Universidad Europea

GRADUATION PROJECT

Degree in Dentistry

PREVENTIVE STRATEGIES AND CLINICAL MANAGEMENT IN DENTISTRY FOR PATIENTS UNDERGOING BISPHOSPHONATE TREATMENT

Madrid, academic year 2025/2026

Identification number: 178

RESUMEN

Introducción: Dado el aumento del uso de los bifosfonatos y otros fármacos relacionados, los profesionales de la odontología deben ser conscientes de los riesgos asociados e implementar medidas preventivas de forma temprana para garantizar un manejo seguro de estos pacientes. La osteonecrosis de los maxilares relacionada con medicamentos es una complicación relevante asociada a los fármacos antirresortivos como los bifosfonatos y el denosumab. El manejo dental preventivo se ha propuesto como una estrategia clave para reducir su incidencia y otras complicaciones. **Objetivo:** Aprender a gestionar a un paciente en tratamiento con bifosfonatos y saber cómo prevenir cualquier complicación en la consulta dental. **Métodos:** Se realizó una revisión de la literatura que incluyó 9 estudios seleccionados según criterios de inclusión previamente definidos. Se analizaron diferentes diseños de estudio, incluyendo ensayos clínicos aleatorizados, estudios de cohortes y estudios observacionales. Los principales resultados evaluados fueron la incidencia de osteonecrosis de los maxilares relacionada con medicamentos, los protocolos preventivos y los enfoques de manejo clínico. **Resultados:** Los estudios incluidos mostraron que la evaluación dental preventiva antes de iniciar la terapia antirresortiva se asocia con una menor incidencia de osteonecrosis de los maxilares relacionada con medicamentos. El seguimiento regular y el mantenimiento de la salud oral durante la terapia también parecen reducir su riesgo de aparición. La exodoncia fue identificada como un factor desencadenante importante de osteonecrosis. Terapias complementarias como el plasma rico en plaquetas, la ozonoterapia y las técnicas de preservación del alveolo mostraron resultados prometedores en la mejora de la cicatrización. **Conclusión:** El manejo dental preventivo y un enfoque multidisciplinario desempeñan un papel importante en la reducción del riesgo de osteonecrosis de los maxilares relacionada con medicamentos. La evaluación cuidadosa del paciente, la estratificación del riesgo y la planificación del tratamiento individualizado son esenciales en la práctica clínica. Sin embargo, se necesitan más estudios estandarizados para establecer protocolos clínicos claros.

PALABRAS CLAVE

Odontología, bisfosfonatos, estrategias preventivas, manejo dental, osteonecrosis de los maxilares**.**

ABSTRACT

Introduction: Given the increasing use of bisphosphonates and related drugs, dental professionals must be aware of associated risks and implement preventives measures early to ensure safe management of these patients. Medication-related osteonecrosis of the jaw is a relevant complication associated with antiresorptive drugs such as bisphosphonates and denosumab. Preventive dental management has been proposed as a key strategy to reduce its incidence and other complications. **Objective:** Learn how to manage a patient undergoing bisphosphonate treatment and know how to prevent any complication in the dental chair. **Methods:** A literature review was conducted including 9 studies selected according to predefined inclusion criteria. Different study designs were analysed, including randomized clinical trials, cohort studies, and observational studies. The main outcomes evaluated were medication-related osteonecrosis of the jaw incidence, preventive protocols, and clinical management approaches. **Results:** The included studies showed that preventive dental assessment before starting antiresorptive therapy is associated with a lower incidence of medication-related osteonecrosis of the jaw. Regular follow-up and maintenance of oral health during the therapy also appear to reduce its risk of appearance. Tooth extraction was identified as a major triggering factor of osteonecrosis. Adjunctive therapies such as platelet-rich fibrin, ozone therapy, and socket preservation techniques showed promising results in improving healing outcomes. **Conclusion:** Preventive dental management and a multidisciplinary approach play an important role in reducing the risk of medication-related osteonecrosis of the jaw. Careful patient evaluation, risk stratification, and individualized treatment planning are essential in clinical practice. However, further standardized studies are needed to establish clear clinical protocols.

KEYWORDS

Dentistry, bisphosphonates, dental management, osteonecrosis of the jaw, preventive strategies.

TABLE OF CONTENTS

1. INTRODUCTION 1

1.1. A link between oral and systemic health 1
1.1.1 Importance of oral health in general well-being 1
1.1.2 Evidence linking systemic diseases and oral conditions 1
1.1.3 Relevance of this relationship in clinical dentistry 1

1.2. Bisphosphonates as systemic medication 2
1.2.1 Therapeutic indications 2
1.2.2 Mechanism of action: inhibition of osteoclasts and bone resorption 3
1.2.3 Types and routes of administration 4

1.3. Adverse effects of bisphosphonates and pathogenesis of medication-related osteonecrosis of the jaw (MRONJ). 5
1.3.1 Definition and characteristics of medication-related osteonecrosis of the jaw (MRONJ). 5
1.3.2 Risk factors 6
1.3.3 Main pathophysiological hypotheses 7

1.4. The role of the dentist in patient management 7
1.4.1 Pre-treatment phase 8
1.4.2 Management during therapy 8
1.4.3 Long-term follow-up 10

2. OBJECTIVE 11

3. MATERIAL AND METHODS 12

3.1 Databases consulted 12

3.2. Keywords and search strategy 12

3.3. Inclusion and exclusion criteria 13

3.4 Study selection process 14

3.5 PICO Question 14

3.6 PRISMA Diagram 15

4. RESULTS 17

5. DISCUSSION 19

6. CONCLUSIONS 21

7. SUSTAINABILITY 22

8. BIBLIOGRAFY 23

1. INTRODUCTION

1.1. A link between oral and systemic health

1.1.1 Importance of oral health in general well-being

Many people may see oral health as less important than systemic health, not knowing that the mouth usually shows and has an impact on the general state of the body.
For them, oral health still seems separated from general health, as if the rest of the body is unaffected by events in the mouth. Still, more recent data shows the contrary.
A fundamental aspect of general health, oral health affects not just physical capability but also mental and emotional well-being. Research has shown that poor self-rated oral health is associated with more psychological stress, more depressive symptoms and a lower quality of life (1).

1.1.2 Evidence linking systemic diseases and oral conditions

Recent evidence highlights the close interrelationship between oral and systemic health; with oral conditions both influencing and being influenced by systemic diseases. In fact, oral diseases such as periodontitis and dental caries are closely linked with systemic disorders, including diabetes mellitus and hypertension (2). We can potentially add Alzheimer's disease and chronic kidney disease. Nevertheless, obesity still needs research to prove its link with oral health (3). This bidirectional relationship underscores the importance of viewing the oral system as an integral part of general health.

1.1.3 Relevance of this relationship in clinical dentistry

The clinical importance of the relationship between systemic health and orofacial health becomes evident when dentists recognize how patients' perceptions of their mouth condition reflect more general well-being.
According to a study of older people, individuals who rated their oral health as bad exhibited reduced life satisfaction and greater levels of sadness and stress, therefore implying that oral condition might act as a clear sign of overall health (1).
For dentists, this means that comprehensive patient assessment should go beyond teeth and gums to include psychosocial factors and systemic risk profiles, thereby reinforcing the role of dental care in overall health management.

1.2. Bisphosphonates as systemic medication

1.2.1 Therapeutic indications

Bisphosphonates are a class of antiresorptive agents widely prescribed for the prevention and treatment of bone-related disorders such as osteoporosis, Paget's disease or metastatic lesions (4).

1.2.1.1 Osteoporosis

A chronic disorder, osteoporosis causes a major loss of bone mass and makes bones fragile. Its internal structure declines in strength and density faster than it can be replaced. This imbalance makes bones more porous and more likely to break over time, even during basic movements. This disease is more common in older people; however, it can also affect younger individuals when metabolic or hormonal factors interfere with normal bone remodelling. Bisphosphonates are indicated against osteoporosis to stabilize bone loss and reduce fracture risk, especially in postmenopausal women and elderly men who experience increased bone fragility or in conditions where bone resorption is accelerated (5,6).

In treating secondary osteoporosis linked to long-term corticosteroid usage, immobilisation, or chronic disease, bisphosphonates can be helpful in paediatric practice.

In these cases, the treatment helps improve bone mineral density and reduce the likelihood of deformities and fractures during growth (6).

1.2.1.2 Paget's disease

Paget's disease of bone is a chronic disorder in which the normal cycle of bone breakdown and rebuilding becomes irregular. Indeed, it leads to areas of excessive, anarchic bone remodelling and structurally weakened bone (7).

In patients affected by this condition, bisphosphonates are used to suppress this excessive bone remodelling caused by overactive osteoclasts (7). By controlling abnormal bone resorption, they help relieve bone pain and prevent deformities and fractures associated with the disease (7). The effectiveness of bisphosphonates in reducing disease activity has made them the cornerstone of Paget's disease management.

1.2.1.3 Therapeutic indications in Oncology

Bisphosphonates play an essential role in oncology. They are often used in the management of cancers that affect the skeleton, breasts, prostate, and multiple myeloma (5). By lowering bone destruction, they help to control skeletal-related events, they also relieve pain and prevent pathological fractures or hypercalcemia. Their molecular characteristics allow them to target bone tissue with great affinity, and recent research has investigated their use in bisphosphonate-based conjugates for targeted cancer therapy (5). The capacity of these agents to influence both tumour behaviour and bone metabolism emphasizes their value in multimodal cancer care.

Beyond their skeletal and oncologic effects, bisphosphonates may have wider systemic benefits (8). Some studies have found that prolonged bisphosphonate use is linked to lower mortality and higher survival rates, perhaps as a result of anti-tumour or anti-inflammatory properties (8). Even though these results are still being studied, they show that bisphosphonates have therapeutic possibilities that go beyond just bone metabolism.

From metabolic bone illnesses to cancer, the broad spectrum of indications for which bisphosphonates are generally given points to their vital need in contemporary medicine. However, their prolonged use makes dental awareness even more vital as the same process that protect bone could later affect tissue responses and healing in maxillofacial areas.

1.2.2 Mechanism of action: inhibition of osteoclasts and bone resorption

Considering their major influence on bone metabolism, bisphosphonates have become a mainstay in treating disorders affecting skeletal integrity and connect general health issues with focused oral and bone therapies (4).

Bisphosphonates mostly block bone resorption by influencing osteoclasts, which are the cells in charge of bone breakdown.

These compounds have a strong attraction for hydroxyapatite crystals once given, which lets them attach to bone surfaces, especially in places where remodelling is most active (9).

Osteoclasts absorb bisphosphonate molecules during bone resorption, which then interfere with necessary cellular processes. Non-nitrogenous bisphosphonates are processed by osteoclasts to produce poisonous ATP analogues that induce cell death.

On the other hand, nitrogen-containing bisphosphonates like zoledronate or alendronate stop the mevalonate pathway, which reduces the amount of important prenylated proteins that osteoclast need to work and live (9).

Their therapeutic efficacy in conditions marked by high bone loss is explained by this suppression of osteoclast action, which results in lower bone turnover and hence increased skeletal stability (7).

These processes also aid to reduce tumour-induced bone resorption in oncology, therefore restricting the release of growth factors that might promote cancer development (5).

In fact, bisphosphonates could slow down healing processes, especially in the jaw, where bone turnover is naturally high, because they significantly lower bone remodelling and angiogenesis (9).

This biological reaction is the cause of problems like medication-related osteonecrosis of the jaw (MRONJ), which remains a major concern in dental and surgical care.

1.2.3 Types and routes of administration

Depending on the administration of bisphosphonates, they act against specific types of conditions. Bisphosphonate compounds can be administered either orally or intravenously, depending on the disease severity and therapeutic goal.

1.2.3.1 Oral pathway

On one hand, oral administration (less potent than intravenous one) is mostly used to counteract osteoporosis. Patients take this medication orally to “strengthen bones” (ex: alendronate, risedronate) (4).

In fact, this administration route is most commonly prescribed for long-term management diseases because of its simple use and because it is generally well tolerated (9).

It could also be used for Paget’s disease, where heightened osteoclastic activity is followed by disorganized and rapid bone formation. (7)

1.2.3.2 Intravenous pathway (IV)

On the other hand, intravenous forms , including pamidronate and zoledronic acid, are reserved for patients requiring stronger antiresorptive effects, such as those with bone metastases or multiple myeloma (5,9). It might also be administered to counteract fibrous dysplasia or Paget’s disease in severe cases (4).

Intravenous therapy achieves higher plasma concentrations and a more potent inhibition of osteoclasts, but it is also more closely associated with the risk of medication-related osteonecrosis of the jaw (5).

Once administered, bisphosphonates display a strong affinity for hydroxyapatite, leading to their accumulation in mineralized tissues (8). They bind tightly to bone surfaces and can remain embedded for years, continuing to exert their biological effect long after the drug is discontinued. This prolonged skeletal retention contributes to their therapeutic efficacy by maintaining bone density, nevertheless it also means that any adverse effects may persist for extended periods.

From a dental perspective, this property has significant clinical implications, as even patients who have stopped bisphosphonate therapy can remain at risk for complications such as impaired bone healing and MRONJ (8).

1.3. Adverse effects of bisphosphonates and pathogenesis of medication-related osteonecrosis of the jaw (MRONJ).

Despite their therapeutic benefits, oral bisphosphonates have been associated with complications involving the digestive system and other body systems, which may influence treatment tolerance and patient compliance (10).

In dentistry, one of the complications that often goes along with bisphosphonate treatment is medication-related osteonecrosis of the jaw (MRONJ) (10).

It happens when parts of the jawbone lose their blood supply and necrosis begins, usually in the upper or lower jaw. The problem is similar to bone that stays exposed or a tooth socket that just does not heal properly. This condition is observed more often in people who receive intravenous nitrogen-based bisphosphonates, but it can also appear after long-term oral treatment, especially when the medication has been used for several years.(10)

1.3.1 Definition and characteristics of medication-related osteonecrosis of the jaw (MRONJ).

Bisphosphonate-related osteonecrosis of the jaw (BRONJ), more broadly referred to as medication-related osteonecrosis of the jaw (MRONJ), is a medical condition identified by the presence of exposed bone, or bone that can be probed through a fistula, in the maxillofacial region. It persists for at least eight weeks in a person who has received anti-resorptive or anti-angiogenic therapy and has not undergone radiation therapy to the jaws (9,11,12).

This standardized definition, established by the American Association of Oral and Maxillofacial Surgeons (AAOMS), allows clinicians to differentiate MRONJ from other osteonecrosis conditions (11).

Although relatively rare, MRONJ represents a serious complication for patients treated with bisphosphonates. Clinically, affected patients may present with symptoms such as pain, swelling, mucosal ulceration, fistula formation, and exposed necrotic bone that may lead to

secondary infection (9,13). Radiographically, affected sites often display mixed sclerotic and radiolucent patterns, cortical irregularities, and bone sequestrum (13).

The severity of MRONJ can vary from asymptomatic bone exposure to extensive necrosis with pathological fracture or extraoral fistula formation, making early diagnosis crucial (9).

In addition, the American Dental Association provides updated recommendations on the risk of MRONJ associated with oncology agents and outlines preventive strategies for dental practitioners managing these patients (14).

Despite ongoing research, evidence from systematic reviews suggests that no single intervention guarantees complete resolution of the disease. However, conservative management resolves ~70-80% of early cases. This lets us understand the importance of prevention and multidisciplinary management (9,12).

1.3.2 Risk factors

1.3.2.1 Duration of therapy

The development of MRONJ is multifactorial, with both systemic and local elements contributing to its onset (9,11–13). The duration of antiresorptive therapy is among the strongest predictors. According to AAOMS classification, patients who have received oral bisphosphonate treatment for less than 4 years and have no additional comorbidities are considered at low risk. In contrast, those with more than 4 years of therapy, or with contributing systemic conditions are categorized as high-risk individuals (9,11).

1.3.2.2 Drug type

The potency and route of administration also influence risk of adverse effects. Intravenous zoledronic acid and pamidronate, which achieve higher bone concentrations, are associated with greater risk than oral agents like alendronate (11,13).

1.3.2.3 Dental interventions

Depending on the treatment undergone, there are varying degrees of osteonecrosis risk. In fact, dental extractions, implant placement, and periodontal or endodontic surgery remain the most frequent local precipitating factors (9,11).

Actually, patients should not stop bisphosphonate treatment on their own or at the dentist's request without consulting their physician, as it does not reduce the risks significantly (11).

Systemic comorbidities such as diabetes, cancer, corticosteroid use, and poor oral hygiene further compound the risk (12,13).

From a preventive standpoint, identifying these predisposing conditions before initiating antiresorptive treatment and maintaining rigorous oral health care are essential measures to reduce MRONJ occurrence (9,11,12).

1.3.3 Main pathophysiological hypotheses

1.3.3.1 Reduced bone remodelling and vascularization

The biological mechanisms leading to medication-related osteonecrosis of the jaw (MRONJ) are complex and multifactorial (4,5,8,9,11,13). The main hypothesis involves the suppression of bone remodelling caused by the long-term inhibition of osteoclastic activity.
As bone turnover slows, microdamage accumulates, and the capacity for repair diminishes, especially in the alveolar bone, which is constantly remodelled through mastication and dental stress (9,11).

At the same time, these drugs can reduce local vascularization by limiting new blood vessel formation, compromising nutrient and oxygen delivery to bone tissue (13). This ischemic environment delays healing and makes the jaw particularly prone to necrosis following trauma or dental extraction.

1.3.3.2 Impaired mucosal healing and infection

In addition, bisphosphonates can exert toxic effects on oral soft-tissue cells, such as keratinocytes and fibroblasts, weakening oral mucosa and delaying wound closure (4). Once the mucosal barrier is disrupted, oral bacteria may colonize exposed bone surfaces, leading to chronic inflammation and infection that perpetuate the necrotic process (5,8).
In summary, MRONJ likely results from a mix of factors: less bone renewal, limited blood circulation and reduced oxygen supply, more infection, all happening in the jaws which are subjected to high mechanical stress due to mastication.

1.4. The role of the dentist in patient management

For dental practitioners, knowledge of the effects of bisphosphonate therapy is essential to guarantee safe and successful patient care. Handling these patients requires anticipating possible complications, early identification of risk factors, and adapting the treatment plan appropriately.

1.4.1 Pre-treatment phase

1.4.1.1 Oral evaluation

Dentists can greatly lower the odds of complications and help preserve general health as well as oral health, by maintaining good communication with the medical team and emphasizing prevention.

Managing patients on antiresorptive therapy requires dental practitioners to adopt a proactive, ordered approach. The dentist must act not only as a clinician treating teeth and gums, but also as a coordinator of the patient's whole oral-systemic health condition, especially in individuals taking bone-modifying agents such as bisphosphonates (4).

For instance, pre-treatment dental revision and elimination of oral infection foci are essential steps to reduce the risk of medication-related osteonecrosis of the jaw (MRONJ) when these medications are used (15).

1.4.1.2 Patient education

Reducing the chance of complications with bisphosphonate treatment starts with patient education as it is quite important (16,17).

Since many people are unaware bisphosphonates may affect oral healing or raise susceptibility to jawbone issues, the dentist should carefully detail how these drugs interact with regular dental care. Patients should be informed about the importance of maintaining strict oral hygiene, attending regular check-ups, and reporting any discomfort such as persistent pain, swelling, or exposed bone (16). Clear instructions on daily cleaning techniques, the proper use of antibacterial mouthwashes, and the avoidance of habits that may traumatize the oral tissues, such as ill-fitting prostheses or hard foods, contribute significantly to prevention (17). In addition, patients should understand the need to communicate their medication history to all healthcare providers and they shouldn't stop taking their medicine unless a doctor tells them to. When patients are actively involved and understand the reasons behind preventive recommendations, adherence improves and the overall risk of MRONJ is reduced (16,17).

1.4.2 Management during therapy

1.4.2.1 Minimally invasive procedures

For patients already on bisphosphonate treatment, the first goal is to reduce any operation that might weaken their bones (4,15,18–20). These drugs' repressed bone turnover slows recovery and increases the likelihood of complications. Conservative treatments including

endodontic treatment, periodontal stabilization, or restoration should always be preferred over extractions (15). These options reduce inflammation while preventing direct trauma to the bone, which is particularly important in patients receiving high-dose antiresorptive therapy for oncologic conditions (4).

1.4.2.2 Surgical precautions when intervention is necessary

If surgery cannot be avoided, meticulous preparation and an atraumatic approach are crucial (18). Small incisions should be made, flap management should be gentle, and any sharp bony edges should be smoothed to prevent any future discomfort.

Whenever possible, getting primary closure helps soft-tissue recovery in a setting where recovery is sometimes slower. Since local inflammation raises the possibility of delayed healing, infection control is a crucial part of surgical planning. Depending on clinical judgment and the recommendations of oncology-focused rules, antiseptic procedures and antibiotic prophylaxis could be used (4,19).

For patients receiving high-risk bisphosphonate, antibiotic prophylaxis should be considered before invasive dental procedures involving bone or mucosal disruption, such as extractions or implant placement.

The suggested approach is a single dose of oral amoxicillin 2 g 1h before the procedure. If the patient is allergic to penicillin, we would recommend oral azithromycin or clarithromycin 500 mg 1h before the procedure.

If the patient is a child, we would recommend 50 mg/kg of amoxicillin 1 h before the treatment. After the procedure, antibiotic coverage may be extended for 24-48 hours and combined with antiseptic rinse such as 0,12% Chlorhexidine (21).

Regular postoperative follow-up helps to identify any delayed healing or new complication early on.

1.4.2.3 Monitoring and maintenance

Continuous monitoring is required during active treatment to spot early symptoms of mucosal damage, prosthetic trauma, or tissue irritation (20).

Adjustments to removable appliances, softening of sharp dental surfaces, and reinforcement of oral hygiene habits all contribute to a stable environment. Regular check-ups give a chance to assess healing potential, spot changes in soft tissues, and strengthen patient knowledge on symptoms not to be disregarded such as continuous pain or exposed bone (19,20). This ongoing awareness guarantees that minor complications are handled fast to prevent them from developing into more severe consequences.

1.4.3 Long-term follow-up

Long-term follow-up is clearly essential since the pharmacological effects of these agents may persist while the patient remains at risk. In fact, the risk persists for 1–5 years after bisphosphonate discontinuation (20). Clear communication with the medical provider, documenting drug history, counselling patients about the risks and benefits, and scheduling check-ups are all integral components of effective care in this context (20).

Clinicians may greatly help to provide safer outcomes and maintain both oral and systemic health in this vulnerable group of patients by adopting a preventive attitude followed by an interprofessional cooperation into dental operations.

2. OBJECTIVE

General objective:

Evaluate how to manage a patient undergoing bisphosphonate treatment and know how to prevent any complication in the dental chair.

3. MATERIAL AND METHODS

This Final Degree Project was carried out as a documentary research study, following a structured methodology to ensure the reliability, reproducibility and scientific validity of the information collected.

The research process was organized into four main phases:

- identification of the research question
- systematic literature search
- study selection based on predefined eligibility criteria
- extraction and organization of the data for analysis

3.1 Databases consulted

The bibliographic search was conducted between October 2025 and January 2026, using the electronic resources available through the CRAI–UEM Library. The following databases were consulted:

- PubMed
- MEDLINE Complete
- Dentistry and Oral Science Source
- CINAHL with Full text
- Google scholar (with CRAI institutional access)

These databases were selected due to their relevance in biomedical and dental research and their wide coverage of peer-reviewed scientific literature.

3.2. Keywords and search strategy

The search used combinations of controlled vocabulary (MeSH) and free-text keywords related to the topic. The main terms included:

“bisphosphonates”
“osteoporosis”
“Paget’s disease”
“dentistry”
“clinical management”
“complications”
“osteonecrosis of the jaw”

“MRONJ”

“oral health”

“general health”

“prevention”

“cancer”

“treatment methods”

“antibiotic prophylaxis”

These terms were combined using Boolean operators (AND, OR) to refine the search. Example of search strategies included:

- (bisphosphonates) AND (dental management)
- (bisphosphonates) AND (osteonecrosis of the jaw OR MRONJ) AND prevention
- (osteoporosis OR Paget’s disease) AND (bisphosphonates) AND (dental treatment)
- (cancer) AND (bisphosphonates) AND (complications)

Final Boolean research for PICO question: (bisphosphonates) AND (dental prevention OR preventive strategies) AND (osteonecrosis of the jaw OR MRONJ).

3.3. Inclusion and exclusion criteria

Inclusion

- Publications between 2020 and 2026
- Documents translated in English
- Peer-reviewed, full-text scientific articles
- Randomized clinical trials, cohort studies and observational studies
- Studies addressing bisphosphonate therapy and its dental implications

Exclusion

- Publications prior to 2020
- Studies unrelated to dentistry or MRONJ
- Non-scientific or non peer-reviewed sources
- Animal or in vitro studies
- Systematic reviews
- Articles without full-text availability

Although systematic reviews provide a high-level of evidence, they were excluded to avoid duplication of data and to allow direct analysis of primary studies relevant to the research question.

3.4 Study selection process

The initial search across all databases identified a total of 835 records. After applying filters (publication date, study type, and full text-availability), 61 articles remained for eligibility assessment.

Following full-text screening based on the inclusion and exclusion criteria, 9 studies were selected for inclusion in the systematic analysis. These studies consisted exclusively of primary research articles (randomized clinical trials, cohort and cross-sectional studies) directly addressing the PICO question.

A total of 30 references were used throughout this Final Degree Project to support the introduction, theoretical framework and discussion.

Moreover, key professional documents, such as the AAOMS 2022 Position Paper, the Cochrane Review (2022), and the ADA 2023 resource, were added manually due to their high clinical relevance, although they were not part of the systematic selection process.

3.5 PICO Question

The research question was structured using this PICO framework:

P (Population): Patients receiving bisphosphonate therapy (oral or IV).

I (Intervention): Dental preventive strategies and clinical management approach.

C (Comparison): Patients not following preventive guidelines, or alternative management strategies.

O (Outcome): Reduction of complications, particularly medication-related osteonecrosis of the jaw (MRONJ), and improved oral health outcomes.

Complete PICO question:

In patients undergoing bisphosphonate therapy (P), do structured dental preventive measures and specific clinical management protocols (I), compared to standard dental care or absence of preventive strategies (C), reduce the risk of medication-related osteonecrosis of the jaw and other oral complications (O)?

3.6 PRISMA Diagram

The study selection process was conducted in accordance with PRISMA 2020 guidelines and is illustrated in Figure 1.
The PRISMA flow diagram includes only the studies selected to answer the PICO research question and does not represent the total number of references used in the overall manuscript.

Boolean research for PICO question: (bisphosphonates) AND (dental prevention OR preventive strategies) AND (osteonecrosis of the jaw OR MRONJ).

The bibliographic search was realized using a selection of major biomedical and dental databases in order to ensure a comprehensive and systematic identification of relevant peer-reviewed studies:

- Medline Complete: 516 sources
- Dentistry and Oral Science source: 216 sources
- CINAHL with Full text: 113 sources

The selection process resulted in 9 studies chosen for in-depth analysis.

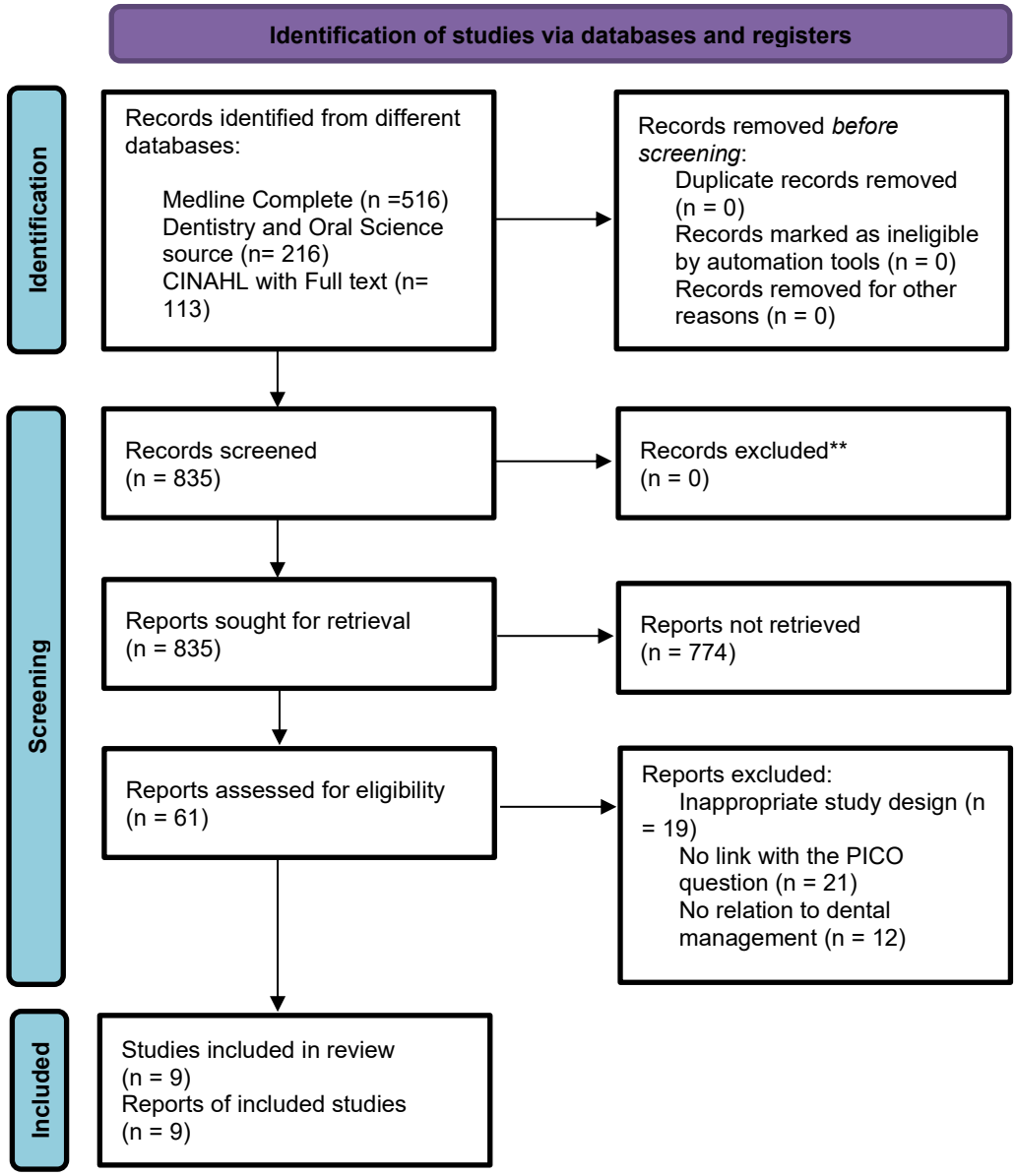


Figure 1. PRISMA flow diagram of the literature search and study selection process.

4. RESULTS

Author (year)	Study design	Sample / population	Medication	Intervention / comparison	Outcome / follow-up	Main results
Di Fede et al. (2024) (22)	Randomized single-center clinical trial	n=117; patients at risk of MRONJ requiring tooth extraction	Antiresorptive and anti-angiogenic drugs	Extraction + oxygen-ozone infiltration vs extraction without ozone	Post-extraction healing (IPR); 6 weeks	Improved healing in early phases; no significant difference in remodelling or total IPR score.
Bacci et al. (2021) (23)	Retrospective observational study	n=99; symptomatic multiple myeloma patients	IV bisphosphonates, mainly zoledronic acid	Dental treatment before therapy vs after therapy started	Incidence of BRONJ; 5 years	No BRONJ in pre-treatment group; 5 BRONJ cases and 2 osteonecrotic areas in post-treatment group.
Besi et al. (2024) (24)	Prospective observational cohort study	n=39 (63 extractions); mixed conditions	Bisphosphonates and/or denosumab	Extraction with L-PRF (leukocyte and platelet rich fibrin) vs without L-PRF	Occurrence of MRONJ; 10-12 weeks	No MRONJ in L-PRF group; 5 high-risk controls showed MRONJ signs.
Kizub et al. (2020) (25)	Randomized clinical trial	n=6018; women with stage I-III breast cancer	Zoledronic acid, ibandronate, clodronate	Randomized treatment with prevention guidelines and regular check-ups	Development of BRONJ during follow-up	BRONJ in 48 patients (0.8%); highest incidence with zoledronic acid.
Lin et al. (2026) (26)	Retrospective case series	n=106 (249 extractions); high- and low-risk patients	Bisphosphonates and denosumab	Extraction with socket preservation, antibiotic prophylaxis, >3 months drug withdrawal	Incidence of MRONJ after extraction; 3-6 months	MRONJ prevented in 99.6% of extractions; 1 case after early denosumab restart; 100% prevention in high-risk group.
Parise et al. (2022) (27)	Case-control study	n=20; oncologic patients	IV zoledronic acid	L-PRF prevention/treatment vs conventional surgery	Successful healing; 6 months	No MRONJ in prevention L-PRF group; faster healing and fewer complications.

Alrmali (2023) (28)	Prospective clinical case series	n=13; prevention and treatment patients	IV zoledronic acid or oral alendronate	PRF plugs after extraction; no control	Prevention of MRONJ; 12-48 months	100% MRONJ prevention; one flap dehiscence in treatment group only.
Mauceri et al. (2026) (29)	Retrospective multicenter comparative cohort study	n=202; metastases or myeloma patients	IV zoledronic acid	Intensive protocol (check-ups, exodontia 1 month before therapy) vs standard protocol	Incidence of MRONJ; 2012-2015	MRONJ 2.3% vs 13.9%; extractions, ill-fitting prostheses, and periodontitis were major risk factors.
Mirelli et al. (2022) (30)	Retrospective cohort study	n=434; osteoporosis and/or oncologic disease	Mainly alendronate, zoledronate, pamidronate, denosumab	Dental monitoring and prevention program; no control	Incidence of MRONJ; 2006-2020	MRONJ in 34 patients (7.8%); higher incidence with zoledronate and pamidronate.

Table 1. Summary of studies included in the systematic analysis

5. DISCUSSION

This review aimed to analyse the preventive and management strategies for medication-related osteonecrosis of the jaw (MRONJ) in patients receiving antiresorptive drugs. A total of 9 studies were included in the results table, with different study designs such as randomized clinical trials, retrospective cohort studies, and observational studies. Overall, the studies evaluated several preventive approaches, including preventive dental programs, surgical protocols for dental extractions, and adjunctive therapies such as platelet-rich fibrin (PRF), ozone therapy, and socket preservation techniques (22–30).

One of the main findings observed across several studies is the importance of preventive dental care before starting antiresorptive therapy. Studies evaluating preventive dental protocols showed that patients who underwent dental assessment and treatment before beginning bisphosphonate therapy presented a lower incidence of MRONJ compared with those who received dental treatment after the start of medication (23). These results support current recommendations suggesting that potential oral infections should be treated before initiating antiresorptive therapy.

Similarly, another study comparing two preventive protocols in patients treated with zoledronic acid showed that a more intensive preventive strategy including check-ups before and after the therapy begins, exodontia 1 month before starting zoledronate, was associated with a lower incidence of MRONJ (29). These findings highlight the importance of identifying and treating potential oral infections before antiresorptive therapy begins.

Some of the studies included in the table also focused on improving healing after tooth extraction, which is one of the most common triggering factors for MRONJ. Different adjunctive therapies were investigated. For example, ozone therapy was evaluated as a method to improve early healing after extraction (22), while other studies analysed the use of platelet concentrates such as L-PRF, which may promote tissue regeneration and wound healing (24,27). In addition, one study investigated a protocol including socket preservation, antibiotic prophylaxis and drug withdrawal reporting a very low incidence of MRONJ after extractions (26).

Other studies included in the review did not focus on a specific intervention but instead evaluated risk factors associated with MRONJ development**.** For example, a large clinical trial involving breast cancer patients reported a relatively low overall incidence of BRONJ, although the risk differed depending on the type of bisphosphonate used (25). Another retrospective

cohort study also analysed the incidence of MRONJ and identified several associated factors in patients receiving antiresorptive drugs (30).

However, several limitations should be considered when interpreting these results. First of all, the included studies were heterogeneous, both in terms of study design and interventions evaluated. Some studies focused on preventive dental programs, while others evaluated surgical techniques or analysed epidemiological data. In addition, some studies had relatively small sample sizes, which may limit the generalizability of their findings. The differences in patient populations, medications, and follow-up periods also make direct comparison between studies difficult.

Despite these limitations, the results presented in this review suggest that prevention and early dental management play an important role in reducing the risk of MRONJ. Preventive dental assessment before starting antiresorptive therapy, careful management of dental extractions, and regular follow-up appear to be important measures for improving patient outcome.

6. CONCLUSIONS

Ultimately, dental management of patients on bisphosphonate therapy should focus on a specific protocol to avoid any complication in the dental chair. The available scientific evidence indicates that the prevention of medication-related osteonecrosis of the jaw (MRONJ) is primarily based on early dental management and the implementation of preventives measures prior to the initiation of bisphosphonate therapy.

Conservative management strategies, including minimally invasive dental procedures and strict oral hygiene protocols, play a key role in reducing the incidence of MRONJ in patients at risk.

Adjunctive therapies such as platelet-rich fibrin and ozone therapy show promising results, particularly in early phases. Nevertheless, their long-term effectiveness remains unclear.

The development of MRONJ is multifactorial, involving systemic conditions, type of medication, therapy duration and local risk factors. As a dentist, this highlights the need for individualized patient consideration.

In fine, interdisciplinary collaboration between dental and medical professionals is essential to optimize prevention, early diagnosis and treatment outcomes.

7. SUSTAINABILITY

Management and Prevention of Medication - Related Osteonecrosis of the Jaw (MRONJ) is a function of Sustainable Principles of Healthcare.

Preventive dental care leads to fewer complexities in surgical management, lower hospitalizations, reduced need for long-term therapies, resulting in reduced healthcare costs and consumption of resources.

Socially, early prevention provides a better quality of life for patients by avoiding pain, infection, and functional impairment caused by MRONJ. It enhances education and awareness on oral health for the patient, promoting responsible health behaviours.

Economically, preventive strategies are more cost-effective than treatment of advanced stages of MRONJ which usually entails multidisciplinary management and long - term follow-up.

Environmentally, reducing surgery and use of medicine will decrease the number of resources used by the healthcare system including medical waste.

Consequently, the implementation of preventive dental protocols in patients receiving antiresorptive therapy enhances a sustainable healthcare system by enhancing patient outcomes while also optimally using resources.

8. BIBLIOGRAFY

1. Kolli BD, Pachava S, Talluri D, Veligatla SM, Patnala J, Selvaraj VK. Assessment of self-perceived oral health status, psychological well-being and life satisfaction among geriatric population. J Indian Assoc Public Health Dent. 2023;21(2):183–189.

2. Natarajan P, Madanian S, Marshall S. Investigating the link between oral health conditions and systemic diseases: a cross-sectional analysis. Sci Rep. 2025;15(1):10476.

3. Takefuji Y. Oral health's role in disease prevention. Br Dent J. 2024;236(10):733–734.

4. Lee ES, Tsai MC, Lee JX, Wong C, Cheng YN, Liu AC, et al. Bisphosphonates and their connection to dental procedures: exploring bisphosphonate-related osteonecrosis of the jaws. Cancers. 2023;15(22):5366.

5. Mbese Z, Aderibigbe BA. Bisphosphonate-based conjugates and derivatives as potential therapeutic agents in osteoporosis, bone cancer and metastatic bone cancer. Int J Mol Sci. 2021;22(13):6869.

6. Ciancia S, Högler W, Sakkers RJB, Appelman-Dijkstra NM, Boot AM, Sas TCJ, et al. Osteoporosis in children and adolescents: how to treat and monitor? Eur J Pediatr. 2022;182(2):501–511.

7. Tenshin H, Delgado-Calle J, Windle JJ, Roodman GD, Chirgwin JM, Kurihara N. Osteocytes and paget's disease of bone. Curr Osteoporos Rep. 2024;22(2):266–72.

8. Billington EO, Reid IR. Benefits of bisphosphonate therapy: beyond the skeleton. Curr Osteoporos Rep. 2020;18(5):587–96.

9. Yılmaz A, Arı I, Samunahmetoğlu E, Hürmüzlü S, Çetiner S. Diagnosis of medication-related osteonecrosis of the jaw and alternative treatment methods. Cumhur Dent J. 2025;28(2): 278-286.

10. Psimma C, Psimma Z, Willems HC, Klüter WJ, Van Der Maarel-Wierink CD. Oral bisphosphonates: adverse effects on the oral mucosa not related to the jaw bones. A scoping review. Gerodontology. 2022;39(4):330–338.

11. Ruggiero SL, Dodson TB, Aghaloo T, Carlson ER, Ward BB, Kademani D. American association of oral and maxillofacial surgeons' position paper on medication-related osteonecrosis of the jaws—2022 update. J Oral Maxillofac Surg. 2022;80(5):920–43.

12. Beth-Tasdogan NH, Mayer B, Hussein H, Zolk O, Peter JU. Interventions for managing medication-related osteonecrosis of the jaw. Cochrane Oral Health Group, editor. Cochrane Database Syst Rev [Internet]. 2022 Jul 12 [cited 2025 Oct 29];2022(7). Available from: http://doi.wiley.com/10.1002/14651858.CD012432.pub3

13. Kuroshima S, Al-Omari FA, Sasaki M, Sawase T. Medication-related osteonecrosis of the jaw: a literature review and update. genesis. 2022;60(8–9):e23500.

14. American Dental Association. Oncology Agents and Medication-Related Osteonecrosis of the Jaw [Internet]. American Dental Association; 2023 [cited 2025 Dec 1]. Available from: https://www.ada.org/resources/ada-library/oral-health-topics/oncology-agents-and-medication-related-osteonecrosis-of-the-jaw.

15. Zavalloni G, Spinelli A, Coppini M, Mauceri R, Campisi G, Lenzi J, et al. Endodontic treatment and management of patients under antiresorptive treatment: a scoping review on MRONJ risk. Clin Oral Investig. 2025;29(10):466.

16. Saur FG, Keinki C, Cramer A, Buentzel J, Hübner J. Education and communication on the topic of osteonecrosis of the jaw when taking bone-stabilizing drugs. Clin Exp Dent Res. 2024;10(6):e70024.

17. Lima-Souza RAD, Leonel ACLDS, Duarte ÂLBP, Castro JFLD, Carvalho EJDA, Perez DEDC. Awareness of patients receiving bisphosphonates: a cross-sectional study. Braz Oral Res. 2022;36:e0126.

18. Byrne H, O'Reilly S, Weadick CS, Brady P, Ríordáin RN. How we manage medication-related osteonecrosis of the jaw. Eur J Med Res. 2024;29(1):402.

19. Dipalma G, Inchingolo AD, Guglielmo M, Palumbo I, Riccaldo L, Morolla R, et al. Monoclonal antibodies and osteonecrosis of the jaw: a systematic review of risk, incidence, and clinical management in dentistry. Khalaf K, editor. Int J Dent. 2025;2025(1):2557594.

20. Golu MV, Bogozi BB, Petrovan C, et al. Maxillary osteonecrosis of the jaw: a multidisciplinary approach, communication strategies, and technological tools for prophylaxis. Rom J Stomatol. 2024;70(1):52–6.

21. Vidović Juras D, Škrinjar I, Križnik T, Andabak Rogulj A, Lončar Brzak B, Gabrić D, et al. Antibiotic prophylaxis prior to dental procedures. Dent J. 2024;12(11):364.

22. Di Fede O, La Mantia G, Del Gaizo C, Mauceri R, Matranga D, Campisi G. Reduction of MRONJ risk after exodontia by virtue of ozone infiltration: a randomized clinical trial. Oral Dis. 2024;30(8):5183–94.

23. Bacci C, Cerrato A, Dotto V, Zambello R, Barilà G, Liço A, et al. The importance of alliance between hematologists and dentists: a retrospective study on the development of bisphosphonates osteonecrosis of the jaws (BRONJ) in multiple myeloma patients. Dent J. 2021;9(2):11.

24. Besi E, Pitros P. The role of leukocyte and platelet-rich fibrin in the prevention of medication-related osteonecrosis of the jaw, in patients requiring dental extractions: an observational study. Oral Maxillofac Surg. 2024;28(2):785–93.

25. Kizub DA, Miao J, Schubert MM, Paterson AHG, Clemons M, Dees EC, et al. Risk factors for bisphosphonate-associated osteonecrosis of the jaw in the prospective randomized trial of adjuvant bisphosphonates for early-stage breast cancer (SWOG 0307). Support Care Cancer. 2021;29(5):2509–17.

26. Lin LH, Wang CH, Lu SY. Successful prevention of medication-related osteonecrosis of the jaw after dental extractions by socket preservation with alloplast plus tetracycline in patients taking antiresorptive drugs. J Dent Sci. 2026;21(1):468–74.

27. Parise GK, Costa BN, Nogueira ML, Sassi LM, Schussel JL. Efficacy of fibrin-rich platelets and leukocytes (L-PRF) in tissue repair in surgical oral procedures in patients using zoledronic acid—case–control study. Oral Maxillofac Surg. 2022;27(3):507–12.

28. Alrmali A, Saleh MHA, Kurdi SMS, Sabri H, Meghil MM, Wang H. Prevention and management of drug-induced osteonecrosis of the jaws using platelet-rich fibrin: a clinical feasibility study. Clin Exp Dent Res. 2023;9(5):791–798.

29. Mauceri R, La Mantia G, Di Fede O, Fusco V, Marcianò A, Coppini M, et al. Medication-related osteonecrosis of the jaw primary prevention: multidomain long-term intervention versus pre-bisphosphonate treatment standalone dental intervention. A retrospective multi-center comparative cohort study. Support Care Cancer. 2026;34(2):135.

30. Mirelli C, Marino S, Bovio A, Pederielli S, Dall'Agnola C, Gianni AB, et al. Medication-related osteonecrosis of the jaw in dental practice: a retrospective analysis of data from the Milan cohort. Dent J. 2022;10(5):89.