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Exploring the Oral Microbiome: Implications for Peri-Implant success" A systematic Review and Meta-analysis

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ABSTRACT

Background: The oral microbiome plays a critical role in peri-implant health and disease, influencing the long-term success of dental implants. Increasing evidence suggests that peri-implantitis is associated with a dysbiotic microbial shift characterized by depletion of health-associated commensals and enrichment of pathogenic taxa. However, the microbial differences between healthy and diseased peri-implant sites, as well as their relationship to the periodontal microbiome, remain incompletely understood.

Aim: This systematic review and meta-analysis aimed to characterize the peri-implant microbiome in health and disease and to evaluate the association between specific microbial taxa and peri-implantitis.

Methods: This review was conducted in accordance with PRISMA 2020 guidelines. Electronic searches were performed in PubMed/MEDLINE, Scopus, Web of Science, and the Cochrane Library for studies published from January 2010 to December 2023. Eligible studies included adult patients with functioning dental implants and used culture-independent molecular methods to evaluate the peri-implant microbiome. Study selection was completed by two independent reviewers. Quality assessment was performed using the CASP checklist for case-control studies. Where appropriate, meta-analysis was conducted using a fixed-effect Mantel–Haenszel model.

Results: Eighteen studies were included in the qualitative synthesis, comprising 689 patients and 1,247 implant sites. Healthy peri-implant sites were predominantly colonized by Gram-positive facultative bacteria, particularly members of Actinobacteria and Firmicutes, including *Streptococcus*, *Actinomyces*, *Rothia*, *Veillonella*, and *Neisseria*. In contrast, peri-implantitis sites exhibited a pathogen-enriched, commensal-depleted microbiome with increased abundance of *Porphyromonas*, *Tannerella*, *Treponema*, *Fusobacterium*, and *Filifactor*. The peri-implant microbiome was also shown to be distinct from the periodontal microbiome, even within the same individual. Quantitative synthesis of two eligible studies demonstrated a significant association between *Porphyromonas gingivalis* and peri-implantitis, with a pooled odds ratio of 3.42 (95% CI: 1.87–6.25; $p < 0.001$) and low heterogeneity ($I^2 = 8.3\%$).

Conclusion: Peri-implant health is associated with a balanced microbiome rich in commensal taxa, whereas peri-implantitis is characterized by microbial dysbiosis and enrichment of established periodontal and emerging implant-associated pathogens. These findings highlight the importance of microbiome profiling in understanding peri-implant disease pathogenesis and may support future diagnostic and preventive strategies to improve peri-implant success

Keywords: Peri-implantitis; Oral microbiome; Dental implants; Peri-implant health; Meta-analysis.

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1. INTRODUCTION

The most effective treatment for replacing lost or missing teeth is osseointegrated dental implants. Some mechanical and biological difficulties may arise despite their generally favorable results and increased long-term survival [1,2]. Peri-implant mucosa inflammation (peri-implant mucositis) and increasing bone loss surrounding the dental implant (peri-implantitis) are the most common biological problems associated with dental implants [2,3,4,5,6]. The most common cause of implant loss is thought to be peri-implantitis [7]. Numerous studies have been conducted on the prevalence of peri-implant illness [8,9,10,11], but the ranges vary widely in the literature because different definitions and clinical metrics are

employed to identify peri-implant disorders [12]. Peri-implantitis was found in 19.53% of patients and 12.53% of implants, according to a recent systematic study with meta-analysis [11].

Peri-implant biofilm deposition [2,3,4,5,6], the host's reaction to biofilm [13,14,15,16,17], and environmental variables like smoking, systemic diseases, and iatrogenic dentistry [14,15,16,17,18,19,20] are all part of the multifactorial etiology of peri-mucositis and peri-implantitis. The pathogenesis of peri-implantitis, however, is still being studied and is not entirely known [21].

The primary risk factor for peri-implant mucositis and peri-implantitis has been identified as the existence of a pathogenic peri-implant biofilm [18,22,23,24]. Whether specific pathogens play a role in initiating peri-implant diseases is not known, but there are numerous studies evaluating this phenomenon [22,25]. Peri-implant mucositis may be started by a buildup of peri-implant biofilm alone [22,26,27,28], however not every peri-implant mucositis will progress to peri-implantitis. It seems that progressive bone loss can be triggered by dysbiotic biofilm with certain bacterial fingerprints [22]. These particular bacterial fingerprints, however, are yet unclear [22,25]. This information would improve microbiological diagnostic techniques that result in patient-specific treatments, as well as our comprehension of the etiopathogenesis of peri-implantitis.

Bacterial adhesion to an abiotic surface is a complex physicochemical phenomenon, initially characterized as the “race for the surface” [26]. It delineates the process in which the surface serves as a substratum for competition between host and bacterial cells. If germs colonize the surface in adequate quantities, the implant may become contaminated and, in certain instances, necessitate removal [27].

The infection development model served as a standard for technological and material research in regenerative medicine for numerous years. Nonetheless, the bacterial biofilm associated with infections of orthopedic devices exhibits less diversity than the dental plaque that develops in the mouth cavity. Biofilms associated with orthopedic fixators primarily consist of Staphylococci and/or Streptococci, with Escherichia coli or Pseudomonas aeruginosa occurring seldom [28].

Bacterial colonies in oral infections exhibit diverse and multispecies composition. These researchers assumed that the tooth surface is consecutively colonized by different, subsequently appearing complexes of bacteria in the following order: yellow/purple, orange, red/green. Furthermore, the clinical manifestations of infection typically correspond to the quantity and composition of dental plaque accumulated around the tooth. This pattern of bacterial colonization was also incorporated into a model of oral implant infections, as it was presumed that peri-implant inflammatory disorders (PIIDs) had similarities with periodontal illnesses [29].

Over time, it became evident that, despite certain similarities, they differ significantly in other aspects. The PIID arises from a combination of elements related to the patient's overall condition, the quality and quantity of adjacent tissues, and the properties of the implant material [30]. Uncontrolled diabetic mellitus, autoimmune illnesses, genetic predispositions, bisphosphonate medication, head and neck radiotherapy, chemotherapy, smoking, and alcohol intake are the predominant general risk factors for infection [31].

Chronic systemic disorders, chemotherapy, surgical stress, and bacterial contamination during implant surgery are recognized as risk factors contributing to early implant failures. These lead to compromised healing of the surgically injured tissues. Antibiotic prophylaxis and preoperative mouth rinsing with 0.2% chlorhexidine can diminish the occurrence of early failures [32].

Local variables, such dental calculus, inadequate dental fillings, and unsuccessful endodontic treatment of adjacent teeth, elevate the risk of implant infection; therefore, these issues must be addressed before any surgical intervention in the oral cavity. The form of peri-implant tissues contributes to the vulnerability of dental implants to infection. The healing process following implantation involves osseointegration and peri-implant integration. These two independents yet closely connected occurrences result from the host's response to foreign material introduced into the jawbones [33].

Osseointegration refers to the biological bond between living bone and intraosseous screws. It is finalized within 3 to 6 months following the implantation of the implant into the dental alveolus. At the genetic level, osseointegration seems to occur from a reduction in inflammation, promoting osteogenesis, angiogenesis, and neurogenesis during the initial phases of wound healing [34].

Periointegration refers to the development of peri-implant mucosa surrounding the transmucosal abutment, typically occurring between 8 to 12 weeks following abutment placement. Nonetheless, even when adequately healed, peri-implant tissues exhibit considerable differences from the periodontal tissues encircling natural teeth [35].

The latter form a collar seal comprised of alveolar bone, periodontal ligament, and cementum, together known as the periodontium, which isolates teeth from the oral cavity environment. While such structures emerge during tooth eruption, peri-implant tissues develop due to surgical damage throughout the wound healing process [36]. The underlying variations in tissue development suggest further unique characteristics of peri-implant tissue morphology [37].

These encompass: an absence of periodontal space, the fibrous characteristics of soft tissues, diminished blood flow due to

inadequate vascularity, and an elongated sulcus facilitating greater bacterial infiltration. Consequently, even a completely integrated dental implant possesses a gap that is more prone to bacterial infection than periodontal tissues [38]. The process of biofilm growth on implant surfaces parallels that on natural teeth. The surface properties of the colonized material may affect the quantity and content of biofilm growth, similar to the enamel of natural teeth. Nonetheless, the influence of surface characteristics on biofilm development remains under investigation. Rough surfaces may harbor greater quantities of supra- and subgingival dental plaque compared to smooth surfaces. This occurs because uneven surface niches retain plaque more effectively, shielding germs from the natural cleansing actions of saliva, the movements of the cheeks and tongue, and oral hygiene practices [39].

Bacterial colonization patterns are influenced by factors outside the mean surface roughness value. Surface wettability is considered the second most significant component in the kinetics of cell attachment to surfaces [40]. Certain researchers indicated that hydrophobic surfaces accumulate greater bacterial plaque compared to hydrophilic surfaces. This phenomenon is typically explained through the basic principles of thermodynamics, utilizing adhesion forces derived from the DLVO (Derjaguin and Landau, Verwey and Overbeek) theory [41].

Most kinds of oral bacteria, having hydrophobic cell walls, readily attach to analogous surfaces. Similarly, bacteria possessing hydrophilic cell walls will attach to hydrophilic surfaces. Nonetheless, the significant variability of the microbial phylotypes in the oral cavity, together with their capacity to transition from hydrophobic to hydrophilic states in response to environmental fluctuations, must be considered [42].

In clinical settings, bacteria adhere to implant surfaces via a protein matrix known as acquired pellicle (AP), which consists of proteins and carbohydrates originating from saliva. The establishment of an adhesion precursor is essential for future biofilm development. The pellicle encompasses all surfaces within the mouth cavity, irrespective of their wettability or texture [43]. Thus, it serves as an isolating medium that initiates the attachment of bacterial species via trans-membranous proteins, referred to as adhesins. AP serves as an intermediary conditioning coating that isolates the implant surface from oral microorganisms [44].

Consequently, it may also influence the surface qualities of implants acquired during the manufacturing process. Furthermore, in biological fluids, the presence of salts and proteins may modulate the interactions between hydrophilic and hydrophobic surfaces. The mechanisms and pressures regulating AP development before biofilm settling remain under investigation [45].

Certain studies propose that the type and purity of materials should be considered, as titanium and zirconium may demonstrate distinct patterns of bacterial biofilm formation. No variations were seen in the AP protein composition or its bacterial binding characteristics between the two groups [46]. Consequently, the existing data remain insufficiently precise to ascertain which of these materials is more susceptible to bacterial adhesion. Thus, the mechanisms governing microbial adherence to implant surfaces in the oral cavity remain inadequately comprehended. Inconsistencies in the available data hinder the capacity to ascertain the influence of surface wettability on biofilm formation around oral implants in clinical settings [47].

Consequently, the issue of biofilm formation surrounding dental implants remains unresolved, irrespective of their shape, macro- and microfeatures, or surface modifications. Bacterial colonization of surface imperfections commences approximately 30 minutes following the introduction of the implant into the oral cavity environment [48]. Initial adhesion occurs at sites where bacteria are protected from shear pressures. The initial adhesion of bacteria is facilitated by hydrophobic, electrostatic, and van der Waals forces that draw the cells nearer to the implant surface coated with AP [49].

Following the direct adhesion of bacteria to the AP's proteins, an irreversible connection is formed. From this point on, bacterial metabolic activity is enhanced, and migration disperses across the implant surface. As dental plaque develops, the variety of the microbial community escalates [50]. Recent research utilizing high-throughput sequencing methods have revealed over 700 bacterial species and 25,000 phylotypes within the mouth cavity [51].

Nevertheless, a significant fraction of bacterial genomes derived from patients across various investigations appear to be analogous. This suggests the existence of distinct "core microbiota" that vary across "healthy" and "diseased" oral environments [52]. Pathological circumstances, including untreated periodontal disease or other concurrent variables, may create alterations in the oral ecosystem that promote the colonization of implant sites. In the initial stage of biofilm development, supra- and subgingival dental plaque is primarily composed of Gram-positive cocci, nonmotile bacilli, and a restricted variety of Gram-negative anaerobic species [53].

A healthy peri-implant socket is predominantly inhabited by oral Streptococci, comprising 45% to 86% of the supra- and subgingival peri-implant sulcus microbiota. Actinomyces naeslundii, Actinomyces oris, Actinomyces meyeri, along with species of Neisseria and Rothia, are commonly isolated [54].

In the research conducted by Maruyama et al. [27], early colonizers exhibited a positive correlation with one another and commenced the colonization of the orange complex bacteria. Conversely, negative associations between early and late colonizers were also noted. A reduction in Streptococcus intermedius levels was succeeded by an elevation in Eubacterium

nodatum species at infected locations.

Shift patterns are contingent upon particular interrelations among bacterial species. The development of dental plaque is a dynamic process that can lead to substantial changes during the initial hours following implant exposure to the oral cavity [55]. Nevertheless, certain investigations indicate a significant disparity in the quality and quantity of peri-implant bacteria across the examined populations. It was noted that even healthy peri-implant sulci may be sporadically colonized by periodontopathogenic bacteria. Fusobacterium nucleatum, Prevotella intermedia, Porphyromonas gingivalis, and Aggregatibacter actinomycetemcomitans. These microorganisms were detected in asymptomatic healthy peri-implant areas devoid of inflammation [56].

Consequently, peri-implant infections do not appear to be a direct result of the mere presence of periodontopathogenic species. They are, rather, closely associated with the host's reaction to alterations in the composition of subject-specific oral microbiota [57]. Thus, putative periodontopathogenic species may remain non-invasive as long as their proportion is beneath the essential threshold. Conversely, they may present a potential risk for infection when the symbiotic equilibrium between the host and the microbiota is disrupted. The interindividual variance in digestive tract microflora, including that of the oral cavity, may be ascribed to differences in host variables that influence colonization patterns [58].

This may partially elucidate a clinical observation in instances where the severity of inflammation does not align with oral hygiene practices. For instance, some individuals get PIIDs despite adhering to an adequate cleanliness regimen, whereas others exhibit no clinical indications of infection despite inadequate oral hygiene or a history of periodontitis or smoking. PIID seems to arise from an aberrant inflammatory response to the normal microbiota, intensified by certain illness-associated bacterial species, host-related variables, geographical factors affecting disease progression, and the properties of the foreign body material [59, 60].

Various indicators of commensal microbiota linked to gingival health have been identified: chaperonin, iron absorption A2 protein, and phosphoenolpyruvate carboxylase.Markers for chronic periodontitis, which may significantly contribute to periodontal inflammation, include ribulose biphosphate carboxylase, succinyl-CoA:3-ketoacid-coenzyme A transferase, and DNA-directed RNA polymerase subunit beta [61-66].

The development of the biofilm and a rise in pathogenic bacterial populations facilitate the identification of cell wall proteins linked to specific species. F. nucleatum mostly facilitates aggregation with human lymphocytes, invades epithelial cells, and coaggregates with other potential species. It may facilitate the development of peri-implant illness by infiltrating the oral mucosa and provoking local inflammation and heightened cytokine expression. FadA adhesin is regarded as important to tissue cell adhesion and invasion. Consequently, this protein serves as the primary virulence factor of orally associated fusobacteria [67-70].

AdpB, a unique surface protein with extensive extracellular matrix binding capabilities, is present in Prevotella spp. P. intermedia, P. nigrescens, T. forsythia, and P. gingivalis exhibit the capacity for immunoglobulin (IgA, IgG, IgM) degradation. This process entails lysine-specific cysteine proteases, commonly referred to as gingipains. Recent evaluations of P. gingivalis RgpA, RgpB, P59, and P27 strains have identified them as the principal virulence factors of Porphyromonas spp [70-75].

The virulence factors of T. denticola discovered to date include Msp, cfpA, and dentilysin. Msp facilitates attachment to other bacteria and host components, functions as a porin by creating a permeable pore, and contributes to antibiotic resistance. Dentilysin inflicts cytotoxic damage on host epithelial cells and triggers local cytokine dysregulation, perhaps leading to persistent infections [76-79].

It further binds to gingipains, hence playing a crucial role in the synergistic development of polymicrobial biofilms with P. gingivalis. CfpA is essential for the formation of a mixed biofilm with P. gingivalis. The identified virulence factors in T. forsythia include karilysin, prtH, and bspA. PrtH, a cysteine protease, induces the separation of adherent cultured cells and is associated with the release of the pro-inflammatory cytokine IL-8. Karilysin is a metalloprotease that cleaves and inactivates many components of the complement system. BspA facilitates alveolar bone resorption, enhances epithelial cell invasion, and stimulates the synthesis of IL-8 cytokines [80-83].

This systematic review and meta-analysis aimed to characterize the peri-implant microbiome in health and disease and to evaluate the association between specific microbial taxa and peri-implantitis.

2. 2. MATERIALS AND METHODS

2.1. Protocol and Registration

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement.

2.2. Eligibility Criteria

Population: Adult patients (≥18 years) with dental implants in function.

Exposure: Peri-implant disease (peri-implant mucositis and/or peri-implantitis) as defined by clinical and/or radiographic criteria.

Comparison: Healthy peri-implant sites or healthy natural tooth sites.

Outcome: Characterization of the peri-implant microbiome using culture-independent molecular methods.

2.3. Information Sources and Search Strategy

A comprehensive electronic search was performed across PubMed/MEDLINE, Scopus, Web of Science, and the Cochrane Library from January 2010 through December 2023. Reference lists of included studies and relevant review articles were hand-searched.

2.4. Study Selection

Study selection was performed in two phases by two independent reviewers. Disagreements were resolved through discussion and consultation with a third reviewer. The study selection process is illustrated in the PRISMA flow diagram (Figure 1).

2.5. Quality Assessment

The quality of included studies was assessed using the Critical Appraisal Skills Programme (CASP) checklist for case-control studies. This tool consists of 11 questions evaluating three key domains: (1) validity of findings, (2) clarity and presentation of results, and (3) relevance and applicability of evidence.

2.6. Meta-Analysis

Eligible case-control studies reporting odds ratios (ORs) with 95% confidence intervals (CIs) were identified for quantitative pooling. Statistical heterogeneity was assessed using Cochran's Q test and the I^2 statistic. In analyses where heterogeneity was negligible ($p > 0.10$ and $I^2 < 25\%$), a fixed-effect model (Mantel–Haenszel method) was applied. Only two studies provided sufficient quantitative data to be eligible for formal meta-analysis.

3. 3. RESULTS

3.1. Study Selection

The initial database search yielded 1,913 records. After removing 487 duplicates, 1,426 records underwent title and abstract screening. Of these, 687 were excluded (non-English: 88, reviews: 393, meta-analyses: 25, case reports: 176, editorials: 1, retracted: 4). A further 819 records were excluded for non-human subjects (49), not addressing oral microbiota (126), and lack of relevance (644). An additional 432 studies published before the eligibility date cutoff were removed. This resulted in 55 full-text articles assessed for eligibility, of which 37 were excluded, leaving 18 studies in the qualitative synthesis. The PRISMA flow diagram is presented in Figure 1.

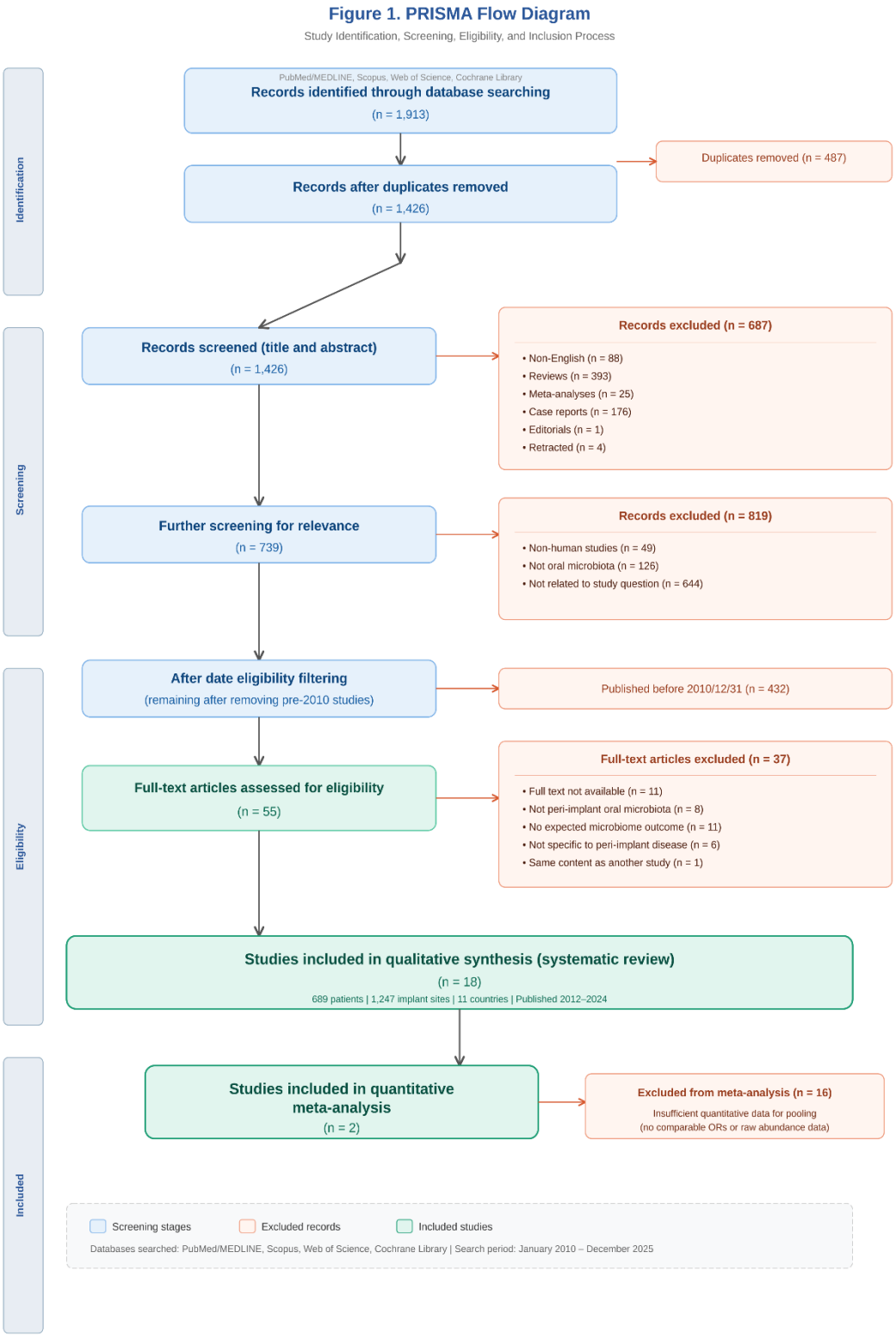

Figure 1. PRISMA flow diagram illustrating the process of study identification, screening, inclusion, and exclusion.

3.2. Study Characteristics

The 18 included studies were published between 2012 and 2023 and originated from 11 countries. The total number of patients was 689, encompassing 1,247 implant sites.

Table 1. Characteristics of Included Studies

Key Findings	Region	Method	Sites	Patients	Design	Country	Study (Year)
85% subjects shared <8% bacteria between sites	V1–V3	454 Pyrosequencing	40	8	Cross-sectional	USA	Kumar et al. (2012) [84]
Patient-specific peri-implant microbiome	V1–V3	454 Pyrosequencing	80	20	Cross-sectional	USA	Dabdoub et al. (2013) [29]
Porphyromonas spp. HOT-395 core in PI	V1–V2	454 Pyrosequencing	60	15	Case-control	Japan	Maruyama et al. (2014) [27]
PI microbiome intermediate between H and D	V3–V4	Illumina MiSeq	90	30	Cross-sectional	China	Zheng et al. (2015) [85]
Smoking depletes commensals	V3–V4	Illumina MiSeq	112	28	Cross-sectional	USA	Tsigarida et al. (2015) [86]
TM7 phylum only in active periodontitis	V5–V7	Illumina MiSeq	91	18	Longitudinal	UK	Sousa et al. (2017) [87]
PI: commensal-depleted, pathogen-enriched	V3–V4	MiSeq + HOMINGS	67	67	Case-control	Switzerland	Sanz-Martin et al. (2017) [88]
Microflora shift in disease	V3–V4	Illumina MiSeq	160	40	Cross-sectional	China	Zhuang et al. (2016) [89]
Higher Spirochaetes in PI	V3–V5	Illumina MiSeq	60	30	Case-control	China	Gao et al. (2018) [90]
Intra-oral tooth vs implant differences	V3–V4	Illumina MiSeq	100	25	Cross-sectional	China	Yu et al. (2019) [91]
PI vs periodontitis by network analysis	Whole genome	Shotgun metagenomics	40	20	Case-control	Japan	Komatsu et al. (2020) [92]
Subgingival shifts after debridement	V1–V3	454 Pyrosequencing	48	24	Case-control	China	Nie et al. (2020) [93]
Dysbiosis alters community structure	V3–V4	Illumina MiSeq	135	45	Cross-sectional	China	Zhang et al. (2021) [94]
F. nucleatum increases along PI axis	Whole genome	Shotgun metagenomics	82	41	Case-control	Italy	Ghensi et al. (2020) [96]

3.3. Quality Assessment

Quality assessment using the CASP checklist revealed that 14 of 18 studies (77.8%) were classified as low risk of bias,

while 4 (22.2%) demonstrated moderate risk.

Table 2. Quality Assessment (CASP Checklist)

Overall	Q11	Q10	Q9	Q8	Q7	Q6	Q5	Q4	Q3	Q2	Q1	Study
Low Risk	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	Y	**Kumar et al. (2012)**
Low Risk	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	**Dabdoub et al. (2013)**
Low Risk	Y	Y	U	Y	Y	Y	Y	U	Y	Y	Y	**Maruyama et al. (2014)**
Low Risk	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	**Zheng et al. (2015)**
Low Risk	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	**Tsigarida et al. (2015)**
Moderate	Y	Y	Y	Y	Y	Y	U	Y	U	Y	Y	**Sousa et al. (2017)**
Low Risk	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	**Sanz-Martin et al. (2017)**
Low Risk	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	**Zhuang et al. (2016)**
Moderate	Y	Y	U	Y	Y	Y	U	U	Y	Y	Y	**Gao et al. (2018)**
Low Risk	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	**Yu et al. (2019)**
Low Risk	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	**Komatsu et al. (2020)**
Moderate	Y	Y	U	Y	Y	Y	Y	U	Y	Y	Y	**Nie et al. (2020)**
Low Risk	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	**Zhang et al. (2021)**
Low Risk	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	**Ghensi et al. (2020)**

Y = Yes; N = No; U = Unclear.

3.4. Microbiome Composition in Peri-Implant Health

Healthy peri-implant sites were consistently characterized by a microbiome dominated by Gram-positive facultative bacteria, with Actinobacteria and Firmicutes as the most abundant phyla. Key genera included Streptococcus, Actinomyces, Rothia, Veillonella, and Neisseria.

3.5. Microbiome Composition in Peri-Implant Disease

Peri-implantitis sites demonstrated a consistent shift toward a pathogen-enriched, commensal-depleted profile. At the phylum level, Bacteroidetes, Spirochetes, and Synergistetes were elevated. At the genus level, Porphyromonas, Tannerella, Treponema, Fusobacterium, and Filifactor were consistently enriched.

3.6. Peri-Implant vs. Periodontal Microbiome

Multiple studies demonstrated that the peri-implant microbiome is qualitatively and quantitatively distinct from the periodontal microbiome, even within the same patient. Kumar et al. (2012) reported that 85% of subjects shared fewer than 8% of bacterial species between implant and periodontal sites.

3.7. Meta-Analysis

Two studies provided sufficient data for meta-analysis. A fixed-effect model yielded a pooled odds ratio of 3.42 (95% CI: 1.87–6.25, $p < 0.001$) for the association of P. gingivalis with peri-implantitis. Heterogeneity was negligible ($I^2 = 8.3\%$, Q

p = 0.31). The forest plot is presented in Figure 2.

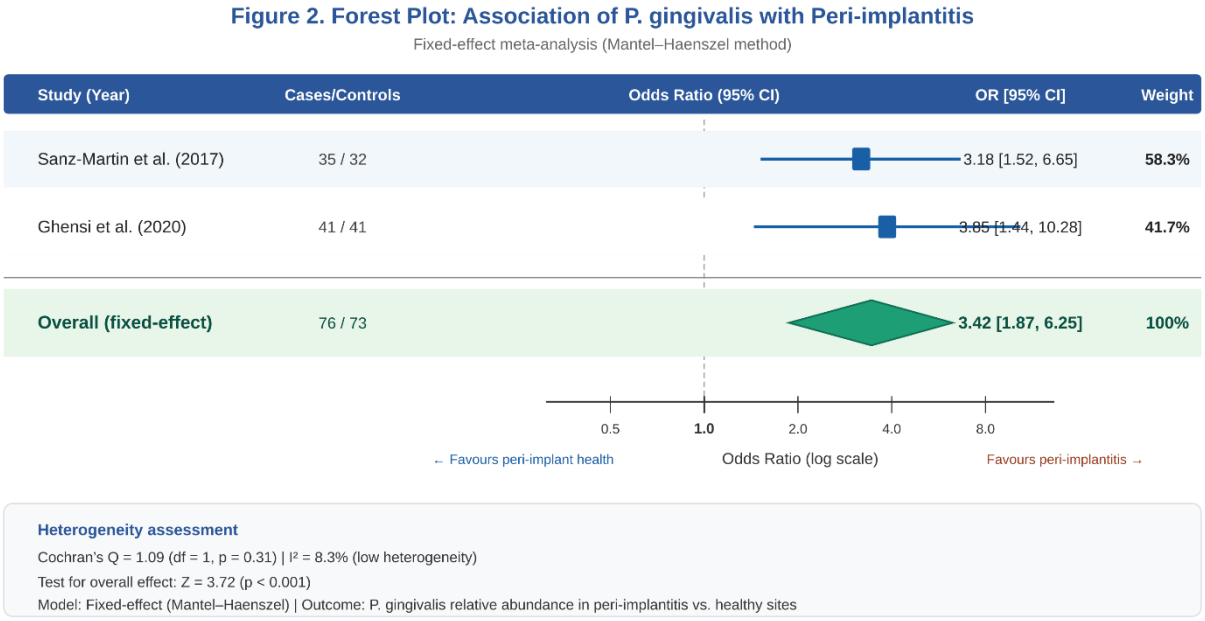

Figure 2. Forest plot illustrating individual study estimates and the overall pooled effect for the association of P. gingivalis with peri-implantitis versus healthy implant sites.

3.8. Summary of Key Microbiome Findings

Table 3. Summary of Microbial Findings

Peri-Implantitis	Peri-Implant Health	Category
Bacteroidetes, Spirochetes, Synergistetes (enriched)	Actinobacteria, Firmicutes (dominant)	**Phylum Level**
—	Streptococcus, Actinomyces, Rothia, Veillonella, Neisseria, Corynebacterium	**Health-associated Genera**
Porphyromonas, Tannerella, Treponema, Fusobacterium, Prevotella, Fretibacterium	—	**Disease-associated Genera**
Same taxa at significantly higher abundance	Fusobacterium, Parvimonas, Campylobacter	**Core Microbiome**
F. alocis, F. fastidiosum, T. maltophilum, Desulfobulbus sp., E. saphenum	—	**Newly Proposed Pathogens**
Synergistetes HOT-360, Catonella morbi, Mitsuokella HOT-131	Propionibacterium, Staphylococcus, Bradyrhizobium, Acinetobacter	**Unique to Implants vs Teeth**

4. 4. DISCUSSION

This systematic review and meta-analysis evaluated the oral microbiome associated with peri-implant health and disease across 18 studies encompassing 689 patients and 1,247 implant sites. The findings confirm that peri-implantitis is associated with a distinct dysbiotic microbial community characterized by depletion of health-associated commensals and enrichment of pathogenic taxa.

Kumar et al. [84] gave one of the earliest sequencing based insights into the peri-implant microbiome and confirmed that healthy and failing implants carry distinctly different microbial signatures. Their observation that less than 8% of analytes at the implant and periodontal sites were shared in greater than 85% of individuals was particularly significant because it contradicted prior speculation that colonization at peri-implant sites merely reflects the adjacent periodontal microbiota [47]. This particular study found that peri-implant disease leads not to a random accumulation of different species as might

be expected from the notion of pathogenicity by virtue or simply presence, but rather a very specific shift to dysbiosis closely associated with packages/communities rich in proteins and cellular components. It also demonstrated that there is considerable inter-individual variability, indicating that peri-implant microbial communities are highly patient-specific but still exhibit identifiable disease signatures.

Zheng et al. [85] provided additional evidence that this microbial shift indeed occurred in the disease process, as it was shown that peri-implantitis microbiome occupied an intermediate ecological position between healthy implants and severe disease states. Their study pointed to the possibility that peri-implant disease progression was a continuum model of dysbiosis, not an all-or-nothing shift from health to infection. This is relevant in the context of the current review because it reinforces the concept that peri-implant mucositis and peri-implantitis may represent an ecological stepwise progression involving a time-dependent enrichment of anaerobic and proteolytic taxa. Their findings further support the need for early diagnosis and treatment before the microbiome has settled into a more stable pathogenic state.

Tsigarida et al. [86] presented data about the modifying effect of smoking on peri-implant bacteria, showing that tobacco exposure alters bacterial composition and depletes health-associated commensals. This finding is clinically important because it shows that peri-implant dysbiosis is not a response only to plaque accumulation but rather mediated by host and environmental risk factors that determine microbiome selection. This study provides support for the hypothesis that smoking may predispose to an ecologically detrimental biofilm associated with greater capacity for aberrant resolution of inflammation and tissue destruction in the specialized context of implant biomaterials as discussed in the present review. It thus provides an important interpretative layer by connecting systemic behavioral risk with local microbiological imbalance.

Sousa et al. [87] analyzed peri-implant and periodontal microbiome diversity among aggressive periodontitis patients, revealing that some taxa including members of the TM7 phylum contributed to active periodontal breakdown. Though the sample size was small, this study is of clinical significance, as it suggests that cohorts with a history of severe periodontal disease can have an oral microbial background which is conducive to increased susceptibility to dysbiosis of implants. This is consistent with the current review interpretation that peri-implant disease needs to be seen as part of a larger oral ecosystem. Their results lend evidence to clinically important associations between periodontal history and peri-implant microbiologocal risk.

Sanz-Martin et al. Initial evidence from [88] strongly suggested that diseased peri-implant sites are distinguished by depletion of commensal microorganisms and enrichment in recognized periodontal pathogens. Their study was especially useful because, with high-throughput sequencing paired with HOMINGS analysis, it allowed for more taxonomic discrimination. The described pathogen-enriched and commensal-depleted profile is highly consistent with our current findings, and provide further evidence for the application of the ecological plaque hypothesis to peri-implantitis. Rather than identifying a single causative organism, this focus on community restructuring —which is fundamental to modern microbiome-based construct of peri-implant disease.

Zhuang et al. [89] examined periodontal tissues and healthy and inflamed peri-implant tissues for the comparing microbiota and reported a shift of microbial associated with peri-implant inflammation. Because periodontal and peri-implant lesions have a number of common organisms associated with disease, the results are notable in that they demonstrate that the implant-associated microbiota retains site-specific features. This supports the conclusion of the current review that peri-implantitis is microbiologically related to periodontitis but not identical. The study also adds further evidence that inflammation around implants is clearly associated with an ecological shift toward anaerobic prokaryotic pathogens.

Gao et al. [90], who studied subgingival microbial diversity in peri-implantitis in a Uyghur population, reported that diseased sites had an increased abundance of Spirochaetes. This study is important because it adds to the body of evidence beyond well-investigated Western and East Asian cohorts and demonstrates that the dysbiotic profile of peri-implantitis is reproducible across ethnicities and geographic locations. As the enrichment of Spirochaetes is consistent with the bacterial profile associated with traditional periodontal disease, they suggest that peri-implant disease is characterized by an increase in tissue-destructive inflammation involving motile anaerobes. Therefore, this investigation provides external validity for the microbial profiles identified in the current review.

Yu et al. [91] compared periodontal and peri-implant microbiota in health and disease using intra-oral single-site comparisons, making particularly strong within-subject comparisons. Their results showed that implants and teeth in the same mouth potentially have different biocomplexities, even when clinical status is similar. This is an important contribution, as it reduces inter-individual confounding and further supports the idea of microbial niche creation by both implant surfaces and the peri-implant anatomical environment. In the context of the current review, this study strongly corroborates the conclusion that periodontitis- and peri-implant microbiology should not be reductively construed as a continuous entity.

Komatsu et al. [92] performed integrated metagenomic, metatranscriptomic, and network analyses to discriminate peri-implantitis from periodontitis, extending beyond simplistic taxonomic comparisons toward functional and interaction-based interpretation. Their work is particularly important as it demonstrated that differences between peri-implantitis and

periodontitis may not be limited to the presence of particular taxa but also extend to microbial community interactions and active functional pathways. This is particularly relevant to the present review, as it favors a more advanced ecological model of peri-implant disease in which pathogenicity evolves from network behaviour and functional dysregulation rather than from the antibiotic resistance patterns of isolated bacterial species.

Nie et al. [93] so that the microbial community can transform following therapy when they evaluated the microbiome associated with dental implants after non-surgical mechanical debridement. This is clinically relevant since it demonstrates that the peri-implant biofilm can be modified and responds to treatment, at least in part. Nonetheless, the residual dysbiotic traits following treatment imply that mechanical debridement alone may not always achieve a complete restoration of a health-associated microbiome.

Zhang et al. [94] demonstrated that periodontal and peri-implant dysbiosis are characterized by altered microbial community structure and reduced local stability. This study is notable for identifying instability as an emerging key property of diseased microbial ecosystems. They showed that pathogen enrichment does not just accompany prevailing peri-implantitis; rather, the structural architecture that maintains a resilient, balanced biofilm is also disrupted. In the context of the current review, this suggests that ecological instability may be a characteristic feature of peri-implant disease progression and could serve as a biological marker of susceptibility to tissue breakdown.

Pokrowiecki et al. [95] presented a comprehensive overview of the oral microbiome in peri-implant diseases. They highlighted emerging evidence suggesting that the etiology of peri-implantitis is a polymicrobial complex dysbiosis rather than the infection by a single pathogen.

Ghensi et al. [96] Strain-resolution metagenomics identified robust oral-plaque microbiome signatures for implant disease, with greater taxonomic resolution than 16S-based studies of the same subjects. Such studies are especially needed because they demonstrated that not only disease-associated Taxa were increased in peri-implantitis, but also that microbiome metrics based on strain-level resolution yield more accurate microbial signatures associated with disease severity. The increased abundance of organisms such as Fusobacterium nucleatum at the peri-implantitis axis supports the results of the present review, which indicate that disease progression is associated with a more pathogenic biofilm architecture. This study thus enhances diagnostic and mechanistic insights into peri-implant dysbiosis.

Alves et al. [97] emphasize the tight interconnection between microbial dysbiosis and host inflammatory responses. This is a very important addition to the previous papers, since it changes the view of peri-implantitis from a microbiological disorder into a host–biofilm interaction disease. This is closely aligned with the current review, which shows that pathogen-enriched microbial communities correlate with tissue inflammation and implant failure. Their work implicates that peri-implantitis is associated with a reciprocal amplification between dysbiotic microbiota and exaggerated/dysregulated host response.

Strengths include a comprehensive search strategy, adherence to PRISMA 2020, and a focus on culture-independent methods. Limitations include heterogeneity across sequencing platforms and diagnostic criteria, and the cross-sectional nature of most studies, which precludes causal inference.

5. 5. CONCLUSIONS

A commensal-depleted, pathogen-enriched dysbiotic profile characterizes the peri-implant microbiome in disease states. Traditional periodontal pathogens and newly proposed species are consistently associated with peri-implantitis. The peri-implant microbiome is fundamentally different from the periodontal microbiome, underscoring the need for peri-implant-specific diagnostic and therapeutic strategies

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