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Establishing and validating a risk prediction model for peri-implantitis based on meta-analysis and machine learning methods

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Data extraction.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 7 July 2025 and was last updated on 7 July 2025.

INTRODUCTION

Review question / Objective PICOS Framework: Population (P): Adult patients with dental implants. Intervention/Exposure (I): Established risk factors (e.g., periodontitis, diabetes, smoking, poor plaque control, thin gingival biotype, insufficient keratinized mucosa, iatrogenic factors like implant design/surgical technique). Comparator (C): Patients without these risk factors or with different risk profiles. Outcomes (O): Incidence of peri-implantitis (defined as soft tissue inflammation + progressive bone loss). Study Design (S): Systematic review and meta-analysis of observational studies (cohort, case-control, cross-sectional) followed by machine learning model development/validation.

Rationale Peri-implantitis is one of the most common complications in implant repair, which is a chronic inflammatory disease characterized by soft tissue inflammation and progressive loss of hard tissue . It has a high incidence rate, with incidence rates at the patient and implant levels ranging from 8.9% to 56.6% and 4.8% to 27.9%, respectively. The main clinical manifestations of peri implantitis are inflammation, bleeding, pain, and bone loss around the implant . The risk factors are complex and not completely clear at present. According to previous studies, they mainly include patient related factors such as periodontitis, diabetes, smoking, poor plaque control, thin gingival biotype, insufficient width of keratinized mucosa, as well as iatrogenic factors such as implant operation scheme, implant model, implant site, superstructure retention mode, etc. These risk factors can promote the occurrence and development of peri implant through a variety of complex mechanisms . Due to the unclear early symptoms, peri implantitis cannot attract the attention of patients and doctors in a timely manner, which poses difficulties for its early prevention and diagnosis. In addition, the uncertainty of risk factors for peri implantitis and

the complexity of related mechanisms also increase the difficulty of early prevention of peri implantitis. Therefore, comprehensively exploring the risk factors of peri implantitis and finding a simple, fast, and reliable method to predict the risk of peri implantitis and identify high-risk populations can help clinical doctors develop personalized plans for early prevention and treatment to reduce the incidence of peri implantitis.At present, oral clinical and imaging examinations are the main tools for screening peri implantitis, which rely more on the experience and judgment of medical personnel and are easily influenced by subjective factors. In addition, imaging examinations usually only detect bone tissue changes when inflammation is more pronounced, and may be difficult to capture small lesions in soft tissue inflammation or early bone tissue. Therefore, routine examinations are difficult to detect early or mild symptoms of peri implantitis in a timely manner. Machine learning prediction models are commonly used tools for disease risk prediction, which can predict the risk of peri implantitis by analyzing clinical data to achieve early prevention and intervention. However, currently the vast majority of available peri implantitis risk prediction models are constructed using population-based data, mostly in small sample sizes and small-scale studies, with limited representativeness. Their predictive performance needs to be further improved. Furthermore, it remains to be confirmed whether the weighting of each risk factor in these models is reasonable. Building predictive models based on high-quality meta-analysis results can avoid data loss, ensure sufficient sample size, and compensate for the instability of predictive models. The purpose of this article is to develop and validate a stable, reliable, and easily applicable risk prediction model for peri implantitis based on meta-analysis and machine learning methods, providing reference information for the prevention, early clinical diagnosis, and treatment of peri implantitis in clinical practice.Specifically, there are the following points: 1. Systematically synthesize evidence on peri-implantitis risk factors via meta-analysis.2.Develop/validate an ML-based prediction model using pooled high-quality data to improve early risk stratification.3.Address clinical gaps by providing a tool for personalized prevention and timely intervention.

Condition being studied Peri-implantitis is a chronic inflammatory disease affecting the tissues surrounding dental implants, characterized by progressive bone loss and soft tissue inflammation. Clinically manifested through bleeding on probing, suppuration, increased probing depths, and radiographic evidence of bone resorption, this condition represents one of the most significant complications in implant dentistry. With reported incidence rates ranging from 8.9% to 56.6% at the patient level and 4.8% to 27.9% at the implant level, peri-implantitis poses substantial clinical and economic burdens. The disease shares pathogenic mechanisms with periodontitis but exhibits distinct features due to the unique implant-tissue interface. Early stages often present asymptomatically, leading to delayed diagnosis until substantial bone loss has occurred, which may ultimately result in implant failure requiring complex regenerative therapies or explantation. Current diagnostic approaches rely heavily on subjective clinical examinations and late-stage radiographic changes, while the multifactorial etiology involves a complex interplay of patient-related factors such as diabetes, smoking and poor oral hygiene, along with iatrogenic factors including implant design and surgical technique. The therapeutic outcomes remain unpredictable due to heterogeneous microbial profiles and variable host responses. This systematic review and meta-analysis aims to clarify the key risk factors contributing to peri-implantitis development, addressing critical gaps in current understanding and providing evidence to support improved prevention and early intervention strategies.

METHODS

Search strategy Computers searched PubMed, The Cochrane Library, Web of Science, EMbase, CNKI, VIP, and WanFang databases from their inception to August 2024 by adopting the MeSH heading search strategy or searching keywords including “peri-Implantitis/peri-implantitis/periimplantitis/periimplant disease*/peri-implant disease*/peri-implant inflammat*/dental implant disease*/dental implant inflammation*/oral implant disease*/oral implant inflammation*” “risk factor*/factor risk*/associate factor*/relevant factor*/influence factor*/predictive factor*”.Search by combining topic words with free words and connecting them with Boolean logical operators, and trace the references included in the literature.

1.1 Databases & Timeframe
Searched from inception to August 2024:PubMed/MEDLINE • EMBASE • Cochrane LibraryWeb of Science • CNKI • VIP • WanFang

1.2 PubMed Search Syntax
#1 "Peri-Implantitis"[Mesh] OR "Dental Implants/adverse effects"[Mesh]

#2 (periimplantitis[tiab] OR "peri-implant disease*"[tiab] OR "dental implant inflammation*"[tiab])
#3 #1 OR #2
#4 "Risk Factors"[Mesh] OR "Multivariate Analysis"[Mesh]
#5 (risk factor*[tiab] OR predictor*[tiab] OR "multivariate model"[tiab])
#6 #4 OR #5
#7 "Cohort Studies"[Mesh] OR "Longitudinal Studies"[Mesh] OR "Retrospective Studies"[Mesh]
#8 #3 AND #6 AND #7
#9 Filters: Humans, English/Chinese

1.3 EMBASE Search Syntax
1. exp peri-implantitis/ or (periimplantitis or "peri-implant disease*" or "dental implant inflammation*").ti,ab.
2. exp "risk factor"/ or (risk factor* or predictor* or "multivariate model").ti,ab.
3. exp cohort analysis/ or exp longitudinal study/ or exp retrospective study/
4. 1 and 2 and 3
5. limit 4 to (human and (english or chinese) and yr="1980-2024")

1.4 Cochrane Library (CENTRAL)
#1 MeSH descriptor: [Peri-Implantitis] explode all trees
#2 (periimplantitis OR "peri-implant disease*" OR "implant-associated infection*"):ti,ab,kw
#3 #1 OR #2
#4 MeSH descriptor: [Risk Factors] explode all trees
#5 ("risk factor*" OR predictor* OR "multivariate analysis"):ti,ab,kw
#6 #4 OR #5
#7 MeSH descriptor: [Cohort Studies] explode all trees
#8 (cohort OR longitudinal OR prospective OR retrospective):ti,ab,kw
#9 #7 OR #8
#10 #3 AND #6 AND #9

1.5 Web of Science (Core Collection)
TS=((periimplantitis OR "peri-implant disease*" OR "dental implant complication*")
AND
("risk factor*" OR predictor* OR "multivariate model")
AND
(cohort OR longitudinal OR prospective OR retrospective))
Refined by:
LANGUAGES: (ENGLISH OR CHINESE)
DOCUMENT TYPES: (ARTICLE OR PROCEEDINGS PAPER)
Timespan: 1980-2024

1.6 CNKI
SU=('Periimplantitis' OR' Periimplantitis' OR 'Periimplantitis' OR' Periimplantitis' OR 'Infection')
AND
SU=('Risk Factors' OR' Risk Factors' OR 'Predictive Factors' OR' Multivariate Analysis')
AND
SU=('Queue Study' OR 'Longitudinal Study' OR 'Prospective Study' OR 'Retrospective Study')
Time range: 1980-2024
Literature classification: Medical and Health
Support Fund: Unlimited

1.7 VIP
(M='Periimplantitis' OR' Periimplantitis')
*
(M=('Risk Factors' OR' Risk Prediction ')+M=(' Queue Study 'OR' Prospective Study ')
Search scope: All journals
Time limit: 1980-2024
Subject limitation: Oral Science

1.8 WanFang
Topic: "Periimplantitis" or "Periimplantitis" or "Implant Infection"
AND
Topic: ("Risk Factors" or "Prediction Model")
AND
Topic: ("Queue Studies" or "Longitudinal Studies")
Time: 1980-2024
Literature type: Journal paper
Discipline classification: Oral ScienceComputers searched PubMed, The Cochrane Library, Web of Science, EMbase, CNKI, VIP, and WanFang databases from their inception to August 2024 by adopting the MeSH heading search strategy or searching keywords including “peri-Implantitis/peri-implantitis/periimplantitis/periimplant disease*/peri-implant disease*/peri-implant inflammat*/dental implant disease*/dental implant inflammation*/oral implant disease*/oral implant inflammation*” “risk factor*/factor risk*/associate factor*/relevant factor*/influence factor*/predictive factor*”.Search by combining topic words with free words and connecting them with Boolean logical operators, and trace the references included in the literature.

Participant or population The target population for this study consists of adult patients (aged 18 years or older) who have undergone dental implant treatment, encompassing all implant types, locations, and prosthetic restorations. This includes individuals with varying health statuses, ranging from systemically healthy patients to those with predisposing conditions such as diabetes mellitus or osteoporosis, as well as those with local risk factors including a history of periodontitis or

current smoking status. The study population involves patients with successfully osseointegrated implants that have been in function for a minimum of three months post-loading, representing the full spectrum of peri-implant conditions from healthy peri-implant tissues to various disease stages including peri-implant mucositis and peri-implantitis. The research incorporates data from diverse clinical settings including general dental practices, specialty periodontal or implant clinics, and academic centers, with consideration given to global populations to account for potential geographical variations in risk factor profiles. Particular attention is paid to patient subgroups demonstrating early signs of peri-implant inflammation, high-risk populations such as smokers, diabetics and patients with a history of periodontitis, as well as long-term implant recipients with more than five years of functional loading. The study explicitly excludes animal studies, small case reports or series with fewer than ten participants, and research focusing exclusively on implant survival outcomes without specific assessment of peri-implantitis parameters.The specific inclusion and exclusion criteria are as follows：

1.Inclusion Criteria

（1）Study Design: Prospective/retrospective cohorts, case-control (n≥50 implants)

（2）Participants: Adults (≥18y) with dental implants, minimum 12-month follow-up

（3）Outcome: Peri-implantitis defined as:Clinical: BOP(+) AND probing depth ≥6mm,

（4）Radiographic: Bone loss ≥3mm from implant shoulder

（5）Data Requirement: Adjusted RR/OR with 95% CI for ≥1 risk factor

2.Exclusion Criteria

（1）Case reports, reviews, in vitro/animal studies

（2）Studies without clear diagnostic criteria

（3）Duplicate publications with overlapping cohorts.

Intervention The intervention component of this study systematically evaluates both modifiable and non-modifiable risk factors associated with peri-implantitis development in dental implant patients. The primary exposures of interest include: (1) patient-related factors such as systemic conditions (diabetes mellitus, osteoporosis), behavioral factors (smoking status, oral hygiene practices), and local anatomical characteristics (gingival biotype, keratinized mucosa width); (2) implant-related factors including surgical protocol (immediate vs delayed placement), prosthetic design (cemented vs screw-retained restorations), and biomaterial characteristics (implant surface topography, alloy composition); and (3) maintenance-related factors encompassing professional supportive peri-implant therapy protocols and recall interval frequency. These interventions/exposures are analyzed through their documented association with peri-implantitis incidence, with particular emphasis on dose-response relationships where applicable (e.g., pack-years of smoking, glycemic control levels in diabetics). The study employs rigorous methods to standardize the measurement and classification of these exposures across included studies, utilizing validated diagnostic criteria and established clinical parameters to ensure consistent data extraction and analysis. Special consideration is given to potential confounding variables and interaction effects between multiple risk factors in the development of peri-implant pathology.

Comparator The comparator groups for this study comprise dental implant patients without the examined risk factors or with differing risk profiles, serving as reference populations to evaluate relative peri-implantitis risk. Systemically healthy patients without conditions like diabetes or osteoporosis are compared to affected individuals, while non-smokers provide baseline data against varying levels of tobacco exposure. Patients demonstrating optimal local conditions - including sufficient keratinized mucosa width and no history of periodontitis - are contrasted with those exhibiting these risk factors. Regarding implant characteristics, conventional machined surfaces serve as controls for modified surface topographies, and standard delayed placement protocols are compared to immediate placement approaches. Prosthetic design comparisons focus on screw-retained versus cemented restorations. Maintenance-related comparators include patients adhering to regular professional supportive therapy versus those with irregular or no maintenance care, with particular attention to varying recall interval frequencies. The analysis prioritizes studies providing quantitative exposure measures, such as HbA1c levels for glycemic control or pack-years for smoking history, to enable dose-response evaluations. Where applicable, the lowest-risk patient subgroups are designated as reference categories, maintaining consistency with source study classifications while allowing stratification by exposure intensity. This comprehensive comparator framework facilitates robust assessment of both modifiable and non-modifiable factors influencing peri-implantitis development across biological, technical, and maintenance-related domains.

Study designs to be included Prospective or retrospective cohort studies, case-control studies, and cross-sectional studies.

Eligibility criteria
Inclusion Criteria:
Study Design:prospective/retrospective cohort studies, case-control studies, and cross-sectional studies with clearly defined diagnostic criteria for peri-implantitis.Studies reporting quantitative data on risk factors and peri-implantitis outcomes.
Population:Human studies involving adult patients (≥18 years) with at least one osseointegrated dental implant.Minimum follow-up duration of 1 months post-loading for longitudinal studies.
Outcome Measures:
Studies must explicitly define peri-implantitis using standardized criteria (e.g., presence of bleeding/suppuration, probing depth ≥5 mm, and radiographic bone loss ≥2 mm).Reporting of at least one risk factor (e.g., smoking, diabetes, implant design) with measurable association to peri-implantitis.
Language and Publication:
Peer-reviewed articles published in English or with available English translations.No date restrictions applied to capture historical and contemporary evidence.

Exclusion Criteria:
Study Design:Case reports, conference abstracts, editorials, and non-peer-reviewed literature.
Studies with fewer than 20 implants or 10 patients to ensure adequate sample size.
Population:Animal or in vitro studies.Patients with implants placed in grafted or augmented bone without separate analysis.
Data Quality:Studies lacking clear diagnostic criteria for peri-implantitis.Incomplete data (e.g., missing risk factor quantification or outcome measures).
Redundancy:Duplicate publications or overlapping datasets (only the most comprehensive study included).

Information sources To ensure a comprehensive and systematic literature search, the following information sources were utilized:
Electronic Databases:PubMed/MEDLINE、The Cochrane Library、Web of Science、EMbase、CNKI、VIP、WanFang
Grey Literature:Conference proceedings (e.g., IADR, EAO, AAP);Government reports, theses/dissertations (via ProQuest Dissertations);Institutional repositories and academic theses
Supplementary Search Strategies:Hand-searching reference lists of included studies and relevant reviews; Contacting corresponding authors for unpublished or incomplete data; Searching Google Scholar (first 200 hits screened for relevance)
Search Timeframe:No date restrictions will be applied to capture historical and contemporary evidence.
Language Consideration:Non-English studies will be included if an English abstract is available and key data can be extracted (with translation assistance if needed).

Main outcome(s) The main outcome measure of the study was whether peri-implantitis occurred.Studies must explicitly define peri-implantitis using standardized criteria (e.g., presence of bleeding/suppuration, probing depth ≥5 mm, and radiographic bone loss ≥2 mm).
Reporting of at least one risk factor (e.g., smoking, diabetes, implant design) with measurable association to peri-implantitis.

Data management This study used Excel 2019 and Endnote X7 software for literature screening, management, and data extraction. Import the literature search results into Endnote X7 software, and have two researchers independently screen and evaluate the quality of the literature based on the inclusion and exclusion criteria. Controversies will be discussed and decided by two researchers, and when a consensus cannot be reached, the opinion of a third researcher will be sought. After discussion by the research group, a literature data extraction table was developed, which was independently extracted by two researchers. The extracted data included first author, publication year, country, research type, sample size, and risk factors. The last two researchers will cross check the extracted data, and if there is any dispute, it will be resolved through discussion. If there is no consensus, the opinion of the third researcher will be sought.

Quality assessment / Risk of bias analysis The literature quality evaluation of the included cohort studies and case-control studies was conducted using the Newcastle Ottawa Scale (NOS), which was scored from three aspects: selection of study subjects, comparability between groups, and determination of results. The maximum score for the scale is 9 points, with a score of ≥ 6 indicating high-quality research. The included cross-sectional studies were evaluated using the cross-sectional study evaluation criteria developed by the Agency for Healthcare Research and Quality (AHRQ) in the

United States, with a maximum score of 11 on the scale and a score of ≥ 8 being considered a high-quality study. This study excluded all non high quality studies to ensure the quality of the included literature. A funnel plot is a commonly used method for evaluating publication bias, which can determine publication bias by observing the distribution of effect points on both sides of the centerline in each study. This study generated funnel plots for meta-analysis of all risk factors and further evaluated publication bias using Begg's test and Egger's test.

Strategy of data synthesis This study used Stata12.0 software for meta-analysis, including heterogeneity testing, merging of effect sizes and drawing of forest plots, sensitivity analysis, and publication bias testing. All test results have statistical significance with P0.05, I2<50%), a fixed effects model will be used for combined analysis of effect sizes; If there is significant heterogeneity between studies (P ≤ 0.05, I2 ≥ 50%), a random effects model will be used for combined analysis of effect sizes. Use Z-test to determine whether the combined RR values of meta-analysis have statistical significance, with P<0.05 indicating statistical significance. Incorporate the statistically significant risk factors identified through systematic review and meta-analysis into the risk scoring table for implant periarthritis, and assign scores to each factor. Select appropriate sensitivity analysis results, calculate the regression coefficients of each risk factor based on the merged RR and its 95% CI, and construct a prediction model using machine learning methods.

Subgroup analysis This study will conduct subgroup analyses to explore potential sources of heterogeneity and examine the consistency of associations between risk factors and peri-implantitis across different clinical scenarios. The planned subgroup analyses include:1.Implant Characteristics: (1) Implant surface modification (e.g., machined vs. rough surfaces). (2) Implant length and diameter. (3) Prosthetic connection type (e.g., internal vs. external hex).2.Patient-Related Factors: (1) Smoking status (current/former/never smokers). (2) History of periodontitis (yes/no). (3) Presence of diabetes (stratified by glycemic control).3.Methodological Factors: (1) Study design (prospective vs. retrospective). (2) Follow-up duration (<5 years vs. ≥5 years). (3) Diagnostic criteria for peri-implantitis.4.Geographic Regions:European vs. Asian vs. American studies.These subgroup analyses will be performed when sufficient data are available (typically requiring ≥3 studies per subgroup). Between-subgroup differences will be assessed using meta-regression or interaction tests (p<0.05 considered significant). The results will help identify context-specific risk patterns and guide clinical decision-making.

Sensitivity analysis For risk factors with significant heterogeneity, this study used sensitivity analysis to partially correct for heterogeneity. This study conducted sensitivity analysis by excluding each study one by one and observing the degree of impact of each excluded study on the total effect size. If a study has significant heterogeneity, it should be excluded before merging the effect sizes. If there are fewer studies included (<4), different models will be used to analyze the same data for sensitivity analysis, observing the changes in combined RR. If the combined RR values of different models do not change significantly, then the results of the meta-analysis are considered stable.

Country(ies) involved China.

Keywords Peri-implantitis, Risk factors,Meta-analysis, Machine learning, Prediction model.

Contributions of each author

Author 1 - Yuxiang Chen - CY conceived and designed this study, participated in data collection, analysis, and interpretation, and was responsible for manuscript writing.
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