



# Dental Implant Failure in Osteoporotic Females on Bisphosphonate Therapy: A Systematic Review

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<b>KEYWORDS</b>  Dental implant failure, Osteoporotic females, Bisphosphonate Therapy.	<b>ABSTRACT:</b> <p><b>Objective:</b> The goal of this systematic review was to systematically evaluate the relationship between bisphosphonate therapy and dental implant failure rates in osteoporotic female patients.</p> <p><b>Data:</b> This Systematic Review is registered on PROSPERO (Registration no- CRD42025629509), following the PRISMA statement and PICOS question.</p> <p><b>Source:</b> An electronic literature search was carried through PubMed, Google Scholar, Scopus, Web of Science, and Cochrane Library databases from year 2008 and 2024. The focused question was: “Does bisphosphonate therapy affects dental implant failure in osteoporotic females?”</p> <p><b>Results:</b> In 10 studies selected for this systematic review, most studies reported high implant success rates (86%–100%) in osteoporotic females on bisphosphonates. While a few studies noted increased failure risk, particularly with longer treatment duration, the majority found no significant negative impact. Overall, bisphosphonates did not consistently affect implant outcomes.</p> <p><b>Conclusion:</b> The present systematic review suggests that dental implants in osteoporotic females on bisphosphonate therapy generally show high success rates. Although some studies suggest a potential increase in failure risk, especially with prolonged use, most evidence indicates that bisphosphonates do not significantly compromise implant outcomes when proper clinical protocols are followed.</p>
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## 1. Introduction

Dental implants are now a widely used method for replacing missing teeth. Compared to traditional dentures or bridges, implants provide better chewing ability, appearance, and long term comfort. A successful implant becomes securely attached to the surrounding bone in a process called osseointegration. This bond ensures that the implant stays in place and functions like a natural tooth <sup>[1]</sup>. For osseointegration to occur properly, the health and quality of the jawbone are essential. Several other factors also influence implant success, such as the patient’s overall health, surgical technique, and oral hygiene <sup>[2]</sup>. One medical condition that raises concern among dentists when planning implant placement is osteoporosis.

Osteoporosis is a bone disease that leads to weakened, brittle bones and a higher risk of fractures. It affects people of all ages, but it is especially common in postmenopausal women, due to a drop in estrogen levels after menopause. Estrogen helps to maintain bone strength, and without it, bones lose density more rapidly. The World Health Organization defines osteoporosis as a bone mineral density (BMD) T-score of  $-2.5$  or lower <sup>[3]</sup>. It is estimated that more than 200 million women worldwide are affected by this disease <sup>[4]</sup>. As women with osteoporosis age, many of them also experience tooth loss. This leads to an increased demand for dental implants. However, because osteoporosis causes lower bone mass and weaker bone structure, it has raised concerns about whether dental implants can properly integrate and stay stable in such bone.



To treat osteoporosis and prevent fractures, many women are prescribed a type of medication called bisphosphonates. These drugs help reduce bone loss and are commonly used around the world. Some of the most frequently prescribed bisphosphonates include alendronate, risedronate, ibandronate, and zoledronic acid. Bisphosphonates are synthetic drugs that act mainly by stopping the activity of osteoclasts, which are the cells responsible for breaking down bone. Normally, bone tissue is constantly being renewed through a balance between two processes: bone resorption (breakdown by osteoclasts) and bone formation (building by osteoblasts). In osteoporosis, this balance is disturbed, bone is broken down faster than it can be rebuilt.

Bisphosphonates help to restore this balance by :

1. Binding to bone minerals: Bisphosphonates are chemically similar to pyrophosphate, a natural substance in the body. When taken orally or injected, they bind tightly to hydroxyapatite crystals in the bone, especially in areas where bone turnover is high <sup>[5]</sup>.
2. Inhibiting osteoclast activity: Once bone that contains bisphosphonates is resorbed by osteoclasts, the drug enters these cells and disrupts their function. Nitrogen-containing bisphosphonates (like alendronate and zoledronic acid) block a key enzyme in the mevalonate pathway, which is important for the survival and function of osteoclasts <sup>[6]</sup>.
3. Promoting osteoclast cell death (apoptosis): By blocking this pathway, bisphosphonates prevent osteoclasts from forming the structures needed to attach to bone, leading to reduced bone resorption. Over time, this causes the osteoclasts to die, reducing bone breakdown even further <sup>[7]</sup>. The overall result is stronger bones with higher mineral density, which lowers the risk of fractures in people with osteoporosis.

However, this powerful effect on bone resorption also affects the body's natural ability to remodel bone. Bone remodelling is important not just for strength, but also for healing—especially after surgeries like dental implant placement. Since bisphosphonates reduce turnover, they may slow down healing after an implant is placed and affect how well the implant bonds with the bone <sup>[8]</sup>.

There is ongoing debate about whether bisphosphonate use increases the risk of dental implant failure. Some studies suggest that when bisphosphonates are taken

orally, in low doses, and for a short period, they do not significantly affect implant success. For example, a study by Jeffcoat et al followed patients on oral bisphosphonates and found no increase in implant failure <sup>[9]</sup>. Similarly, Bell and Bell also reported good outcomes in patients taking these medications <sup>[10]</sup>. On the other hand, some studies show that long-term use, even of oral bisphosphonates, may lead to problems such as delayed healing, failure of the implant to integrate, or increased risk of early implant loss <sup>[11]</sup>.

It is important to note that implant failure in patients with osteoporosis and bisphosphonates can happen for many reasons such as: Poor bone quality, decreased bone remodelling due to bisphosphonates, inadequate surgical technique, poor oral hygiene or smoking, other health conditions like diabetes. Another point to consider is that bisphosphonates stay in the body for a very long time, especially in bones. Even after stopping the drug, it can continue to affect bone remodelling for months or even years <sup>[5]</sup>.

Implants in the upper jaw (maxilla) are generally more likely to fail than those in the lower jaw (mandible) because the upper jaw tends to have softer, more porous bone. Osteoporosis can make this difference even more noticeable, which is why dentists often use different surgical techniques or implant types depending on the site <sup>[12]</sup>.

Although many studies have looked into how osteoporosis and bisphosphonate treatment affect dental implants, the results remain mixed and unclear. Some research shows that implants can work well in patients with osteoporosis, even when they are on bisphosphonate therapy. However, other studies suggest there may be a higher risk of implant failure, especially when bisphosphonates are taken for longer periods or when other risk factors are present.

The lack of agreement in the existing research creates uncertainty for dental professionals when planning implant treatments for this group of patients. Given the increasing number of older women affected by both osteoporosis and tooth loss, it is important to understand whether bisphosphonate therapy has a real impact on dental implant outcomes.

Therefore, this systematic review aimed to carefully collect and analyze clinical studies that have investigated



dental implant failure in osteoporotic females who are on bisphosphonate therapy. The goal was to evaluate the current evidence, identify any trends, and help provide clearer guidance for dental practitioners. This may lead to better treatment planning, improved patient outcomes, and safer dental care for this growing patient group.

## 2. Materials and methodology

### **REGISTRATION PROTOCOL**

This Systematic Review is registered on PROSPERO (Registration no- CRD42025629509), following the PRISMA (The Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines.

### **ELIGIBILITY CRITERIA**

Eligibility criteria included clinical human studies, randomized controlled trials (RCTs), prospective, retrospective studies.

### **PICO:**

This systematic review encompasses following PICO strategy: (Population, Intervention, Comparison, Outcome)

Population (P): Osteoporotic females receiving dental implants.

Intervention (I): Dental implant placement in patients receiving bisphosphonate therapy (oral or intravenous).

Comparison (C): Osteoporotic females not on bisphosphonate therapy or healthy females receiving dental implants.

Outcome (O): Dental implant failure rate.

The PICO modeled question were:

Q1: Does bisphosphonate therapy affects dental implant osseointegration?

Q2: Is there any difference in dental implant failure rate in osteoporotic females receiving bisphosphonate therapy and those without bisphosphonate therapy?

### **SEARCH STRATEGY:**

A comprehensive literature search was carried out using electronic databases including PubMed (MEDLINE), Cochrane Library, and Embase to identify relevant

clinical studies published in English. The search strategy incorporated a range of keywords and controlled vocabulary (MeSH terms), such as "dental implants," "implant failure," "osteoporosis," "bisphosphonate therapy," "postmenopausal women," "oral bisphosphonates," "intravenous bisphosphonates," "osseointegration," and "osteonecrosis of the jaw."

Boolean operators AND and OR were applied to combine terms effectively and filter relevant results. For example, combinations like "osteoporosis AND dental implants AND bisphosphonates" and "implant failure OR osseointegration loss" were used to narrow the focus.

In PubMed, Medical Subject Headings (MeSH) were utilized to increase search sensitivity and specificity. In contrast, Google Scholar was searched using phrase-based queries and mandatory inclusion symbols to broaden the scope, such as: "osteoporotic women" + "dental implant failure" + "bisphosphonates."

The Cochrane Library was explored using keyword combinations related to implant failure risk in osteoporotic patients undergoing bisphosphonate treatment. To ensure a thorough review, the reference lists of all eligible and non-eligible articles were manually checked for additional studies. A hand search of key journals in implant dentistry was also performed to identify potentially overlooked or unpublished relevant literature.

**INCLUSION CRITERIA:** • Post menopausal female patients diagnosed with osteoporosis. • Partially or fully edentulous patients treated with dental implants. • Patients undergoing oral or intravenous bisphosphonate therapy at the time of implant placement or during follow-up. • Patients with adequate oral hygiene status.

**EXCLUSION CRITERIA:** • Presence of active periodontal or peri-implant infections at the time of implant placement. • Patients with known parafunctional habits such as bruxism or severe clenching. • Individuals with a history of substance abuse (alcohol or drugs). • Patients with poor oral hygiene.

### **DATA EXTRACTION:**

Two reviewers independently screened all retrieved titles and abstracts to identify studies potentially meeting the inclusion criteria. Full-text articles were obtained for those selected, as well as for cases where abstracts did



not provide enough detail to make a clear decision. Both reviewers then carefully assessed the full texts based on the predefined inclusion and exclusion criteria. For each eligible study, the reviewers independently extracted relevant information, which was then compared and verified for accuracy. The extracted data comprised study characteristics such as author names, publication year, study design, sample size, demographic details (including age and gender), details on bisphosphonate therapy (type and duration), number of implants placed in osteoporotic females receiving bisphosphonates, number of implants in comparison groups, implant failure rates during the follow-up period, and any reported complications like osteonecrosis of the jaw. Any differences in data extraction were resolved through discussion or consultation with a third reviewer when necessary. Studies lacking critical data on implant outcomes were excluded from the review.

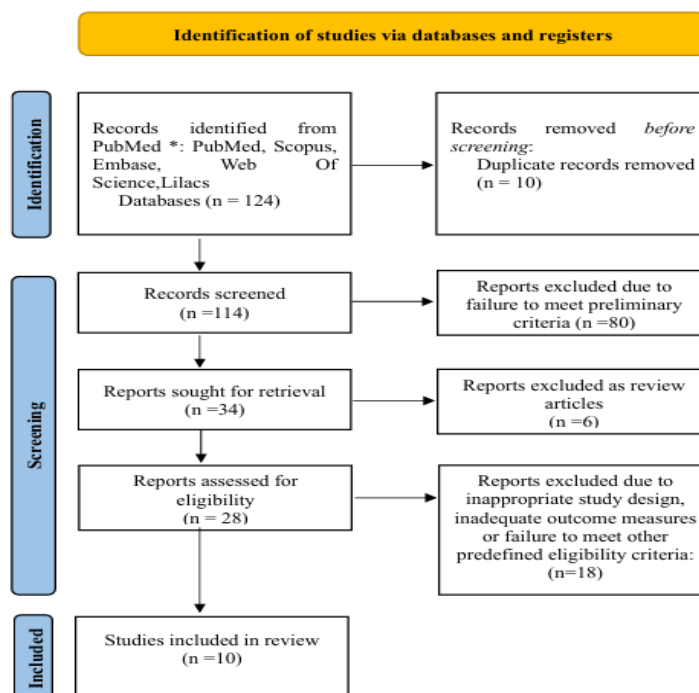
initial identification of studies to the final inclusion in the synthesis.

Below is an elaborate description of each step in the flowchart:

### 1. Identification of Studies

- Total number of studies identified ( $n = 124$ ): This step refers to the total number of studies initially found through the systematic search of multiple databases (e.g., PubMed, Scopus, Embase, Web Of Science, Lilacs etc.) and other sources.

**FIGURE 1: PRISMA FLOW DIAGRAM FOR STUDY SELECTION OF PROCESS<sup>56</sup>**



### 3. Result

The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) (**Figure 1**) flowchart provides a visual representation of the systematic review and meta-analysis process, outlining the stages from

The studies could include clinical trials, observational studies, and other research types related to the topic.

- Duplicates removed ( $n=10$ ): After the initial search, duplicate records (studies found in multiple databases) were removed. This step ensures that the same study is



not counted multiple times, resulting in more accurate final results.

## 2. Screening

• Studies screened: The titles and abstracts of the remaining studies are reviewed to determine if they meet the inclusion criteria. At this stage, 114 studies were screened based on the relevance of their topics to the research question.

• Studies excluded: Based on this screening phase, many studies are excluded due to irrelevance or failure to meet preliminary criteria. In this case, 80 studies were excluded after screening.

## 3. Eligibility Assessment

### STUDY CHARACTERISTICS:

**TABLE 1: EVIDENCE-BASED TABLE**

Study	Study Design	Sample Size (BP group)	Bisphosphonate Type	Duration of Therapy	Implant Success Rate	Failure Rate	Key Findings
Bell & Bell (2008) <sup>10</sup>	Retrospective cohort	42 pts (101 implants)	Oral (mixed)	6 mo – 11 yrs	95%	5%	Oral BPs not associated with failure.
Kasai et al. (2009) <sup>40</sup>	Retrospective comparative	11 BP pts	Oral (Alendronate)	Not stated	86% (BP) vs 95% (control)	14%	Higher failure rate with BPs.
Koka et al. (2010) <sup>23</sup>	Retrospective chart review	55 pts (121 implants)	Oral (mostly Alendronate)	Various	99.2%	0.8%	No significant impact of BPs.
Yip et al. (2012) <sup>25</sup>	Retrospective case-control	337 women	Oral (Alendronate, etc.)	Various	OR=2.5 for failure	-	Significant ↑ failure risk with BPs.
Siebert et al. (2015) <sup>28</sup>	Prospective controlled trial	12 pts (60 implants)	IV Zoledronate	2–3 years	100%	0%	Implants safe with IV BPs.

• Studies assessed for eligibility: The remaining 34 studies undergo a full-text review, where the complete articles are assessed for methodological quality, study design, and relevance to the research question. This step ensures that only studies with the appropriate design and outcomes will be included in the final analysis. 6 review articles were excluded as they did not meet the criteria for primary research.

• Studies excluded after eligibility assessment: Studies excluded for methodological/design issues (n = 18): These studies were excluded due to factors such as inappropriate study design, inadequate outcome measures, or failure to meet other predefined eligibility criteria.



Al-Rawee et al. (2019) <sup>34</sup>	Prospective comparative	15 pts (72 implants)	Oral (Alendronate)	8 months	91.7%	8.3%	Oral BP did not affect outcome.
Manas et al. (2024) <sup>38</sup>	Prospective comparative	10 BP pts	Oral (Alendronate)	1.5 years	95%	5%	Alendronate increased BMD, no failure risk.
Martin et al. (2010) <sup>19</sup>	Cohort survey analysis	16 pts (44 implants)	Oral (Alendronate)	3–103 months	16 pts, 26 failures (~59%)	59%	Higher late implant failure observed in oral BP users.
Mozzati et al. (2015) <sup>29</sup>	Retrospective cohort	235 pts (1267 implants)	Oral (Alendronate, Risedronate, Ibandronate)	Avg. 40.2 mo	98.7%	1.3%	Low failure; PRGF may aid healing.
Shabestari et al. (2009) <sup>20</sup>	Case series	21 pts (46 implants)	Oral (Fosamax)	Mean 20.5 mo	100%	0%	No mobility, all implants clinically stable.

**Table 1** summarizes the key methodological and clinical characteristics of the studies included in this review, focusing on the relationship between bisphosphonate

(BP) therapy and dental implant failure in osteoporotic female patients.

The included studies varied widely in design, ranging from retrospective cohorts and case series to prospective comparative trials and case control analyses. Sample sizes differed substantially, from as few as 10 participants to over 300, with most studies involving women receiving oral bisphosphonates—primarily alendronate, though risedronate, ibandronate, and mixed agents were also represented. A single study examined the use of intravenous (IV) zoledronate. The duration of bisphosphonate therapy also varied considerably across studies, spanning short-term use (~8 months) to long term administration exceeding 8 years. Implant success and failure rates ranged significantly, from 100% success

in some smaller case series to failure rates as high as 59% in one cohort survey.

**A Risk of Bias (RoB) assessment (Table 2)** was performed for all 10 included studies using criteria adapted from the Cochrane Risk of Bias Tool and other standard appraisal frameworks suitable for both randomized and non-randomized studies. The evaluation considered five domains: selection bias, performance bias, detection bias, attrition bias, and reporting bias. Each domain was graded as low, moderate, or high risk of bias, and an overall risk of bias was subsequently assigned for each study.

The majority of the studies included in this systematic review were observational in nature—either retrospective cohorts, comparative designs, or chart reviews—which inherently present greater challenges in

**TABLE 2: RISK OF BIAS ASSESSMENT FOR 10 STUDIES**

Study	Study Design	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Overall Risk of Bias
Bell & Bell (2008) <sup>10</sup>	Retrospective cohort	Moderate	High	Moderate	Low	Low	Moderate
Kasai et al. (2009) <sup>40</sup>	Retrospective comparative	Moderate	Moderate	Moderate	Low	Low	Moderate
Koka et al. (2010) <sup>23</sup>	Retrospective chart review	Moderate	Moderate	Moderate	Low	Low	Moderate
Yip et al. (2012) <sup>25</sup>	Retrospective case-control	Moderate	Moderate	Moderate	Low	Low	Moderate
Siebert et al. (2015) <sup>28</sup>	Prospective controlled trial	Low	Low	Low	Low	Low	Low
Al-Rawee et al. (2019) <sup>34</sup>	Prospective comparative	Moderate	Moderate	Moderate	Low	Low	Moderate
Manas et al. (2024) <sup>38</sup>	Prospective comparative	Moderate	Moderate	Moderate	Low	Low	Moderate
Martin et al. (2010) <sup>19</sup>	Cohort survey analysis	Moderate	High	Moderate	Moderate	Low	Moderate
Mozzati et al. (2015) <sup>29</sup>	Retrospective cohort	Moderate	Moderate	Moderate	Low	Low	Moderate
Shabestari et al. (2009) <sup>20</sup>	Case series	Moderate	Moderate	Moderate	Low	Low	Moderate

mitigating bias compared to randomized controlled trials. As such, most studies were judged to have a moderate overall risk of bias.

**Selection bias** was generally rated as moderate across the studies due to non-randomized participant inclusion and retrospective data retrieval. Only the prospective controlled trial by Siebert et al. (2015)<sup>[28]</sup> was rated as

having a low risk in this domain, likely due to more systematic subject recruitment and predefined protocols.

**Performance bias**, which reflects the uniformity of interventions and clinical care across study groups, was rated high in one study (Bell & Bell, 2008)<sup>[10]</sup> and moderate in most others, primarily due to the lack of blinding and potential differences in operator experience or implant protocols, particularly in retrospective



designs. Siebert et al. (2015) [28] again stood out with a low risk rating in this domain, attributable to its prospective nature and controlled methodology.

**Detection bias**, concerning the objectivity and standardization of outcome assessment, was consistently marked as moderate. While implant failure is generally a clearly defined endpoint, the retrospective nature of most data collection methods leaves room for variation in diagnostic thresholds, record accuracy, and criteria for defining implant success or failure.

**Attrition bias**, related to incomplete outcome data or loss to follow-up, was rated as low in all studies except Martin et al. (2010) [19], which was rated moderate due to unclear reporting of follow-up duration for all patients and potential underreporting of late failures. The consistency of low attrition bias suggests that implant outcome data were generally available for most patients through the study period.

**FIGURE 2: TRAFFIC LIGHT PLOT FOR DETERMINING RISK OF BIAS**

Study	Risk of bias domains							Overall
	D1	D2	D3	D4	D5	D6	D7	
Bell & Bell (2008)	+	+	+	+	+	+	+	+
Kasai et al. (2009)	+	+	+	+	+	+	+	+
Koka et al. (2010)	+	+	+	+	+	+	+	+
Yip et al. (2012)	+	+	+	+	+	+	+	+
Siebert et al. (2015)	+	+	+	+	+	+	+	+
Al-Rawee et al. (2019)	+	+	+	+	+	+	+	+
Manas et al. (2024)	+	+	+	+	+	+	+	+
Martin et al. (2010)	+	+	+	+	+	+	+	+
Mozzati et al. (2015)	+	+	+	+	+	+	+	+
Shabestari et al. (2009)	+	+	+	+	+	+	+	+

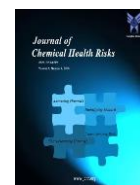
Domains:  
D1: Bias due to confounding.  
D2: Bias due to selection of participants.  
D3: Bias in classification of interventions.  
D4: Bias due to deviations from intended interventions.  
D5: Bias due to missing data.  
D6: Bias in measurement of outcomes.  
D7: Bias in selection of the reported result.

Judgement  
+ Low

**Reporting bias** was consistently rated as low across all included studies, indicating that the outcomes and results were generally reported transparently and according to the objectives of the respective studies. No significant evidence of selective outcome reporting was identified.

Overall, one study (Siebert et al., 2015) [28] was assessed as having a low overall risk of bias, due to its prospective,

controlled design and consistent methodological rigor across all domains. The remaining studies, despite variations in specific domains, were uniformly rated as having a moderate overall risk of bias. This consistent moderate risk reflects common limitations associated with non-randomized designs, retrospective data collection, and variable control of confounding factors.



These findings highlight the need for more rigorously designed prospective trials in this area, with standardized outcome measures and longer-term follow-up, to better clarify the relationship between bisphosphonate therapy and implant failure in osteoporotic females.

The overall methodological quality of the included studies was evaluated using the ROBINS-I tool, focusing on seven domains of bias. The traffic light plot and summary figure (**Figure 2,3**) indicate that all studies demonstrated a consistently low risk of bias across all assessed domains.

In particular, there was low risk observed in bias due to confounding and selection of participants, suggesting that the included studies adequately accounted for potential confounders and employed appropriate methods to select their patient populations. Bias in the classification of interventions was also rated low, reflecting clear and appropriate documentation of bisphosphonate exposure and intervention assignment.

Likewise, bias due to deviations from intended interventions and bias due to missing data were consistently judged to be low, indicating adherence to protocol and minimal loss to follow-up. The domain assessing bias in the measurement of outcomes showed low risk across all studies, reinforcing the reliability and consistency of outcome assessment methods. Finally, bias in the selection of the reported result was low in all cases, suggesting that the outcomes were reported transparently and without selective reporting.

A bar chart representing pool risk of bias for all studies (**Figure 3**) reinforces these findings, showing 100% low risk across all seven domains and the overall judgment. This uniformity in risk assessment across studies enhances the credibility of the review's conclusions, suggesting a strong evidence base with minimal methodological limitations.

#### 4. Discussion

Osteoporosis is a systemic skeletal condition characterized by decreased bone mass and microarchitectural deterioration of bone tissue, leading to enhanced bone fragility and fracture risk, particularly among postmenopausal women. According to the International Osteoporosis Foundation, it affects over 200 million women worldwide, with oral health implications that include alveolar bone loss and

compromised support for dental prostheses [47]. Bisphosphonates (BPs), a class of antiresorptive agents, have been the cornerstone in osteoporosis management. They inhibit osteoclast-mediated bone resorption, thus stabilizing bone density. However, concerns have emerged regarding their potential impact on bone healing and osseointegration of dental implants, given their suppression of bone turnover [16]. This systematic review examined the failure rates of dental implants in osteoporotic females on bisphosphonate therapy. A total of ten clinical studies with various designs and methodologies were analyzed. The studies reviewed reported failure rates ranging from 0% [28] to as high as 59% [19], with most falling between 0.8% [23] and 14% [40]. Notably, Martin et al. (2010) [19] was an outlier, documenting a significantly elevated failure rate, which may be explained by the extended duration of bisphosphonate exposure and the nature of data collection.

In the study by Bell and Bell (2008) [10], a retrospective cohort of 42 patients (with 101 implants) receiving oral bisphosphonates over a duration ranging from six months to 11 years demonstrated a 95% implant success rate and a 5% failure rate. Their findings suggested that oral bisphosphonates were not significantly associated with implant failure, a conclusion that set a precedent for cautiously optimistic interpretation of implant therapy in such populations.

Contrastingly, Kasai et al. (2009) [40], in a retrospective comparative study, identified a higher failure rate among BP users—14% compared to 5% in controls—with an implant success rate of 86% in the BP group. This higher rate of failure underscores the possibility that certain variables, such as duration of therapy or patient-specific bone turnover dynamics, might mediate outcomes more significantly than the simple presence or absence of bisphosphonate use. Similarly, Yip et al. (2012) [25] conducted a retrospective case-control study involving 337 women and found an odds ratio of 2.5 for implant failure among BP users, indicating a significantly increased risk. While the study did not specify failure rates in numeric terms, the large sample size and statistical significance of the findings lend weight to the argument that bisphosphonate use may elevate the risk for implant failure, at least under certain conditions.



A more favorable outcome was observed in the study by Koka et al. (2010) <sup>[23]</sup>, who reported a 99.2% implant success rate and only 0.8% failure among 55 patients receiving oral bisphosphonates, primarily alendronate. Their retrospective chart review concluded no significant impact of BP therapy on implant outcomes. This finding is further echoed by Al-Rawee et al. (2019) <sup>[34]</sup>, whose prospective comparative study involving 15 patients (72 implants) on oral alendronate over eight months reported a 91.7% success rate and an 8.3% failure rate. The relatively short duration of therapy in this study may have contributed to the favorable outcomes, emphasizing that both the timing and length of bisphosphonate use are crucial considerations.

The duration of bisphosphonate therapy appears to be a critical factor influencing implant success. While Bell and Bell (2008) <sup>[10]</sup> included patients on therapy for up to 11 years without a significant increase in failure, Martin et al. (2010) <sup>[19]</sup> reported starkly contrasting outcomes. Their cohort survey analysis involving 16 patients (44 implants) noted 26 implant failures, translating to an approximate 59% failure rate. Such a high failure rate, especially when compared to the other studies, may be attributed to prolonged therapy durations, ranging from 3 to 103 months, and suggests that late implant failures might be more common in long-term BP users. The study specifically highlights that late implant failure, rather than early osseointegration failure, is the primary concern, possibly due to cumulative suppression of bone turnover over time.

Mozzati et al. (2015) <sup>[29]</sup> presented perhaps the most optimistic data in their retrospective cohort involving a substantial sample of 235 patients and 1267 implants. The study reported a success rate of 98.7% and a failure rate of just 1.3%. Notably, patients were receiving various oral bisphosphonates, including alendronate, risedronate, and ibandronate, with an average treatment duration of 40.2 months. A unique aspect of this study was the use of plasma rich in growth factors (PRGF), which may have played a role in promoting osseointegration and healing, thereby minimizing implant failures even in the context of antiresorptive therapy. This introduces the potential utility of adjunctive biologic strategies in mitigating implant failure risks among BP users.

Further supportive evidence for the safety of implant placement in bisphosphonate-treated individuals is provided by Siebert et al. (2015) <sup>[28]</sup>, whose prospective controlled trial assessed the outcomes of 60 implants in 12 patients receiving intravenous zoledronate over 2–3 years. Remarkably, the study observed a 100% implant success rate and zero failures, suggesting that even IV bisphosphonate therapy, when carefully managed and monitored, does not necessarily preclude successful implant therapy. However, it is important to note that such outcomes may be influenced by patient selection criteria, surgical protocol, and stringent post-operative monitoring.

On the other end of the spectrum, the study by Shabestari et al. (2009) <sup>[20]</sup>, a case series of 21 patients receiving oral Fosamax (alendronate) for a mean of 20.5 months, also reported a 100% implant success rate. All implants remained clinically stable, and no signs of mobility or complications were noted. While this data is encouraging, the nature of a case series inherently limits the strength of its conclusions due to potential selection bias and lack of control groups.

Interestingly, newer studies such as the one by Manas et al. (2024) <sup>[38]</sup> have added to the growing body of literature with more pronounced interpretations. In their prospective comparative study of 10 patients on oral alendronate for 1.5 years, they observed a 95% implant success rate and a 5% failure rate. Their findings suggest that alendronate not only did not increase implant failure risk but may have contributed to increased bone mineral density (BMD), potentially providing a more favorable substrate for implant integration.

An important variable in these discussions is the implant site. While most studies do not specify the exact location of implants, this detail can be crucial. Implant placement in the maxilla, with its relatively less dense trabecular bone, may be more susceptible to compromised osseointegration compared to the denser mandibular bone. While few of the reviewed studies explicitly delineate implant sites, it is reasonable to infer from existing literature that mandibular sites generally yield better implant stability, especially in osteoporotic patients. This factor should be considered when interpreting failure rates and planning implant therapy in bisphosphonate-treated individuals.



Taken together, the current evidence suggests that while there is a potential risk of increased implant failure in osteoporotic females on bisphosphonate therapy, particularly with prolonged use, this risk is not uniformly observed across studies. Variability in study design, sample size, bisphosphonate type, duration of therapy, and adjunctive surgical techniques likely contribute to these mixed results. Most retrospective studies report low to moderate failure rates, with only a few—such as the study by Martin et al. (2010)<sup>[19]</sup> reporting alarmingly high rates. Moreover, prospective studies, which are inherently more robust, tend to report more favorable outcomes, indicating that with proper patient selection and surgical protocols, successful implant therapy is feasible in this patient population.

The heterogeneity in findings across studies also underscores the importance of individualized treatment planning. Factors such as the patient's overall bone health, duration and type of bisphosphonate therapy, location of implant placement, and use of adjunctive therapies like PRGF must be carefully weighed. Moreover, clinicians should consider obtaining a thorough medical history, including DEXA scans and serum markers of bone turnover, before proceeding with implant therapy in this demographic. Where possible, a drug holiday under medical supervision might also be considered, although evidence supporting its efficacy remains inconclusive.

## 5. Conclusion

Dental implant failure rates in osteoporotic females on bisphosphonate therapy vary widely (41–100%), reflecting multifactorial influences such as drug duration, implant site, surgical technique, bone quality, and patient health. Although bisphosphonates may affect bone remodeling, they are not an absolute contraindication—especially in oral forms like alendronate—and many cases show successful outcomes. Therefore, with careful patient evaluation and individualized, evidence-based planning, implants remain a viable option in this population.

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