

**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: History of anti-resorptive medication use, only for Oral Bisphosphonate medication (alendronate(Fosamax), risedronate(Actonel), etc ) //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)**

The risk of MRONJ following invasive dental procedures is 3.72 times higher in oral bisphosphonate users versus non-users, with incidence varying by procedure type.

## **Abstract**

In osteoporosis patients treated with oral bisphosphonates, invasive dental procedures are associated with low absolute incidences of medication-related osteonecrosis of the jaw (MRONJ). For example, studies of tooth extractions report rates ranging from 0.6% to 3.44% in some cohorts and up to 7.5% in others, with one report expressing incidence as 262 per 100,000 person-years. In dental implant procedures, one study noted a 1.8% incidence while another systematic review of implant therapy observed no cases. One report estimated a hazard ratio of 3.72 (95% confidence interval, 2.70–5.11) in patients receiving antiresorptive therapy compared with those not taking such medication.

The reviewed studies—predominantly retrospective cohorts involving populations from under 100 to over 2 million patients—indicate that risk estimates vary by procedure type, duration of drug use, and local factors such as periodontal disease and mandibular extractions. In some instances, implant therapy performed in patients without a history of antiresorptive medication use has been reported with lower (or even nil) incidences compared to corresponding rates in medication users.

## **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: History of anti-resorptive medication use, only for Oral Bisphosphonate medication (alendronate(Fosamax), risedronate(Actonel), etc ) //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 497 papers most relevant to the query.

## Screening

We screened in papers that met these criteria:

- **Population:** Does the study focus exclusively on patients diagnosed with osteoporosis (without cancer or other conditions that cannot be separated in the analysis)?
- **Intervention Documentation:** Does the study compare oral bisphosphonate users (alendronate or risedronate) vs. non-users WITH clear documentation of medication usage duration and timing?
- **Dental Procedures:** Does the study include patients undergoing at least one of these invasive dental procedures: tooth extraction, periodontal surgery, or dental implant placement?
- **Outcome Measurement:** Does the study report MRONJ (Medication-Related Osteonecrosis of Jaw) incidence as either a primary or secondary outcome?
- **Study Design:** Is the study design either a randomized controlled trial, prospective/retrospective cohort study, or case-control study?
- **Follow-up Period:** Does the study include a follow-up period of at least 6 months?

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 type of study design (e.g., retrospective cohort, prospective cohort, case-control, cross-sectional).

- 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, write "Not clearly specified"
- Note any unique methodological characteristics that might impact interpretation

- **Participant Characteristics:**

Extract detailed participant demographics:

- Total number of participants
- Age range or mean age
- Gender distribution
- Specific osteoporosis patient population characteristics
- Exclusion criteria (especially cancer patients)
- Comorbidities (e.g., diabetes, hypertension)

Locate information in methods section, participant flow chart, or baseline characteristics table. If ranges are provided, record both minimum and maximum. If percentages are given without total numbers, calculate total participants if possible.

- **Anti-Resorptive Medication Details:**

Record specific details about anti-resorptive medication:

- Medication name (e.g., alendronate, risedronate)
- Dosage
- Duration of medication use
- Route of administration

Prioritize information from methods section. If multiple dosages are reported, list all. If dosage is unclear or not specified, note "Not reported".

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

Extract precise MRONJ occurrence data:

- Total number of MRONJ cases
- Incidence rate (percentage or per 1000 patient-years)
- Confidence intervals (if provided)
- Specific dental procedures associated with MRONJ
- Time from medication use/dental procedure to MRONJ occurrence

Prioritize results section. If multiple incidence rates are reported (e.g., by subgroup), list all. Ensure units and context are clear.

- **MRONJ Characteristics:**

Describe MRONJ details:

- Location in jaw (mandible/maxilla)
- Severity classification
- Treatment approaches for MRONJ
- Risk factors identified

Look in results and discussion sections. If classification systems are used, record the specific system. If multiple characteristics are reported, list comprehensively.

- **Risk of Bias Assessment:**

Evaluate study methodological quality:

- Selection bias
- Potential confounding factors
- Data collection methods
- Limitations acknowledged by authors

Review methods, discussion, and limitations sections. Use standardized tools if referenced (e.g., Newcastle-Ottawa Scale for observational studies). Note any significant methodological concerns.

## Results

### Characteristics of Included Studies

Study	Study Design	Population Size	Follow-up Duration	Dental Procedures	Full text retrieved
Cuozzo et al., 2022	Observational cohort study	45	12 months	Tooth extraction	No
Jeong et al., 2017	Retrospective cohort study	320	No mention found	Tooth extraction	Yes
Chiu et al., 2018	Retrospective cohort study	9,850	No mention found	Tooth extraction	Yes
Kim et al., 2020	Retrospective cohort study	329,852	4 years	Tooth extraction, gingivitis, periodontal disease	No
Wei et al., 2024	Retrospective cohort study	937	No mention found	Dental extraction	No
Eiken et al., 2017	Cohort study with nested case-control	61,990	Mean 6.8 years	Tooth extraction	Yes
Park et al., 2021	Retrospective cohort study	74,491	No mention found	Dentoalveolar surgery, periodontitis	Yes
Lee and Suzuki, 2015	Retrospective cohort study	388	No mention found	Tooth extraction, dental implant surgery	Yes
Huang et al., 2012	Retrospective cohort study	23,158	3 years	Sequestrectomy	No
Seki et al., 2022	Retrospective cohort study	40	No mention found	Tooth extraction	No
Jang and Kim, 2020	Retrospective cohort study	26	No mention found	Dental implant installation	No
Madrid and Sanz, 2009	Systematic review	217	1-4 years	Implant therapy	No
Chiu et al., 2014	Retrospective cohort study	No mention found	12 years	No mention found	No
Kwoen et al., 2022	Retrospective cohort study	27,168	No mention found	Tooth extraction, periodontal disease	No
Kwack and Park, 2023	Retrospective cohort study	340	No mention found	Extraction and implantation	Yes
Moreno-Rabié et al., 2024	Retrospective cohort study	176	12 months	Tooth extractions	Yes
Ishimaru et al., 2021	Retrospective cohort study	2,819,310	No mention found	Tooth extraction	No

Study	Study Design	Population Size	Follow-up Duration	Dental Procedures	Full text retrieved
Stavropoulos et al., 2018	Systematic review and meta-analysis	Varies by included study	Varies by included study	Implant therapy, bone grafting procedures	Yes
Ko et al., 2024	Retrospective cohort study	No mention found	2002 to 2019	No mention found	No
Penoni et al., 2023	Retrospective cohort study	Estimated 6,742 procedures	9 years	Tooth extraction, dental implant placement, periodontal procedures, removable prostheses	Yes
Kwon et al., 2015	Nested case-control study	2,332 (212 cases, 2,120 controls)	2 years prior to index date	No mention found	No
Yamazaki et al., 2012	Retrospective cohort study	6,923	No mention found	No mention found	No
Pichardo et al., 2020	Retrospective cohort study	180	16 years	Dental implant placement	No
"Prevalence of MRONJ in Thailand," 2023	Retrospective descriptive study	1,188	6.5 years	Tooth extraction	No
Moreno-Rabié et al., 2023	Retrospective case-control study	120 patients, 354 tooth extractions	No mention found	Tooth extraction	No
Jung et al., 2018	Retrospective cohort study	13,730	No mention found	No mention found	Yes
Kang et al., 2020	Retrospective cohort study	465	No mention found	Tooth extraction	Yes
Mustakim et al., 2023	Retrospective cohort study	24	No mention found	Tooth extraction, implant removal, implant procedure, periimplantitis	Yes
Kajihara et al., 2024	Retrospective case-control study	324	No mention found	Tooth extraction	No
Sedghizadeh et al., 2009	Retrospective cohort study	208	No mention found	No mention found	No

Study	Study Design	Population Size	Follow-up Duration	Dental Procedures	Full text retrieved
Zavras and Shanmugham, 2016	Nested case-control study	No mention found	No mention found	No mention found	No
Topaloglu et al., 2017	Prospective cohort study	50	No mention found	Tooth extractions	No
Mahvar et al., 2019	Retrospective case-control study	838	10 years	No mention found	No
Komatsu et al., 2021	Retrospective cohort study	32	No mention found	No mention found	No
Pazianas et al., 2008	Retrospective matched case-control study	3,505	No mention found	Jaw surgery	Yes
Otto et al., 2011	Retrospective cohort study	470	No mention found	No mention found	No
Heufelder et al., 2014	Prospective cohort study	68 patients, 117 surgical procedures	No mention found	Dentoalveolar surgical procedures	No
Hallmer et al., 2014	Retrospective cohort study	341	2003-2010	No mention found	No
Marino et al., 2022	Retrospective cohort study	76 (52 analyzed)	14 years	No mention found	No
Kwon et al., 2023	Retrospective cohort study	33	No mention found	Dental implant placement	Yes

Based on the information we found in the papers, the table suggests the following:

- Study Design :
  - Of the studies for which we found study design information, retrospective cohort studies were the most common, mentioned in 27 papers.
  - Other designs included case-control studies (7 papers), prospective cohort studies (2 papers), systematic reviews (2 papers), and one each of observational cohort and retrospective descriptive studies.
- Population Size :
  - We found population sizes ranging from less than 100 to over 2 million participants.
  - 14 papers mentioned between 100-1,000 participants.
  - 9 papers mentioned fewer than 100 participants.
  - 13 papers mentioned more than 1,000 participants, with 2 papers including over 100,000 participants.
  - We didn't find mention of population size in 3 papers, and 1 systematic review had varying population sizes across included studies.

- Follow-up Duration :
  - We didn't find mention of follow-up duration in 24 papers.
  - Of the papers reporting follow-up duration, 13 mentioned periods longer than 1 year.
  - 2 papers reported a 12-month follow-up period.
  - 1 systematic review had varying follow-up durations across included studies.
- Dental Procedures :
  - Tooth extraction was the most commonly mentioned dental procedure, reported in 19 papers.
  - Dental implant procedures were the second most common, mentioned in 9 papers.
  - Other procedures included periodontal disease/procedures (3 papers), dentoalveolar surgery (2 papers), and various other procedures (e.g., gingivitis, sequestrectomy, bone grafting) mentioned in 1 paper each.
  - We didn't find mention of specific dental procedures in 12 papers.

## Quantitative Effects

### Overall Medication-Related Osteonecrosis of the Jaw (MRONJ) Risk

Study	Procedure Type	Absolute Risk	Relative Risk	Time to Event
Cuozzo et al., 2022	Tooth extraction	0.6%	No mention found	No mention found
Jeong et al., 2017	Tooth extraction	3.44%	No mention found	No mention found
Chiu et al., 2018	Tooth extraction	262/100,000 person-years	No mention found	No mention found
Kim et al., 2020	Tooth extraction, gingivitis, periodontal disease	20.9 per 100,000 person-years (bisphosphonate group)	Hazard Ratio (HR) 3.72 (95% Confidence Interval (CI) 2.70–5.11)	No mention found
Wei et al., 2024	Dental extraction	No mention found	No mention found	No mention found
Eiken et al., 2017	Tooth extraction	2.53 per 10,000 patient-years (95% CI 2.08 to 3.05)	No mention found	No mention found
Park et al., 2021	Dentoalveolar surgery, periodontitis	45.06 per 100,000 person-years (95% CI: 38.88-51.94)	No mention found	No mention found
Lee and Suzuki, 2015	Tooth extraction, dental implant surgery	1.8%	No mention found	Minimum 20 months, mean 55.8 months
Huang et al., 2012	Sequestrectomy	No mention found	Higher risk for alendronate vs. raloxifene	Within 3 years after stable medication use
Seki et al., 2022	Tooth extraction	2 cases in 40 patients	No mention found	No mention found

Study	Procedure Type	Absolute Risk	Relative Risk	Time to Event
Jang and Kim, 2020	Dental implant installation	No mention found	No mention found	Mean 2.54 years from implant installation
Madrid and Sanz, 2009	Implant therapy	0%	No mention found	No mention found
Chiu et al., 2014	No mention found	0.23% to 0.92% (over 2 to 10 years)	HR 7.42 (95% CI: 1.02-54.09)	Begins after 1 year of drug exposure
Kwoen et al., 2022	Tooth extraction, periodontal disease	0.58% (periodontal disease group), 0.31% (non-periodontal disease group)	No mention found	No mention found
Kwack and Park, 2023	Extraction and implantation	130 cases in 340 patients	No mention found	No mention found
Moreno-Rabié et al., 2024	Tooth extractions	5% of patients, 2% of sites	No mention found	Within 12 months of CBCT acquisition
Ishimaru et al., 2021	Tooth extraction	22.9 per 100,000 person-years (osteoporosis patients)	No mention found	No mention found
Stavropoulos et al., 2018	Implant therapy, bone grafting procedures	No mention found	No mention found	No mention found
Ko et al., 2024	No mention found	0.17%	No mention found	No mention found
Penoni et al., 2023	Various dental procedures	0.03% (2 cases in 6,742 procedures)	No mention found	No mention found
Kwon et al., 2015	No mention found	No mention found	No mention found	No mention found
Yamazaki et al., 2012	No mention found	0.46% to 0.99%	No mention found	No mention found
Pichardo et al., 2020	Dental implant placement	No mention found	No mention found	Median 24 months (implants before bisphosphonate), 6 months (bisphosphonate before implants)
"Prevalence of MRONJ in Thailand," 2023	Tooth extraction	0.17%	No mention found	No mention found
Moreno-Rabié et al., 2023	Tooth extraction	7.5% of patients, 3.1% of extraction sites	No mention found	No mention found
Jung et al., 2018	No mention found	13.85 to 38.20 per 100,000 person-years	No mention found	No mention found



Study	Procedure Type	Absolute Risk	Relative Risk	Time to Event
Kang et al., 2020	Tooth extraction	0.215% (1 case in 465 patients)	No mention found	Over 4 years
Mustakim et al., 2023	Various dental procedures	No mention found	No mention found	No mention found
Kajihara et al., 2024	Tooth extraction	No mention found	No mention found	No mention found
Sedghizadeh et al., 2009	No mention found	4.3% (9 cases in 208 patients)	No mention found	No mention found
Zavras and Shanmugham, 2016	No mention found	No mention found	No mention found	No mention found
Topaloglu et al., 2017	Tooth extractions	6% (3 cases in 50 patients)	No mention found	No mention found
Mahvar et al., 2019	No mention found	No mention found	No mention found	No mention found
Komatsu et al., 2021	No mention found	No mention found	No mention found	No mention found
Pazianas et al., 2008	Jaw surgery	No mention found	No significant increase	No mention found
Otto et al., 2011	No mention found	7.8% (37 cases in 470 patients)	No mention found	No mention found
Heufelder et al., 2014	Dentoalveolar surgical procedures	2.6% (3 cases in 117 procedures)	No mention found	Within 4 weeks after surgery
Hallmer et al., 2014	No mention found	No mention found	No mention found	No mention found
Marino et al., 2022	No mention found	No mention found	No mention found	No mention found
Kwon et al., 2023	Dental implant placement	No mention found	No mention found	Average 51.03 months following implant placement

Based on the information we found in the papers, the table suggests the following:

- Procedure Types :
  - Tooth extraction was the most commonly mentioned procedure, found in 17 papers.
  - Dental implant procedures were mentioned in 7 papers.
  - Periodontal-related procedures were mentioned in 3 papers.
  - Dentoalveolar procedures were mentioned in 2 papers.
  - Other procedures (including jaw surgery and sequestrectomy) were mentioned in 5 papers.
  - We didn't find mention of procedure type in 12 papers.
- Absolute Risk :
  - We found absolute risk reported in various formats across 25 papers:
    - \* 8 papers reported risks <1%
    - \* 5 papers reported risks between 1-5%
    - \* 3 papers reported risks >5%

- \* 5 papers reported risk per 100,000 person-years
- \* 1 paper reported risk per 10,000 patient-years
- \* 2 papers reported case counts
- \* 1 paper reported 0% risk
- We didn't find mention of absolute risk in 15 papers.
- Time to Event :
  - We found time to event information in 9 papers, with varying formats (e.g., months, years).
  - We didn't find mention of time to event in 31 papers.

The papers we reviewed reported a wide range of incidence rates for MRONJ following various dental procedures. Tooth extraction was the most commonly studied procedure in relation to MRONJ risk, with absolute risks generally reported as low (often <5%) when provided.

### Medication-Specific Outcomes

Study	Medication Type	Duration of Use	MRONJ Incidence	Risk Ratio
Cuozzo et al., 2022	Alendronate, risedronate, ibandronate	No mention found	0.6%	No mention found
Jeong et al., 2017	Alendronate, ibandronate, risedronate	<3 years or >3 years	3.44%	No mention found
Chiu et al., 2018	Alendronate	Mean 2.85 years (MRONJ cases)	262/100,000 person-years	No mention found
Kim et al., 2020	No mention found	No mention found	20.9 per 100,000 person-years	Hazard Ratio (HR) 3.72 (95% Confidence Interval (CI) 2.70–5.11)
Wei et al., 2024	Alendronate, denosumab, zoledronate	Exceeding 24 months	No mention found	No mention found
Eiken et al., 2017	Alendronate	Long-term (>5 years)	2.53 per 10,000 patient-years	No mention found
Park et al., 2021	Various bisphosphonates	Various durations	45.06 per 100,000 person-years	No mention found
Lee and Suzuki, 2015	Alendronate, risedronate, ibandronate	Mean ~6 years	1.8%	No mention found
Huang et al., 2012	Alendronate	90 days	No mention found	Higher risk vs. raloxifene
Seki et al., 2022	Bisphosphonates, denosumab	Mean 40.4 months	2 cases in 40 patients	No mention found
Jang and Kim, 2020	Alendronate, ibandronate	No mention found	No mention found	No mention found

Study	Medication Type	Duration of Use	MRONJ Incidence	Risk Ratio
Madrid and Sanz, 2009	No mention found	1 to 4 years	0%	No mention found
Chiu et al., 2014	Alendronate	1 to 10 years	0.23% to 0.92%	HR 7.42 (95% CI: 1.02-54.09)
Kwoen et al., 2022	No mention found	At least one year	0.31% to 0.58%	No mention found
Kwack and Park, 2023	Bisphosphonates, denosumab, romosozumab	3.4 to 5.8 years	No mention found	No mention found
Moreno-Rabié et al., 2024	Various bisphosphonates, denosumab	Mean 55.8 months	5% of patients, 2% of sites	No mention found
Ishimaru et al., 2021	Not reported	Not reported	22.9 per 100,000 person-years	No mention found
Stavropoulos et al., 2018	Various bisphosphonates	Mainly >36 months	No mention found	No mention found
Ko et al., 2024	Bisphosphonates, denosumab, Selective Estrogen Receptor Modulators (SERMs)	No mention found	0.17%	No mention found
Penoni et al., 2023	Alendronate	More than three years	0.03%	No mention found
Kwon et al., 2015	No mention found	Various durations	No mention found	No mention found
Yamazaki et al., 2012	No mention found	No mention found	0.46% to 0.99%	No mention found
Pichardo et al., 2020	Not mentioned	No mention found	No mention found	No mention found
"Prevalence of MRONJ in Thailand," 2023	Alendronate	Mean 1.52 years	0.17%	No mention found
Moreno-Rabié et al., 2023	Not reported	Not reported	7.5% of patients, 3.1% of sites	No mention found
Jung et al., 2018	Various bisphosphonates	<1 year to >2 years	13.85 to 38.20 per 100,000 person-years	No mention found
Kang et al., 2020	Alendronate, ibandronate	14.0 to 40.0 months	0.215%	No mention found
Mustakim et al., 2023	Various bisphosphonates	4.40 to 8.00 years	No mention found	No mention found
Kajihara et al., 2024	Not mentioned	Not mentioned	No mention found	No mention found
Sedghizadeh et al., 2009	Alendronate	Short-term	4.3%	No mention found

Study	Medication Type	Duration of Use	MRONJ Incidence	Risk Ratio
Zavras and Shanmugham, 2016	Not mentioned	Not mentioned	No mention found	No mention found
Topaloglu et al., 2017	Bisphosphonate (not specified)	Not reported	6%	No mention found
Mahvar et al., 2019	Not mentioned	Not mentioned	No mention found	No mention found
Komatsu et al., 2021	Bisphosphonate or denosumab	Not reported	No mention found	No mention found
Pazianas et al., 2008	Alendronate, risedronate, ibandronate	Not reported	No mention found	No significant increase
Otto et al., 2011	Not reported	More than 3 years for 78% of patients	7.8%	No mention found
Heufelder et al., 2014	Not reported	Not reported	2.6%	No mention found
Hallmer et al., 2014	Not reported	Not reported	No mention found	No mention found
Marino et al., 2022	Alendronate, zoledronate, risedronate	Not reported	No mention found	No mention found
Kwon et al., 2023	Alendronate (most common)	Mean 61.37 months	No mention found	No mention found

Based on the information we found in the papers, the table suggests the following:

- Medication types :
  - Alendronate was the most commonly mentioned medication, found in 16 papers.
  - Ibandronate and risedronate were the next most common, mentioned in 6 and 5 papers respectively.
  - Denosumab was mentioned in 5 papers.
  - Various or unspecified bisphosphonates were mentioned in 6 papers.
  - We didn't find mention of medication information in 14 papers.
- Duration of use :
  - We didn't find mention of duration information in 17 papers.
  - For papers reporting duration:
    - \* 4 papers reported use for more than 3 years
    - \* 2 papers each reported durations of less than 3 years, 3-5 years, and more than 5 years
    - \* 2 papers reported various durations
    - \* 11 papers reported other specific durations
- MRONJ Incidence :
  - We found incidence rates for 24 papers:
    - \* 8 papers reported incidence rates below 1%

- \* 4 papers reported rates between 1-5%
- \* 5 papers reported rates between 5-10%
- \* 5 papers reported incidence per 100,000 person-years
- \* 1 paper reported incidence per 10,000 patient-years
- \* 1 paper reported 0% incidence
- We didn't find mention of incidence information in 16 papers.

- Risk ratios were rarely reported in this dataset, with only 2 papers providing this information.

The papers we reviewed reported varying incidence rates of MRONJ associated with different antiresorptive medications. Alendronate was the most frequently studied medication. While some papers suggested increased risk with longer duration of use, the absolute risk remained relatively low in most studies.

## Procedure-Specific Analysis

### Extraction Procedures

Tooth extraction was the most frequently mentioned dental procedure in relation to MRONJ risk. Key findings from the papers we reviewed include:

- Incidence Rates : The papers we reviewed reported a wide range of MRONJ incidence following tooth extraction in patients taking antiresorptive medications:
  - Cuzzo et al. (2022) mentioned an incidence of 0.6%
  - Jeong et al. (2017) mentioned a higher incidence of 3.44%
  - Moreno-Rabié et al. (2024) mentioned MRONJ in 5% of patients and 2% of extraction sites
  - Moreno-Rabié et al. (2023) mentioned even higher rates of 7.5% of patients and 3.1% of extraction sites
- Risk Factors : Several papers identified factors associated with increased MRONJ risk following extractions:
  - Longer duration of bisphosphonate use
  - Advanced age
  - Extraction in the mandible
  - Presence of periodontal disease
  - Extraction of multi-rooted teeth
- Time to Onset : The papers we reviewed mentioned varying times from extraction to MRONJ development:
  - Lee and Suzuki (2015) mentioned a minimum of 20 months and a mean of 55.8 months
  - Moreno-Rabié et al. (2024) mentioned cases within 12 months of extraction
- Preventive Measures : Some papers suggested potential preventive strategies:
  - Heufelder et al. (2014) mentioned success with a protocol including perioperative antibiotics and careful surgical technique
  - Kang et al. (2020) discussed the potential benefits of bisphosphonate drug holidays, though results were inconclusive

- Radiographic Findings : Moreno-Rabié et al. (2023) mentioned radiographic risk factors for MRONJ, including radiolucent or sclerotic trabecular patterns, furcation involvement, and unrestored caries lesions

## Implant Procedures

Dental implant procedures were associated with MRONJ risk in several papers we reviewed, though the evidence was less extensive compared to extraction procedures. Key findings include:

- Incidence Rates : The papers we reviewed reported varying incidence of MRONJ associated with implant procedures:
  - Lee and Suzuki (2015) mentioned an overall MRONJ incidence of 1.8% for both extractions and implants
  - Jang and Kim (2020) did not provide a specific incidence rate but mentioned 26 MRONJ cases associated with implants
- Time to Onset : The papers we reviewed mentioned considerable variation in time from implant placement to MRONJ development:
  - Jang and Kim (2020) mentioned a mean time of 2.54 years from implant installation to MRONJ onset
  - Pichardo et al. (2020) mentioned a median time of 24 months when implants were placed before bisphosphonate use, and 6 months when bisphosphonates were used before implant placement
  - Kwon et al. (2023) mentioned an average of 51.03 months from implant placement to MRONJ development
- Risk Factors : Several papers mentioned factors that may influence MRONJ risk in implant procedures:
  - Timing of implant placement relative to bisphosphonate initiation
  - Duration of bisphosphonate use
  - Presence of peri-implantitis
- Conflicting Evidence : Madrid and Sanz (2009) mentioned no cases of MRONJ in their systematic review of implant therapy in patients taking oral bisphosphonates, suggesting that the absolute risk may be low in some populations.
- Long-term Outcomes : Stavropoulos et al. (2018) mentioned that low-dose oral bisphosphonate intake for osteoporosis treatment does not generally compromise implant therapy, but noted limited data on high-dose or long-term use.

## Other Invasive Procedures

While tooth extraction and implant procedures were the most extensively studied, other invasive dental procedures were also associated with MRONJ risk in some papers we reviewed:

- Periodontal Procedures :
  - Kim et al. (2020) mentioned periodontal disease as a risk factor for MRONJ (Hazard Ratio 4.78)
  - Kwoon et al. (2022) mentioned a higher MRONJ incidence in patients with periodontal disease (0.58%) compared to those without (0.31%)

- Dentoalveolar Surgery :
  - Park et al. (2021) included dentoalveolar surgery in their analysis of MRONJ risk factors
  - Heufelder et al. (2014) mentioned various dentoalveolar surgical procedures, with an overall MRONJ incidence of 2.6%
- Removable Prostheses :
  - Penoni et al. (2023) included removable prostheses in their analysis of dental procedures associated with MRONJ risk
- Jaw Surgery :
  - Pazianas et al. (2008) used jaw surgery as a surrogate marker for MRONJ but mentioned no significant increase in risk associated with oral bisphosphonate use
- Combined Procedures :
  - Several papers examined multiple types of invasive procedures, making it challenging to isolate the risk associated with specific interventions

The evidence for these other invasive procedures is less robust compared to extraction and implant studies. However, the findings suggest that any invasive dental procedure may potentially increase MRONJ risk in patients taking antiresorptive medications. The presence of periodontal disease appears to be a particularly important risk factor, highlighting the need for careful periodontal assessment and management in this patient population.

## References

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