
Revisiting Socransky's Complexes: A Review Suggesting Updated New Bacterial Clusters (GF-MoR complexes) for Periodontal and Peri-Implant Diseases and Conditions

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Review

Revisiting Socransky's Complexes: A Review Suggesting Updated New Bacterial Clusters (GF-MoR complexes) for Periodontal and Peri-Implant Diseases and Conditions

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Abstract: The aim of this review was to identify newly discovered bacteria from individuals with periodontal/peri-implant diseases and organize them in new clusters (GF-MoR complexes) to update Socransky's complexes (1998). The focus question was developed based on the PCC (Population, Concept, Context) strategy: "In patients with periodontal and/or peri-implant disease, what bacteria (microorganisms) were detected through laboratory assays?" The search strategy was applied to PubMed/MEDLINE, PubMed Central, and Embase. The search keyterms, combined with Boolean markers, were: (1) bacteria, (2) microbiome, (3) microorganisms, (4) biofilm, (5) niche, (6) native bacteria, (7) gingivitis, (8) periodontitis, (9) peri-implant mucositis, and (10) peri-implantitis. The search was restricted to 1998–2024 and English language. The bacteria groups in the oral cavity obtained/found were retrieved and were included in the GF-MoR complexes which were based on the disease/condition, presenting six groups: (1) Health, (2) Gingivitis, (3) Peri-implant mucositis, (4) Periodontitis, (5) Peri-implantitis, and (6) Necrotizing and Molar-Incisor (M-O) pattern Periodontitis. The percentual found per group refers to the number of times a specific bacterium was found associated with a particular disease. A total of 381 articles were found; 162 articles were eligible for full-text reading ($k=0.92$); 9 articles were excluded with justification, and 153 were included in this review ($k=0.98$). Most of the studies reported results for Health condition, Periodontitis, and Peri-implantitis (3 out of 6 GF-MoR clusters), limiting the number of bacteria found in the other groups. Therefore, it is essential to understand that bacterial colonization is a dynamic process, and the bacteria present in one group can also be present in other one or others, such as observed with the bacteria found in all groups (*Porphyromonas gingivalis*, *Tannarella forsythia*, *Treponema denticola*, and *Aggregatibacter actinomycetemcomitans*) (GF-MoR's red Triangle); the second most observed bacteria were grouped at GF-MoR's blue Triangle: *Porphyromonas spp.*, *Prevotella spp.*, and *Treponema spp.*, present in 5 of the six groups; and the third most detected bacteria were clustered in the grey Polygon (GF-MoR's grey Polygon): *Fusobacterium nucleatum*, *Prevotella intermedia*, *Campylobacter rectus*, and *Eikenella corrodens*. These three geometric shapes had the most relevant bacteria for periodontal and peri-implant diseases. Specifically, per group, GF-MoR's Health had 58 species; GF-MoR's Gingivitis presented 16 bacteria; the GF-MoR's Peri-implant mucositis included 17 bacteria; GF-MoR's Periodontitis group had 101 different bacteria; GF-MoR's Peri-implantitis presented 61 bacteria; and the last group was a combination of Necrotizing diseases and Molar-Incisor (M-I) pattern Periodontitis, with seven bacteria. Observing the top seven bacteria of all groups, all were gram-negative; Groups 4 and 5 (Periodontitis and Peri-implantitis) presented the same top seven bacteria. **Conclusion:** For the first time in the literature, GF-MoR's complexes are presented, gathering the bacteria according to the condition found and including more bacteria

than Socransky's complexes. On this understanding, this study can drive future research into treatment options for periodontal and peri-implant diseases, guiding future studies and collaborating to prevent and worsen systemic conditions. Moreover, it permits the debate about the evolution of the bacterial clusters correlated to periodontal and peri-implant diseases and conditions.

Keywords: bacteria; bacterium; complexes; clusters; periodontitis; peri-implantitis; peri-implant mucositis; gingivitis; periodontal health

1. Introduction

In the human oral cavity's damp and organically rich environment, it is no surprise for many to understand that one's mouth is an ecosystem where an immense variety of microorganisms endure and thrive. Considering the lifestyle and genomic differences of all individuals, every person can host different types of organisms in their oral cavity, including bacteria, fungi, viruses, and even protozoa. However, a standard balance of predominant species is found in most healthy human beings. Unfortunately, a lack of convincing *in vivo* studies that determine precisely what role fungi and protozoa have in maintaining a healthy, symbiotic environment in the host's oral cavity currently exists, leaving most studies focusing on the most abundant organism of the oral cavity, bacteria [1].

A review published in 2018 aimed to research within the expanded Human Oral Microbiome Database (eHOMD) to determine which of the cultivable and uncultivable bacteria found in the oral cavity are indicative of health [2]. With the advantage of 16S rDNA profiling, six broad phyla were found to inhabit the healthy oral cavity and constitute 96% of total oral bacteria, including: *Firmicutes*, *Actinobacteria*, *Proteobacteria*, *Fusobacteria*, *Bacteroidetes*, and *Spirochaetes*. A relatively steady balance of these incalculable colonies, in quantity and quality, maintains equilibrium for a stable, and therefore healthy, oral cavity for the host.

Within the field of Periodontology, most current research is focused on its four most prevalent diseases: Gingivitis, Periodontitis, Peri-implant mucositis, and Peri-implantitis. Periodontal disease is estimated to affect between 45 and 50% of the global population, with 11.2% diagnosed with severe periodontitis [3]. It refers to an infection of the tissues surrounding and supporting the teeth. The collection of bacteria on teeth and gingiva forms biofilm. Failure to remove the biofilm/plaque through regular brushing and flossing can allow the slim to harden into calculus, requiring removal only from a dentist (professional care). Early stages of periodontal disease are called gingivitis; it is an inflammation (including, but not limited to, redness, swelling, and profuse bleeding on probing [BoP]) of the gums induced, most of the time, by dental plaque. However, gingivitis can also be caused by certain drugs, stress, malnutrition, genetic and acquired diseases, viral and fungal infections, allergies, and trauma. If gingivitis is not correctly treated or resolved, it may evolve, but not necessarily, into a severe form of the disease known as periodontitis [4]. Periodontitis is advanced inflammation of the supporting tissues of the dentition (including the alveolar bone, gingiva, cementum, and periodontal ligaments), marked by the irreversible loss of bone tissue. All these processes happen due to the dysbiosis process, and over time, the periodontal apparatus's destruction can occur, potentially leading to tooth loss [5].

The subgingival periodontal microbiome has been a heavily studied topic. In 1998, Socransky et al.'s research [6] identified many microorganisms and didactically divided them into clusters (Figure 1), becoming an essential aspect of education, research, and treatments. Understanding specific bacteria's role in periodontal diseases has guided the evolution of research in microbiological diagnosis and treatment strategies [7,8], targeting interventions to prevent and treat periodontitis effectively.

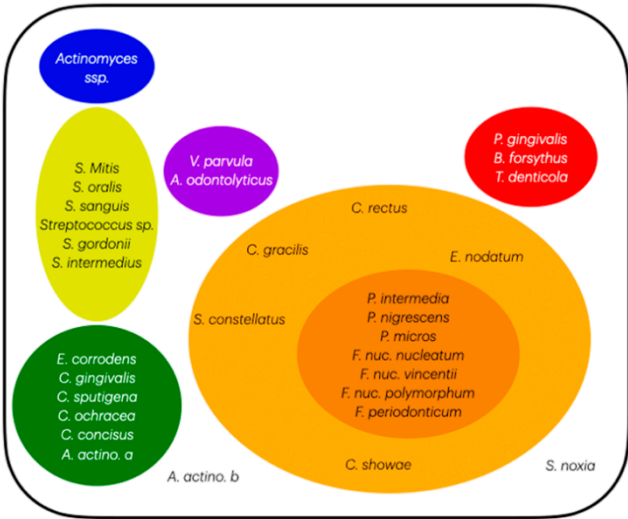


Figure 1. Socransky’s complexes with adaptation including the blue complex.

Socransky's bacterial complexes in periodontics are essential for understanding the microbial composition associated with oral health and periodontal disease through a framework that categorizes the periodontal bacteria into different complexes based on their pathogenicity. Then, according to Socransky et al. [6], microorganisms inhabiting the oral cavity consisted of 5 major complexes devised by the severity of each microorganism. Although this research established a profound understanding and framework of the microorganisms related to periodontal diseases, this information is outdated. It poses a vital need to update the microorganisms associated with developing periodontal and peri-implant diseases. In addition, since the article was presented in 1998 [6], there has been no robust collective article suggesting the identification and updates of newly found bacteria that have been recognized through more recent research.

Identifying specific microorganisms within one’s subgingival microbiome has been crucial in understanding the pathogenesis of periodontal and peri-implant diseases. Similar to periodontitis’ effect on natural teeth, peri-implant diseases affect the tissues around a dental implant; peri-implant mucositis affects only the soft tissue, whereas hard and soft tissues are affected in peri-implantitis [9,10]. Moreover, these insights about microorganisms have driven the development of diagnostic tools, influenced treatment protocols, and informed preventive strategies. On the same hand, peri-implant disease development has been, currently, broadly relevant regarding understanding the relationship between one’s oral microbiome and disease onset and progression. In a recent study analyzing the prevalence of pre-peri-implantitis and peri-implantitis, the authors determined that 31.3% of the patients had pre-peri-implantitis at the patient level and 56.6% had peri-implantitis. At the implant level, 31.7% were affected by pre-peri-implantitis and 27.9% by peri-implantitis [11]. The results indicate that a significant number of both patients and implants were affected by early and advanced inflammation around the dental implants.

The development of peri-implantitis leads the patient to poor clinical outcomes, such as bleeding on probing (BoP), progressive marginal bone loss (MBL), purulent secretion, exacerbated bone remodeling, and, in severe cases, the need for explantation as a last resort available [12]. As a result, understanding the relevant microorganisms present in periodontal/peri-implant diseases is a key factor for prevention and treatment; likewise, understanding the pathogenesis of the disease is vital for understanding dysbiosis, homeostasis, allostasis, and when the relationship between microbiota and host becomes detrimental to the host [13].

Thus, the goal of this review was to identify newly discovered bacteria from individuals with periodontal/peri-implant diseases, organizing them in new clusters (GF-MoR complexes) to update Socransky’s complexes. This aim is essential in advancing the knowledge regarding periodontal/peri-implant diseases [14,15] to help clinicians identify bacterial clusters correlated to the disease’s

specificity. Mapping and identifying bacteria in the oral cavity enable professionals to understand infections better and create personalized treatment plans; additionally, since oral bacteria can be linked to systemic health issues [16,17], knowing the specific species can help clinicians anticipate potential systemic diseases in patients and refer them to the appropriate specialists.

2. Materials and Methods

This review deployed a systematic methodology to organize the findings better and keep the results transparent. The focus question was developed based on the PCC (Population, Concept, Context) strategy: “In patients with periodontal and/or peri-implant disease, what bacteria (microorganisms) were detected through laboratory assays?”

2.1. Search Strategy

The bibliographic search used three electronic databases: PubMed/MEDLINE, PubMed Central, and Embase. The search key terms with the relative Boolean markers (AND, OR) were: (1) bacteria, (2) microbiome, (3) microorganisms, (4) biofilm, (5) niche, (6) native bacteria, (7) gingivitis, (8) periodontitis, (9) peri-implant mucositis, and (10) peri-implantitis. In addition, the search was restricted to the period 1998–2024 (1998, because it was the publication date of the last complexes [Socransky's complexes]) and English language articles.

2.2. Study Selection and Eligibility Criteria

Two investigators (G.M. and W.R.) independently followed the search and selection of studies, and a third author (G.V.O.F) collaborated in case of disagreement regarding the selection of articles. The inclusion criteria were: (1) human studies, (2) patients aging over 18 years, (3) clinical trials, randomized controlled clinical trials, comparative studies, case-control studies, cross-sectional studies, and cohort studies, (4) articles aiming to evaluate the microorganisms in the oral cavity and correlate them with the diagnosis, (5) articles published between 1998 and 2024, and (6) publications in the English language. The exclusion criteria were: (1) studies involving *animals* or only *in vitro* part, (2) reviews, letters to the editor, and case reports, (3) lack of information about the bacteria and diagnosis found.

2.3. Data Extraction

All the information reported that matched this study's goal was retrieved. Two authors (G.M. and W.R.) performed this step; a third author (G.V.O.F.) was consulted in case of disagreement. Specifically, all the bacteria groups in the oral cavity obtained/found were retrieved.

2.4. Socransky's Complexes

Figure 1 shows the complexes published in 1998 [6]. Socransky's blue complex is an adaptation for better organization; originally, five complexes were described: green, purple, yellow, orange, and red. The red complex plays a significant role in the pathogenesis of periodontal diseases such as gingivitis and periodontitis and is known for its association with severe periodontitis, includes *Bacteroides forsythus* (*Tannerella forsythia*), *Porphyromonas gingivalis*, and *Treponema denticola* [18–20]; this red complex is strictly correlated with periodontally-diseased sites and is the most common bacteria, key pathogens, in periodontal disease progression [18,20]. The presence of these pathogens is associated with dysbiotic changes in the oral microbiome, which can lead to increased inflammation and tissue destruction [18,21,22].

The other complexes, such as the orange complex, are linked to dysbiosis of the native microbiota and the development of gingivitis and later periodontitis [23,24]. The orange complex is considered the precedent of the red complex for colonization and proliferation. It consists of *Fusobacterium nucleatum*, *Prevotella intermedia*, *Prevotella nigrescens*, *Peptostreptococcus micros* [8,25], *Streptococcus constellatus*, *Eubacterium nodatum*, *Campylobacter showae*, *Campylobacter gracilis*, and *Campylobacter rectus*. The yellow complex comprises several streptococcus species: *Streptococcus*

sanguis, *Streptococcus oralis*, *Streptococcus mitis*, *Streptococcus gordonii*, and *Streptococcus intermedius*. The green complex included three *Capnocytophaga spp.*, *Campylobacter concisus*, *Eikenella corrodens*, and *Aggregatibacter actinomycetemcomitans (serotype a)*. The fifth complex (purple) incorporates *Veillonella parvula* and *Actinomyces odontolyticus*, whereas the blue complex (adaptation of the article for a better organization) included *Actinomyces spp.*

2.5. GF-MoR’s Complexes Organization

The bacteria retrieved from each included study and associated with disease/condition were registered for the GF-MoR group development. The GF-MoR complexes were based on the disease/condition, permitting to gather bacteria in six groups: (1) Health, (2) Gingivitis, (3) Peri-implant mucositis, (4) Periodontitis, (5) Peri-implantitis, and (6) Necrotizing and Molar-Incisor (M-O) pattern periodontitis (Figure 3). The percentual found refers to the number of times a specific bacterium was associated with a particular disease; hence, a percentual number was calculated to sort them from the most common to the least identified bacteria. It is worth reporting that bacteria from the healthy conditions can be present in any other complex and vice-versa, even though the bacterium was not perceptually found in the included studies.

3. Results

A total of 381 articles were found. Therefore, after screening by title and abstract and removing duplicates, 162 articles were eligible for full-text reading (k=0.92). In this step, nine articles were excluded: six due to a lack of information and three because of availability. Hence, 153 articles were included (k=0.98) (Figure 2, Table 1).

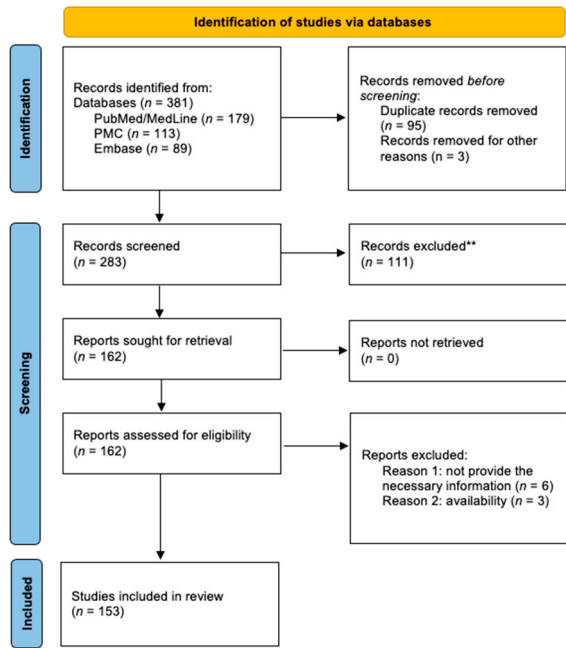


Figure 2. Flowchart for screening and selection of studies.

Table 1. List of articles included.

COD E	Study (Title, Authors, Journal, Year of publication, doi)	
	<u>Effects of a stabilized stannous fluoride dentifrice on clinical, immunomodulatory, and microbial outcomes in a human experimental gingivitis model.</u>	
7	Fine N, Barbour A, Kaura K, Kerns KA, Chen D, Trivedi HM, Gomez J, Sabharwal A, McLean JS, Darveau RP, Glogauer M. J Periodontol. 2024;95(5):421-431. doi: 10.1002/JPER.22-0710	

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- 8 Omega-3 nanoemulgel in prevention of radiation-induced oral mucositis and its associated effect on microbiome: a randomized clinical trial.
Morsy BM, El Domiaty S, Meheissen MAM, Heikal LA, Meheissen MA, Aly NM. BMC Oral Health. 2023;23(1):612. doi: 10.1186/s12903-023-03276-5
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- 10 Effect of scaling and root planing with and without minocycline HCl microspheres on periodontal pathogens and clinical outcomes: A randomized clinical trial.
Arnett MC, Chanthavisouk P, Costalonga M, Blue CM, Evans MD, Paulson DR. J Periodontol. 2023;94(9):1133-1145. doi: 10.1002/JPER.23-0002
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- 11 Effect of laser-assisted reconstructive surgical therapy of peri-implantitis on protein biomarkers and bacterial load.
Di Gianfilippo R, Wang CW, Xie Y, Kinney J, Sugai J, Giannobile WV, Wang HL. Clin Oral Implants Res. 2023;34(4):393-403. doi: 10.1111/clr.14059
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- 12 A Placebo-Controlled Trial to Evaluate Two Locally Delivered Antibiotic Gels (Piperacillin Plus Tazobactam vs. Doxycycline) in Stage III-IV Periodontitis Patients.
Ilyes I, Rusu D, Rădulescu V, Vela O, Boariu MI, Roman A, Surlin P, Kardaras G, Boia S, Chinnici S, Jentsch HFR, Stratul SI. Medicina (Kaunas). 2023;59(2):303. doi: 10.3390/medicina59020303
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- 15 Clinical Evaluation of Diode Laser-Assisted Surgical Periodontal Therapy: A Randomized Split-Mouth Clinical Trial and Bacteriological Study.
Doğan ŞB, Akça G. Photobiomodul Photomed Laser Surg. 2022;40(9):646-655. doi: 10.1089/photob.2022.0035
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- 17 Different scaling and root planing strategies in Turkish patients with aggressive periodontitis: A randomized controlled clinical trial.
Mamaklioğlu D, Karched M, Kuru L, Kuru B, Asikainen S, Doğan B. Int J Dent Hyg. 2022;20(2):347-363. doi: 10.1111/idh.12592
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- 19 Chemomechanical preparation influences the microbial community and the levels of LPS, LTA and cytokines in combined endodontic-periodontal lesions: A clinical study.
Gomes BPFA, Berber VB, Marinho ACS, Louzada LM, Arruda-Vasconcelos R, Passini MRZ, Lopes EM, Pecorari VGA, Chen T, Paster BJ. J Periodontal Res. 2022;57(2):341-356. doi: 10.1111/jre.12964
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- 21 The microbiome of dental and peri-implant subgingival plaque during peri-implant mucositis therapy: A randomized clinical trial.
Philip J, Buijs MJ, Pappalardo VY, Crielaard W, Brandt BW, Zaura E. J Clin Periodontol. 2022;49(1):28-38. doi: 10.1111/jcpe.13566
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- 25 Evaluation of different materials used for sealing of implant abutment access channel and the peri-implant sulcus microbiota: A 6-month, randomized controlled trial.
Rubino CV, Katz BG, Langlois K, Wang HH, Carrion JA, Walker SG, Collier JL, Iacono VJ, Myneni SR. Clin Oral Implants Res. 2021;32(8):941-950. doi: 10.1111/clr.13787
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- 28 Effectiveness of single versus multiple sessions of photodynamic therapy as adjunct to scaling and root planing on periodontopathogenic bacteria in patients with periodontitis.
Muzaheed, Acharya S, Hakami AR, Allemailem KS, Alqahtani K, Al Saffan A, Aldakheel FM, Divakar DD. Photodiagnosis Photodyn Ther. 2020;32:102035. doi: 10.1016/j.pdpdt.2020.102035
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- 29 Effects on clinical outcomes of adjunctive moxifloxacin versus amoxicillin plus metronidazole in periodontitis patients harboring Aggregatibacter actinomycetemcomitans, Porphyromonas gingivalis, and Tannerella forsythia: exploratory analyses from a clinical trial.

- Ardila CM, Hernández-Casas C, Bedoya-García JA. Quint Int. 2021;52(1):20-29. doi: 10.3290/j.qi.a44927
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- 34 Clinical and microbiological effect of frequent subgingival air polishing on periodontal conditions: a split-mouth randomized controlled trial.
Sekino S, Ogawa T, Murakashi E, Ito H, Numabe Y. Odontology. 2020;108(4):688-696. doi: 10.1007/s10266-020-00493-0
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- 39 Clinical and Microbiological Evaluation of Surgical and Nonsurgical Treatment of Aggressive Periodontitis.
Cirino CCDS, Vale HFD, Casati MZ, Sallum EA, Casarin RCV, Sallum AW. Braz Dent J. 2019;30(6):577-586. doi: 10.1590/0103-6440201902930
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- 41 Clinical and microbiological outcomes of photodynamic and systemic antimicrobial therapy in smokers with peri-implant inflammation.
Deeb MA, Alsahhaf A, Mubarak SA, Alhamoudi N, Al-Aali KA, Abduljabbar T. Photodiagnosis Photodyn Ther. 2020;29:101587. doi: 10.1016/j.pdpdt.2019.101587
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- 43 Short-term effects of hyaluronic acid on the subgingival microbiome in peri-implantitis: A randomized controlled clinical trial.
Soriano-Lerma A, Magán-Fernández A, Gijón J, Sánchez-Fernández E, Soriano M, García-Salcedo JA, Mesa F. J Periodontol. 2020;91(6):734-745. doi: 10.1002/JPER.19-0184
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Reinhardt B, Klocke A, Neering SH, Selbach S, Peters U, Flemmig TF, Beikler T. Clin Oral Investig. 2019;23(10):3905-3914. doi: 10.1007/s00784-019-02821-3
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- 47 Periodontal condition in Japanese coronary heart disease patients: A comparison between coronary and non-coronary heart diseases.
Aoyama N, Kobayashi N, Hanatani T, Ashigaki N, Yoshida A, Shiheido Y, Sato H, Takamura C, Yoshikawa S, Matsuo K, Izumi Y, Isobe M. J Periodontal Res. 2019;54(3):259-265. doi: 10.1111/jre.12626
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- 48 Impact of dental cement on the peri-implant biofilm-microbial comparison of two different cements in an in vivo observational study.
Korsch M, Marten SM, Walther W, Vital M, Pieper DH, Dötsch A. Clin Implant Dent Relat Res. 2018;20(5):806-813. doi: 10.1111/cid.12650
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Wang H, Ai L, Zhang Y, Cheng J, Yu H, Li C, Zhang D, Pan Y, Lin L. Biomed Res Int. 2018;2018:1805793. doi: 10.1155/2018/1805793
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- 51 What is the influence of tonsillectomy on the level of periodontal pathogens on the tongue dorsum and in periodontal pockets.
Diener VN, Gay A, Soyka MB, Attin T, Schmidlin PR, Sahrman P. BMC Oral Health. 2018;18(1):62. doi: 10.1186/s12903-018-0521-7
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- 52 Diamond burs versus curettes in root planing: a randomized clinical trial.
Türktekin F, Buduneli N, Lappin DF, Türk T, Buduneli E. Aust Dent J. 2018;63(2):242-252. doi: 10.1111/adj.12602
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Gao X, Zhou J, Sun X, Li X, Zhou Y. Medicine (Baltimore). 2018;97(5):e9774. doi: 10.1097/MD.0000000000009774
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- 54 Clinical and microbiological evaluation of the effect of Lactobacillus reuteri in the treatment of mucositis and peri-implantitis: A triple-blind randomized clinical trial.
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Tada H, Masaki C, Tsuka S, Mukaibo T, Kondo Y, Hosokawa R. J Prosthodont Res. 2018;62(1):89-96. doi: 10.1016/j.jpor.2017.06.006
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Stokman MA, van Winkelhoff AJ, Vissink A, Spijkervet FK, Raghoobar GM. Clin Oral Investig. 2017;21(2):717-724. doi: 10.1007/s00784-016-1941-x
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Öztürk VÖ, Emingil G, Bostanci N, Belibasakis GN. Clin Oral Implants Res. 2017;28(9):e111-e120. doi: 10.1111/clr.12937
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Seymour GJ, Palmer JE, Leishman SJ, Do HL, Westerman B, Carle AD, Faddy MJ, West MJ, Cullinan MP. J Periodontal Res. 2017;52(1):61-73. doi: 10.1111/jre.12369
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Corrêa MG, Oliveira DH, Saraceni CH, Ribeiro FV, Pimentel SP, Cirano FR, Casarin RC. Lasers Surg Med. 2016;48(10):944-950. doi: 10.1002/lsm.22449
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Most of the studies reported results for Health, Periodontitis, and Peri-implantitis conditions (3 out of 6 GF-MoR clusters) (Figure 3); this fact limited the number of bacteria found in the other groups. Therefore, it is essential to understand that bacterial colonization is a dynamic process; bacteria present in one group can also be present in another or others, such as observed with the bacteria found in all groups (*Porphyromonas gingivalis*, *Tannarella forsythia*, *Treponema denticola*, and *Aggregatibacter actinomycetemcomitans*) (GF-MoR's red Triangle), independent of the condition (Figure 4); the second most observed bacteria were *Porphyromonas spp.*, *Prevotella spp.*, and *Treponema spp.*, present in 5 of the 6 GF-MoR groups (GF-MoR's blue Triangle). The third most detected bacteria were clustered in the grey Polygon (GF-MoR's Polygon) (*Fusobacterium nucleatum*, *Prevotella intermedia*, *Campylobacter rectus*, and *Eikenella corrodens*). These three geometric shapes, but not limited to them, have the most relevant bacteria for periodontal and peri-implant diseases.

3.1. Clusters and the Seven Most Relevant Bacteria per Group

In the Health cluster (Cluster 1), 36 gram-negative bacteria and 22 gram-positive were found (totaling 58 species); the top seven most often bacteria found in this group were all gram-negative: 1. *Campylobacter rectus* (5.56%), 2. *Porphyromonas gingivalis* (5.56%), 3. *Prevotella intermedia* (5.56%), 4. *Tannarella forsythia* (5.56%), 5. *Bacteroidales* spp. (3.33%), 6. *Leptotrichia* spp. (3.33%), and 7. *Porphyromonas* spp. (3.33%).

In Gingivitis (Cluster 2), 16 bacteria were retrieved, all of them gram-negative bacteria. The seven more relevant were: 1. *Prevotella* spp. (25%), 2. *Treponema* spp. (9.38%), 3. *Aggregatibacter actinomycetemcomitans* (6.25%), 4. *Fusobacterium* spp. (6.25%), 5. *Porphyromonas gingivalis* (6.25%), 6. *Porphyromonas* spp. (6.25%), and 7. *Selenomonas* spp. (6.25%).

In the Peri-implant mucositis cluster (Cluster 3), 17 bacteria were detected (3 gram-positive and 14 gram-negative). The seven most significant bacteria (all gram-negative) were: 1. *Prevotella* spp. (12%), 2. *Treponema denticola* (12%), 3. *Tannarella forsythia* (12%), 4. *Aggregatibacter actinomycetemcomitans* (8%), 5. *Fusobacterium nucleatum* (8%), 6. *Porphyromonas gingivalis* (8%), and 7. *Prevotella intermedia* (8%).

In the Periodontitis group (Cluster 4), 54 gram-negative and 47 gram-positive bacteria composed it, totaling 101 different bacteria. Again, the seven most significant bacteria were all gram-negative: 1. *Porphyromonas gingivalis* (11.12%), 2. *Aggregatibacter actinomycetemcomitans* (10.3%), 3. *Tannerella forsythia* (8.43%), 4. *Prevotella intermedia* (7.61%), 5. *Fusobacterium nucleatum* (7.14%), 6. *Treponema denticola* (6.44%), and 7. *Campylobacter rectus* (3.4%).

In Peri-implantitis (Cluster 5), 34 gram-negative and 27 gram-positive bacteria were gathered in this group (61 bacteria). The seven most significant bacteria were all gram-negative and the same as the Periodontitis group, presenting a similar standard of bacteria: 1. *Fusobacterium nucleatum* (9.38%), 2. *Tannarella forsythia* (7.81%), 3. *Porphyromonas gingivalis* (7.29%), 4. *Aggregatibacter actinomycetemcomitans* (6.25%), 5. *Prevotella intermedia* (6.25%), 6. *Treponema denticola* (6.25%), and 7. *Campylobacter rectus* (3.65%).

The last cluster is a combination of Necrotizing diseases and molar-incisor (M-I) pattern Periodontitis (Cluster 6); the seven most important were: 1. *Aggregatibacter actinomycetemcomitans* (29.17%), 2. *Porphyromonas gingivalis* (29.17%), 3. *Tannarella forsythia* (16.67%), 4. *Treponema denticola* (8.33%), 5. *Treponema forsythensis* (8.33%), 6. *Escherichia coli* (4.17%), and 7. *Prevotella intermedia* (4.17%).

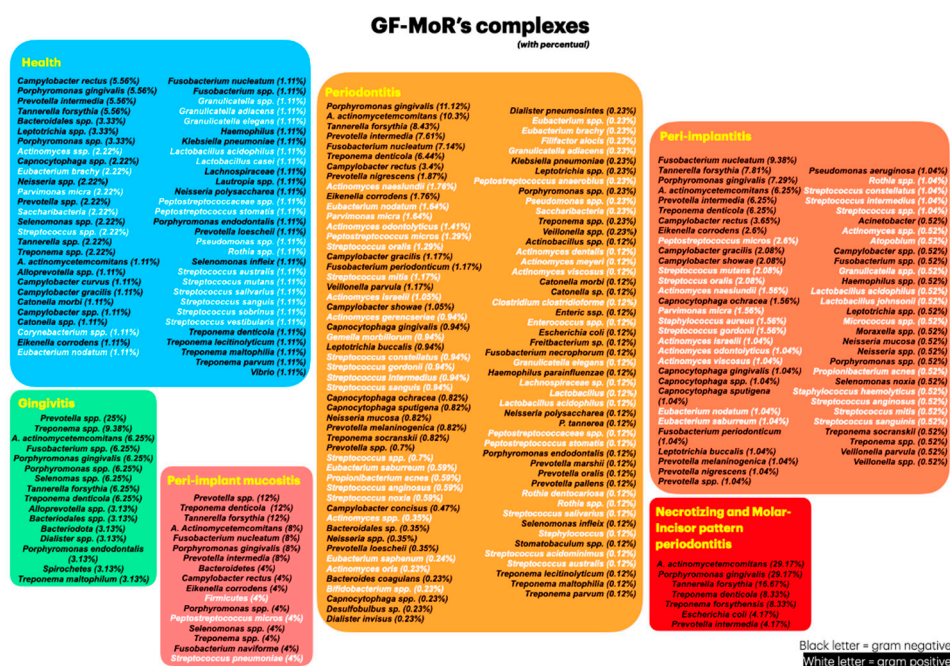


Figure 3. Bacterial organization according to the percentage of citations per condition.

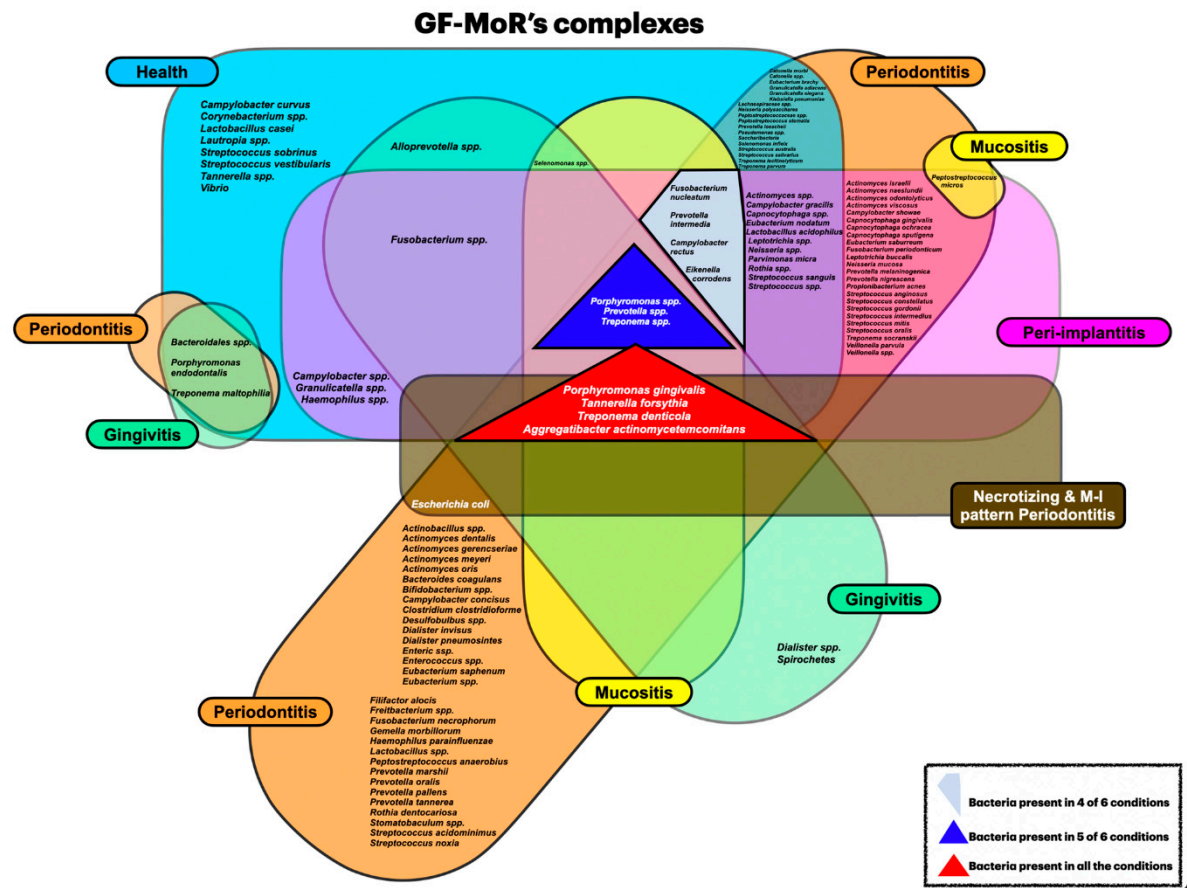


Figure 4. GF-MoR's complexes are organized according to the bacteria's presence in different clusters. (Blue = Healthy condition; Green = Gingivitis; Yellow = Peri-implant mucositis; Orange = Periodontitis; Brown = Necrotizing and M-I pattern Periodontitis; Purple = Peri-implantitis).Socransky's complexes and GF-MoR's complexes.

Socransky et al. [6] did not gather bacteria strictly according to the diseases and condition found as it is being presented in the present study; the authors studied subgingival bacteria in healthy patients and patients with periodontitis. Moreover, they observed the results of community ordination using correspondence analysis, which reinforced the relationships and showed the relationships among the different microbial complexes. All bacteria detected by Socransky et al.'s study were also found and retrieved from the literature published after Socransky et al.'s study. They compound the GF-MoR's groups divided by diseases and conditions, which received many other bacteria.

The Socransky's red complex (*P. gingivalis*, *B. forsythus*, and *T. denticola*), which is wholly part of the GF-MoR's red Triangle, was closely associated with the orange complex (*F. nucleatum*, *P. intermedia*, *P. nigrescens*, *P. micros*, *E. nodatum*, and *S. constellatus*, and *Campylobacter spp.*); *F. nucleatum*, *P. intermedia*, and *Campylobacter rectus* were included in the GF-MoR's grey Polygon (the third most relevant GF-MoR group). In Socransky et al.'s article, the authors also showed the relationships among the *Capnocytophaga spp.*, most of the *Streptococcus spp.* (Socransky's yellow complex), and *E. corrodens* (present in the GF-MoR's Polygon) and *C. concisus* (green complex) were closely related and somewhat associated with the orange complex. The relationship between *A. odontolyticus* and *V. parvula* (Socransky's purple complex) was confirmed by cluster and correspondence analysis [6]; both were also found in the intersection for the GF-MoR's Periodontitis and Peri-implantitis groups. Furthermore, the authors reinforced the distinction between the Socransky's red and orange clusters and the separation of these two groups from the Socransky's green and yellow complexes (Figure 5).

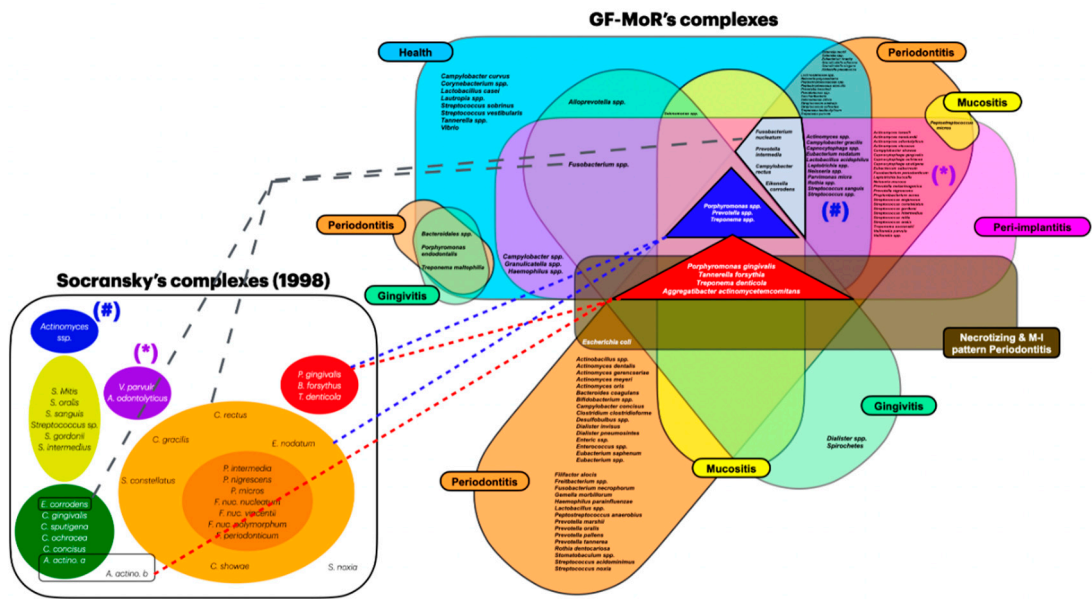


Figure 5. Bacteria allocation in Socransky's and GF-MoR's complexes. ([#] Socransky's blue complex is an adaptation for better organization; originally, five complexes were described: green, purple, yellow, orange, and red).DISCUSSION.

This review aimed to identify newly discovered bacteria from individuals with periodontal/peri-implant diseases and conditions, which were clustered in updated new complexes (GF-MoR complexes). Socransky's complexes, introduced in 1998 [6], categorized oral bacteria based on the subgingival sites of periodontal disease (periodontitis) and healthy conditions, including patients with and without periodontitis. The present study compromised not only periodontitis and health but also gingivitis, peri-implant mucositis, and peri-implantitis.

Thus, knowing the types of bacteria in the periodontal and peri-implant conditions aids clinicians in determining the stage of the disease and choosing the most effective treatment. Understanding the bacteria linked to healthy condition, gingivitis, peri-implant mucositis, and more advanced conditions such as periodontitis and peri-implantitis can help for a more accurate diagnosis and treatment planning, especially in cases where there is a fine line/borderline between conditions as gingivitis and early-stage periodontitis. In addition, verifying whether newly identified bacteria are symbiotic with other bacteria can increase the knowledge of biofilm formation, bacterial community/relationship, structure, and resilience. This insight can help develop strategies to disrupt harmful biofilms and promote a healthy oral microbiome.

Socransky's complexes [6] were pivotal in understanding the microbial dynamics contributing to the Periodontitis conditions. The red, orange, yellow, green, and purple complexes were identified, each with specific bacterial species that exhibit varying pathogenic potentials. Socransky's yellow, green, and adapted blue complexes, including *Streptococcus mitis* and *Actinomyces spp.*, are generally associated with periodontal health; compared, GF-MoR health group has presented a higher number of bacteria. However, their role in the context of disease is complex, as they can also be found in diseased sites, as observed in GF-MoR's complexes, albeit in lower proportions compared to red and orange complex bacteria [26,27]. The presence of these complexes may indicate an attempt by the host to restore a healthy microbial balance, but their efficacy in preventing disease progression remains uncertain.

Socransky's orange complex, particularly *Fusobacterium nucleatum* (a member of the GF-MoR's grey Polygon), is frequently identified in periodontal and peri-implant diseases. This bacterium acts as a bridge between early colonizers and late colonizers, promoting the establishment of pathogenic communities [28,29]. Furthermore, studies have shown that the microbial diversity in peri-implantitis is significantly higher than in healthy implants, with a predominance of gram-negative anaerobic

bacteria [30,31]. This shift in microbial composition is critical for understanding the pathogenesis of peri-implantitis and highlights the importance of maintaining oral hygiene to prevent dysbiosis.

A relevant bacteria associated with peri-implantitis, aggressive and necrotizing periodontitis is *Aggregatibacter actinomycetemcomitans* (A.a.) (Socransky's green complex; GF-MoR's red Triangle) and *Campylobacter rectus* (Socransky's orange complex; GF-MoR's grey Polygon), which are also found in periodontal disease [32–34]. Aggressive forms of periodontitis present with a phenotypic molar-incisor pattern, initiated by A.a., and form concomitants with disease of endodontic origin. In GF-MoR's complexes, A.a. received a higher level of importance than in Socransky's complexes due to its presence in all the groups, the majority in the Necrotizing and M-I pattern Periodontitis (29.17%). Detecting these bacteria in peri-implant or periodontal sites underscores the need to monitor microbial profiles in patients with dental implants or periodontitis. The absence of treatment for any of the diseases studied allows the effects of the disease to progress in a non-linear and accelerating pattern.

The most relevant of the Socransky's complexes, the red complex, includes *Porphyromonas gingivalis*, *Tannerella forsythia*, and *Treponema denticola*, which match with GF-MoR's red Triangle; these bacteria also were present in all GF-MoR's groups summed to A.a. Then, it is possible to affirm that Socransky's red complex and GF-MoR's red Triangle are strongly associated with periodontal and peri-implant disease progression [32,35,36].

3.2. Periodontal and Peri-Implant Diseases and Conditions

Numerous studies have proven that certain species of bacteria play a role in different stages of periodontal disease, from mild gingivitis to advanced periodontitis. Likewise, one study introduced a visual design for clinicians and researchers to easily understand the advancement of a stable, subgingival, pathogenic bacterial colony in periodontal disease [6]. The most virulent and destructive pathogens (*P. gingivalis*, *T. forsythia*, *T. denticola* - Socransky's red complex, and GF-MoR's red Triangle that included also A.a.), with a recent study that reported the importance of *Parvimonas micra* and *Filifactor alocis* as indicative of severe inflammation [37], showed that the "Red complex" has high-risk initiators of intracellular damage during the late stages of periodontal tissue damage. In parallel, with the higher level of those bacteria, there is a substantial decrease in the representation of the strains *Streptococcus sanguinis* (*sanguis*), *Rothia dentocariosa*, *Veillonella parvula*, *Capnocytophaga sputigena*, and *Prevotella intermedia* in the periodontitis pockets relative to the healthy sulcus [37].

Plaque-induced gingivitis is often considered a precursor to periodontitis, but it is not always followed. Studies indicate that bacterial community diversity increases in gingival fluid from individuals experiencing gingival bleeding, a most relevant and common symptom of gingivitis [31,38]. This increase in diversity is linked to the presence of pathogenic bacteria, which disrupt the homeostatic balance of the oral microbiome. The dysbiotic state fosters an environment conducive to inflammation as the immune system responds to the heightened bacterial load [21,31]. Furthermore, the inflammatory response is mediated by various cytokines, including interleukin-1 β , which has been shown to correlate with clinical signs of gingival inflammation [17,21,31].

Periodontitis represents a more advanced stage of periodontal disease, where the inflammatory response leads to the destruction of periodontal tissues, causing attachment loss [17]. It may be multifactorial, but clinicians and researchers can centralize this disease to disrupt the dynamic, symbiotic relationships of the microflora, allowing certain pathogenic species to prosper and thrive. Such disruptions include significant changes in pH or diet, interactions between bacteria, the absence of mechanical forces from mastication and brushing, and several others [39]. Furthermore, research has proven that specific intrinsic and extrinsic factors interact with particular pathogenic bacteria, which can be further discussed. The role of specific bacteria in the etiology of periodontitis has already been well-documented, with *P. gingivalis* being a prominent pathogen due to its virulence factors that facilitate immune evasion and tissue destruction [21,40].

Peri-implant mucositis and peri-implantitis also involve dysbiotic microbial communities similar to those observed in periodontal diseases. Peri-implant mucositis is characterized by inflammation of the mucosal tissues surrounding the implant, often seen in patients with dental

implants. The microbial profile in peri-implantitis has been shown to include members of Socransky's red complex, also members of the GF-MoR's red Triangle, indicating a shared pathogenic mechanism with periodontitis [18,22]. These bacteria can lead to a mucosal barrier breakdown, facilitating further bacterial invasion and inflammation [40,42]. The interplay between the host immune response and the microbial community is critical in determining the outcome of these conditions.

Multiple bacterial species interact synergistically to highlight polymicrobial nature, exacerbating the inflammatory response and contributing to disease progression [18,41]. This complexity underscores the need for a multifaceted approach to treatment, targeting both the microbial community and the host's immune response. The concept of polymicrobial synergy and dysbiosis (PSD) provides a framework for understanding the interactions between different bacterial species in periodontal diseases. This model suggests that the presence of certain bacteria can enhance the pathogenic potential of others, leading to a more severe inflammatory response [8,18]. This fact justifies the importance of Socransky's and GF-MoR's complexes. For instance, the co-occurrence of *P. gingivalis* with other bacteria can amplify the inflammatory response, resulting in more significant tissue destruction [18,41]; for example, bacteria from Socransky's red complex (also present in the GF-MoR's red Triangle), when associated with bacteria from Socransky's orange complex (present in the GF-MoR's grey Polygon), which includes species such as *Fusobacterium nucleatum* and *Prevotella intermedia*, they will play a significant role in the progression of periodontal diseases. These bacteria often co-aggregate with members of the red complex, facilitating their colonization and enhancing pathogenicity [32,43,44]. This highlights the importance of considering the entire microbial community rather than focusing on individual pathogens when studying periodontal and peri-implant diseases.

3.3. Modifiers

Multiple cross-sectional and longitudinal studies have demonstrated that probing pocket depth (PD), clinical attachment loss (CAL), and alveolar bone loss are more prevalent and severe in patients who have uncontrolled diabetes, smoke, or other systemic diseases that can be linked with the pathogenic bacteria of periodontal/peri-implant disease. For smokers, both *in vitro* and *in vivo* studies have proven that smoking can defect chemotaxis and phagocytosis of neutrophils in the periodontium, leading to impaired clearance of bacteria and increasing their colonization [45,46]. Furthermore, smoking inversely correlates with the levels of serum IgG antibodies, particularly for some periodontal pathogens [47,48]. Periodontal/peri-implant pathogens such as *P. gingivalis*, *C. rectus*, and *P. nigrescens* thrive in smokers after adjusting important confounding factors [49].

For patients with uncontrolled diabetes, both Type 1 and Type 2 are associated with elevated levels of systemic markers of inflammation, many of which are found in periodontal and peri-implant diseases as well. Periodontal/peri-implant treatment lowering one's HbA1c has been proven to decrease this ongoing inflammatory response in serum and periodontal tissues, respectively. Hence, accentuating the mutual impact of treatment of each disease, and lack thereof, affects the control of the other. Moreover, one study recovering periodontal pathogens in diabetic and non-diabetic patients found that significantly more individuals with diabetes harbored *P. gingivalis* [50], further outlining the relationship between the two diseases.

Finally, it must not overlook the impact that periodontal/peri-implant diseases and certain systemic diseases have on one another. Examples include cardiovascular disease, gastrointestinal, and colorectal cancer, Alzheimer's disease, and adverse pregnancy outcomes. One study can link many of these systemic diseases with the pathogens of oral disease as well as their metabolic by-products; however, the evidence that there is a mechanism that demonstrates a "cause and effect" relationship has yet to be identified. Furthermore, recent advancements in microbiome research have utilized metagenomic analyses to explore the complex interactions within the oral microbiota. These studies revealed that the microbial composition in individuals with periodontal disease is markedly different from that of healthy individuals [51–53], with specific bacterial taxa associated with disease severity [18,41]. Identifying these microbial signatures can aid in developing targeted therapeutic

strategies, such as probiotics or antimicrobial treatments [54,55], to restore a healthy microbial balance and mitigate inflammation [18,36].

3.4. Limitations of the Study

One significant limitation was that the majority of the studies reported results for Health, Periodontitis, and Peri-implantitis (mainly for the two lasts), limiting the number of bacteria detected in the other clusters (Gingivitis, Mucositis, and Necrotizing and M-I pattern Periodontitis). Moreover, this review used a systematic methodology to standardize the articles' inclusion; therefore, it is recommended that all data presented must be carefully analyzed. In addition, this review did not intend to retrieve and compare techniques used for bacterial analysis, limiting our data for the types of bacteria.

4. Conclusions

Within the limitation of this study and for the first time in the literature, GF-MoR's complexes are presented, gathering the bacteria according to the condition found and including more bacteria than Socransky's complexes. On this understanding, this study can drive future research into treatment options for periodontal and peri-implant diseases, guiding future studies and collaborating to prevent and worsen systemic conditions. Moreover, it permits the debate about the evolution of the bacterial clusters correlated to periodontal and peri-implant diseases and conditions.

Authors' contributions: GVOF, GM, WR, AD, BGSM, JCHF were responsible for the conceptualization and design of the project. GVOF, GM, WR were responsible for the data collection. GVOF, GM, WR, AD, BGSM, JCHF were responsible for the analysis and interpretation of data. GVOF, GM, WR, AD, BGSM, JCHF participated in the investigation, data curation, drafted the manuscript, and made contributions to the revising of the manuscript. All authors read and approved the final manuscript submitted.

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Data Availability Statement: The data used to generate and support this study's findings are available from the corresponding author upon request.

Conflicts of Interest: The authors declare that they have no competing interests.

(All references used in this article [n=153], found in Table 1, should be included in the references of this review.)

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