-analysis will be conducted using Review Manager (RevMan) software. The data will be combined according to the random effects model and planned to be expressed as forest plots. A Funnel graph is planned to measure the selection bias of the study.

Subgroup analysis None.

Sensitivity analysis None.

Country(ies) involved Jordan, Turkey.

Keywords Prostate cancer, Bone metastasis, Osteonecrosis jaw, Anti-resorptive, Bisphosphonate, Denosumab.

Contributions of each author

Author 1 - Yasamin R.M Aljomard - The first author is conceiving and designing the study, and will perform the literature search, screen titles and abstracts, conduct full-text assessment, extract and analyze the data, assess the risk of bias, and draft the manuscript.

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Author 2 - Elif Çiğdem Keleş - The author will be responsible for performing the statistical analysis and verifying the accuracy of the results. Analyses will be conducted with the support of computational tools, and all outputs will be independently reviewed and validated.

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Author 3 - Barış Çağrı Delilbaşı - The author will be assisted in screening titles and abstracts, participate in data extraction, and provide expert assessment of the surgical aspects of the included studies.

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Author 4 - Haluk Barış Kara - The author will oversee the study design and conduct, contribute to data extraction and risk of bias assessment, and will provide critical revision of the manuscript for important intellectual content.

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