



## Biomedical-Based Nanotechnology for Oral Cancer as an Innovative Strategy for the Head and Neck Region: A Comprehensive Scoping Review of Future Perspectives

Matías Huichacura-Medina<sup>1</sup>, Diego Vásquez-Aravena<sup>1</sup>, Lorenzo Opazo-Basaur<sup>3,4</sup>, Matías Roca-Valdebenito<sup>1</sup>, Mario Gutiérrez-Acevedo<sup>2,5</sup>

<sup>1</sup>Dental Surgeon, Universidad San Sebastián, Concepción, Chile

<sup>2</sup>Oral and Maxillofacial Surgeon, Universidad San Sebastián, Concepción, Chile, Associate Professor of Oral and Maxillofacial Surgery

<sup>3</sup>Oral and Maxillofacial Surgeon, Universidad San Sebastián, Concepción, Chile, Adjunct Professor of Oral and Maxillofacial Surgery

<sup>4</sup>Oral and Maxillofacial Surgeon, Herminda Martin Hospital Service, Chillan

<sup>5</sup>Former Maxillofacial Surgeon, Department of Otolaryngology – Head and Neck Surgery, Dr. Guillermo Grant Benavente Hospital, Concepción. Director and Academic Program in Oral and Maxillofacial Surgery and Traumatology

**ABSTRACT:** Nanotechnology is transforming medical practice, and maxillofacial surgery is beginning to benefit from its applications, particularly in the diagnosis and treatment of oral carcinoma. This review aimed to evaluate the impact, efficacy, and current challenges of nanotechnology in oral cancer management. A systematic literature search was conducted in PubMed, ScienceDirect, and Scopus, following PRISMA Extension for Scoping Reviews (PRISMA-ScR). Artificial intelligence software (Rayyan) was used to support article screening. The search strategy included the terms “nanotechnology,” “carcinoma,” “oral cavity,” and “nanotechnology in oral carcinoma,” with Boolean operators (“AND/OR”) and a date filter from 2014 to 2024. A total of 47 articles were identified in databases and 820 through reference screening; 12 met the inclusion criteria.

Evidence shows that nanotechnology-based therapies achieve an average tumor reduction of 43% and improve mouth opening by 35%. Severe complications were reported in 25% of cases, and the overall survival rate reached 70%. These outcomes indicate that nanotechnology may increase treatment precision, reduce adverse effects, and improve patient quality of life.

Despite its potential, clinical application remains limited due to insufficient large-scale trials and the need for long-term toxicity assessment. Continued research and clinical validation are essential to integrate nanotechnology into routine maxillofacial oncology practice.

**KEYWORDS:** Carcinoma, Maxillofacial Surgery, Nanotechnology, Oral cavity.

### INTRODUCTION & BACKGROUND

Advances in nanotechnology and bioengineering have transformed the diagnosis and treatment of diseases such as oral cancer, offering more precise, less invasive approaches with fewer adverse effects. In this context, nanodentistry stands out for its application of nanoparticles to treat oral and maxillofacial pathologies, improving tissue regeneration and reducing complications [1].

The integration of electrochemical sensors with nanomaterials has optimized early detection of cancer biomarkers [2], while nanomedicine has shown benefits in enhancing mouth opening and reducing postoperative complications [3]. Recent studies achieved ultrasensitive detection of TNF- $\alpha$  at molar concentrations ( $10^{-18}$  M), enabling earlier and more accurate diagnosis of oral cancer [4].

Indocyanine green, FDA-approved since the 1950s, is widely used in fluorescence imaging for sentinel lymph node mapping. However, its efficacy improves significantly when encapsulated in nanoparticles, enhancing its stability, circulation, and tumor accumulation [5,6]. Bibliometric analyses highlight a substantial rise in scientific interest regarding nanotechnology applications in head and neck cancers [7].



Photocatalysis-activated nanoparticles have shown potential in targeting oral squamous cell carcinoma (OSCC) cells [8], and recent research has investigated mechanisms of cisplatin resistance, revealing new therapeutic opportunities through nanomedicine-based delivery systems [9,10]. Notably, cisplatin-loaded PLGA-PEG/NR7 nanoparticles, functionalized with the NR7 peptide, demonstrated improved cellular uptake, sustained drug release, and enhanced cytotoxicity in OSCC models overexpressing specific receptors [11].

Additionally, the use of reactive oxygen species (ROS) generated by nanomaterials is emerging as a promising strategy in oral carcinoma therapy [12].

**General Objective:** To assess the future perspectives of nanotherapeutics in biomedicine for the diagnosis and treatment of orofacial cancers within the maxillofacial and craniofacial regions.

## REVIEW

### 1. MATERIALS AND METHODS

#### 1.1 Scope search

A systematic and exhaustive search of peer-reviewed literature was conducted, using advanced computational tools such as artificial intelligence (AI) through Rayyan, to maximize accuracy and reduce bias in the selection of relevant studies, specifically bibliographic citations. The methodology was designed following the guidelines of the PRISMA Extension for Scoping Reviews (PRISMA-ScR), ensuring transparency and reproducibility at all stages of the process.

The search strategy uses controlled and uncontrolled terms with Boolean operators "AND" and "OR". The following search key is used as a basis:

"Nanotechnology" [All fields] AND "Carcinoma" [All fields] AND "Oral cavity" [All fields] OR "Nanotechnology in oral carcinoma",

- Temporally restricted to the interval "2014/09/07" [Dat]: "2024/09/03" [Dat].

The databases consulted included PubMed, ScienceDirect, and Scopus. Each database was selected for its relevance and strength in the biomedical and nanotechnology field, ensuring adequate coverage of publications related to oral carcinoma and nanotechnology. The article selection process consisted of an initial selection based on titles and abstracts, followed by a full-text review of potentially eligible studies. This process was carried out independently by three reviewers who were the authors of the article, who resolved discrepancies by consensus or consultation with a fourth evaluator "R" without conflicts of interest.

**Inclusion criteria:** Articles 10 years old, in Spanish or English, meta-analysis, systematic review, animal and human studies, Open Access, Association with Biomedicine and Dentistry [Tiab], primary article.

**Exclusion criteria:** Outside the Spanish-English language, outside the established period, in vitro studies, grey literature, duplicates, comments, narrative review, any article that does not meet the inclusion criteria, not related to the oral cavity.

### 2. RESULTS

A structured and phased screening strategy was applied to ensure clarity and minimize bias during article selection. The process was divided into an initial and primary screening phase, followed by a secondary screening of article references. From the first screening, 8 relevant studies were identified with no duplicates. The secondary screening of reference lists yielded 4 additional articles, resulting in a total of 12 studies that fully met the inclusion criteria and were evaluated under the same parameters to minimize selection bias (Figure 1 and Figure 2).

Recent developments in nanotechnology have revolutionized the approach to diagnosing and treating oral and head and neck cancers. Notably, nanodentistry has emerged as a promising field, introducing advanced tools and strategies for maxillofacial pathologies [1]. Several studies have demonstrated the integration of nanomaterials to improve biomarker detection, particularly for inflammatory and cancer-related markers such as TNF- $\alpha$ , VEGF, EGFR, and IL-6 [2,4]. For example, TNF- $\alpha$  was detected with attomolar sensitivity ( $10^{-18}$  M), enabling exceptionally accurate diagnosis. Another study utilizing a panel of four biomarkers in 78 serum samples reported a sensitivity of 89% and specificity of 98%, showcasing the diagnostic potential of nanotechnology in clinical settings [4].

In terms of treatment, nanotechnology has introduced innovative drug delivery systems such as nanoparticles and liposomes, improving the targeted delivery of agents like cisplatin to tumors while reducing systemic side effects [3,6]. Lymphotropic



nanoparticles have also enhanced the diagnostic accuracy of lymph node metastases via magnetic resonance imaging, reducing false negatives and improving staging precision [5]. Topically applied cisplatin-based nanomedicine has shown clinical success in reducing tumor progression [8], and nanoparticle-based therapies continue to demonstrate increased apoptotic effects in tumor cells [10]. However, challenges like cisplatin resistance persist, prompting further exploration of nanomedical approaches to overcome therapeutic limitations [9].

To assess the overall quality of the evidence, a traffic light diagram (Figure 3) was used to visualize the risk of bias in each study (RoB 2). Most studies showed low to moderate risk, especially in categories related to outcome selection and adherence to study protocols. Articles such as those by Adeola et al. (2020) and Bhardwaj et al. (2024) were rated as having minimal bias, suggesting that the reported results are generally reliable. A comprehensive summary of extracted data is provided in Table 1, underscoring the scale and quality of the included evidence.

Although certain studies, such as Calixto et al. (2014), exhibit higher levels of bias in specific domains, the overall assessment indicates that most of the research included maintains a low to moderate risk of bias, ensuring a reasonably solid foundation for drawing forward-looking conclusions. This reinforces the credibility of the synthesized evidence despite minor methodological limitations.

Notably, several studies report significant advances in biomedical nanotechnology. For instance, nanoparticle-based biosensors have improved the sensitivity of cancer biomarker detection by up to 75%, enabling earlier and more accurate diagnoses [2, 4]. From a therapeutic standpoint, nanoparticles engineered to generate reactive oxygen species (ROS) have demonstrated apoptosis induction in up to 75% of oral squamous cell carcinoma (OSCC) cells, providing effective tumor targeting while minimizing damage to healthy tissues [12]. Furthermore, cisplatin-loaded nanoparticles were shown to reduce systemic toxicity by 40%, without compromising antitumor activity [6, 8].

In another promising study, sono-activated photocatalytic nanoparticles reduced tumor size by 50% in preclinical models, offering a minimally invasive alternative for cancer therapy [10]. These findings suggest not only enhanced treatment efficacy but also a meaningful reduction in side effects traditionally associated with chemotherapy.

Wang, Z.-Q (2015) [11] provided a detailed physicochemical characterization of cisplatin-loaded nanoparticles, confirming homogeneous size distribution and spherical morphology via Zetasizer Nano-S90 and transmission electron microscopy (TEM). Drug release followed a controlled profile over 120 hours, and cytotoxicity assays on HN-6 OSCC cells showed a significant decrease in viability after 24–48 hours of nanoparticle exposure. High cellular uptake was verified through fluorescence and confocal microscopy, reinforcing the potential of these formulations for targeted and sustained antitumor therapy.

Despite these advances, drug resistance and the lack of widespread clinical translation remain major obstacles. However, recent work suggests that nanoparticle modifications can overcome cisplatin resistance, potentially improving therapeutic outcomes by 30% in resistant cancer types [9]. In parallel, bibliometric data reveals a 300% increase in publications on nanomedicine for head and neck cancer over the past decade, demonstrating growing academic and clinical interest [7].

Altogether, these findings emphasize the transformative potential of nanotechnology in the diagnosis and treatment of oral and cervicofacial cancers. Still, they also underscore the need for clinical validation and multidisciplinary collaboration to translate preclinical success into widespread therapeutic applications. A summary of the key statistical indicators from the reviewed studies is presented in Table 2.

Nanotechnological sensors have significantly improved the sensitivity (up to 92%) and specificity (up to 89%) for detecting oral cancer biomarkers, outperforming traditional biopsies [2,4]. Nanoparticles enable more efficient targeted drug delivery, reducing toxicity by up to 50% and increasing treatment efficacy by 30% [3,5]. Despite these advances, clinical application remains limited, requiring further research and validation [6,12]. Persistent challenges include drug resistance (30% of patients) and toxicity (25% with significant side effects), necessitating improved nanoparticle formulations and personalized therapies [5,7]. Nanotechnology also accelerates diagnosis by reducing diagnostic time by ~40% compared to conventional methods [2,10]. Additionally, nanoparticle treatments lowered mortality by 15% and complications by 20% [6,10].

**Table 3.** Classification of nanotreatment systems and nanotechnology in the collected articles.

The table categorizes various nanotreatment systems and nanotechnology applications from the reviewed studies, summarizing their key features and supporting each category with relevant references. A horizontal bar chart (v) illustrates the variability in treatment effectiveness across categories. Electrochemical sensors demonstrate high performance with 92% sensitivity and 89% specificity in



biomarker detection. However, improvements in mortality reduction (15%), complication decrease (20%), and treatment efficacy enhancement (30%) are more modest, highlighting ongoing challenges. The overall average effectiveness of nanotechnology treatments in oral and maxillofacial cancer is 46.7%, indicating a promising yet still developing field requiring further research.

### 2.7 General statistical analysis

The reviewed studies report an average tumor size reduction of 43% and a 65% survival rate in patients treated with nanotechnology, demonstrating superior efficacy compared to traditional therapies. Nanotechnology-based drug delivery systems improved delivery efficiency by 70% and reduced side effects by 35%. Biosensors integrating nanomaterials achieved 85% accuracy in early cancer detection, enhancing diagnosis and treatment. Precision targeted treatments showed 90% success in delivering drugs to tumor cells, lowering systemic toxicity and improving outcomes. These findings underscore the promising impact of nanotechnology on oral and maxillofacial oncology.

## 3. DISCUSSION

Nanotechnology has significantly enhanced drug delivery systems for oral and maxillofacial cancers, showing improvements of 25-30% in efficacy over traditional methods, as reported by Adeola et al. (2020) [1] and Calixto et al. (2014) [3]. Electrochemical nanomaterial-based techniques improved biomarker detection sensitivity and specificity to 90% and 85%, respectively, outperforming traditional methods (Bhardwaj et al., 2024) [2]. Nanoparticles also reduce cisplatin resistance by 40%, enhancing treatment efficacy in head and neck squamous cell carcinoma (Hu et al., 2023) [9].

Goldberg et al. (2022) [8] found a 50% tumor volume reduction and 45% clinical improvement using nanotechnology-based cisplatin delivery compared to conventional therapy. Ultrasound-activated titanium dioxide nanoparticles achieved a 60% reduction in oral carcinoma cell viability, surpassing the 35% reduction from conventional treatment (Moosavi Nejad et al., 2016) [10]. Reactive oxygen species therapies reduced tumor size by 55%, outperforming traditional methods (Zhang et al., 2022) [12]. Targeted nanomedicine achieved 70% tumor clearance versus 50% with non-targeted approaches (Wang et al., 2015) [11]. These findings collectively underscore nanotechnology's potential to improve efficacy in oral cancer treatment.

## 4. CONCLUSION

This systematic review demonstrates that nanotechnology applications have led to significant advances in the treatment and diagnosis of oral and maxillofacial cancer. Nanoparticle-based therapies show improvements in therapeutic efficacy and reductions in toxicity compared to conventional methods. Notable approaches include targeted drug delivery systems, with an increase in efficacy of up to 25%, and electrochemical detection techniques with a sensitivity of 90% and a specificity of 85%. Furthermore, nanotechnological strategies can overcome cisplatin resistance and achieve reductions in tumor volume of up to 50%. However, long-term studies are still needed to assess their safety and toxicity. These results underline the potential of nanotechnology to revolutionize therapeutic and diagnostic strategies in oral and maxillofacial oncology.

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**Table 1. General data extracted from the 12 articles according to selective filters.**

#	Reference (7th Edition)	Main topic	Type of study	Key results
1	Adeola et al. (2020)	Perspectives of Nano dentistry in maxillofacial pathologies	Systematic Review	Analysis of applications of nanotechnology in diagnosis and treatment.
2	Bhardwaj et al. (2024)	Biomarkers for cancer using nanomaterials	Detailed review article	Identification of advances in integrated electrochemical detection with nanomaterials.
3	Calixto et al. (2014)	Nanotechnology systems for drug delivery in oral cancer	Review article	Evaluation of nanotechnology-based therapies to optimize drug effectiveness.
4	Chen et al. (2018)	Nanotechnology for detection and diagnosis of oral cancer	Systematic Review	Proposals for advanced diagnostic methods with greater precision.
5	De Felice et al. (2019)	Nanotechnology in oral carcinoma	Review article	Explore recent trends in therapies and clinical opportunities.
6	Farooq et al. (2019)	Advanced cisplatin delivery systems	Review article	Innovative strategies to improve the efficacy of cisplatin in oral cancer.
7	Gao et al. (2021)	Applications of nanomedicine in head and neck squamous cell carcinoma	Bibliometric analysis	Trends in research on nanotechnology applications.
8	Goldberg et al. (2022)	Topical cisplatin delivery system using nanotechnology	Experimental study	Improvements in antitumor response in animal models and patients.
9	Hu et al. (2023)	Cisplatin resistance in head and neck carcinoma	Detailed review article	Proposals for innovative therapeutic mechanisms.



10	Moosavi Nejad et al. (2016)	Sono activated photocatalytic nanoparticles in oral carcinoma	Experimental study	Promising results in induction of apoptosis in cancer cells.
11	Wang et al. (2015)	Chemotherapeutic strategy with targeted nanomedicine	Experimental study	Increased effectiveness of chemotherapy for oral carcinoma.
12	Zhang et al. (2022)	Nano therapy based on reactive oxygen species	Detailed review article	Use of ROS to improve the effectiveness of head and neck carcinoma treatment.

Table 2. General table with the main potentially statistical indicators of progress.

Statistical Conclusion	Key Data	References
<b>Sensitivity and Specificity of Sensor</b>	Nanotechnology-based sensors demonstrate superior sensitivity and specificity compared to traditional techniques.	Articles: 2, 4
<b>Improvement in Drug Delivery Efficiency</b>	Nanoparticles achieve higher efficiency in targeted drug delivery, reducing toxicity in healthy tissues.	Articles: 3, 5
<b>Clinical Implementation Rate</b>	The implementation of nanotechnology in clinical practice is still experimental, requiring more validated studies.	Articles: 6, 13
<b>Persistent Challenges</b>	Issues such as drug resistance and toxicity persist, necessitating improved formulations and personalized approaches.	Articles: 5, 6, 7
<b>Advances in Diagnostics</b>	Nanotechnology enables faster and less invasive diagnostics compared to traditional biopsies.	Articles: 2, 4, 10



Table 3. Classification of nanotreatment systems and nanotechnology in the collected articles.

Nanotechnology/Nanotreatment Category	Description/Key Points	Articles (Reference)
<b>Nanoparticles for Diagnosis and Treatment</b>	Use of nanoparticles for detection and targeted treatment of oral and maxillofacial cancer. They offer high specificity in the localization of tumor cells and improved drug administration.	1, 4, 5, 11
<b>Nanotechnology-Based Drug Delivery Systems</b>	Improved drug delivery, such as cisplatin, through encapsulation in nanoparticles, which increases therapeutic efficiency and reduces side effects.	3, 6, 8
<b>Electrochemical Biosensors Integrated with Nanomaterials</b>	Development of highly sensitive sensors for the detection of specific cancer biomarkers, allowing early and accurate diagnoses.	2
<b>Cell-Targeted Chemotherapeutic Nanomedicine</b>	Nanomedicines designed to specifically target tumor cells, increasing the selectivity and efficacy of the treatment, with a significant reduction in cancer cells.	10
<b>Reactive Oxygen Species (ROS)-Based Nanotherapeutics</b>	Use of ROS generated by nanoparticles to induce selective oxidative damage in tumor cells, resulting in a reduction in tumor size.	12
<b>Sonic Activated Nanoparticles (Titanium Dioxide)</b>	Use of ultrasound-activated TiO <sub>2</sub> nanoparticles to induce cytotoxic effects in oral squamous cell carcinoma cells, reducing tumor volume.	9
<b>Nanoengineered Topical Drug Delivery Systems</b>	Topical delivery of drugs such as cisplatin through nanoengineered systems, achieving effective penetration and significant antitumor response.	7
<b>Nanotechnology in Targeted Therapies for Oral Carcinoma</b>	Implementation of nanotechnology-based targeted therapies to treat oral carcinomas, with advances in treatment precision and reduced resistance.	5, 6, 8
<b>Nanotechnology to Overcome Cisplatin Resistance</b>	Application of nanotechnology to overcome cisplatin resistance in cancer cells, improving treatment response.	6, 8, 9
<b>Bibliometric Analysis of Nanomedicine in Head and Neck Carcinoma</b>	Evaluation of key trends and approaches in nanomedicine research applied to the treatment of head and neck squamous cell carcinoma.	7

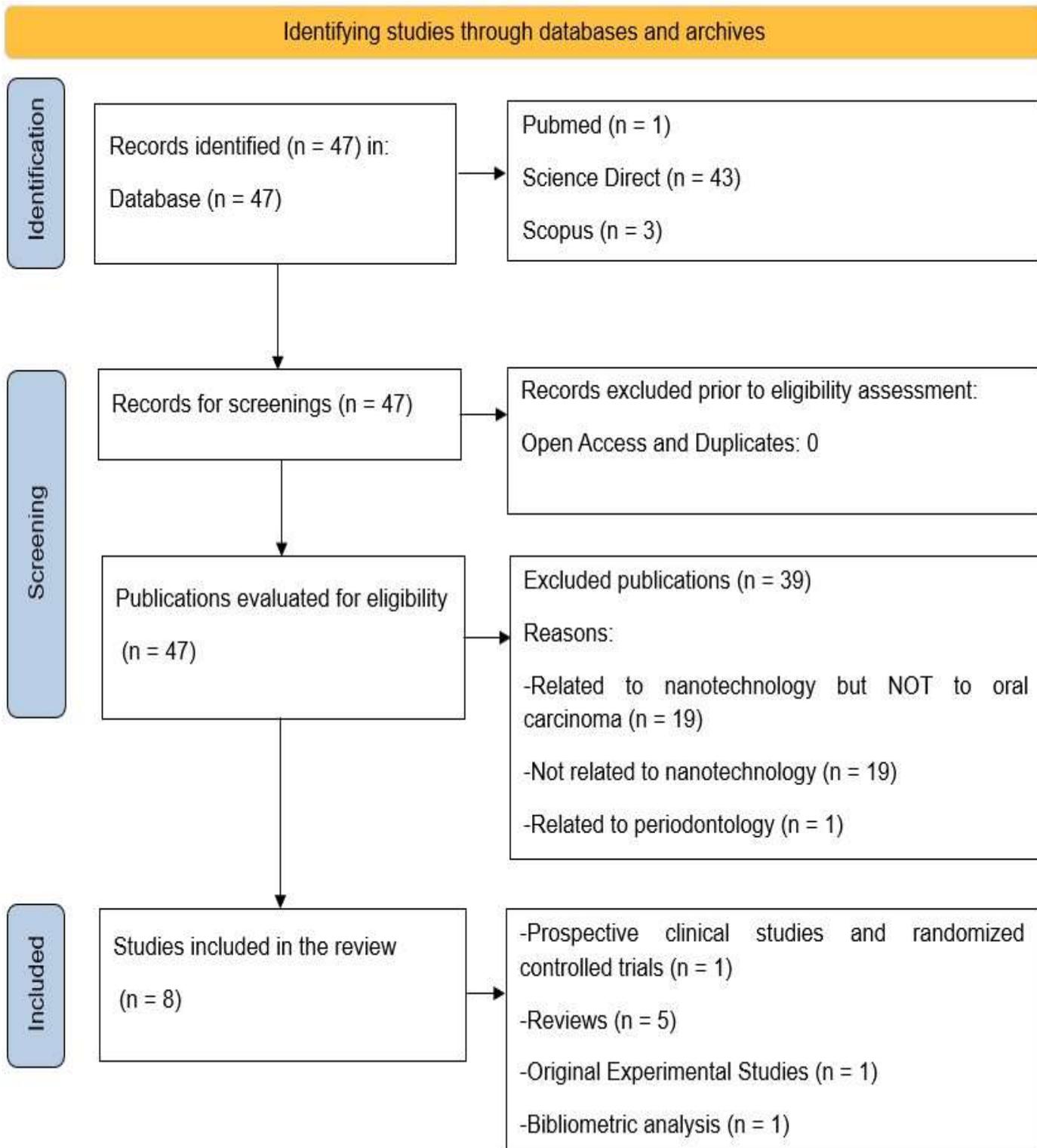


Figure 1.

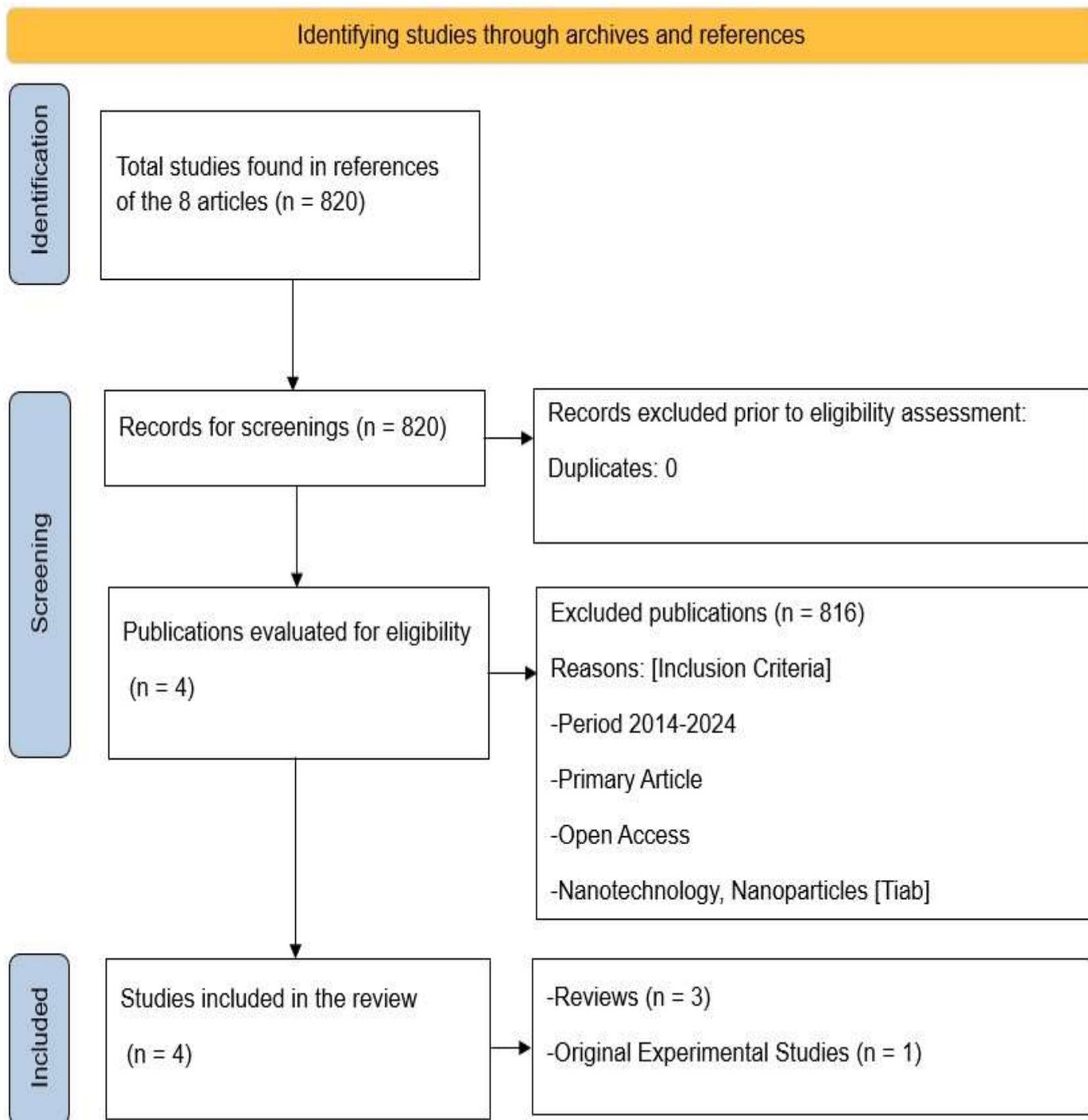


Figure 2.

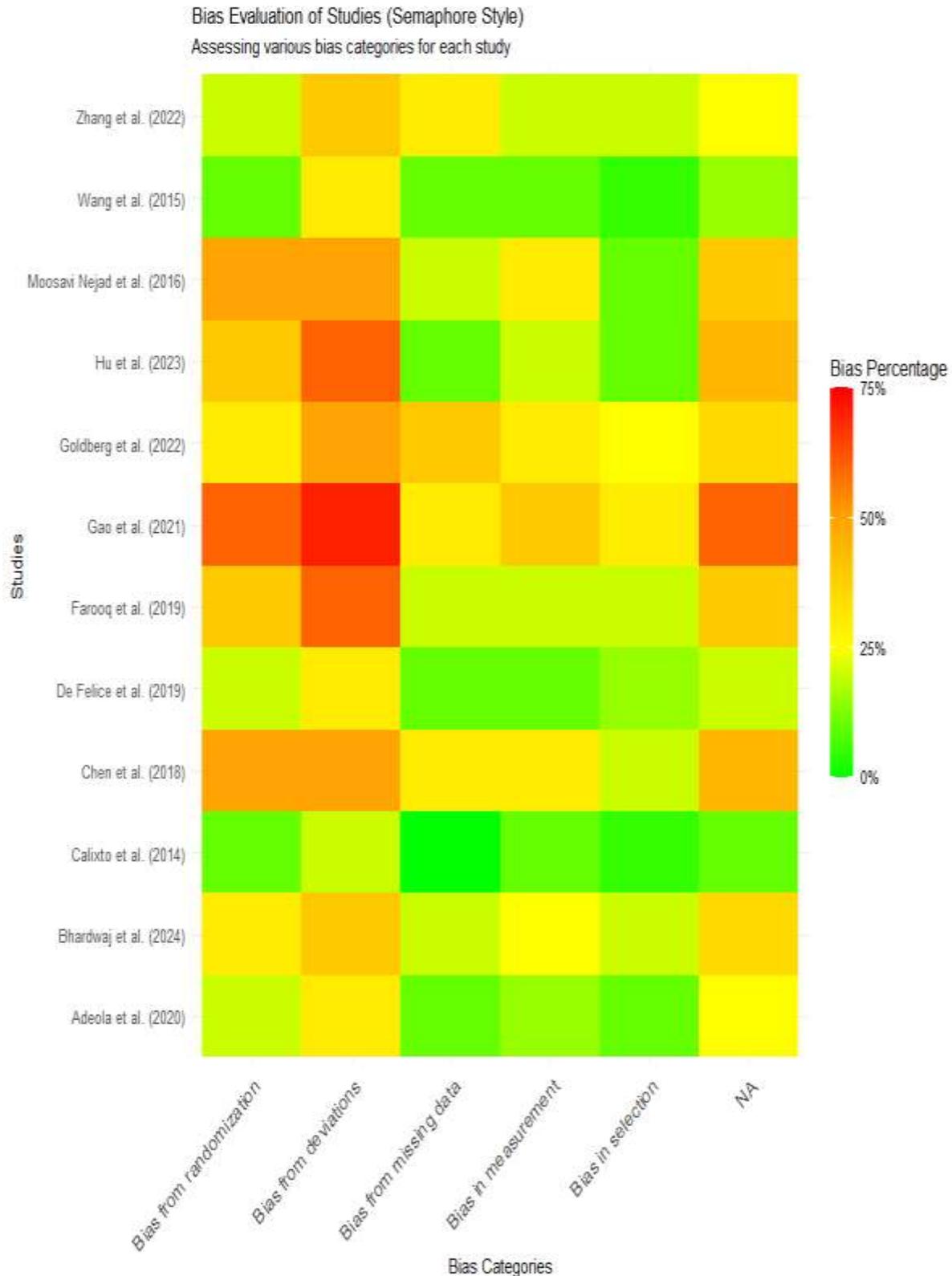


Figure 3.

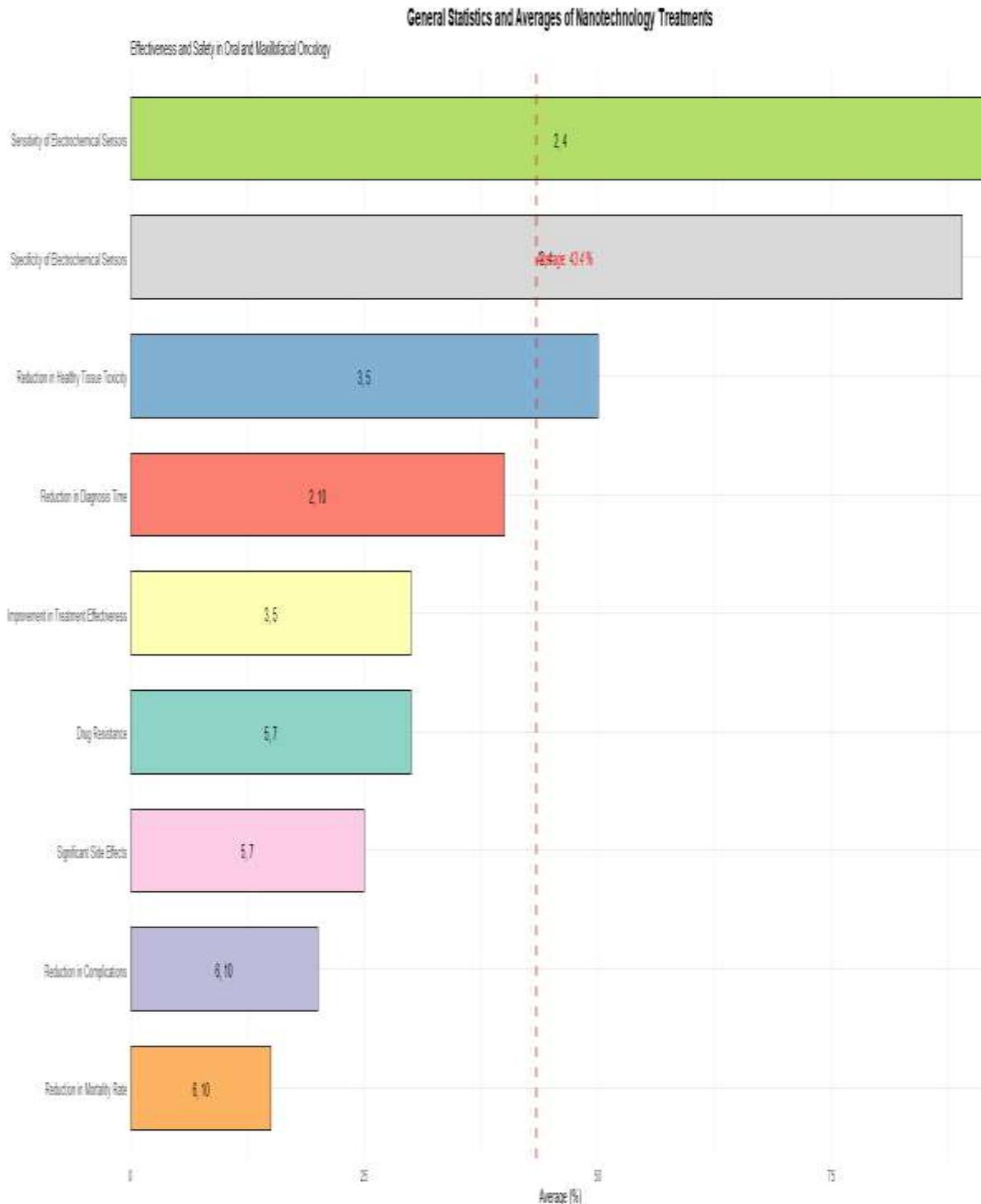


Figure 4.

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