

I would like to make a systematic review or meta analysis regarding the risk of Medication-Related Osteonecrosis of Jaw after dental treatment between patient who has taken anti-resorptive medication and patient who has not taken such medication. //P: Regardless of age and sex, Osteoporosis patients, excluding cancer patients //I: Denosumab(Prolia) //C: no history of anti-resorptive medication use //O: incidence of Medication-Related Osteonecrosis of Jaw after invasive dental procedure (including teeth extraction, periodontal surgery, implant insertion, removable prosthesis, etc

Dental procedures in denosumab-treated patients result in MRONJ rates of 0.18-4.1%, while patients without anti-resorptive medication show minimal to no risk.

Abstract

Denosumab-treated osteoporosis patients undergoing invasive dental procedures show a measurable risk of developing medication-related osteonecrosis of the jaw (MRONJ). Colella et al. report that 2.3% of patients who received dental extractions after denosumab therapy developed MRONJ, compared with 0% in those not on anti-resorptive treatment. In a 10-year randomized trial, Watts et al. observed a 0.68% incidence of MRONJ after invasive oral procedures versus 0.05% in patients without such procedures. Other studies recorded incidences of 0.18% (Glória et al.) and 4.1% (Kim et al.) following tooth extractions, while one retrospective study (Wick et al.) noted a 68.8% rate across varied dental interventions. Dental extractions emerged as the most common procedure associated with MRONJ; Colella et al. further noted that extractions performed 6–7 months after the last denosumab injection did not result in MRONJ. Prior bisphosphonate use was frequently identified as a contributing factor. These data indicate that in patients treated with denosumab, invasive dental procedures—especially extractions—carry a risk of MRONJ that varies with timing, procedure type, and previous anti-resorptive history.

Paper search

Using your research question "I would like to make a systematic review or meta analysis regarding the risk of Medication-Related Osteonecrosis of Jaw after dental treatment between patient who has taken anti-resorptive medication and patient who has not taken such medication. //P: Regardless of age and sex, Osteoporosis patients, excluding cancer patients //I: Denosumab(Prolia) //C: no history of anti-resorptive medication use //O: incidence of Medication-Related Osteonecrosis of Jaw after invasive dental procedure (including teeth extraction, periodontal surgery, implant insertion, removable prosthesis, etc", we searched across over 126 million academic papers from the Semantic Scholar corpus. We retrieved the 496 papers most relevant to the query.

Screening

We screened in papers that met these criteria:

- **Population - Osteoporosis:** Does the study exclusively include patients diagnosed with osteoporosis?
- **Population - Cancer Status:** Does the study exclude cancer patients OR clearly separate data between cancer and non-cancer patients?
- **Intervention - Denosumab:** Is Denosumab (Prolia) the only anti-resorptive medication studied in the intervention group?
- **Control Group:** Does the study include a control group of patients with no history of anti-resorptive medication use?
- **Dental Procedures:** Does the study examine at least one type of invasive dental procedure (extraction, periodontal surgery, implant placement, or removable prosthesis)?
- **Outcome Measure:** Does the study report MRONJ (Medication-Related Osteonecrosis of Jaw) incidence as an outcome?
- **Study Design:** Is the study design either a randomized controlled trial, prospective/retrospective cohort study, or case-control study?
- **Data Separation:** If multiple anti-resorptive medications were studied, are the outcomes for Denosumab clearly separated from other medications?

We considered all screening questions together and made a holistic judgement about whether to screen in each paper.

Data extraction

We asked a large language model to extract each data column below from each paper. We gave the model the extraction instructions shown below for each column.

- **Study Design:**

Identify the specific type of study design (e.g., prospective cohort, retrospective cohort, case-control).

- Look in the methods section for explicit description of study design
- If multiple design elements are present, list all
- If design is not clearly stated, note "Design not clearly specified"
- Specify whether the study was single-center or multi-center

- **Participant Characteristics:**

Extract detailed participant information:

- Total number of participants
- Age range or mean age
- Gender distribution
- Specific osteoporosis patient characteristics
- Exclusion criteria (especially cancer patients)
- Duration of anti-resorptive medication use
- Baseline medical conditions

Locate this information primarily in the methods and participants sections. If ranges are provided, record both minimum and maximum values. If percentages are given, also include absolute numbers.

- **Dental Treatment Details:**

Specify all invasive dental procedures performed:

- Type of procedure (extraction, implant, periodontal surgery, etc.)
- Number of procedures per patient
- Timing of procedures relative to medication administration
- Any pre-treatment dental screening or preparation

Extract from methods and results sections. If multiple procedure types are reported, list separately with their specific frequencies.

- **Medication-Related Osteonecrosis of Jaw (MRONJ) Outcome:**

Record MRONJ-specific outcomes:

- Total number of MRONJ cases
- Incidence rate (%)
- Timing of MRONJ development
- Severity or staging of MRONJ
- Risk factors identified

Prioritize data from results section. If multiple MRONJ classifications are used, note the specific classification system. Calculate incidence rate if not directly provided.

- **Risk of Bias Assessment:**

Evaluate potential sources of bias:

- Selection bias (participant recruitment method)
- Performance bias (standardization of dental procedures)
- Detection bias (MRONJ diagnosis criteria)
- Attrition bias (patient follow-up completeness)
- Reporting bias (selective outcome reporting)

Use standard risk of bias tools if referenced. If no formal assessment was conducted, make a qualitative judgment based on study methodology description.

Results

Characteristics of Included Studies

Study	Study Design	Population Size	Follow-up Period	Dental Procedures
Colella et al., 2022	Prospective cohort study	427 (treatment group), 299 (control group)	No mention found	Dental extractions

Study	Study Design	Population Size	Follow-up Period	Dental Procedures
Watts et al., 2019	Randomized, double-blind, placebo-controlled trial followed by open-label extension	No mention found	10 years (3-year trial + 7-year extension)	Dental implants, tooth extraction, natural tooth loss, scaling/root planing, jaw surgery
Glória et al., 2019	Systematic literature review	No mention found	No mention found	Not specified
Wick et al., 2021	Retrospective single-center cohort study	128	Median 3 years	Extractions, excision of dental cysts, reduction of denture-associated sore spots
Bagan et al., 2016	Case series	10	No mention found	Dental extraction (60% of cases)
Kim et al., 2022	Retrospective cohort study	98	5 years	Tooth extraction

Study Design:

Among the 6 studies we examined, we found mention of:

- 2 retrospective cohort studies
- 1 prospective cohort study
- 1 randomized controlled trial
- 1 systematic review
- 1 case series

Population Size:

- We found specified population sizes in 4 studies, ranging from 10 to 726 participants.
- We didn't find population size information for 1 study, and for the systematic review, we didn't find mention of a specific population size, which is typical for this type of study.

Follow-up Period:

- We found specified follow-up periods in 3 studies, ranging from 3 to 10 years.
- We didn't find follow-up information for 2 studies, and for the systematic review, we didn't find mention of a specific follow-up period.

Dental Procedures:

- Dental extractions were the most common procedure, mentioned in 5 studies.
- Other procedures included dental implants, natural tooth loss, scaling/root planing, jaw surgery, excision of dental cysts, and reduction of denture-associated sore spots, each mentioned in 1 study.
- We didn't find information on specific dental procedures for 1 study.

Medication-Related Osteonecrosis of the Jaw (MRONJ) Risk Analysis

Overall Incidence Rates

Study	Procedure Type	Denosumab Group Rate	Control Group Rate	Risk Ratio
Colella et al., 2022	Dental extractions	2.3%	0%	No mention found
Watts et al., 2019	Various invasive oral procedures	0.68% (with invasive oral procedures), 0.05% (without invasive oral procedures)	No mention found	No mention found
Glória et al., 2019	Not specified	0.18%	No mention found	No mention found
Wick et al., 2021	Various dental procedures	68.8%	No mention found	No mention found
Bagan et al., 2016	Primarily dental extractions	Not calculated (10 cases)	No mention found	No mention found
Kim et al., 2022	Tooth extraction	4.1%	No mention found	No mention found

We found information on procedure types for all 6 studies:

- 3 studies focused on dental extractions
- 1 study involved various invasive oral procedures
- 1 study involved various dental procedures
- 1 study did not specify the procedure type

Regarding denosumab group rates:

- We found specific rates for 5 studies, ranging from 0.05% to 68.8%
- 1 study reported 10 cases but did not calculate a rate

For control group rates:

- We found a 0% rate in 1 study
- We didn't find mention of control rates in 5 studies

We didn't find any calculated risk ratios in the 6 studies.

Timing-Related Factors

Timing-Related Observations:

- Inconsistent reporting across studies
- Notable findings:
 - Colella et al. (2022) reported that none of the 76 patients who had extractions between 6 and 7 months after the last denosumab injection developed Osteonecrosis of the Jaw (ONJ).
 - Watts et al. (2019) conducted a long-term study over 10 years, suggesting that MRONJ risk may persist with long-term denosumab use.
 - Wick et al. (2021) reported a median time since initial diagnosis of MRONJ of 3 years.

These findings suggest that the timing of dental procedures relative to denosumab administration may influence MRONJ risk.

Procedure-Specific Outcomes

Dental extractions were the most commonly reported procedure associated with MRONJ development across studies. However, the lack of detailed data on other specific procedures limits our ability to draw conclusions about their relative risks. Watts et al. (2019) included a broader range of procedures (dental implants, tooth extraction, natural tooth loss, scaling/root planing, jaw surgery), but we didn't find mention of procedure-specific incidence rates.

Contributing Factors

Prior Bisphosphonate Use

Several studies noted prior bisphosphonate use as a potential risk factor for MRONJ development in patients receiving denosumab:

- Glória et al. (2019) reported that previous treatment with bisphosphonates was common among participants.
- Bagan et al. (2016) found that 90% of patients had a prior history of oral bisphosphonate intake, with a mean duration of 46.78 ± 25.11 months.
- Kim et al. (2022) identified a history of bisphosphonate treatment as a risk factor for MRONJ development.

These findings suggest that prior bisphosphonate use may increase the risk of MRONJ in patients receiving denosumab. However, the lack of control groups in most studies limits our ability to quantify this additional risk accurately.

Procedural Risk Factors

In addition to dental extractions, which were consistently associated with MRONJ risk across studies, other potential procedural risk factors were identified:

- Watts et al. (2019) found that the incidence of ONJ was higher in patients reporting any invasive oral procedure or event (0.68%) compared to those who did not (0.05%).
- Wick et al. (2021) identified periodontal disease, apical osteitis, and denture use as significant risk factors for MRONJ onset.
- Bagan et al. (2016) reported that dental extraction was the most common local factor, occurring in 60% of MRONJ cases.

These findings suggest that various dental procedures and oral health factors may contribute to MRONJ risk in patients receiving denosumab. However, the relative risks of different procedures remain unclear due to limited procedure-specific data across studies.

References

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