Primordial and primary prevention of peri-implant diseases: A systematic review and meta-analysis

Maria Clotilde Carra, Nicolas Blanc-sylvestre, Alexandre Courtet, Philippe Bouchard

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SYSTEMATIC REVIEW

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Primordial and primary prevention of peri-implant diseases: A systematic review and meta-analysis

Maria Clotilde Carra[1,2,3] | Nicolas Blanc-Sylvestre[1,2,4] | Alexandre Courtet[1,2] | Philippe Bouchard[1,4]

[1]U.F.R. d'Odontologie, Université Paris Cité, Paris, France

[2]Service of Odontology, Periodontal and Oral Surgery Unit, Rothschild Hospital (AP-HP), Paris, France

[3]Population-Based Epidemiologic Cohorts Unit, Inserm, UMS 11, Villejuif, France

[4]URP 2496, Université Paris Cité, Paris, France

Correspondence
Maria Clotilde Carra and Philippe Bouchard, Department of Periodontology, Université Paris Cité. Service of Odontology of the Rothschild University Hospital, AP-HP, 5, rue Santerre, 75012 Paris, France.
Email: mclotildecarra@gmail.com and philippe.bouchard.perio@gmail.com

Abstract

Aim: This systematic review and meta-analysis aims to assess the efficacy of risk factor control to prevent the occurrence of peri-implant diseases (PIDs) in adult patients awaiting dental implant rehabilitation (primordial prevention) or in patients with dental implants surrounded by healthy peri-implant tissues (primary prevention).

Materials and Methods: A literature search was performed without any time limit on different databases up to August 2022. Interventional and observational studies with at least 6 months of follow-up were considered. The occurrence of peri-implant mucositis and/or peri-implantitis was the primary outcome. Pooled data analyses were performed using random effect models according to the type of risk factor and outcome.

Results: Overall, 48 studies were selected. None assessed the efficacy of primordial preventive interventions for PIDs. Indirect evidence on the primary prevention of PID indicated that diabetic patients with dental implants and good glycaemic control have a significantly lower risk of peri-implantitis (odds ratio [OR] = 0.16; 95% confidence interval [CI]: 0.03–0.96; I^2: 0%), and lower marginal bone level (MBL) changes (OR = −0.36 mm; 95% CI: −0.65 to −0.07; I^2: 95%) compared to diabetic patients with poor glycaemic control. Patients attending supportive periodontal/peri-implant care (SPC) regularly have a lower risk of overall PIDs (OR = 0.42; 95% CI: 0.24–0.75; I^2: 57%) and peri-implantitis compared to irregular attendees. The risk of dental implant failure (OR = 3.76; 95% CI: 1.50–9.45; I^2: 0%) appears to be greater under irregular or no SPC than regular SPC. Implants sites with augmented peri-implant keratinized mucosa (PIKM) show lower peri-implant inflammation (SMD = −1.18; 95% CI: −1.85 to −0.51; I^2: 69%) and lower MBL changes (MD = −0.25; 95% CI: −0.45 to −0.05; I^2: 62%) compared to dental implants with PIKM deficiency. Studies on smoking cessation and oral hygiene behaviors were inconclusive.

Conclusions: Within the limitations of available evidence, the present findings indicate that in patients with diabetes, glycaemic control should be promoted to avoid peri-implantitis development. The primary prevention of peri-implantitis should involve regular SPC. PIKM augmentation procedures, where a PIKM deficiency exists,

may favour the control of peri-implant inflammation and the stability of MBL. Further studies are needed to assess the impact of smoking cessation and oral hygiene behaviours, as well as the implementation of standardized primordial and primary prevention protocols for PIDs.

KEYWORDS
dental implants, implant-supported rehabilitation, mucositis, peri-implant diseases, peri-implantitis, prevention, risk factors, risk indicators, survival

Clinical Relevance

Scientific rationale for study: Risk assessment and risk factor control are necessary to prevent the development of peri-implant diseases in patients who are candidates for dental implant(s) (primordial prevention) and in those who have received dental implant(s) and currently have healthy peri-implant tissues (primary prevention).

Principal findings: Risk factor control is necessary to preserve peri-implant health and to avoid PIDs. In patients with diabetes, special attention should be paid to improving glycaemic control. The primary prevention of peri-implantitis should be based upon regular supportive periodontal/peri-implant care. Increasing PIKM where a deficiency exists may be considered to preserve peri-implant health.

Practical implications: Risk factor control should target all modifiable patient-, implant-, and clinician-related risk factors identified for a specific patient, by implementing multiple preventive interventions simultaneously to maintain peri-implant health over time.

1 | INTRODUCTION

Implant-supported restorations are widely employed for the rehabilitation of partial or complete edentulism. Despite favourable dental implant outcomes and long-term survival rates, the occurrence of peri-implant diseases (PIDs) is common and represents a significant disease burden that needs to be addressed with effective preventive interventions (Gurgel et al., 2017; Jepsen et al., 2015).

PIDs include peri-implant mucositis (hereafter referred to as "mucositis" in this review) and peri-implantitis. They are initiated by dysbiotic microbial biofilms on the hard, non-shedding surfaces of the implant-supported restoration, which causes local inflammation at the level of the peri-implant mucosa (i.e., mucositis) and progressively the peri-implant bone (i.e., peri-implantitis) (Renvert et al., 2018; Salvi et al., 2012). However, the aetiology and pathophysiology of PIDs remain under investigation, with several risk factors/indicators advocated as potential contributors to peri-implant tissue breakdown[1] (Fu & Wang, 2020; Schliephake, 2022). These include smoking (Javed et al., 2019; Rinke et al., 2020), diabetes (Chambrone & Palma, 2019; Genco & Borgnakke, 2020; Jiang et al., 2021), periodontitis (Schwarz et al., 2018), limited/lack of provision of supportive peri-implant care (Jepsen et al., 2015), inadequate personal biofilm control (Renvert & Quirynen, 2015), reduced peri-implant keratinized mucosa (PIKM) (Rinke et al., 2020; Sanz et al., 2022; Thoma et al., 2018, 2021), and some characteristics of the implant-supported restoration design (Koutouzis, 2019; Schwarz et al., 2021; Staubli et al., 2017). Furthermore, genetics, stress, diet, and other lifestyle habits may be considered as potential risk factors for PIDs (Loos et al., 2015; Loos & Van Dyke, 2020). The level of risk, as well as the quality of the associated literature, differs significantly depending on the specific factor considered. Current evidence does not allow the identification of "true" risk factors, that is, specific to PIDs, because of the paucity of long-term prospective longitudinal studies evaluating a potential causal relationship between the exposure (the risk factor) and the outcome (peri-implant health/disease). Moreover, in view of the potential continuum of progression from mucositis to peri-implantitis, similar to gingivitis and periodontitis, peri-implant mucositis is considered a predictor of peri-implantitis (Jepsen et al., 2015).

The European Federation of Periodontology (EFP) has been addressing the importance of PID prevention for several years (Jepsen et al., 2015; Tonetti et al., 2015) by listing a series of recommendations for dental professionals, which include the management of the major risk factors for PIDs (Berglundh et al., 2018). Indeed, risk assessment is part of professional preventive care. An effective preventive approach needs to be personalized to the individual patient's risk profile, addressing all potential local and systemic risk factors for PIDs that can be modified. This personalized approach to prevention also requires specific approaches to patient education and motivation for behavioural change, with patients taking responsibility for their own health under the guidance and support of the oral care team (Tonetti et al., 2015). Preventive measures can even be implemented prior to implant placement in order to prevent exposure to risk factor(s) and ultimately reduce the incidence of new disease. In this situation, we

[1]For the sake of simplicity, the term "risk factors" will be used in this article to generally refer to all indicators that have been significantly associated with PID occurrence despite the difference level of supporting evidence.

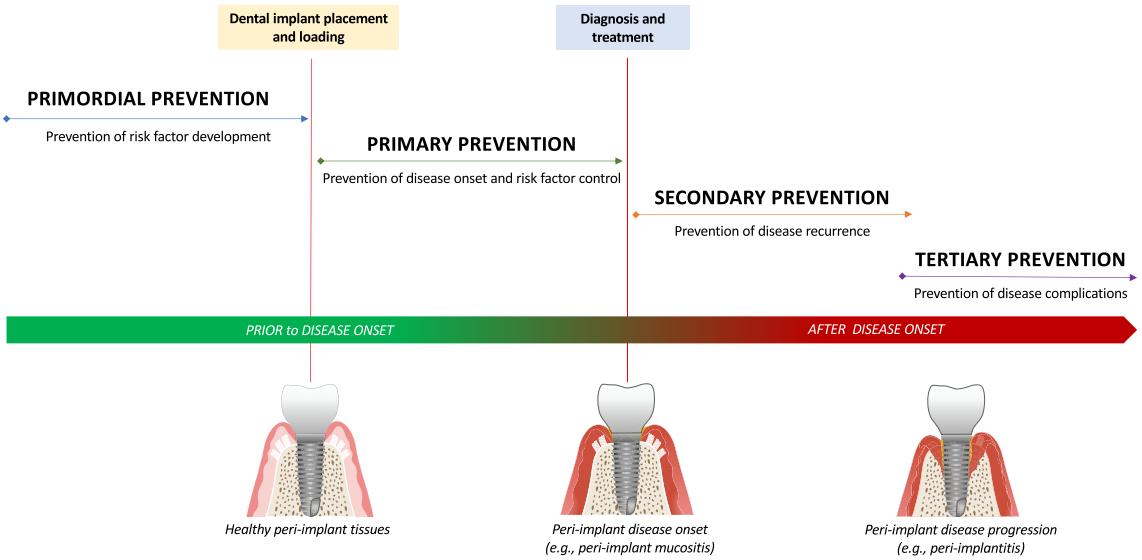


FIGURE 1 Definition of the different types of prevention. Primordial prevention consists in the prevention of risk factor development; it targets the population of individuals who do not have the disease (have not yet received dental implants) to avoid risk factor exposure, for example, promoting healthy behaviours (e.g., no addiction, good oral hygiene, etc.). Primary prevention aims to prevent disease onset by risk factor control in individuals with healthy peri-implant tissues but exposed to known risk factors, for example, applying adequate and personalized oral hygiene for optimal plaque control also around implant-supported restoration(s). Secondary prevention aims at preventing disease recurrence once peri-implant disease (PID) has been diagnosed and treated. Thus, it targets populations of individuals who already have experienced an event of the disease: for example, regular peri-implant supportive care after successful active treatment of PID represents secondary prevention. Finally, tertiary prevention is represented by the prevention of disease complications in individuals who have a chronic disease, for example, promoting interventions to slow down the progression of the PIDs to avoid implant loss.

refer to "primordial prevention" as the earliest prevention modality targeting the underlying risk factors and conditions that promote disease onset (Kisling & Das, 2022) (Figure 1). An example includes promoting healthy behaviours including no tobacco smoking or increased physical activity to prevent non-communicable diseases, such as type-2 diabetes, or harmful behaviours that may increase the risk of PIDs.

Once the dental implant is placed and loaded, the health of the peri-implant tissues must be maintained over time. This is the driver of primary prevention strategies, which target the population of individuals with healthy peri-implant tissues and comprises all interventions that promote risk factor control to prevent the disease from manifesting (Kisling & Das, 2022), for example, educating and motivating the patient in a personalized manner to practice adequate oral hygiene behaviours to effectively control biofilm accumulation around dental implants and their superstructures/restorations. The management of peri-implant mucositis is a preventive measure for the onset of peri-implantitis, but in this situation it represents a form of secondary prevention that is beyond the scope of the present review (Figure 1).

The present study aimed to systematically review the current literature to answer the following focused research question: "What is the efficacy of preventive interventions, involving risk factor control, in patients (i) awaiting dental implant rehabilitation (primordial prevention), or (ii) having dental implant(s) with healthy peri-implant tissues (primary prevention) on the incidence of PIDs?"

2 | METHODS

2.1 | Protocol development and registration

The protocol of the present systematic review and meta-analysis was developed following the PRISMA statement checklist (Moher et al., 2009) and registered in PROSPERO on 10 May 2022 (registration number: CRD42022324733).

2.2 | Eligibility criteria

The main research question was constructed using the PICOS format for interventional studies and the PECOS format for observational studies, as follows:

2.2.1 | PICOS

(P) Participants: Adult patients awaiting dental implant placement or having dental implants with peri-implant health.

(I) Intervention: Interventions to control risk factor(s) for PIDs.

(C) Comparison: Adult patients awaiting dental implant placement or having dental implants with peri-implant health and not receiving any preventive intervention.

(O) Outcomes: The primary outcome was the occurrence of PIDs, including mucositis and peri-implantitis. Any case definition of peri-implant mucositis and peri-implantitis was considered. Because a preventive intervention aims to prevent the occurrence of a disease (i.e., PIDs) but also to maintain health (i.e., peri-implant health), clinical parameters essential to define peri-implant health and diagnose PIDs according to the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions (Berglundh et al., 2018; Caton et al., 2018) were also considered as primary outcome measures, such as bleeding on probing (BOP) (or other indices for peri-implant tissue inflammation), peri-implant probing depth (PPD), suppuration, and radiographic marginal bone level (MBL). Eligible studies must report at least one of the aforementioned primary outcomes to be selected. Biomarkers in saliva or peri-implant fluid and dental implant survival rate were considered as secondary outcomes (Derks et al., 2022).

(S) Study design: Randomized (RCTs) and non-randomized controlled trails (NRCTs), with a minimum of 6 months follow-up from implant loading.

2.2.2 | PECOS

(P) Participants: Adult patients awaiting dental implant placement or having dental implants with peri-implant health.

(E) Exposure: Exposure to a risk factor for PIDs.

(C) Comparison: Adult patients awaiting dental implant placement or having dental implants with peri-implant health no more exposed to the risk factor.

(O) Outcomes: Same as in the PICOS format described above.

(S) Study design: Prospective and retrospective cohort studies and case–control studies (matched or not) with a minimum of 6 months follow-up from implant loading.

Based on the above-mentioned criteria, separate research questions were constructed for each PID risk factor explored.

The efficacy of primordial and primary preventive interventions for PIDs should be ideally assessed in longitudinal and interventional studies. However, because of the difficulties and ethical issues in conducting certain types of RCTs/NRCTs and the expected paucity of literature on PID prevention, prospective and retrospective observational studies were also considered. To assess the efficacy of risk factor control, the target population must be exposed to the risk factor at some point in time. Therefore, studies assessing the association between a risk factor and PID occurrence were not considered. For instance, comparisons between diabetes and non-diabetes patients with dental implants, or smokers versus non-smokers, were not considered. Indeed, the aim of the present study was designed to assess the efficacy of risk factor control on PID prevention, but not to identify the risk factors.

A set of potentially modifiable risk factors were predetermined and searched. We made the pragmatic decision not to include prosthesis-related risk factors because time and resources made them beyond the scope of this review. Therefore, the present systematic review was limited to the following risk factors and their corresponding preventive interventions:

- Poor glycaemic control (as measured by HbA1c [in percentage]) in diabetic and pre-diabetic patients. No threshold was set for HbA1c because of country-related differences and comorbidity-related impact in defining good and poor glycaemic control. The preventive intervention was improving or obtaining glycaemic control.
- Smoking status (as defined by current smoking) and smoking habit (as measured by the quantity [number of cigarettes] or type of smoking habit [e.g., cigarette, e-cigarette, water pipe]). The preventive intervention was the promotion of smoking cessation by any guideline-based strategy.
- Type of and adherence to supportive periodontal/peri-implant care (SPC) protocols. The preventive intervention was promoting and obtaining adequate/regular patient adherence to the SPC employed. Studies comparing the efficacy of different SPC protocols were also considered.
- Width of the PIKM and thickness of the peri-implant soft tissue. A deficiency of PIKM or a thin peri-implant mucosa was considered as a risk factor. The preventive intervention was a surgical procedure for soft tissue augmentation, including PIKM augmentation. To be included, studies had to report the surgical indication, which should clearly be to augment the peri-implant keratinized tissue width or the peri-implant soft tissue thickness.
- Oral hygiene behaviours (including frequency and methods of brushing). The preventive intervention was promoting and achieving optimal/improved patient's oral hygiene behaviour.
- Bruxism/oral parafunction. The preventive intervention was controlling bruxism and oral parafunction with any appropriate therapy.

2.3 | Literature sources and search

The literature search and selection were carried out by two independent reviewers (NBS, AC). The following electronic databases were searched during April 2022 and updated during August 2022: MEDLINE (through PubMed), EMBASE, Cochrane Central Library, BaseSearch, Open Access Thesis and Dissertation (openthesis.org), and ClinicalTrials.gov. A specific research equation was formulated in each database, using appropriate keywords and MeSH terms for exposure and outcomes, as detailed in Table S1. In addition, reference lists from eligible studies and previously published review articles were cross-checked to identify additional pertinent studies. Only articles in English were considered but no publication date limit was applied.

2.4 | Study selection and data extraction

Records from the literature searches were merged into a single list imported into an EndNote library (EndNote software, Clarivate, Cleverbridge GmbH, Gereonstr., Cologne, Germany), in which duplicates

were automatically removed. Two independent reviewers (NBS, AC) undertook the study screening process by using Rayyan software (Intelligent Systematic Review, 2022) to support the reviewers at all different stages of the systematic review. Records were first screened at the title and abstract level. Each record had to be screened and voted upon (to be included or excluded) by the two reviewers, and blinded to the other reviewer's assessment. Any disagreement was resolved by a third author (MCC or PhB) acting as a moderator. Subsequently, reviewers performed a full-text evaluation of the pre-selected articles. Similarly, this evaluation was performed independently, and disagreements were resolved by the moderator to reach the final selection of the articles. Agreement between the reviewers was assessed by calculating Cohen's Kappa.

A dedicated Microsoft EXCEL spreadsheet was created to facilitate the data extraction process, which was conducted by three reviewers (MCC, NBS, AC). Study characteristics and principal findings were collated, analysed, and then summarized into tables to be processed for qualitative and quantitative analyses.

2.5 | Risk-of-bias assessment

Once the full-text article analysis was completed, the reviewers undertook evaluation of the risk of bias, which was assessed using appropriate tools according to the study design. Specifically, the revised Cochrane risk-of-bias tool for randomized trials (RoB-2) (Higgins et al., 2016), the ROBINS-I tool for NRCTs (Sterne et al., 2016), and the Newcastle–Ottawa Scale (NOS) (Stang, 2010) for cohort and case–control studies were employed as needed. Publication bias and sponsoring bias were also evaluated. The source of funding was classified as unknown if not reported in the original studies (Popelut et al., 2010).

2.6 | Data synthesis and analysis

Whenever information essential for inclusion (e.g., duration of follow-up, outcome measures) or potentially relevant data were missing in the published documents, the corresponding authors were contacted by email. When no answer was forthcoming, the record was excluded. The feasibility and appropriateness of meta-analyses was checked once data extraction was completed, and the selected studies were re-grouped by the type of exposure and outcome(s). Outcome measures were extracted as frequency or rate (in percentage), mean (standard deviation, SD), or median (interquartile range, IQR).

For the pooled data analysis, the odds ratio (OR) and 95% confidence intervals (95% CIs) between the compared groups were estimated using the Mantel–Haenszel method for binary outcomes. For continuous data, the mean difference (MD) or the standardized mean difference (SMD) with 95% CI between the groups were estimated using inverse variance weighting. Heterogeneity was assessed by the I^2 statistic, with values <40% considered as negligible, 40%–75% as moderate, and >75% as substantial heterogeneity (https://training.cochrane.org/handbook/current). Random effect models were used as a more conservative approach, as a significant inter-study heterogeneity was expected. The pooled effect was considered significant if $p < .05$. The meta-analysis was performed by using RevMan software (Version 5.3; Cochrane Collaboration) and OpenMetaAnalyst.

3 | RESULTS

3.1 | Study selection and characteristics

By merging the searches of the two independent reviewers on the different databases, 7565 records were initially identified. Figure 2 shows the flow-chart of the study selection. The list of excluded articles after full-text evaluation is provided in Table S2. Finally, 48 articles were selected and distributed according to the type of risk factor. The kappa value was 0.612 (99.2% of agreement) for the selection upon title and abstract, and 0.466 (89.9% of agreement) for the selection after full-text evaluation.

3.2 | Synthesis of the results

3.2.1 | Glycaemic control

No interventional study assessing the efficacy of interventions to improve glycaemic control on peri-implant health and diseases was found. Evidence relies upon 11 observational cohort and case–control studies (Table 1). Seven studies compared well-controlled versus poorly controlled type-2 diabetes patients receiving dental implants (Aguilar-Salvatierra et al., 2016; Al Amri et al., 2016; Al Zahrani & Al Mutairi, 2019; Al-Sowygh et al., 2018; Ghiraldini et al., 2016; Gomez-Moreno et al., 2015; Tawil et al., 2008). Glycaemic control was assessed by measuring HbA1c levels and was defined as good if the value was between 6.1% and 8% in five studies, <7% in one study, and <6% in another study. Poor glycaemic control was defined as HbA1c level ranging between 8.1% and 10% in five studies, >8% in one study, and ranging between 7% and 9% in another study. Three studies also included a group of very poorly controlled type-2 diabetes patients (HbA1c >9 or >10%) (Al-Sowygh et al., 2018; Gomez-Moreno et al., 2015; Tawil et al., 2008). The remaining four studies compared pre-diabetes versus diabetes patients (Abduljabbar et al., 2017; Alrabiah et al., 2018; Alsahhaf et al., 2019; Mokeem et al., 2019), with significant similarities in the study design and methods and overlapping results. The authors were contacted by email to verify whether these studies investigated independent study populations or rather they analysed the same pool of patients. No reply was obtained and therefore these four studies were not included in the meta-analysis.

Pooled data analysis showed a significantly lower rate of peri-implantitis (OR = 0.16; 95% CI: 0.03–0.96; $p = .004$; I^2: 0%) and significantly lower MBL changes over time (MD: −0.36 mm; 95% CI: −0.65 to −0.07; $p < .0001$; I^2: 95%) in patients with good glycaemic control versus poor glycaemic control. The MD values in PPD and

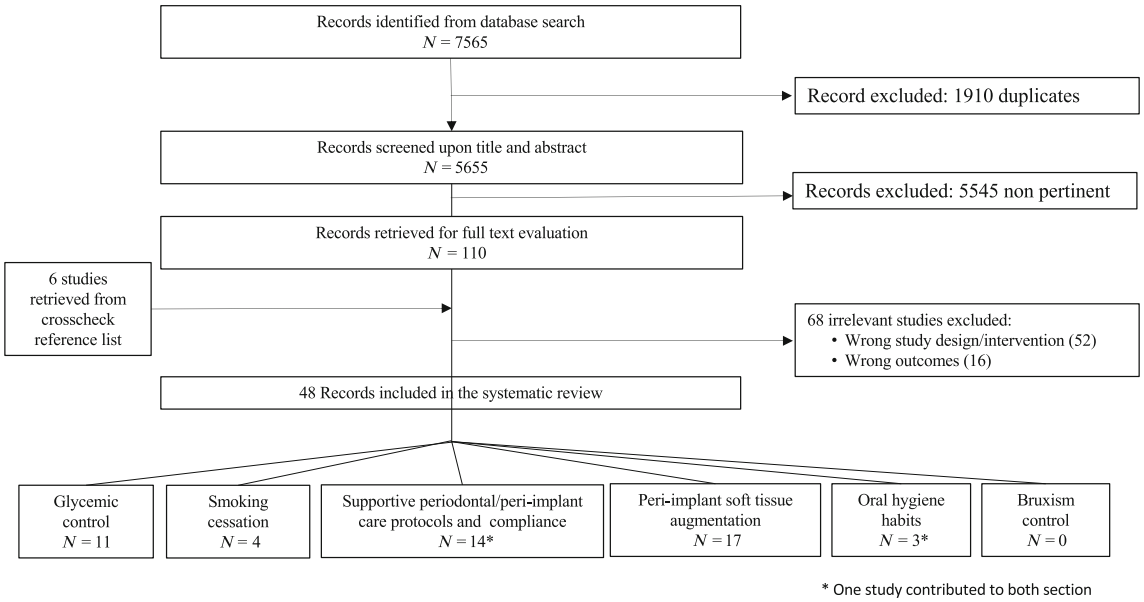


FIGURE 2 Flow-chart of literature search and study selection.

BOP were not significantly different between the groups (Figure 3). Dental implant survival was assessed in five studies (Aguilar-Salvatierra et al., 2016; Al Amri et al., 2016; Al Zahrani & Al Mutairi, 2019; Ghiraldini et al., 2016; Tawil et al., 2008). The estimated mean implant survival was 99% (95% CI: 97.8%–100% based on 253 dental implants) in patients with good glycaemic control and 95.6% (95% CI: 91.4%–99.8% based on 271 dental implants) in patients with poor glycaemic control. Three of these studies reported no implant loss (100% survival) over the study follow-up (ranging from 1 to 7 years) for both good and poor glycaemic control groups. Two studies (Aguilar-Salvatierra et al., 2016; Tawil et al., 2008), which included 309 implants, observed implant loss and were therefore used for meta-analysis; this showed that diabetes patients with poor glycaemic control have a 7.59 times increased risk of dental implant failure compared to patients with good glycaemic control (OR = 7.59; 95% CI: 1.63–35.3; $p = .01$; I^2: 0%). Reasons for implant loss were not clearly specified; they included peri-implant and osseointegration problems occurring 1–3 years after implant placement (Aguilar-Salvatierra et al., 2016; Tawil et al., 2008).

Two studies evaluated biomarkers in the peri-implant sulcular fluid. One study assessed the levels of transforming growth factor-β (TGF-β), fibroblast growth factor (FGF), osteopontin (OPN), osteocalcin (OC), and osteoprotegerin (OPG) in the peri-implant fluid and compared them between patients with good (HbA1c: 6.1%–8%) and poor (HbA1c >8%) glycaemic control, as well as with non-diabetes patients (Ghiraldini et al., 2016). At 12 months, OPN levels were significantly lower in poorly controlled diabetes patients compared with non-diabetes patients, but no difference was observed among diabetes patients, irrespective of the HbA1c values. Another study evaluated the levels of advanced glycation end products (AGEs) in peri-implant sulcular fluid (via ELISA testing) and found a significant positive correlation between AGEs and PPD and MBL in patients with poor glycaemic control (HbA1c >10%), supporting a compromised peri-implant state in these patients (Al-Sowygh et al., 2018).

Regarding pre-diabetes as a potential risk factor, selected studies not included in the meta-analysis showed a significantly worse peri-implant health in pre-diabetes compared to non-diabetes patients, but observed no significant differences between pre-diabetes (defined as HbA1c between 5.7% and 6.4%) and diabetes patients (HbA1c ≥6.5%) (Abduljabbar et al., 2017; Alrabiah et al., 2018; Alsahhaf et al., 2019; Mokeem et al., 2019) (Tables 1 and S3).

3.2.2 | Smoking habits

No interventional study was found. Overall, four studies met the selection criteria and were included (F. Alqahtani et al., 2019; M. A. AlQahtani et al., 2018; ArRejaie et al., 2019; Costa et al., 2022) (Tables 2 and S3). Significant similarities between three studies conducted by the same research team were noted (F. Alqahtani et al., 2019; M. A. AlQahtani et al., 2018; ArRejaie et al., 2019); the authors were contacted to know if they concerned independent patients samples but no answer was obtained. Because of doubts about overlapping data between the study populations, no pooled data analysis was performed.

Among the selected studies, only one described the occurrence of PIDs as a clinical diagnosis, reporting a lower rate of peri-implant mucositis (43.9% vs. 48.6%) and peri-implantitis (19.7% vs. 30.5%) in former smokers compared to current smokers (Costa et al., 2022). The authors observed a direct association between the cumulative smoking exposure and the risk for peri-implantitis as well as the time span since smoking cessation. All studies reported significant clinical

TABLE 1 Characteristics and outcomes of the selected studies analysing the impact of glycaemic control on the prevention of peri-implant diseases.

Reference	Study design	Setting Country	Study time frame Follow-up duration	Study population Total no. patients (no. of implants)	Type of intervention or exposure No. of patients (no. of implants)	Diagnosis of peri-implant mucositis Patient level	 Implant level	Diagnosis of peri-implantitis Patient level	 Implant level	Survival rate	Peri-implant mucosa inflammation (BOP)	Peri-implant probing pocket depth (mm)	Radiographic marginal bone level changes (mm)
Diabetes													
Tawil et al. (2008)	Cohort study	Private periodontal practice Lebanon	NR Mean F-UP: 42.4 months	Consecutive patients with T2DM receiving dental implants *N* = 45 (255)	**HbA1c: <7%** *N* = 22 (103)	NR	NR	0/22 (0%)	0/103 (0%)	99.1%	NR	NR	0.24 ± 0.28
					HbA1c: 7%–9% *N* = 22 (141)	NR	NR	NR	6/141 (4.2%)	96.5%%	NR	NR	0.52 ± 0.75
					HbA1c: >9% *N* = 1 (11)	NR	NR	NR	1/11 (9.1%)	90.9%	NR	NR	1.62
Aguilar-Salvatierra et al. (2016)	Cohort study	University setting Spain	NR F-UP: 24 months	Patients with T2DM receiving immediately loaded dental implants in the aesthetic zone of the upper maxilla *N* = 85 (85)	**HbA1c: ≤6% (no DM)** *N* = 33 (33)	NR	NR	0/33 (0%)	0/33 (0%)	100% at 1 year 100% at 2 year	**0.39 ± 0.04 at 1 year** **0.44 ± 0.07 at 2 year**	2.60 ± 0.18 at 1 year 2.67 ± 0.14 at 2 year	**0.64 ± 0.23 at 1 year** **0.72 ± 0.27 at 2 year**
					HbA1c: 6.1%–8% *N* = 30 (30)	NR	NR	1/30 (3.4%)	1/30 (3.4%)	100% at 1 year 96.6% at 2 year	**0.45 ± 0.07 at 1 year** **0.51 ± 0.05 at 2 year**	2.66 ± 0.27 at 1 year 2.79 ± 0.24 at 2 year	**0.86 ± 0.25 at 1 year** **0.98 ± 0.27 at 2 year**
					HbA1c: 8.1%–10% *N* = 22 (22)	NR	NR	3/22 (13.7%)	3/22 (13.7%)	95.4% at 1 year 86.3% at 2 year	**0.65 ± 0.06 at 1 year 0.74 ± 0.05 at 2 year**	3.57 ± 0.37 at 1 year 3.68 ± 0.48 at 2 year	**1.54 ± 0.43 at 1 year** **1.92 ± 0.38 at 2 year**
Ghiraldini et al. (2016)	Case–control study	University setting Brazil	2012–2013 F-UP: 12 months	Patients with T2DM receiving one posterior dental implant *N* = 51 (51)	**HbA1c: ≤6% (no DM)** *N* = 19 (19)	0%	0%	0%	0%	100%	NR	NR	NR
					HbA1c: 6.1%–8% *N* = 16 (16)	0%	0%	0%	0%	100%	NR	NR	NR
					HbA1c: >8% *N* = 16 (16)	0%	0%	0%	0%	100%	NR	NR	NR
Gomez-Moreno et al. (2015)	Cohort study	University setting Spain	NR F-UP: 36 months	Patients with T2DM receiving dental implants *N* = 67 (67)	**HbA1c: ≤6% (no DM)** *N* = 21 (21)	NR	NR	0%	0%	NR	**0.43 ± 0.05 at 1 year** **0.47 ± 0.05 at 2 year** **0.45 ± 0.06 at 3 year**	2.19 ± 0.22 at 1 year 2.21 ± 0.20 at 2 year 2.26 ± 0.19 at 3 year	0.41 ± 0.18 at 1 year 0.48 ± 0.15 at 2 year 0.53 ± 0.17 at 3 year
					HbA1c: 6.1%–8% *N* = 24 (24)	NR	NR	0%	0%	NR	**0.52 ± 0.06 at 1 year** **0.54 ± 0.06 at 2 year** **0.56 ± 0.07 at 3 year**	2.24 ± 0.20 at 1 year 2.27 ± 0.23 at 2 year 2.30 ± 0.23 at 3 year	0.45 ± 0.15 at 1 year 0.52 ± 0.18 at 2 year 0.57 ± 0.16 at 3 year
						NR	NR	0%	0%	NR	**0.59 ± 0.07 at 1 year**	2.29 ± 0.18 at 1 year	0.51 ± 0.16 at 1 year

(Continues)

TABLE 1 (Continued)

Reference	Study design	Setting Country	Study time frame Follow-up duration	Study population Total no. patients (no. of implants)	Type of intervention or exposure No. of patients (no. of implants)	Diagnosis of peri-implant mucositis Patient level	 Implant level	Diagnosis of peri-implantitis Patient level	 Implant level	Survival rate	Peri-implant mucosa inflammation (BOP)	Peri-implant probing pocket depth (mm)	Radiographic marginal bone level changes (mm)
					HbA1c: 8.1%–10% *N* = 11 (11)						**0.60 ± 0.05 at 2 year** **0.62 ± 0.06 at 3 year**	2.31 ± 0.21 at 2 year 2.34 ± 0.20 at 3 year	0.59 ± 0.16 at 2 year 0.64 ± 0.17 at 3 year
					HbA1c: >10.1% *N* = 11 (11)	NR	NR	0%	0%	NR	**0.62 ± 0.06 at 1 year** **0.63 ± 0.07 at 2 year** **0.72 ± 0.06 at 3 year**	2.33 ± 0.28 at 1 year 2.37 ± 0.26 at 2 year 2.40 ± 0.25 at 3 year	0.54 ± 0.12 at 1 year 0.63 ± 0.16 at 2 year 0.70 ± 0.19 at 3 year
Al Amri et al. (2016)	Cohort study	Hospital setting Saudi Arabia	NR F-UP: 24 months	Partially edentulous T2DM patients receiving immediately loaded dental implants *N* = 91 (91)	**HbA1c: ≤6% (no DM)** *N* = 30 (30)	NR	NR	NR	NR	100%	0.4 ± 0.02 at 1 year 0.4 ± 0.06 at 2 year	1.9 ± 0.04 at 1 year 1.6 ± 0.05 at 2 year	0.45 ± 0.06 at 1 year **0.46 ± 0.16 at 2 year**
					HbA1c: 6.1%–8% *N* = 30 (30)	NR	NR	NR	NR	100%	0.6 ± 0.04 at 1 year 0.62 ± 0.07 at 2 year	2.3 ± 0.18 at 1 year 2.3 ± 0.15 at 2 year	0.54 ± 0.12 at 1 year 0.58 ± 0.15 at 2 year
					HbA1c: 8.1%–10% *N* = 31 (31)	NR	NR	NR	NR	100%	0.63 ± 0.02 at 1 year 0.62 ± 0.05 at 2 year	2.4 ± 0.35 at 1 year 2.3 ± 0.62 at 2 year	0.57 ± 0.07 at 1 year **0.59 ± 0.2 at 2 year**
Al Zahrani and Al Mutairi (2019)	Cohort study	Hospital setting Saudi Arabia	2009–2011 F-UP: 7 years	T2DM patients requiring dental implant *N* = 67 (124)	**HbA1c: ≤6%** *N* = 35 (74)	NR	NR	NR	NR	100%	NR	NR	**0.25 ± 0.35 at 1 year** **0.31 ± 0.22 at 2 year** **0.44 ± 0.31 at 3 year** **0.6 ± 0.18 at 7 year**
					HbA1c: >8% *N* = 32 (50)	NR	NR	NR	NR	100%	NR	NR	**0.48 ± 0.66 at 1 year** **0.64 ± 0.72 at 2 year** **0.83 ± 0.92 at 3 year** **1.12 ± 0.87 at 7 year**
Al-Sowygh et al. (2018)	Case–control study	Private referral dental clinic Greece/ Saudi Arabia	NR F-UP: at least 36 months (Mean: >62 months)	T2DM patients receiving dental implants *N* = 93 (148)	**HbA1c: ≤6% (no DM)** *N* = 26 (42)	NR	NR	NR	NR	NR	**10.8 (6–13.1)**	**1.4 (0.7–2.1)**	**0.8 (0–1.1)**
					HbA1c: 6.1%–8%	NR	NR	NR	NR	NR	**18.2 (11.4–26.7)**	**2.6 (2–2.9)**	**1.7 (1.5–3.1)**

TABLE 1 (Continued)

Reference	Study design	Setting Country	Study time frame Follow-up duration	Study population Total no. patients (no. of implants)	Type of intervention or exposure No. of patients (no. of implants)	Diagnosis of peri-implant mucositis Patient level	 Implant level	Diagnosis of peri-implantitis Patient level	 Implant level	Survival rate	Peri-implant mucosa inflammation (BOP)	Peri-implant probing pocket depth (mm)	Radiographic marginal bone level changes (mm)
					N = 25 (36)								
					HbA1c: 8.1%–10% *N* = 25 (39)	NR	NR	NR	NR	NR	**28.5 (18.9–36)**	**3.1 (2.6–3.9)**	**2.4 (2.1–4.3)**
					HbA1c: >10% *N* = 17 (31)	NR	NR	NR	NR	NR	**31.4 (26.7–34.6)**	**3.3 (2.2–4)**	**2.7 (3.2–5.2)**
Pre-diabetes													
Abduljabbar et al. (2017)	Case–control study	University setting Saudi Arabia	NR Mean F-UP: >6 years	Patients with pre-diabetes or T2DM having received dental implants *N* = 130 (130)	**HbA1c: 4%–5% (no DM)** *N* = 42 (42)	NR	NR	NR	NR	NR	15.2 ± 0.8	2.1 ± 0.1	1.6 ± 0.2
					HbA1c: 5.7%–6.4% *N* = 45 (45)	NR	NR	NR	NR	NR	36.4 ± 4.1	4 ± 0.4	3.4 ± 0.6
					HbA1c: ≥6.5% N = 43 (43)	NR	NR	NR	NR	NR	33.3 ± 3.5	4.2 ± 0.2	3.5 ± 0.4
Alrabiah et al. (2018)	Case–control study	Private referral dental clinic Saudi Arabia	NR F-UP: at least 36 months (Mean: >63 months)	Patients with pre-diabetes or T2DM having received dental implants *N* = 90 (127)	**HbA1c: 4%–5%** *N* = 30 (39)	NR	NR	NR	NR	NR	**13.6 (5.5–15.2)**	**1.3 (0.8–1.9)**	**0.7 (0–1.2)**
					HbA1c: 5.7%–6.4% *N* = 30 (42)	NR	NR	NR	NR	NR	**24.7 (16.1–29.8)**	**2.7 (2.1–3.5)**	**2.1 (1.3–3)**
					HbA1c: ≥6.5% *N* = 30 (46)	NR	NR	NR	NR	NR	**31.4 (21.6–38.2)**	**3.2 (2.4–3.8)**	**2.5 (2–4.2)**
Alsahhaf et al. (2019)	Case–control study	NR Saudi Arabia	2010–2016 F-UP: at least 36 months (Mean: >63 s months)	Patients with pre-diabetes or T2DM having received narrow dental implants *N* = 119 (195)	**HbA1c: 4%–5%** *N* = 40 (52)	NR	NR	NR	NR	NR	0.22 ± 0.04 at 1 year 0.25 ± 0.05 at 2 year **0.21 ± 0.06 at 3 year**	**2.04 ± 0.21 at 1 year** 2.11 ± 0.20 at 2 year 2.18 ± 0.18 at 3 year	0.43 ± 0.20 at 1 year 0.49 ± 0.18 at 2 year 0.51 ± 0.18 at 3 year
					HbA1c: 5.7%–6.4% *N* = 41 (78)	NR	NR	NR	NR	NR	0.38 ± 0.07 at 1 year 0.39 ± 0.07 at 2 year **0.42 ± 0.08 at 3 year**	**2.13 ± 0.20 at 1 year** 2.19 ± 0.21 at 2 year 2.23 ± 0.21 at 3 year	0.51 ± 0.14 at 1 year 0.54 ± 0.17 at 2 year 0.59 ± 0.16 at 3 year

(Continues)

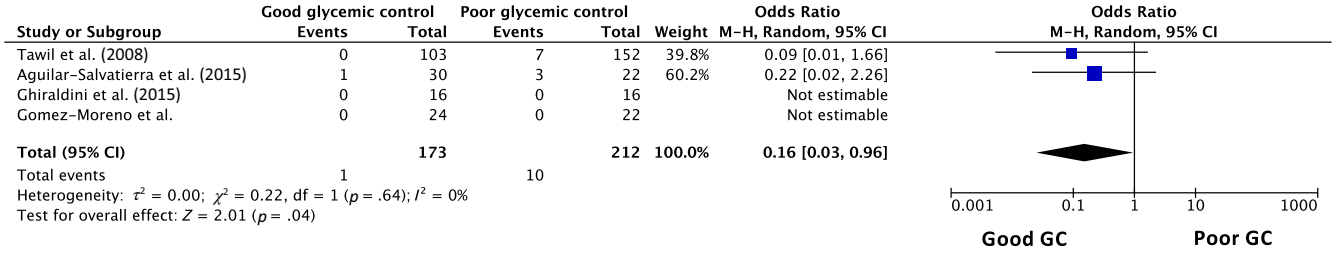
TABLE 1 (Continued)

Reference	Study design	Setting Country	Study time frame Follow-up duration	Study population Total no. patients (no. of implants)	Type of intervention or exposure No. of patients (no. of implants)	Diagnosis of peri-implant mucositis Patient level	 Implant level	Diagnosis of peri-implantitis Patient level	 Implant level	Survival rate	Peri-implant mucosa inflammation (BOP)	Peri-implant probing pocket depth (mm)	Radiographic marginal bone level changes (mm)
					HbA1c: ≥6.5% N = 38 (65)	NR	NR	NR	NR	NR	0.46 ± 0.06 at 1 year 0.49 ± 0.05 at 2 year **0.53 ± 0.07 at 3 year**	**2.32 ± 0.18 at 1 year** 2.35 ± 0.22 at 2 year 2.39 ± 0.18 at 3 year	0.58 ± 0.15 at 1 year 0.62 ± 0.17 at 2 year 0.69 ± 0.17 at 3 year
Mokeem et al. (2019)	Case–control study	NR Saudi Arabia	2016–2017 Mean F-UP: > 59 months	Patients with pre-diabetes or T2DM having received short dental implants *N* = 71 (111)	**HbA1c: 4%–5%** *N* = 25 (32)	NR	NR	NR	NR	NR	**13.6 (5.5–15.2)**	**1.8 (0.7–2.1)**	**0.8 (0–1.3)**
					HbA1c: 5.7%–6.4% *N* = 22 (35)	NR	NR	NR	NR	NR	**24.7 (16.1–29.8)**	**2.2 (2–3.1)**	**1.9 (1.1–2.8)**
					HbA1c: ≥6.5% *N* = 24 (44)	NR	NR	NR	NR	NR	**32.9 (24.7–39.1)**	**3.3 (2.5–3.9)**	**2.7 (2.2–4.1)**

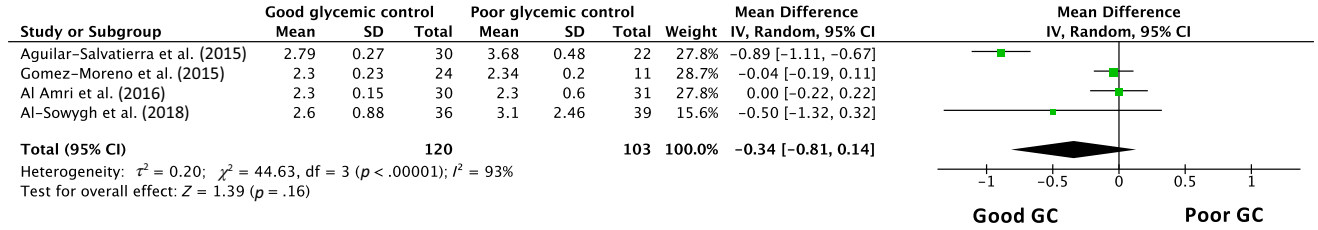
Note: Significant differences between groups in the outcome measures are indicated in bold.

Abbreviations: BOP, bleeding on probing; DM, diabetes mellitus; F-UP, follow-up; HbA1c, glycated haemoglobin; NR, not reported; PPD, periodontal probing depth; T2DM, type-2 diabetes mellitus.

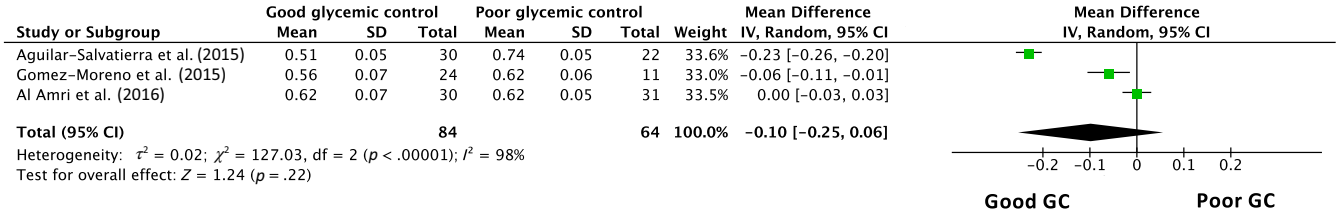
(a) **Diagnosis of peri-implantitis**: comparison between good and poor glycemic control (GC) in type-2 diabetes patients (analysis at the implant level)



(b) **Probing pocket depth (PPD)** : Mean difference between good and poor glycemic control (GC) in type-2 diabetes (analysis at the implant level)



(c) **Bleeding on probing (BOP)**: Mean difference between good and poor glycemic control (GC) in type-2 diabetes patients (analysis at the implant level)



(d) **Marginal bone level (MBL):** Mean difference between good and poor glycemic control (GC) in type-2 diabetes patients (analysis at the implant level)

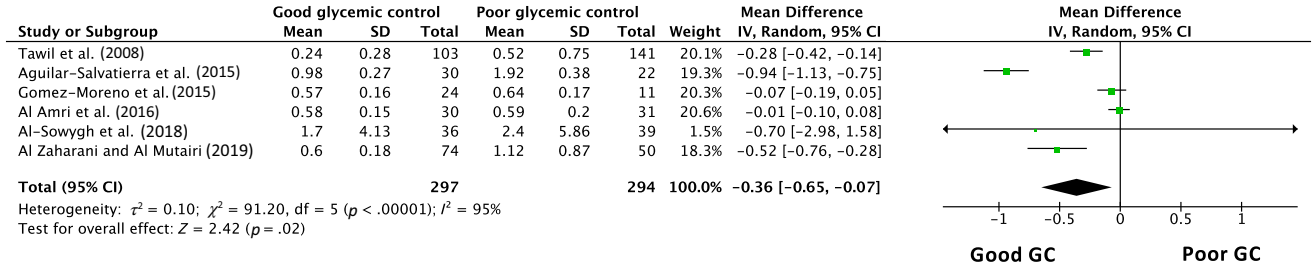


FIGURE 3 Forest plots for the impact of glycaemic control on peri-implant diseases, peri-implant probing depth, bleeding on probing, and marginal bone level.

differences between former smokers, e-cigarette users, waterpipe smokers, and current smokers. The former smoker category showed less peri-implant mucosal inflammation, lower PPD, and lower MBL changes compared to the other categories. Pro-inflammatory marker levels, including MMP-9 (ArRejaie et al., 2019), IL-1β (M. A. AlQahtani et al., 2018; ArRejaie et al., 2019), IL-6 (M. A. AlQahtani et al., 2018), and TNF-α (M. A. AlQahtani et al., 2018), were found to be higher in the peri-implant sulcular fluid of current smokers than in that of e-cigarette users.

TABLE 2 Characteristics and outcomes of the selected studies analysing the impact of smoking cessation strategies on the prevention of peri-implant diseases.

Reference	Study design	Setting Country	Study time frame Follow-up duration	Study population Total no. patients (no. of implants)	Type of intervention or exposure No. of patients (no. of implants)	Diagnosis of peri-implant mucositis		Diagnosis of peri-implantitis		Survival rate	Peri-implant mucosa inflammation/ BOP	Peri-implant probing pocket depth (mm)	Radiographic marginal bone level changes (mm)
						Patient level	Implant level	Patient level	Implant level				
AlQahtani et al. (2018)	Case–control study	NR NR	NR F-UP: at least 36 months (Mean F-UP >47.2 months)	Otherwise systemically healthy adult patients requiring at least 1 dental implant *N* = 160 (253)	**Current smokers** *N* = 40 (71)	NR	NR	NR	NR	NR	**16.7 ± 3.9**	**PPD ≥ 4 mm 7.8% ± 1.2**	**3.6 ± 0.5**
					Waterpipe smokers *N* = 40 (65)	NR	NR	NR	NR	NR	**18.4 ± 2.5**	**PPD ≥ 4 mm 7% ± 1.1**	**3.2 ± 0.6**
					e-cigarette users *N* = 40 (62)	NR	NR	NR	NR	NR	**23.3 ± 5.1**	**PPD ≥ 4 mm 5.3% ± 1.5**	**1.9 ± 0.9**
					Never smokers *N* = 40 (55)	NR	NR	NR	NR	NR	**38.9 ± 19.6**	**PPD ≥ 4 mm 4.4% ± 0.6**	**0.9 ± 0.3**
ArRejaie et al. (2019)	Case–control study	University Setting Saudi Arabia	2016–2017 F-UP: at least 36 months (Mean F-UP >45 months)	Otherwise systemically healthy adult patients requiring dental implants *N* = 95 (159)	**Current smokers** *N* = 32 (59)	NR	NR	NR	NR	NR	**18.4 ± 4.8**	**PPD ≥ 4 mm 23.8% ± 2.7**	**2.3 ± 1.2**
					e-cigarette users *N* = 31 (49)	NR	NR	NR	NR	NR	**14.7 ± 5.3**	**PPD ≥ 4 mm 15.9% ± 1.4**	**1.4 ± 0.9**
					Never smokers *N* = 32 (51)	NR	NR	NR	NR	NR	**39.8 ± 18.1**	**PPD ≥ 4 mm 4.5% ± 0.7**	**0.9 ± 0.3**
AlQahtani et al. (2019)	Case–control study	NR NR	NR Mean F-UP >1.3 years	Young smoker patients requiring dental implants *N* = 137 (137)	**Current smokers** *N* = 35 (35)	NR	NR	NR	NR	NR	**6.8 ± 1.2**	**4.3 ± 0.2**	NR
					Waterpipe smokers *N* = 33 (33)	NR	NR	NR	NR	NR	**7.9 ± 1.8**	**4.4 ± 0.5**	NR
					e-cigarette users *N* = 34 (34)	NR	NR	NR	NR	NR	**6.6 ± 1.3**	**3.2 ± 0.3**	NR
					Never smokers *N* = 35 (35)	NR	NR	NR	NR	NR	**19.8 ± 1.3**	**0.8 ± 0.1**	NR
Costa et al. (2022)	Cohort study	University setting (3 Public Health Centres) Brazil	2008–2019 F-UP: at least 5 years	Patients receiving dental implants *N* = 350 (769)	**Current smokers** *N* = 72 (149)	35/72 (48.6%)	NR	22/72 (30.5%)	NR	NR	**42.8 ± 23.4**	PPD ≥ 5 mm **33.2 ± 15.9**	NR
					Former smokers *N* = 66 (140)	29/66 (43.9%)	NR	13/66 (19.7%)	NR	NR	**53.5 ± 30.2**	PPD ≥ 5 mm **28.5 ± 11.8**	NR

TABLE 2 (Continued)

Reference	Study design	Setting: Country	Study time frame: Follow-up duration	Study population: Total no. patients (no. of implants)	Type of intervention or exposure: No. of patients (no. of implants)	Diagnosis of peri-implant mucositis: Patient level	Diagnosis of peri-implant mucositis: Implant level	Diagnosis of peri-implantitis: Patient level	Diagnosis of peri-implantitis: Implant level	Survival rate	Peri-implant mucosa inflammation/BOP	Peri-implant probing pocket depth (mm)	Radiographic marginal bone level changes (mm)
					Never smokers $N = 212$ (480)	90/212 (42.4%)	NR	39/212 (18.4%)	NR	NR	**56.4 ± 35.6**	PPD ≥ 5 mm **26.3 ± 12.9**	NR

Note: Significant differences between groups in the outcome measures are indicated in bold.
Abbreviations: BOP, bleeding on probing; F-UP, follow-up; NR, not reported; PPD, periodontal probing depth.

3.2.3 | Supportive periodontal/peri-implant care

To assess the efficacy of SPC and different protocols of SPC, 13 observational studies and 1 RCT were found. Overall, nine studies (64.2%) were conducted in private practice settings, most of the time in specialist centres in periodontology or implant dentistry (Tables 3 and S3). Two articles reported different outcomes on the same study population (M. Roccuzzo et al., 2010, 2012), and another two articles reported outcomes of the same study population at different follow-up intervals, at 10 (M. Roccuzzo et al., 2014) and 20 years (A. Roccuzzo et al., 2022). Twelve studies compared patients regularly attending the recommended SPC versus not attending or attending SPC visits irregularly (Aguirre-Zorzano et al., 2013; Alhakeem et al., 2022; Ferreira et al., 2006; Frisch et al., 2020; Hu et al., 2020; Monje et al., 2017; Rinke et al., 2011; A. Roccuzzo et al., 2022; M. Roccuzzo et al., 2010, 2012, 2014; Roman-Torres et al., 2019); one RCT compared four different SPC protocols over a 1-year study period (Ziebolz et al., 2017), and one study compared patients with or without deep residual periodontal pockets during the SPC (Cho-Yan Lee et al., 2012).

Pooled data analyses showed that patients attending SPC regularly were at significantly lower risk of presenting with PIDs (including both peri-implant mucositis and peri-implantitis) (OR = 0.42; 95% CI: 0.24–0.75; $p = .003$; I^2: 57%) during study follow-ups. This was also observed for the specific diagnosis of peri-implantitis, both at the patient level (OR = 0.45; 95% CI: 0.30–0.68; $p = .0002$; I^2: 51%) and at the implant level (OR = 0.26; 95% CI: 0.15–0.46; $p < .0001$; I^2: 21%). No significant between-group difference was observed for the diagnosis of peri-implant mucositis (Figures 4 and S1). In a sensitivity analysis performed excluding those studies that included patients with a history of periodontitis, dental implants under regular SPC showed an OR = 0.23 (95% CI: 0.08–0.64; $p = .005$; I^2: 0%) of developing peri-implantitis compared to dental implants with no SPC (based on two studies; Frisch et al., 2020; Roman-Torres et al., 2019).

Regarding dental implants as the statistical unit, those submitted to regular SPC showed lower PPD (MD: −0.48 mm; 95% CI: −0.67 to −0.29; $p < .0001$; I^2: 32%) and a reduced risk of presenting with an MBL >2 mm (OR: 0.4; 95% CI: 0.25–0.66; $p = .0003$; I^2: 73%) (Figure 5). Irregular SPC was associated with a 3.76 times increased risk of implant failure (95% CI: 1.50–9.45; $p = .005$; I^2: 0%) compared to regular SPC. All studies reporting dental implant survival evaluated study samples that included a proportion of patients with a history of periodontitis. Globally, the estimated mean implant survival was 99.3% (95% CI: 98.6%–100%) in the regular SPC group (based on 564 implants) and 97.8% (95% CI: 95.6%–99.9%) in the irregular SPC group (based on 454 implants). Reasons for implant loss were not specified in the selected studies, but they occurred after implant loading (Frisch et al., 2020; Hu et al., 2020; A. Roccuzzo et al., 2022; M. Roccuzzo et al., 2014).

Only one study evaluated the impact of residual deep periodontal pockets at the remaining natural teeth on the occurrence of PIDs (Cho-Yan Lee et al., 2012). When comparing patients with a history of generalized moderate to severe periodontitis presenting with deep

TABLE 3 Characteristics and outcomes of the selected studies analysing the impact professional periodontal/peri-implant supportive care protocols/compliance on the prevention of peri-implant diseases.

Variable		Setting	Study time frame	Study population	Type of intervention or exposure	Diagnosis of peri-implant mucositis		Diagnosis of peri-implantitis			Peri-implant mucosa inflammation/ BOP	Peri-implant probing pocket depth (mm)	Radiographic marginal bone level changes (mm)
Reference	Study design	Country	Follow-up duration	Total no. of patients (no. of implants)	No. of patients (no. of implants)	Patient level	Implant level	Patient level	Implant level	Survival rate			
Ferreira et al. (2006)	Cross-sectional study	University setting Brazil	NR F-UP: at least 6 months–5 years	Consecutive partially edentulous patients treated with dental implants (including 30 patients with periodontitis) $N = 212$ (578)	**Regular supportive peri-implant therapy** (≤6-month interval) $N = 94$ (NR)	58/94 (61.7%)	NR	8/94 (8.5%)	NR	NR	NR	NR	NR
					Irregular supportive peri-implant therapy (>6-month interval) $N = 118$ (NR)	79/118 (66.9%)	NR	11/118 (9.3%)	NR	NR	NR	NR	NR
M. Rocuzzo et al. (2010, 2012)	Cohort study	Private specialist periodontics/ implantology practice Italy	1996–1998 F-UP: 10 years	Consecutive patients referred for dental implant therapy (including 80 patients with history of periodontitis) $N = 112$ (NR)	**Regular individually tailored supportive periodontal and peri-implant therapy** $N = 79$ (NR)	NR	NR	21/79 (26.6%)	NR	NE	PHP: 12.5 ± 2.4 mPCP: 23 ± 2.7 sPCP: 27.2 ± 2.7	PHP: 3.1 ± 0.5 mPCP: 3.2 ± 0.6 sPCP: 3.9 ± 0.8	MBL > 3 mm: 12 patients (16.4%)
					No supportive periodontal and peri-implant therapy $N = 22$ (NR)	NR	NR	9/22 (40.9%)	NR	NE	PHP: 11.4 ± 4.8 mPCP: 50 ± 4.9 sPCP: 52.1 ± 7.2	PHP: 3.0 ± 0.4 mPCP: 4.3 ± 1.2 sPCP: 3.9 ± 0.7	MBL > 3 mm: 11 patients (50%)
Rinke et al. (2011)	Case–control study	Private practice Germany	1999–2006 Mean F-UP: 68.2 months ±24.8	Consecutive patients referred for dental implant therapy (including patients with history of periodontitis) $N = 89$ (NR)	**Regular supportive periodontal and peri-implant therapy** (3 to 6-month interval) $N = 58$ (NR)	25/58 (43.1%)	NR	2/58 (3.5%)	NR	NR	NR	NR	NR
					Irregular supportive periodontal and peri-implant therapy $N = 31$ (NR)	15/31 (48.4%)	NR	8/31 (25.8%)	NR	NR	NR	NR	NR
Cho-Yan Lee et al. (2012)	Matched case–control study	Private specialist periodontal practice Australia	1995–2005 >5-year F-UP Mean F-UP: 7.99 years ±3.16	Patients with a history of generalized moderate-to-severe chronic periodontitis $N = 30$ (56)	**Residual deep (≥6 mm) periodontal pocket(s) assessed during an individually tailored supportive periodontal therapy** $N = 13$ (23)	NR	NR	7/13 (53.8%)	**10/23 (43.5%)**	NR	NR	**3.18 ± 0.63**	**0.68 ± 1.08 MBL > 2 mm: 26.1%**
					No residual pocket during an individually tailored supportive periodontal therapy $N = 17$ (33)	NR	NR	4/17 (23.5%)	**5/33 (15.2%)**	NR	NR	**2.67 ± 0.44**	**0.23 ± 0.84 MBL > 2 mm: 6.1%**
Aguirre-Zorzano et al. (2013)	Case–control study	University setting Spain	NR F-UP: 1 year	Patients with a history of treated chronic periodontitis $N = 49$ (246)	**4-monthly supportive periodontal therapy** $N = 27$ (123)	1/27 (3.7%)	NR	5/27 (18.5%)	NR	100%	NR	NR	**0.16 ± 0.15**
					No supportive periodontal therapy $N = 22$ (123)	5/22 (22.7%)	NR	11/22 (50%)	NR	99.2%	NR	NR	**0.62 ± 0.94**

TABLE 3 (Continued)

Variable		Setting	Study time frame	Study population	Type of intervention or exposure	Diagnosis of peri-implant mucositis		Diagnosis of peri-implantitis			Peri-implant mucosa inflammation/ BOP	Peri-implant probing pocket depth (mm)	Radiographic marginal bone level changes (mm)
Reference	Study design	Country	Follow-up duration	Total no. of patients (no. of implants)	No. of patients (no. of implants)	Patient level	Implant level	Patient level	Implant level	Survival rate			
M. Roccuzzo et al. (2014), A. Roccuzzo et al. (2022)	Cohort study	Private specialist periodontal practice Italy	1998–2001 F-UP: 10 years (2014) And 20 years (2022)	Consecutive patients receiving dental implants, including 91 patients with history of moderate or severe periodontitis *N* = 123 (252) At 20 years: *N* = 84 (172)	**Regular supportive therapy** *N* = 75 (156) At 20 year: *N* = 58 (117)	NR	NR	At 10 years Overall: 37/52 (71.1%) PHP: 4/19 (21%) mPCP: 13/25 (52%) sPCP: 20/31 (64.5%) At 20 years Overall: 27/58 (46.5%) PHP: 5/17 (29.4%) mPCP: 6/17 (35.3%) sPCP: 16/24 (66.7%)	At 10 years Overall: 24/156 (15.4%) PHP: 2/32 (6.2%) **mPCP: 4/52 (7.7%)** **sPCP: 18/72 (25%)**	At 10 years PHP: 100% mPCP: 100% sPCP: 98.6% At 20 years Overall: 96.6% PHP: 100% mPCP: 97.1% sPCP: 94.2%	At 10 years PHP: 15.8 ± 10.5 mPCP: 20.1 ± 10.8 sPCP: 20.3 ± 8.6 At 20 years PHP: 21 ± 18.4; mPCP: 21.9 ± 26.3; sPCP: 20.4 ± 22.1	At 10 years PHP: 4.2 ± 0.9 mPCP: 4.2 ± 1.1 sPCP: 4.6 ± 1.3 At 20 years PHP: 3.9 ± 0.9 mPCP: 4.1 ± 1.4 sPCP: 4.1 ± 1.3	NR
					Irregular supportive therapy *N* = 48 (96) At 20 year: *N* = 27 (55)	NR	NR	At 10 years Overall: 23/48 (47.9%) PHP: 2/13 (15.4%) mPCP: 11/21 (52.4%) sPCP: 10/14 (71.4%) At 20 years Overall: 13/27 (48.1%) PHP: 2/5 (40%) mPCP: 8/13 (61.5%) sPCP: 3/9 (33.3%)	At 10 years Overall: 42/96 (43.7%) PHP: 4/22 (18.2%) **mPCP: 20/44 (45.5%)** **sPCP: 18/30 (60%)**	At 10 years PHP: 100% mPCP: 93.2% sPCP: 93.3% At 20 years Overall: 85.4; PHP: 75% mPCP: 85.2% sPCP: 90%	At 10 years PHP: 22.2 ± 14.8 mPCP: 31.2 ± 13.1 sPCP: 43.2 ± 25.6 At 20 years PHP: 45.8 ± 29.3; mPCP: 41.3 ± 27.8; sPCP: 56.8 ± 20.7	At 10 years PHP: 4.8 ± 1.3 mPCP: 5.1 ± 1.4 sPCP: 5.4 ± 1.5 At 20 years PHP: 4.2 ± 2.6 mPCP: 4.7 ± 1.5 sPCP: 5.3 ± 1.0	NR

(Continues)

TABLE 3 (Continued)

Variable		Setting	Study time frame	Study population	Type of intervention or exposure	Diagnosis of peri-implant mucositis		Diagnosis of peri-implantitis			Peri-implant mucosa inflammation/ BOP	Peri-implant probing pocket depth (mm)	Radiographic marginal bone level changes (mm)
Reference	Study design	Country	Follow-up duration	Total no. of patients (no. of implants)	No. of patients (no. of implants)	Patient level	Implant level	Patient level	Implant level	Survival rate			
Monje et al. (2017)	Cross-sectional study	Private specialist periodontal practice Spain	2016–2017 Mean F-UP: 46.85 months ±5.8	Consecutive patients treated with dental implants for fixed prosthetic rehabilitation $N = 115$ (206)	**Regular supportive peri-implant therapy** $N = NR$	22.8%	19.3%	**4.5%**	**2.4%**	NE	NE	NE	NE
					Erratic supportive peri-implant therapy $N = NR$	NE	NE	**26.3%**	**19%**	NE	NE	NE	NE
					No supportive peri-implant therapy $N = NR$	NE	NE	**14.3%**	**8.7%**	NE	NE	NE	NE
Ziebolz et al. (2017)	Multicentre RCT	Private dental hygiene practice (12 centres) Germany	F-UP: 1 year	Partially and fully edentulous patients with at least one dental implant-supported restoration (including 49 patients with a history of moderate or severe periodontitis) $N = 62$ (101)	**3-monthly supportive peri-implant therapy with curette, sonic scaler, polishing with prophylaxis brush** $N = 17$ (24)	NR	NR	NR	NR	100%	5.9%	2.21 ± 1.32	NR
					3-monthly supportive peri-implant therapy with curette, air polishing, polishing with prophylaxis brush $N = 15$ (26)	NR	NR	NR	NR	100%	13.3%	2.31 ± 1.54	NR
					3-monthly supportive peri-implant therapy with curette, sonic scaler, polishing with prophylaxis brush, CHX varnish $N = 16$ (30)	NR	NR	NR	NR	100%	6.3%	2.23 ± 1.28	NR
					3-monthly supportive peri-implant therapy with curette, air polishing, polishing with prophylaxis brush, CHX varnish $N = 14$ (21)	NR	NR	NR	NR	1 00%	7.1%	2.05 ± 1.32	NR
Roman-Torres et al. (2019)	Case–control study	University setting Brazil	Dental implant placement in 2007 F-UP: 7 years	Consecutive patients rehabilitated with dental implant-supported overdentures $N = 66$ (396)	**Regular supportive peri-implant therapy (at least once/year for 7 years)** $N = 44$ (264)	NR	NR	NR	1/264 (0.4%)	NR	81/264 (31%)	2.72 ± 0.69	NR
					No supportive peri-implant therapy (over the 7-year study period) $N = 22$ (132)	NR	NR	NR	1/132 (0.75%)	NR	121/132 (92%)	3.10 ± 0.83	NR

TABLE 3 (Continued)

Variable		Setting	Study time frame	Study population	Type of intervention or exposure	Diagnosis of peri-implant mucositis		Diagnosis of peri-implantitis			Peri-implant mucosa inflammation/ BOP	Peri-implant probing pocket depth (mm)	Radiographic marginal bone level changes (mm)
Reference	Study design	Country	Follow-up duration	Total no. of patients (no. of implants)	No. of patients (no. of implants)	Patient level	Implant level	Patient level	Implant level	Survival rate			
Frisch et al. (2020)	Case–control study	Private practice Germany	2006–2007 form implant placement 2012–2014 for outcomes assessment Mean F-UP: 7.76 years ±3.07	Patients who were provided with implant-supported prostheses of all types included in a supportive implant therapy program *N* = 91 (219)	**Regular supportive peri-implant care (at least once/year)** *N* = 48 (98)	NR	**30/98 (30.6%)**	NR	**4/98 (4.1%)**	100%	NR	3.76 ± 0.86	**1.02 ± 0.85** **MBL > 2 mm: 21.4%**
					No supportive peri-implant care *N* = 43 (121)	NR	**82/121 (67.8%)**	NR	**21/121 (17.4%)**	98.4%	NR	4.07 ± 1.18	**1.53 ± 1.46** **MBL > 2 mm: 40.5%**
Hu et al. (2020)	Case–control study	Hospital setting Singapore	2005–2012 Mean F-UP: 6.8 years (range: 4.5–11 years)	Consecutive patients receiving dental implants (including 77 patients with a history of treated periodontitis) *N* = 200 (284)	**Regular supportive peri-implant care (at least once/year)** *N* = 100 (150)	NR	NR	**6/100 (6%)**	**6/150 (4%)**	98.7%	NR	NR	**0.19** **MBL ≥ 2 mm: 0.7%**
					No supportive peri-implant care *N* = 100 (134)	NR	NR	**20/100 (20%)**	**23/134 (17.2%)**	97.8%	NR	NR	**0.63** **MBL ≥ 2 mm: 9.7%**
Alhakeem et al. (2022)	Case–control study	University setting Iran	2010–2012 Mean F-UP: 7.3 ± 1.4 years	Consecutive patients receiving dental implants (including 47 patients with a history of severe periodontitis) *N* = 88 (186)	**Regular supportive care** *N* = 76 (165)	NR	NR	NR	17/165 (26.1%)	100%	137/165	PPD ≥ 4 mm 24/165 (14.5%)	MBL ≥ 3 mm: 25/165
					Irregular supportive care *N* = 12 (21)	NR	NR	NR	1/21 (4.8%)	100%	4/21	PPD ≥ 4 mm 1/21 (4.8%)	MBL ≥ 3 mm: 1/21

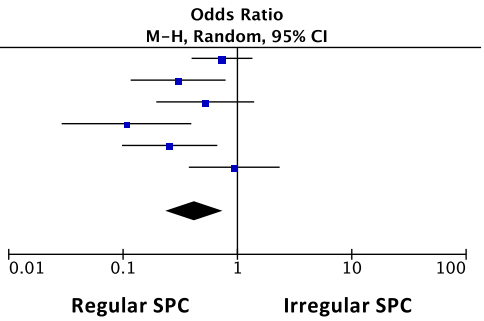
Note: Significant differences between groups in the outcome measures are indicated in bold.

Abbreviations: BOP, bleeding on probing; F-UP, follow-up; MBL, marginal bone level; mPCP, moderately periodontally compromised patients; NE, not estimable; NR, not reported; PHP, periodontally healthy patients; PPD, pocket probing depth; sPCP, severely periodontally compromised patients.

(a) **Diagnosis of peri-implant disease** (including both peri-implant mucositis and peri-implantitis): comparison between regular and irregular SPC (analysis at the patient level)

Study or Subgroup	Regular SPC Events	Regular SPC Total	Irregular SPC Events	Irregular SPC Total	Weight	Odds Ratio M-H, Random, 95% CI
Ferreira et al. (2006)	66	94	90	118	22.5%	0.73 [0.40, 1.35]
Rinke et al. (2011)	27	58	23	31	16.4%	0.30 [0.12, 0.79]
Roccuzzo et al. (2012)	21	79	9	22	15.9%	0.52 [0.20, 1.40]
Aguirre-Zorzano et al. (2013)	6	27	16	22	11.8%	0.11 [0.03, 0.40]
Hu et al. (2020)	6	100	20	100	16.3%	0.26 [0.10, 0.67]
Roccuzzo et al. (2022)	27	58	13	27	17.1%	0.94 [0.38, 2.34]
Total (95% CI)		**416**		**320**	**100.0%**	**0.42 [0.24, 0.75]**
Total events	153		171			

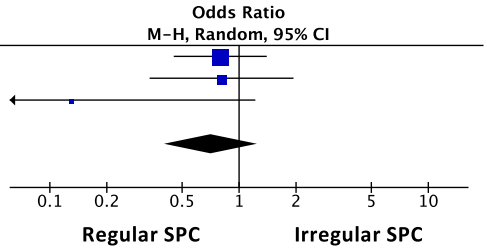
Heterogeneity: $\tau^2 = 0.28$; $\chi^2 = 11.57$, df = 5 ($p = .04$); $I^2 = 57\%$
Test for overall effect: $Z = 2.96$ ($p = .003$)



(b) **Diagnosis of peri-implant mucositis**: comparison between regular and irregular SPC (analysis at the patient level)

Study or Subgroup	Regular SPC Events	Regular SPC Total	Irregular SPC Events	Irregular SPC Total	Weight	Odds Ratio M-H, Random, 95% CI
Ferreira et al. (2006)	58	94	79	118	61.0%	0.80 [0.45, 1.40]
Rinke et al. (2011)	25	58	15	31	32.9%	0.81 [0.34, 1.94]
Aguirre-Zorzano et al. (2013)	1	27	5	22	6.1%	0.13 [0.01, 1.22]
Total (95% CI)		**179**		**171**	**100.0%**	**0.72 [0.41, 1.26]**
Total events	84		99			

Heterogeneity: $\tau^2 = 0.05$; $\chi^2 = 2.43$, df = 2 ($p = .30$); $I^2 = 18\%$
Test for overall effect: $Z = 1.16$ ($p = .25$)



(c) **Diagnosis of peri-implantitis**: comparison between regular and irregular SPC (analysis at the patient level)

Study or Subgroup	Regular SPC Events	Regular SPC Total	Irregular SPC Events	Irregular SPC Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Ferreira et al. (2006)	8	94	11	118	13.2%	0.90 [0.35, 2.35]
Rinke et al. (2011)	2	58	8	31	14.9%	0.10 [0.02, 0.52]
Roccuzzo et al. (2012)	21	79	9	22	15.3%	0.52 [0.20, 1.40]
Aguirre-Zorzano et al. (2013)	5	27	11	22	14.6%	0.23 [0.06, 0.82]
Hu et al. (2020)	6	100	20	100	27.9%	0.26 [0.10, 0.67]
Roccuzzo et al. (2022)	27	58	13	27	14.1%	0.94 [0.38, 2.34]
Total (95% CI)		**416**		**320**	**100.0%**	**0.45 [0.30, 0.68]**
Total events	69		72			

Heterogeneity: $\chi^2 = 10.24$, df = 5 ($p = .07$); $I^2 = 51\%$
Test for overall effect: $Z = 3.76$ ($p = .0002$)

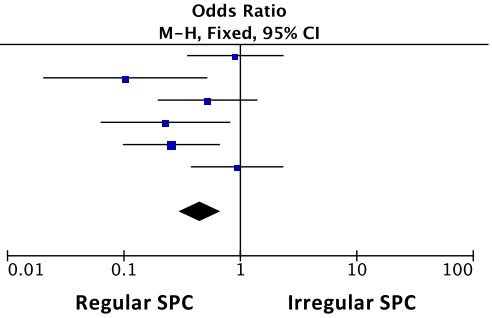


FIGURE 4 Forest plots for the impact of regular versus irregular supportive periodontal/peri-implant care on peri-implant diseases.

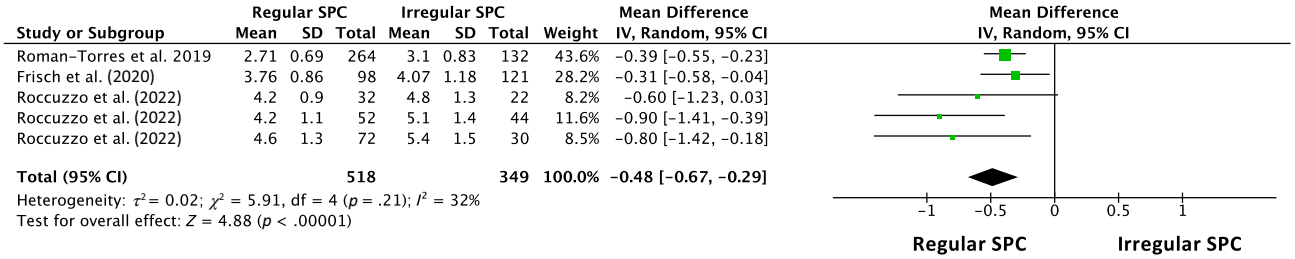
residual pockets (≥6 mm) during the SPC with patients with a history of generalized moderate to severe periodontitis but without residual deep pockets, a significantly higher occurrence of peri-implantitis (3.5% vs. 15.2%, implant-level analysis) was observed when deep residual pockets were present.

The only RCT included in this subsection about SPC (Ziebolz et al., 2017) compared four different SPC protocols, including a 3-monthly SPC with curette, with sonic scaler or air polishing, and with or without chlorhexidine varnish application. No significant differences were noted between the groups in term of PPD, BOP, and survival at 1 year.

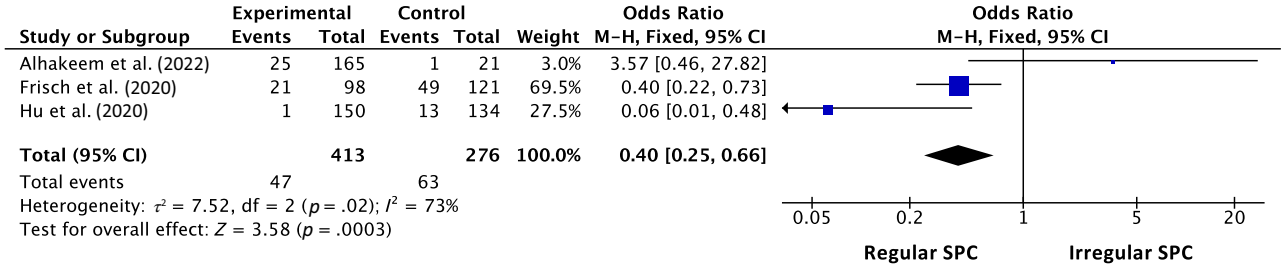
3.2.4 | Peri-implant soft tissue width and thickness

Overall, 17 studies were selected, including 9 RCTs, 4 NRCTs, 3 case–control studies, and 1 cohort study (Tables 4 and S3). Six studies (Buyukozdemir Askin et al., 2015; Kikuchi et al., 2022; Oh et al., 2017, 2020; M. Roccuzzo et al., 2016; Zheng et al., 2021) compared peri-implant tissue health parameters between sites with PIKM deficiency receiving a free gingival graft (FGG) to increase PIKM width versus no intervention. When pooling all studies together, meta-analyses showed a non-significant difference in PPD between the PIKM-augmented and non-augmented sites but a significantly lower clinical

(a) **Probing pocket depth (PPD)**: comparison between regular and irregular SPC (analysis at the implant level)



(b) **Marginal bone level (MBL) > 2 mm**: comparison between regular and irregular SPC (analysis at the implant level)



(c) **Implant survival**: comparison between regular and irregular SPC (analysis at the implant level)

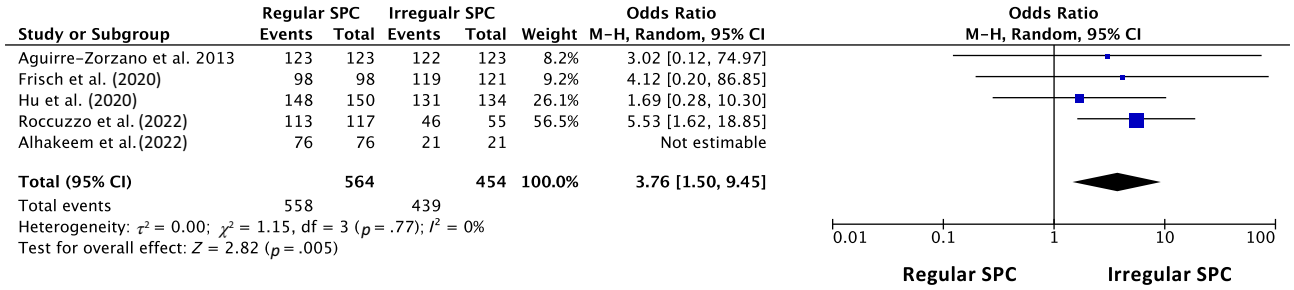


FIGURE 5 Forest plots for the impact of regular versus irregular supportive periodontal/peri-implant care on peri-implant probing depth, bleeding on probing, and marginal bone level.

soft tissue inflammation index (BOP/GI) (SMD = −1.18; 95% CI: −1.85 to −0.51; p = .0006; I^2: 69%) around the dental implants receiving FGG to augment PIKM (Figure 6). Concerning the mean MBL, based on data from four studies, a significant difference in favour of PIKM-augmented sites (SMD: −0.25; 95% CI: −0.45 to −0.05; p = .01; I^2: 62%) was also noted. When excluding from pooled data analysis cohort and case–control studies, the results were consistent with no statistical heterogeneity. No difference in PPD (SMD: −0.25; 95% CI: −0.63 to −0.13; p = .20; I^2: 0%; based on 107 implants) but a significant difference in peri-implant mucosa inflammation (SMD: −1.5; 95% CI: −1.93 to −1.06; p < .0001; I^2: 0%; based on 107 implants) and MBL changes (SMD: −0.33; 95% CI: −0.55 to −0.11; p = .003; I^2: 0%; based on two studies, 66 implants) was noted between PIKM-augmented sites versus non-augmented sites. Only one study (Buyukozdemir Askin et al., 2015) evaluated inflammatory biomarkers in peri-implant sulcular fluid, namely the IL-1β concentration, which was not different between PIKM-augmented and non-augmented sites.

Three studies compared peri-implant tissue health parameters between sites with thin peri-implant soft tissues receiving and not receiving a soft tissue augmentation procedure (by connective tissue graft [CTG] or allogenic membrane) to increase tissue thickness (Bienz et al., 2017; Hosseini et al., 2020; Linkevicius et al., 2015). Concerning the clinical parameters defining peri-implant health, no significant differences were reported for peri-implant mucosa inflammation (BOP or mBI), PPD, and MBL. For this latter parameter, pooled data analysis based on two studies including 107 implants (Hosseini et al., 2020; Linkevicius et al., 2015) showed a non-significant difference between CTG-augmented sites versus non-augmented sites (MD: −0.75 [−2.18 to 0.68], p = .32; I^2: 99%). They all reported a survival rate of 100% (follow-up duration 1–5 years).

TABLE 4 Characteristics and outcomes of the selected studies analysing the impact of peri-implant soft tissue augmentation on peri-implant health and diseases.

Reference	Study design	Setting Country	Study time frame Follow-up duration	Study population Total no. of patients (no. of implants)	Type of intervention or exposure No. patients (no. of implants)	Surgical procedure	Diagnosis of peri-implant mucositis Patient level	 Implant level	Diagnosis of peri-implantitis Patient level	 Implant level	Survival rate	Peri-implant mucosal inflammation/ BOP	Peri-implant probing depth (mm)	Radiographic marginal bone level changes (mm)
Peri-implant keratinized mucosa (PIKM) augmentation: Comparison between augmented and non-augmented sites														
Buyukozdemir Askin et al. (2015)	NRCT	University setting Turkey	NR F-UP: 6 months	Systemically and periodontally healthy patients requiring dental implants *N* = 18 (60)	**Inadequate PIKM width (≤2 mm) treated with FGG** *N* = NR (20)	Surgery performed at least 1 year after implant loading	NR	NR	NR	NR	NR	0.65 ± 0.42 (GI) 30% (BOP)	2.29 ± 0.5	0.55 ± 0.39
					Inadequate PIKM width (≤2 mm) treated with SPC only *N* = NR (20)	-	NR	NR	NR	NR	NR	1.31 ± 0.33 (GI) 95% (BOP)	2.29 ± 0.65	0.81 ± 0.61
					Adequate PIKM width (>2 mm) *N* = NR (20)	-	NR	NR	NR	NR	NR	0.56 ± 0.44 (GI) 25% (BOP)	2.43 ± 0.81	0.72 ± 0.49
Roccuzzo et al. (2016)	Cohort study	Specialized private practice Italy	1998–2002 F-UP: 10 years	Consecutive patients requiring dental implant in the posterior mandible (including 74 patients with history of moderate periodontitis) *N* = 98 (98)	**Implants surrounded by PIKM** *N* = 63 (63)	-	NR	NR	**8/63 (12.7%)**	**8/63 (12.7%)**	NR	23.4 ± 18.4	3.13 ± 0.59	0.34 ± 0.38
					Implants surrounded by alveolar mucosa without additional FGG *N* = 24 (24)	FGG was performed during the SPC whenever the patient reported soreness and insufficient plaque control	NR	NR	**18/35 (51.4%)** **NR**	**18/35 (51.4%)**	NR	33.3 ± 25.2	2.77 ± 0.70	0.50 ± 0.38
					Implants placed in alveolar mucosa with additional FGG *N* = 11 (11)		NR	NR			NR	27.3 ± 26.1	2.95 ± 0.80	0.56 ± 0.39
Oh et al. (2017, 2020)	RCT	University setting USA	2012–2014 F-UP: 18 months (2017) And 48 months (2020)	Patients with history of moderate periodontitis and with PIKM <2 mm on the facial side of a dental implant *N* = 28 (41) At 48 months: *N* = 23 (32)	**FGG** *N* = 14 (21) At 48 months *N* = 11 (18)	Surgery performed at least 6 months after implant loading	NR	NR	NR	NR	100%	0.8 ± 1.1	3 ± 1 (mesial) 2.9 ± 1.1 (distal)	At 18-month F-UP: **0 ± 0.2 (mesial)** **0.06 ± 0.3 (distal)** At 48-month F-UP: 0 ± 0.5 (mesial) **0 ± 0.5 (distal)**
					Oral prophylaxis only *N* = 14 (20) At 48 months *N* = 7 (8)	-	NR	NR	NR	NR	100%	2.1 ± 0.9	3.7 ± 1.5 (mesial) 3.5 ± 1.4 (distal)	At 18-month F-UP: **0.38 ± 0.3 (mesial)** **0.25 ± 0.3 (distal)** At 48-month F-UP: 0.3 ± 0.4 (mesial)

TABLE 4 (Continued)

Reference	Study design	Setting Country	Study time frame Follow-up duration	Study population Total no. of patients (no. of implants)	Type of intervention or exposure No. patients (no. of implants)	Surgical procedure	Diagnosis of peri-implant mucositis Patient level	 Implant level	Diagnosis of peri-implantitis Patient level	 Implant level	Survival rate	Peri-implant mucosal inflammation/ BOP	Peri-implant probing depth (mm)	Radiographic marginal bone level changes (mm)
														0.4 ± 0.3 (distal)
Zheng et al. (2021)	RCT	University setting China	2018–2020 F-UP: 12 months	Consecutive patients requiring dental implant placement in posterior area with a PIKM width <2 mm on the buccal side *N* = 26 (26)	**FGG** *N* = 13 (13)	Surgery performed before implant placement	NR	NR	NR	NR	100%	1.92 ± 6.93 (BOP) 0.62 ± 0.19 (GI)	3.1 ± 0.9	NR
					No surgery *N* = 13 (13)	-	NR	NR	NR	NR	100%	11.57 ± 12.94 (BOP) 1.06 ± 0.33 (GI)	3.3 ± 1.1	NR
Kikuchi et al. (2022)	Multicentric case–control study (PSM)	University/ private practice setting Japan	1996–2015 Mean F-UP: 55.8 months	Patients with at least 1 dental implant in function over 4 years (including 871 patients with a history of periodontitis) *N* = 545 (1626)	**FGG or APF** *N* = NR (66)	NR	NR	NR	NR	NR	NR	NR	NR	NR	**0.081 ± 0.4**
					PIKM ≥ 2 mm *N* = NR (987)	-	NR	NR	NR	NR	NR	NR	NR	**0.18 ± 0.66**
					PIKM <2 mm *N* = NR (573)	-	NR	NR	NR	NR	NR	NR	NR	**0.44 ± 0.87**

Reference	Study design	Setting Country	Study time frame Follow-up duration	Study population Total no. patients (no. of implants)	Type of intervention or exposure No. of patients (no. of implants)	Surgical procedure	Diagnosis of peri-implant mucositis Patient level	 Implant level	Diagnosis of peri-implantitis Patient level	 Implant level	Survival rate	Peri-implant mucosal inflammation/ BOP	Peri-implant probing depth (mm)	Radiographic marginal bone level changes (mm)
Peri-implant soft tissue thickness augmentation: Comparison between augmented and non-augmented sites														
Linkevicius et al. (2015)	NRCT	Private practice Lithuania	NR F-UP: 1 year	Partially edentulous, systemically healthy patients receiving dental implants *N* = 103 (103)	**Thin peri-implant soft tissues** *N* = 34 (34)	-	NR	NR	NR	NR	100%	NR	NR	**1.81 ± 0.06**
					Thin peri-implant soft tissues thickened with allogenic membrane *N* = 35 (35)	Simultaneous to implant placement	NR	NR	NR	NR	100%	NR	NR	**0.34 ± 0.05**
					Thick peri-implant soft tissue *N* = 34 (34)	-	NR	NR	NR	NR	100%	NR	NR	**0.47 ± 0.07**
Bienz et al. (2017)	Case–control study	University setting Switzerland	2002–2005 F-UP: 5 years	Partially edentulous patient with dental implants placed in the maxillary aesthetic area *N* = 18 (18)	**Subepithelial CTG** *N* = 8 (8)	Surgery performed 3–4 months after implant placement and 4–6 weeks prior to abutment connection	NR	NR	NR	NR	100%	31% (13–75)	3.67 (2.67–5)	NR
					No surgery *N* = 10 (10)	-	NR	NR	NR	NR	100%	31% (0–75)	3.33 (2–6.67)	NR
	NRCT				**CTG**		NR	0%	NR	0%	100%	mBI 0: 87.5%	NR	0.11 ± 0.45

(Continues)

TABLE 4 (Continued)

Reference	Study design	Setting Country	Study time frame Follow-up duration	Study population Total no. patients (no. of implants)	Type of intervention or exposure No. of patients (no. of implants)	Surgical procedure	Diagnosis of peri-implant mucositis Patient level	 Implant level	Diagnosis of peri-implantitis Patient level	 Implant level	Survival rate	Peri-implant mucosal inflammation/ BOP	Peri-implant probing depth (mm)	Radiographic marginal bone level changes (mm)
Hosseini et al. (2020)		University setting Denmark	2009–2010 F-UP: 5 years	Patients with tooth agenesis in the anterior maxilla requiring dental implant placement $N = 19$ (33)	$N = 10$[a] (10)	Surgery performed 2–3 months after immediately placed implants if thin phenotype						mBI 1: 12.5% mBI 2: 0%		
					No surgery $N = 15$[a] (23)	-	NR	0%	NR	1/23 (4.3%)	100%	mBI 0: 55% mBI 1: 40% mBI 2: 5%	NR	0.12 ± 0.33

Reference	Study design	Setting Country	Study time frame Follow-up duration	Study population Total no. patients (no. of implants)	Type of intervention or exposure No. of patients (no. of implants)	Surgical procedure	Diagnosis of peri-implant mucositis Patient level	 Implant level	Diagnosis of peri-implantitis Patient level	 Implant level	Survival rate	Peri-implant mucosal inflammation/ BOP	Peri-implant probing depth (mm)	Radiographic marginal bone level changes (mm)
Peri-implant soft tissue augmentation: Comparison between different techniques														
Lorenzo et al. (2012)	RCT	University setting and private practice (2 centres) Spain	2008–2009 F-UP: 6 months	Systemically healthy patients with at least 1 dental implant with minimal or no PIKM (<1 mm) $N = 24$ (24)	**Xenogenic collagen matrix** $N = 12$ (12)	Performed to increase PIKM after implant loading	NR	NR	NR	NR	NR	0.2 ± 0.63 (GI)	1.6 ± 0.52	NR
					Free CTG $N = 12$ (12)		NR	NR	NR	NR	NR	0.33 ± 0.65 (GI)	2.08 ± 1.08	NR
Frisch et al. (2015)	Case–control study	Specialized private practice Germany	1993–2011 Mean F-UP: 12.1 years ±4.9	Patients with a width <1 mm of PIKM at a minimum of one dental implant $N = 60$ (105)	**FGG** $N =$ NR (32)	Surgeries were performed during the SPC program	NR	14/32 (44%)	NR	1/32 (3.1%)	96.61%	NR	3.84 ± 1.10	NR
					CTG $N =$ NR (27)		NR	9/27 (33%)	NR	1/27 (3.7%)		NR	3.78 ± 0.88	NR
					No intervention $N = 30$ (46)	-	NR	15/46 (32.6%)	NR	0 (0%)	100%	NR	3.86 ± 0.89	NR
Basegmez et al. (2013)	RCT	University setting Turkey	February–June 2011 F-UP: 6 months	Systemically healthy patients with at least 2 adjacent dental implants in the mandible presenting inadequate attached mucosa (<1.5 mm) $N = 36$ (72)	**Acellular Dermal Matrix Allografts** $N = 18$ (36)	Surgeries performed at the second stage surgery, prior to implant loading	NR	NR	NR	NR	NR	0.29 ± 0.33	3.22 ± 0.15	NR
					FGG $N = 18$ (36)		NR	NR	NR	NR	NR	0.19 ± 0.17	3.33 ± 0.27	NR
Cairo et al. (2017)	RCT	NR Italy	2013–2016 F-UP: 6 months	Patients in the need of soft tissue augmentation around dental implants $N = 58$ (58)	**Xenogeneic collagen matrix** $N = 28$ (28)	Performed at the second-stage surgery	NR	NR	NR	NR	100%	NR	2.8 ± 0.2	0.2 ± 0.4
					CTG $N = 30$ (30)		NR	NR	NR	NR	100%	NR	2.9 ± 0.3	0.2 ± 0.4

TABLE 4 (Continued)

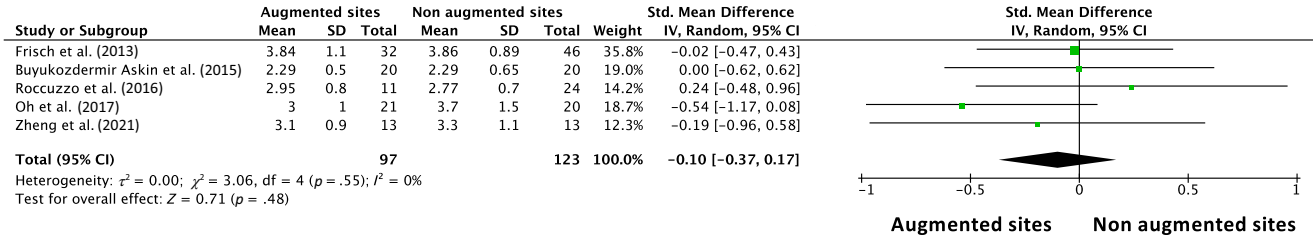
Reference	Study design	Setting Country	Study time frame Follow-up duration	Study population Total no. patients (no. of implants)	Type of intervention or exposure No. of patients (no. of implants)	Surgical procedure	Diagnosis of peri-implant mucositis Patient level	 Implant level	Diagnosis of peri-implantitis Patient level	 Implant level	Survival rate	Peri-implant mucosal inflammation/ BOP	Peri-implant probing depth (mm)	Radiographic marginal bone level changes (mm)
Vellis et al. (2019)	NRCT (split mouth)	University setting USA	NR F-UP: 6 months	Patients with controlateral dental implants with <1 mm of PIKM at the facial site *N* = 30 (60)	**Xenogenic collagen matrix** *N* = 30 (30)	Performed on loaded implants on the same day for both sides	NR	NR	NR	NR	100%	0.23 ± 0.72	1.56 ± 0.67	NR
					FGG *N* = 30 (30)		NR	NR	NR	NR	100%	0.13 ± 0.57	1.56 ± 0.62	NR
Thoma et al. (2020, 2022)	RCT	University setting Switzerland	2012–2018 F-UP: 3 (2020) and 5 years (2022)	Patients in the need of soft tissue augmentation around dental implants *N* = 17 (17)	**Xenogenic collagen matrix** *N* = 8 (8)	Performed after implant placement	NR	NR	NR	NR	NR	NR	NR	At 3 years: 0.5 ± 1 At 5 years: 0.4 ± 1.1
					CTG *N* = 9 (9)		NR	NR	NR	NR	NR	NR	NR	At 3 years: 0.4 ± 0.3 At 5 years: 0.47 ± 0.6
Huang et al. (2021)	RCT	University setting China	2017–2020 F-UP: 6 months	Patients presenting with at least 1 site with PIKM ≤2 mm in the edentulous region after dental implant surgery *N* = 26 (38)	**Xenogenic collagen matrix** *N* = 12 (18)	NR	NR	NR	NR	NR	NR	0.33 ± 0.64	1.45 ± 0.54	NR
					FGG *N* = 13 (19)		NR	NR	NR	NR	NR	0.11 ± 0.27	1.36 ± 0.35	NR

Note: Significant differences between groups in the outcome measures are indicated in bold.

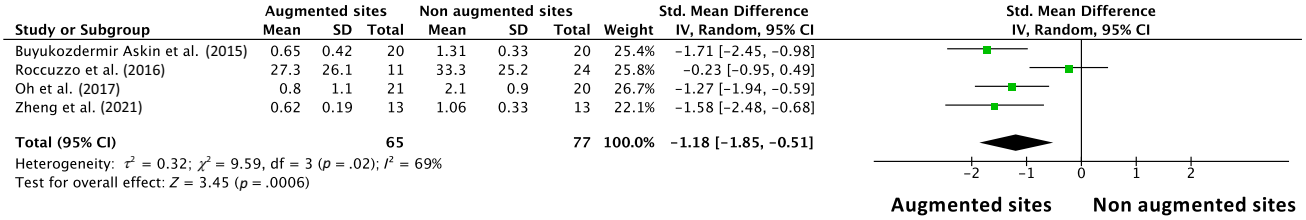
Abbreviations: APF, apically positioned flap; BOP, bleeding on probing; CTG, connective tissue graft; FGG, free gingival graft; F-UP, follow-up; GI, gingival index; KT, keratinized tissue; mBI, modified bleeding index; NR, not reported; NRCT, non-randomized controlled trail; PPD, pocket probing depth; PSM, propensity score matching; RCT, randomized controlled trail; SPC, supportive periodontal/peri-implant care.

[a]6 split-mouth.

(a) Probing pocket depth (PPD): comparison between implant sites with augmented and non-augmented PIKM



(b) Bleeding on probing: comparison between implant sites with augmented and non-augmented PIKM



(c) Marginal bone level: comparison between implant sites with augmented and non-augmented PIKM

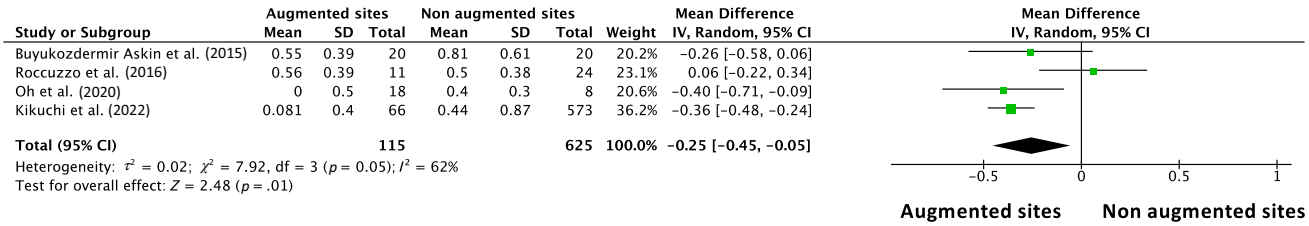


FIGURE 6 Forest plots for impact of peri-implant keratinized mucosa augmentation versus no augmentation on peri-implant probing depth, bleeding on probing, and marginal bone level.

Overall, only three studies reported the occurrence of PIDs (Frisch et al., 2015; Hosseini et al., 2020; M. Roccuzzo et al., 2016). The first study defined peri-implantitis as the presence of BOP, PPD ≥5 mm, and a radiographic bone loss ≥3.5 mm (Frisch et al., 2015). During a mean follow-up of 12 years, three groups receiving FGG or CTG or no intervention were compared. No statistical differences were found between groups. The second study, a 10-year prospective cohort, observed a significantly higher rate of PIDs for dental implants with PIKM deficiency compared to implants surrounded by PIKM (51.4% vs. 12.7%; $p < .0001$) (Roccuzzo et al., 2016). The authors also reported a significantly lower soreness for implants surrounded by PIKM or placed in the alveolar mucosa receiving FGG compared to implants surrounded by alveolar mucosa and not receiving FGG (M. Roccuzzo et al., 2016). The third study was a controlled clinical trial with a small sample size (19 patients) and observed a 4.3% rate of peri-implantitis in the control group compared to 0% in the test group receiving CTG (partial split-mouth design) (Hosseini et al., 2020). Meta-analysis was performed by pooling together two studies comparing CTG versus no intervention (Frisch et al., 2015; Hosseini et al., 2020), and including 37 implants in CTG-augmented sites versus 69 implants in non-augmented sites. It showed no significant difference between the two groups for the rate of incident peri-implantitis (OR = 1.97; 95% CI: 0.2–19.72; $p = .56$; I^2: 0%).

Eight studies (Basegmez et al., 2013; Cairo et al., 2017; Frisch et al., 2015; Huang et al., 2021; Lorenzo et al., 2012; Thoma et al., 2020, 2022; Vellis et al., 2019) assessed the efficacy of alternative techniques for peri-implant soft tissue augmentation, namely FGG, CTF, use of xenogenic collagen matrix (XCM), or acellular dermal matrix. Two articles reported the outcomes of the same RCT, at 3 and 5 years of post-trail follow-up (Thoma et al., 2020, 2022). Pooled data analyses found no difference between CTG/FGG versus XCM for mean PPD, MBL, and BOP (Figure 7).

3.2.5 | Oral hygiene behaviours

Three studies were selected (Alhakeem et al., 2022; Swierkot et al., 2013; Truhlar et al., 2000), including two RCTs and one case–control study (Table 5). No meta-analysis was possible. One multicentre RCT found a significant difference in favour of

counter-rotational powered toothbrush in term of peri-implant mucosa inflammation and implant survival compared to manual toothbrushing over a 2-year follow-up period (Truhlar et al., 2000). The other RCT, comparing sonic versus manual toothbrush over a 1-year trial, concluded that both toothbrushes maintain peri-implant tissue health over time (Swierkot et al., 2013). Finally, the case–control study indicated that the frequency of tooth brushing (at least twice a day vs. at most once a day) had no impact on peri-implant PPD, MBL, and BOP (Alhakeem et al., 2022).

3.2.6 | Other risk factors

No study was found concerning bruxism (or oral parafunction) control in patients awaiting or having received dental implants. Similarly, no study was found addressing the efficacy of behavioural strategies to improve lifestyle in order to maintain peri-implant health and prevent PIDs. Most of the interventions to control risk factors for PIDs remained unexplored.

3.3 | Primordial prevention of PIDs

No study investigated the impact of promoting healthy behaviours prior to implant placement to avoid risk factor development. To further explore this important topic, we revised the studies included in order to try to assess whether any preventive action was undertaken (and thus described) prior to implant placement. The results of this critical appraisal are reported in Table 6. Over the 48 articles included, high heterogeneity was noted; 15 of them (31.2%) clearly stated that periodontal diseases were assessed and treated prior to implant placement. Nineteen studies (39.5%) promoted adherence to SPC and 20 of them (41.7%) considered smoking as an exclusion (or non-inclusion) criterion. Fourteen studies (29%) stated that oral hygiene instructions were given to the patient prior to implant placement, but only a few described the specific OH instructions given.

3.4 | Risk of bias

The ROB assessment for case–control and cohort studies is reported in Table S4. Overall, 32 studies were evaluated based on the NOS system; 14 studies were found to be at high risk (<6 stars) and 18 at low risk of bias (≥6 stars). Concerning the RCTs included, the ROB assessment (ROB-II) is reported in Table S5. Only 2 of 12 trials were judged at low risk of bias. Finally, the four NRCTs were judged to be at moderate risk based on ROBINS-I scale as detailed in Table S6. Only 16 of 48 (33.3%) studies did not declare the source of funding (thus classified as unknown). Similarly, in 12 studies (25%), no declaration about potential conflicts of interest was found. The studies included were published over a period of 22 years (2000–2022).

4 | DISCUSSION

The present systematic review and meta-analysis was designed to assess the efficacy of risk factor control in preventing PIDs. None of the available studies was designed to provide direct evidence for both primordial and primary preventive interventions for PIDs. The present results are therefore inferred from observational and interventional studies with various working hypotheses that were not originally developed to test the efficacy of a preventive measure on the occurrence of PIDs. However, comparing patients exposed and not exposed to risk factors or benefitting or not benefitting from interventions that may decrease the consequence of risk may be useful to elucidate the role of risk factor control in the prevention of PIDs.

4.1 | Main findings

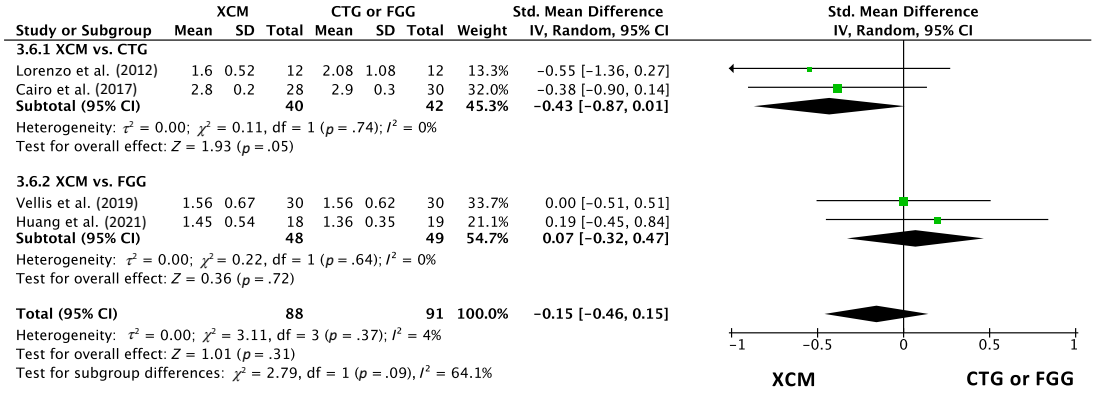
Overall, risk factor control appeared to impact positively on preserving peri-implant health and preventing PIDs, with differences related to the specific risk factor considered.

4.1.1 | Impact of glycaemic control

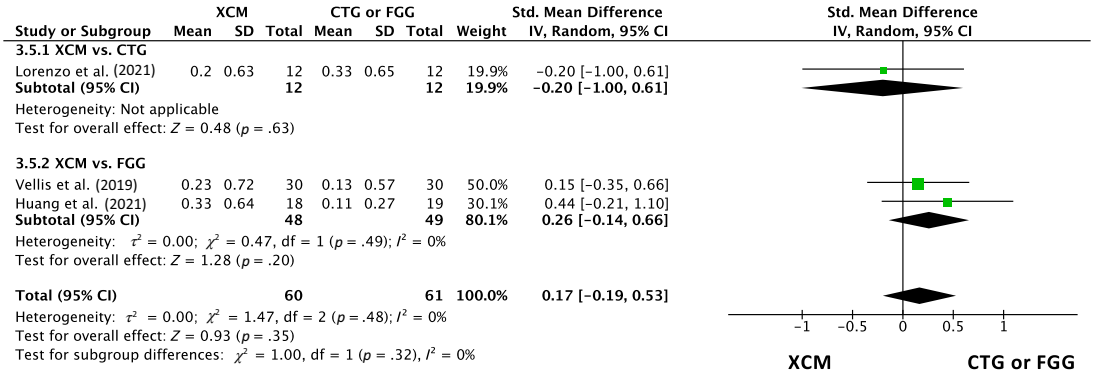
The present meta-analyses showed that diabetes patients with poor glycaemic control (HbA1c >8%) have an increased risk of peri-implantitis and MBL changes over time compared to diabetes patients with a good glycaemic control. Evidence is consistent among the studies but limited and with a mean implant survival rate that may be considered as acceptable in both groups (95.6% and 99%, respectively). The results were reported at the dental implant level only because it was not possible to collect data using the patient as the statistical unit, even though a patient-level analysis would be more appropriate since diabetes is a systemic disease. Pooled-data analyses failed to show differences in PPD and BOP. Since the risk of peri-implantitis is increased, this could be interpreted as conflicting with its case definition, which included increased PPD and BOP (Berglundh et al., 2018). However, a mean difference in MBL was determined. This supports the central role of peri-implant bone loss as a major clinical feature of peri-implantitis (Carral et al., 2021). Pre-diabetes patients may also be seen to be at risk for PIDs, but insufficient data exist to assess this risk compared to controlled or poorly controlled diabetes.

Overall, the present findings were based on 11 studies, of which 4 (36.4%) were judged at high risk of bias. The clinical and statistical heterogeneity was high, which indicates a need for caution in the interpretation of the results. Moreover, no data were available on the type of action taken to control diabetes mellitus (e.g., lifestyle modifications, medications) in patients with good or poor glycaemic control. Finally, 7 of 11 studies were performed in Saudi Arabia where the prevalence of diabetes was estimated at 18.7% in 2021 (https://www.worldbank.org/en/home), one of the highest in the world. This limits the external validity of the data when dealing with European countries. Nevertheless, taken together, the present findings provide

(a) **Probing pocket depth**: comparison between implant sites augmented with xenogenic collagen matrix (XCM) vs. connective tissue graft (CTG) or free gingival graft (FGG)



(b) **Bleeding on probing**: comparison between implant sites augmented with xenogenic collagen matrix (XCM) vs. connective tissue graft (CTG) or free gingival graft (FGG)



(c) **Marginal bone level**: comparison between implant sites augmented with xenogenic collagen matrix (XCM) vs. connective tissue graft (CTG) or free gingival graft (FGG)

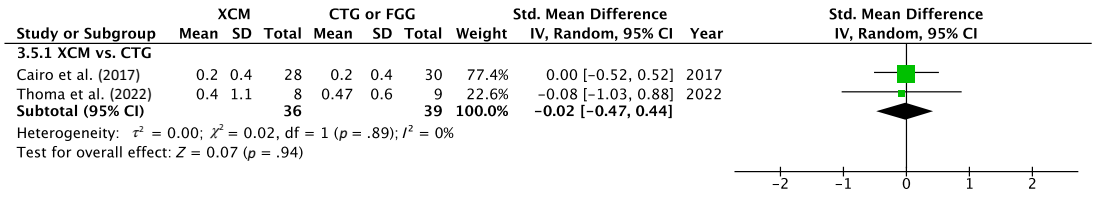


FIGURE 7 Forest plots for impact of different peri-implant soft tissue augmentation procedures on peri-implant probing depth, bleeding on probing, and marginal bone level.

additional evidence-based support to promote optimal glycaemic control in patients with diabetes mellitus undergoing dental implant therapy.

4.1.2 | Impact of smoking cessation

Based on the four studies included in this systematic review, there is insufficient evidence to determine whether smoking cessation or the use of e-cigarettes and other smoking habits are associated with a decreased risk for PIDs compared to current smoking (F. Alqahtani et al., 2019; M. A. AlQahtani et al., 2018; ArRejaie et al., 2019). The best evidence available was represented by the cohort study conducted by Costa et al. The authors showed that the longer the time since smoking cessation, the lower was the occurrence of peri-implantitis: former smokers who quit smoking 6–10 years earlier had a significantly lower OR for peri-implantitis (OR = 0.49; 0.20–0.72) compared to current smokers (Costa et al., 2022). Thus, efforts should

TABLE 5 Characteristics and outcomes of the selected studies analysing the impact of oral hygiene habits on the prevention of peri-implant diseases.

Reference	Study design	Setting Country	Time frame Follow-up duration (months)	Study population Total no. patients (no. of implants)	Type of intervention or exposure No. of patients (no. of implants)	Diagnosis of peri-implant mucositis Patient level	 Implant level	Diagnosis of peri-implantitis Patient level	 Implant level	Survival rate	Peri-implant mucosa inflammation/BOP	Peri-implant probing pocket depth (mm)	Radiographic marginal bone level changes (mm)
Truhlar et al. (2000)	Multicentre RCT	Hospital setting USA	NR F-UP: 24 months	Dental implants placed in Veterans Administration Medical Centres *N* = NR (2966)	**Counter-rotational powered toothbrush** *N* = NR (1409)	NR	NR	NR	NR	**96.1%**	NE—but significantly lower than manual care group	NR	NR
					Manual home-care *N* = NR (1557)	NR	NR	NR	NR	**94.1%**	NE	NR	NR
Swierkot et al. (2013)	RCT	Hospital setting Germany	2008–2010 F-UP: 12 months	Patients treated for periodontitis with at least 1 posterior dental implant *N* = 83 (290)	**Sonic toothbrush** *N* = 42 (NR)	NR	NR	NR	NR	NR	0.27 ± 0.26	3.37 ± 0.85	NR
					Manual toothbrush *N* = 41 (NR)	NR	NR	NR	NR	NR	0.28 ± 0.38	3.19 ± 0.81	NR
Alhakeem et al. (2022)	Case–control study	University setting Iran	2010–2012 Mean F-UP: 7.3 ± 1.4 years	Consecutive patients receiving dental implants (including 47 patients with a history of severe periodontitis) *N* = 88 (186)	**Brushing at least twice/day** *N* = 55 (119)	NR	NR	NR	14/119 (11.8%)	100%	13/119 (10.9%)	PPD ≥ 4 mm: 85/119	MBL ≥ 3 mm: 19/119
					Brushing at most once/day *N* = 33 (67)	NR	NR	NR	4/67 (6%)	100%	12/67 (17.9%)	PPD ≥ 4 mm: 56/67	MBL ≥ 3 mm: 7/67

Note: Significant differences between groups in the outcome measures are indicated in bold.

Abbreviations: BOP, bleeding on probing; F-UP, follow-up; NE, not estimable; NR, not reported; RCT, randomized controlled trail.

TABLE 6 Primordial prevention actions reported in the selected studies.

Variable / Reference	Oral hygiene instructions given prior to implant placement	Achievement of optimal plaque control prior to implant placement	Achievement of low gingival inflammation prior to implant placement	Treatment(s) of periodontal disease prior to implant placement	Promoting smoking cessation	Promoting adherence to periodontal and peri-implant supportive care	Promoting/ monitoring glycaemic control
Glycaemic control							
Tawil et al. (2008)	-	-	-	✓	✓	✓	✓
Aguilar-Salvatierra et al. (2016)	✓	✓	-	✓	Smoking as exclusion criterion	-	✓
Ghiraldini et al. (2016)	-	-	-	✓	Smoking as exclusion criterion	✓	✓
Gomez-Moreno et al. (2015)	-	✓	-	-	Smoking as exclusion criterion	-	✓
Al Amri et al. (2016)	✓	-	-	-	Smoking as exclusion criterion	✓	✓
Abduljabbar et al. (2017)	-	-	-	-	Smoking as exclusion criterion	-	✓
Alrabiah et al. (2018)	-	-	-	-	Smoking as exclusion criterion	-	-
Al-Sowygh et al. (2018)	-	-	-	-	Smoking as exclusion criterion	-	-
Alsahhaf et al. (2019)	-	-	-	-	Smoking as exclusion criterion	✓	✓
Al Zahrani and Al Mutairi (2019)	-	-	-	-	Smoking as exclusion criterion	✓	✓
Mokeem et al. (2019)	-	-	-	-	Smoking as exclusion criterion	-	✓
Smoking cessation strategies							
AlQahtani et al. (2018)	-	-	-	-	-	-	-
ArRejaie et al. (2019)	-	-	-	-	✓	-	Diabetes as exclusion criterion
Alqahtani et al. (2019)	-	-	-	-	-	-	Diabetes as exclusion criterion
Costa et al. (2022)	-	-	-	-	-	-	-
Supportive care protocols/compliance							
Ferreira et al. (2006)	✓	-	-	-	Smoking as exclusion criterion	-	-
M. Rocuzzo et al. (2010, 2012)	✓	✓	✓	✓	-	✓	-

TABLE 6 (Continued)

Variable / Reference	Oral hygiene instructions given prior to implant placement	Achievement of optimal plaque control prior to implant placement	Achievement of low gingival inflammation prior to implant placement	Treatment(s) of periodontal disease prior to implant placement	Promoting smoking cessation	Promoting adherence to periodontal and peri-implant supportive care	Promoting/ monitoring glycaemic control
Rinke et al. (2011)	✓	✓	✓	✓	-	✓	-
Aguirre-Zorzano et al. (2013)	-	-	-	✓	-	✓	-
Roccuzzo et al. (2014, 2022)	✓	✓	✓	✓	-	✓	-
Monje et al. (2017)	✓	-	-	✓	-	-	Diabetes as exclusion criterion
Ziebolz et al. (2017)	-	✓	-	-	Smoking as exclusion criterion	✓	Diabetes as exclusion criterion
Roman-Torres et al. (2019)	-	-	-	-	Smoking as exclusion criterion	-	Diabetes as exclusion criterion
Frisch et al. (2020)	-	-	-	-	-	-	-
Hu et al. (2020)	-	-	-	✓	-	-	-
Alhakeem et al. (2022)	-	-	-	✓	-	-	-
Peri-implant soft tissue augmentation							
Lorenzo et al. (2012)	✓	✓	-	-	-	✓	-
Frisch et al. (2015)	-	-	-	✓	Smoking as exclusion criterion	✓	-
Basegmez et al. (2013)	-	-	-	-	Smoking as exclusion criterion	-	Diabetes as exclusion criterion
Linkevicius et al. (2015)	✓	✓	✓	-	Smoking as exclusion criterion	✓	Diabetes as exclusion criterion
Buyukozdemir Askin et al. (2015)	✓	✓	-	-	Smoking as exclusion criterion	-	-
Roccuzzo et al. (2016)	✓	✓	✓	✓	-	✓	-
Bienz et al. (2017)	-	✓	-	-	-	-	-
Cairo et al. (2017)	-	✓	✓	-	-	-	Diabetes as exclusion criterion
Oh et al. (2017, 2020)	✓	-	-	-	Smoking as exclusion criterion	✓	Diabetes as exclusion criterion
Vellis et al. (2019)	-	-	-	-	-	✓	-
Hosseini et al. (2020)	-	-	-	-	-	-	-
Huang et al. (2021)	✓	-	-	-	Smoking as exclusion criterion	✓	-

(Continues)

TABLE 6 (Continued)

Reference	Variable	Oral hygiene instructions given prior to implant placement	Achievement of optimal plaque control prior to implant placement	Achievement of low gingival inflammation prior to implant placement	Treatment(s) of periodontal disease prior to implant placement	Promoting smoking cessation	Promoting adherence to periodontal and peri-implant supportive care	Promoting/monitoring glycaemic control
Zheng et al. (2021)		✓	✓	✓	✓	-	-	-
Thoma et al. (2020, 2022)		-	-	-	-	-	-	Diabetes as exclusion criterion
Kikuchi et al. (2022)		-	-	-	✓	✓	✓	-
Oral hygiene habits								
Truhlar et al. (2000)		-	-	-	-	-	-	-
Swierkot et al. (2013)		-	-	-	-	Smoking as exclusion criterion	-	Diabetes as exclusion criterion

Note: ✓ Reported in the article.

be made to promote smoking cessation in routine dental practice as recommended by recent guidelines (Herrera et al., 2022; Holliday et al., 2021; Sanz et al., 2020; WHO, 2017). However, this does not appear to have been performed in the selected studies; of the 48 studies, only in 3 the authors clearly stated that smoking cessation interventions were undertaken prior to implant placement, whereas in most of them (20/48) smoking was considered as an exclusion (or non-inclusion) criterion for patient selection, leaving essentially unexplored the impact of promoting smoking reduction or cessation prior to implant placement or after implant loading to prevent PIDs.

4.1.3 | Impact of adherence to SPC

The 14 studies dealing with SPC support, the cardinal role of regular SPC to maintain peri-implant health as well as dental implant survival was emphasized (Cortellini et al., 2019). Indeed, irregular or no SPC over time was associated with a significantly higher risk of peri-implantitis and worse clinical parameters at the patient and dental implant level. Interestingly, at the patient level, the occurrence of mucositis was not significantly different between groups. This may be due to the limited number of study/patients included in the meta-analysis or to the case definition of mucositis (e.g., based on clinical vs. radiographic examinations that did not show bone loss). Most of the studies included patients with a history of periodontitis (treated prior to implant placement), for whom SPC also plays a central role in preventing periodontitis recurrence (Sanz et al., 2020), which in turn may have an impact on peri-implant health (Carra et al., 2022; Cho-Yan Lee et al., 2012; Cortellini et al., 2019). Thus, considering the impact of irregular SPC on peri-implant health, effective and individualized SPC protocols should always be considered in case of dental implant placement and must include all preventive and therapeutic actions necessary to maintain peri-implant health (Sanz et al., 2020). Efforts should be made to increase the patient's knowledge about the importance of follow-up after implant therapy to increase motivation and adherence to SPC (Amerio et al., 2020).

4.1.4 | Impact of augmenting PIKM and peri-implant soft tissue thickness

Overall, there is no evidence to support peri-implant soft tissue augmentation procedures as effective preventive measures for PIDs. No study was designed to assess their role over time, and no conclusion can be drawn to date. However, implants receiving PIKM augmentation procedures showed lower peri-implant inflammation (BOP/GI) and lower MBL changes compared to implants with PIKM width deficiency, suggesting that effective keratinized tissue width augmentation procedures may contribute to maintaining peri-implant health. Few studies observed PIDs events (probably due to short follow-ups), and the incidence of PIDs was not different between augmented and non-augmented sites. Similarly, survival was reported in only three studies, and this hampers any clear conclusion. Concerning the type

of soft-tissue augmentation procedures, no difference was observed for CTG, FGG, or XCM in terms of PPD, BOP, and MBL, but differences in the indication may exist. It is noteworthy that PIKM deficiency was defined differently among the selected studies, encompassing a width of PIKM of <1, 2, or 3 mm, and different techniques were applied. A high variability in the timeline at which the augmentation procedure was performed (before or after dental implant placement, simultaneously to the dental implant placement, at the stage 2 surgery, after dental implant loading, etc.) reflects the high clinical heterogeneity of the included studies. Most of the studies described clinical peri-implant outcomes in the short term (6–12 months follow-up), whereas only two observational studies reported the occurrence of PIDs over a 10- (M. Roccuzzo et al., 2016) and 12-year follow-up (Frisch et al., 2015). Therefore, care must be taken regarding the interpretation of the results, although pooled data analyses (and sensitivity analyses) suggest that augmented PIKM may contribute to peri-implant health, probably ensuring a more resistant peri-implant mucosal seal (Sanz et al., 2022), associated with lower biofilm accumulation, soft-tissue inflammation, mucosal recession, and MBL (Giannobile et al., 2018; Ramanauskaite et al., 2022). This hypothesis should be verified in future studies involving soft tissue augmentation procedures performed with a preventive intent towards PIDs and should also specifically assess the benefits/harms ratio taking into account the invasiveness of the intervention and the expected benefits (risk reduction), which to date cannot be evaluated.

4.1.5 | Impact of oral hygiene behaviours

Very few studies investigated the impact of different oral health (OH) behaviours on peri-implant health and diseases. The three studies included were inconclusive about the type of toothbrush to use (e.g., powered or manual) or the frequency of toothbrushing that is most effective on peri-implant health. Further studies are awaited because OH remains the key factor to avoid plaque accumulation and peri-implant tissue inflammation (Fu & Wang, 2020). Specific and personalized OH instructions should be given to patients prior to implant placement, and then reviewed at each therapeutic step and when the final implant-supported restoration is loaded, to ensure adequate cleanliness of the prosthetic rehabilitation. This is a complex and difficult task for patients, requiring time, dexterity, and motivation.

4.2 | Methodological considerations and study limitations

As mentioned previously, no direct evidence was found assessing the efficacy of primordial and primary preventive interventions for PIDs. This represents the main limitation of the present systematic review and meta-analyses, whose findings are mainly derived from observational studies comparing exposed versus non-exposed groups of patients or two types of intervention not originally delivered to prevent PIDs. Thus, caution should be taken in the critical appraisal of the results, particularly because we are mostly dealing with indirect evidence, heterogenous studies (in terms of design and working hypothesis), and almost 58% of included studies presented with moderate to high risk of bias. Moreover, only 33% of the studies declared whether funding was received or not, which may also represent a source of bias. Finally, most of the results were reported at the dental implant level only. There are many reasons to privilege the patient as a statistical unit. First, there is a philosophical consideration: we treat the patients, not implants. Second, there is a statistical consideration: dental implants are not independent of the teeth and of each other. Third, there is a medical consideration: when dealing with general health, such as glycaemic control or behaviours, such as smoking, the patient is involved.

Regarding primordial prevention, the lack of data is mainly due to a precise definition of what the ideal peri-implant health is. It seems that each author has a personalized prevention programme that best fits the type of study design. Several components should be included in the definition of the ideal peri-implant health that should be reached prior to dental implant placement.

Regarding primary prevention, another limiting factor is the duration of the follow-up, which was highly variable between the studies. In the present systematic review, a follow-up of a minimum of 6 months was set as a selection criterion; this may be a sufficient time lag to detect some signs of peri-implant inflammation but is likely too short to diagnose peri-implantitis. For this reason, most of the studies with a short-term follow-up did not report PID rates or did not observe any case of PIDs. This should be considered when interpreting the present results, knowing that the risk of PIDs may be dependent on the duration of the exposure to the risk factor(s) (e.g., smoking, poorly controlled diabetes, irregular SPC). Very limited data were available specifically on the prevention of peri-implant mucositis, a predictor of peri-implantitis, and various disease case definitions were used. Further, in the selected studies, several different dental implant brands and several different surgical protocols were applied, leading to considerable clinical heterogeneity, which must be taken into account in the critical appraisal of the results.

The biological factors evaluated in the present review were predetermined, based on the available evidence supporting their impact on the peri-implant tissues. It is possible that other unknown factors may have an effect on peri-implant health. PIDs are more likely to exhibit a multifactorial aetiology (Fu & Wang, 2020; Schliephake, 2022), in which several patient-, implant-, and clinician-related risk factors interact and contribute to the development of PIDs. If this model is accepted, the risk factor control should target all modifiable risk factors identified for a specific patient, meaning implementing multiple preventive interventions simultaneously to be effective in maintaining peri-implant health over time.

Finally, for complex diseases such as PIDs, considering that one isolated risk factor cannot cause a disease on its own and that a practitioner treats patients not dental implants, special attention should be paid to the statistical unit of analysis. PIDs should be explored at the patient level, and specific clinical diagnoses of peri-implantitis or

mucositis should be reported on the top of the clinical parameters such as BOP, PPD, and MBL.

4.3 | Implications for future research

- Interventional studies targeting specific preventive measures are needed to gather direct evidence on the efficacy of risk factor control for PIDs.
- Studies should be designed with a follow-up period long enough for the outcomes (e.g., PIDs) to occur.
- Analysis should be performed at the dental implant level and at the patient level.
- Promoting healthy behaviours prior to implant placement to avoid risk factor development (primordial prevention) is probably the most effective strategy to avoid implant complications and PIDs in the long term. In this context, an ideal definition of peri-implant health at the patient level is needed in order to provide an adequate tool to explore primordial prevention in future research.
- The efficacy of preventive measures should be also assessed in specific subsets of patients (e.g., elderly patients, those with comorbidities), in order to assist clinicians in performing personalized medicine.

4.4 | Implications for clinical practice

Based on the biological risk factors reviewed in the present article, in patients with healthy implants, the following preventive approaches should be implemented:

- Considering the impact of irregular SPC on peri-implant health, and since inadequate information/motivation appears to be the main patient-reported reason for non-adherence to SPC (Amerio et al., 2020), efforts should be made to increase patients' knowledge about the importance of follow-up after implant therapy and also to increase the dental professionals' skills in motivating patients' behavioural changes.
- Preventing interventions may include
  - Promotion of glycaemic control in patients with diabetes
  - Smoking cessation counselling
  - PIKM augmentation procedure, in cases of deficiency in keratinized tissue width around implants (and in absence of surgical contraindications)
  - Personalization of OH instructions, accounting for specific patient- and implant-related characteristics.

5 | CONCLUSIONS

Within the limitations of this systematic review, the following conclusions can be drawn:

1. Primary prevention of peri-implantitis relies on regular SPC.
2. In diabetes patients receiving dental implants, glycaemic control is essential for primary prevention of peri-implantitis.
3. An increase of PIKM width may contribute to maintaining peri-implant health.

Further studies are needed to evaluate the impact of smoking cessation and oral hygiene behaviors on the primary prevention of PIDs. A definition for the ideal peri-implant health (at the patient level) is critical to explore primordial prevention. There is an urgent need for standardized primordial and primary prevention protocols for PIDs.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Maria Clotilde Carra https://orcid.org/0000-0002-5717-3274
Nicolas Blanc-Sylvestre https://orcid.org/0000-0002-0559-1837
Alexandre Courtet https://orcid.org/0000-0001-7634-0878
Philippe Bouchard https://orcid.org/0000-0003-2500-3219

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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