Received: 3 November 2020 | Revised: 25 March 2021 | Accepted: 3 May 2021

DOI: 10.1111/clr.13766

SYSTEMATIC REVIEW

CLINICAL ORAL IMPLANTS RESEARCH WILEY

Influence of width of keratinized tissue on the prevalence of peri-implant diseases: A systematic review and meta-analysis

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Abstract

Aim: To evaluate the influence of the width of keratinized tissue (KT) on the prevalence of peri-implant diseases, and soft- and hard-tissue stability.

Materials and methods: Clinical studies reporting on the prevalence of peri-implant diseases (primary outcome), plaque index (PI), modified plaque index (mPI), bleeding index (mBI), bleeding on probing (BOP), probing pocket depths (PD), mucosal recession (MR), and marginal bone loss (MBL) and/or patient-reported outcomes (PROMs; secondary outcomes) were searched. The weighted mean differences (WMD) were estimated for the assessed clinical and radiographic parameters by employing a random-effect model that considered different KT widths (i.e., <2 and ≥2 mm).

Results: Twenty-two articles describing 21 studies (15 cross-sectional, five longitudinal comparative studies, and one case series with pre–post design) with an overall high to low risk of bias were included. Peri-implant mucositis and peri-implantitis affected 20.8% to 42% and at 10.5% to 44% of the implants with reduced or absent KT (i.e., <2 mm or 0 mm). The corresponding values at the implant sites with KT width of ≥2 mm or >0 mm were 20.5% to 53% and 5.1% to 8%, respectively. Significant differences between implants with KT < 2 mm and those with KT ≥ 2 mm were revealed for WMD for BOP, mPI, PI, MBL, and MR all favoring implants with KT ≥ 2 mm.

Conclusion: Reduced KT width is associated with an increased prevalence of peri-implantitis, plaque accumulation, soft-tissue inflammation, mucosal recession, marginal bone loss, and greater patient discomfort.

KEYWORDS
dental implant, keratinized mucosa, peri-implant diseases, systematic review

1 | INTRODUCTION

Peri-implant diseases are defined as inflammatory lesions occurring in tissues surrounding dental implants (Berglundh et al. 2018; Schwarz, Becker, et al., 2018; Schwarz, et al., 2018). At peri-implant mucositis sites, inflammation is strictly restricted to the surrounding mucosa, while at sites affected by peri-implantitis, the mucosal inflammation is associated with loss of supporting bone (Berglundh et al. 2018; Schwarz, Becker, et al., 2018; Schwarz, Derks, et al., 2018). While the disease is clearly linked to a bacterial etiology, numerous local and systemic factors have recently been identified that may increase the probability of its occurrence (Heitz-Mayfield & Salvi, 2018; Schwarz, Becker,

et al., 2018; Schwarz, Derks, et al., 2018). Among them, the absence or a reduced width (i.e., ≤2 mm) of keratinized tissue (KT) was suggested as factor that could jeopardize the long-term maintenance of peri-implant tissue health (Gobbato et al. 2013; Heitz-Mayfield & Salvi, 2018; Lin et al. 2013; Schwarz, Becker, et al., 2018; Schwarz, Derks, et al., 2018). In particular, previous clinical studies have pointed to the absence or reduced KT width as negatively affecting self-performed oral hygiene measures and subsequently increasing implants' susceptibility to inflammatory complications (Perussolo et al. 2018; Roccuzzo et al. 2016; Souza et al. 2016; Ueno et al. 2016). Accordingly, soft-tissue augmentation to gain KT has been recommended and shown to improve tissue inflammatory conditions and to stabilize marginal bone levels compared to control sites (Thoma et al. 2018).

In a clinical setting, a threshold of ≤2 mm is frequently used to define KT width as inadequate (Canullo et al. 2016; Esfahanizadeh et al. 2016; Monje & Blasi, 2019; Perussolo et al. 2018; Souza et al. 2016; Ueno et al. 2016). In particular, a reduced KT band (<2 mm) at dental implants was related to higher plaque accumulation and mucosal inflammation, as well as pro-inflammatory mediators (Boynueğri et al., 2013). In addition, the presence of KT has been shown to have an impact on immunological parameters, with a negative correlation with prostaglandin E2 levels (Zigdon & Machtei, 2008). On the contrary, previous experimental data have indicated that KT amounts exceeding the aforementioned threshold (i.e., range: 2 to 10 mm) had limited effects on the onset of peri-implant mucosal inflammation, but instead affected the disease's resolution following therapy (Schwarz, Becker, et al., 2018; Schwarz, Derks, et al., 2018). Nonetheless, the relevance of the amount of KT for the long-term maintenance and stability of peri-implant soft and hard tissues remains unclear. Therefore, the present systematic review aimed at addressing the following PECO question: "In patients with dental implants (Population), what is the influence of the reduced width of KT (i.e., KT < 2 mm; Exposure) compared to implant sites with a width of KT ≥ 2 mm (Comparison), on the prevalence of peri-implant diseases, soft- and hard-tissue stability, as reported in cross-sectional, case–control, cohort, controlled clinical trials (CCTs), randomized clinical trials (RCTs), longitudinal studies, and case series with a pre–post design (Study design)?"

2 | MATERIAL AND METHODS

The review protocol was developed and structured according to the PRISMA (Preferred Re-porting Items for Systematic Review and Meta-Analyses) Statement (Moher et al. 2009). The review was registered in PROSPERO, an international prospective register of systematic reviews (CRD42020211773). Ethics approval was not required for this systematic review.

2.1 | PECO question

In patients with dental implants (Population), what is the influence of the reduced width of KT (i.e., KT < 2 mm; Exposure) compared to implant sites with a width of KT ≥ 2 mm (Comparison), on the prevalence of peri-implant diseases, soft- and hard-tissue stability, as reported in cross-sectional, case–control, cohort, CCTs, RCTs, longitudinal studies, and case series with a pre–post design (Study design)?

Population: Patients with dental implants;
Exposure: Presence of KT < 2 mm;
Comparison: Presence of KT ≥ 2 mm;
Outcome: *primary outcome*: Occurrence of peri-implant mucositis and/or peri-implantitis based on case definitions used in respective studies; *secondary outcomes:* plaque index (PI), probing depth values (PD), bleeding on probing (BOP)/bleeding index (BI), marginal bone level (MBL) changes, and patient reported outcomes on self-assessment of oral hygiene (PROMs).

2.2 | Inclusion and exclusion criteria

Inclusion criteria:

1. Cross-sectional, case–control, cohort (retrospective and prospective), CCTs, RCTs, longitudinal studies, and case series with a pre–post design including ≥10 patients with dental implants in function at least 6 months, reporting on the association between the amount of KT at implant sites and clinical and/or radiographic outcomes and/or the occurrence of peri-implant diseases; and
2. Studies providing case definitions of peri-implant mucositis and peri-implantitis.

Exclusion criteria:

1. Animal studies;
2. Case reports; and
3. Studies reporting on zygomatic or pterygoid implants.

2.3 | Information source and search

Three electronic databases (MEDLINE [via PubMed], Embase [via OVID], and The Cochrane Library) were searched for relevant articles published until September 2020. The search filter "humans" will be applied. A hand search of the bibliographies of all full-text articles and the following Journals was conducted: "Clinical Oral Implants Research", "Clinical Implant Dentistry and Related Research", "European Journal of Oral Implantology", "Implant Dentistry", "International Journal of Oral & Maxillofacial Implants", "International Journal of Periodontics and Restorative Dentistry", "Journal of Clinical Periodontology", "Journal of Oral Implantology", "International Journal of Oral and Maxillofacial Surgery", "Journal of Periodontology", "Journal of Prosthetic Dentistry", "Open Dentistry Journal", and "Journal of Implants and Advanced Clinical Dentistry". Furthermore, search of the

gray literature (conference proceedings, expert contact, and study register) was performed for potentially relevant articles.

The following MeSH and free-text search terms were used.

2.3.1 | Population

dental implant [MeSH] OR dental implants [MeSH]

2.3.2 | Exposure

keratinized mucosa OR KT OR attached mucosa

2.3.3 | Outcome

peri-implant diseases OR periimplant diseases OR peri-implantitis [Mesh term] OR periimplantitis [Mesh term] OR peri-implant mucositis OR periimplant mucositis OR mucositis [Mesh term] OR peri-implant infection OR periimplant infection OR biological complications OR probing depth OR marginal bone loss OR BOP OR bleeding on probing[Mesh term]

Population AND Exposure AND Outcome

2.4 | Study selection

During the first literature selection stage, according to the defined inclusion criteria, the titles and abstracts of all identified studies were screened for eligibility by two independent reviewers (A.R. and F.S). In the second stage, the full texts of potentially eligible articles were reviewed and evaluated according to the aforementioned exclusion criteria. Differences between reviewers were resolved by discussion and consulting the third reviewer (R.S.). The level of inter-examiner agreement for the first and second literature selection stages was expressed by Cohen's kappa scores.

2.5 | Data collection

From among the selected articles that fulfilled the inclusion criteria, the following data were retrieved and extracted into pre-defined templates:

General and patient-related information: study design, follow-up period/implant functioning time, setting, study funding, number of patients and implants, jaw (maxilla/mandible), location (anterior/posterior), and patient-related information, including age, gender, smoking status, history of periodontitis, and supportive maintenance program;

Implant and prosthetic design-related data: implant type/brand, bone augmentation procedures, time of implant placement (immediate/delayed), two- or one-stage implant placement, prosthetic design (single crown/bridge/full-arch prostheses), and loading protocol (conventional/immediate); and

Association between amount of KT and implant success (i.e., prevalence of peri-implant mucositis and/or peri-implantitis, PD values, BOP/BI values, and MBL), and PROMs.

2.6 | Risk of bias in individual studies

Methodological quality of the included observational studies (i.e., cross sectional, case series, and longitudinal) was assessed based on the Newcastle-Ottawa Quality Assessment Scale for Cohort studies (Wells et al., 2009).

2.7 | Data analyses

Descriptive analysis was conducted to evaluate the prevalence of peri-implant diseases. Quantitative analysis was performed for the investigated clinical and radiographic outcomes. Studies that used the implant as statistical unit were considered for meta-analysis. Heterogeneity among studies, meta-analysis for the final values (i.e., weighted mean differences and 95% confidence intervals, and random-effect model to account for potential methodological differences between studies), and forest plots were assessed using a commercially available software program considering implant as a statistical unit (Review Manager [RevMan] version 5.2. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2012).

3 | RESULTS

3.1 | Search and screening

The screening process yielded 829 articles, 40 of which were selected for full-text evaluation (agreement = 86.15%, kappa = 0.723; 95% CI: 0.487 to 0.894; Figure 1). Upon analysis of the full texts, 18 studies were excluded mainly due to the lack of reporting on any primary outcome or because the outcomes were addressed without specifying KT width (agreement = 97.8%, kappa = 0.80; 95% CI: 0.74 to 0.85; Table 1). Finally, 22 articles describing 21 studies were included in the review.

3.2 | Characteristics of the included studies

The characteristics and results reported in the included studies are presented in Tables 2–5. Publication years ranged from 1994 to 2020. Fifteen included studies were cross-sectional analyses, five were longitudinal comparative studies, and one was a case series with a pre–post design.

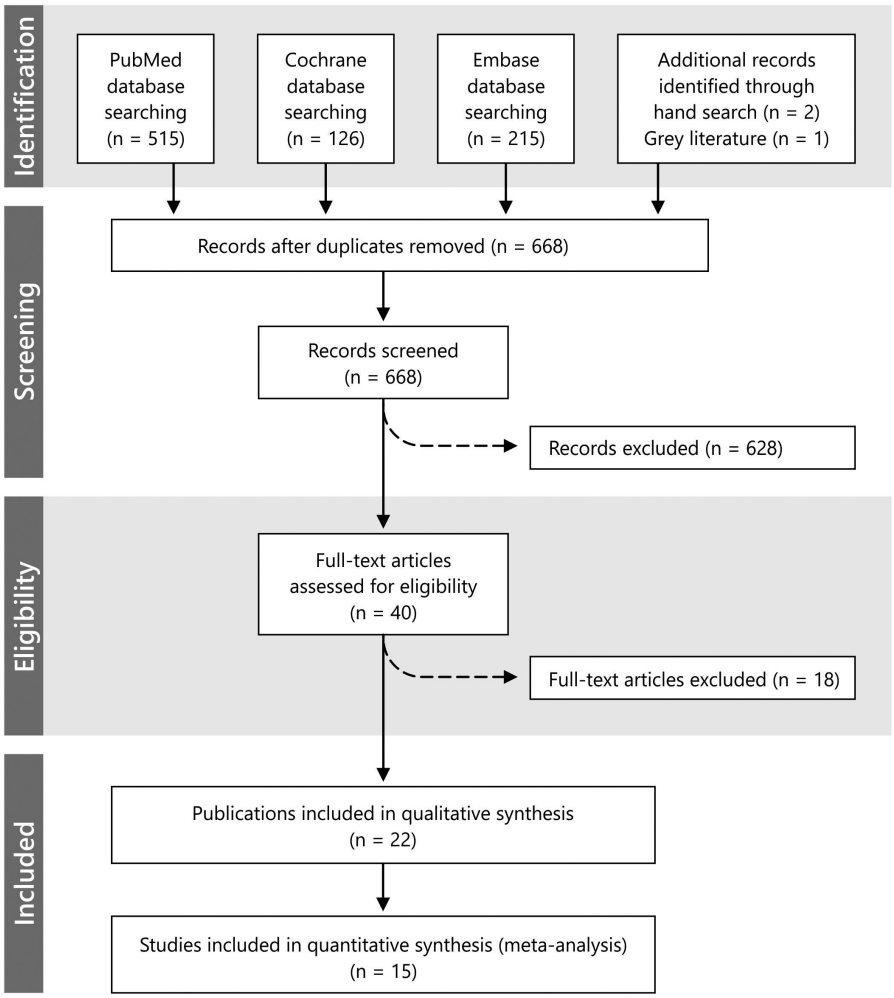

FIGURE 1 Literature search flowchart

TABLE 1 Excluded studies and reasons for exclusion (n = 18)

Reason for exclusion	Studies
Report on peri-implant infection without specifying the diagnosis (i.e., peri-implant mucositis or peri-implantitis)	Gurgel et al. (2020)
Does not provide information on clinical and/or radiographic outcomes	Mameno et al. (2020), Bonino et al. (2018)
Report on the incidence of peri-implant disease/clinical parameters without specifying the KT width	Gunpinar et al. (2020), Vignoletti et al. (2019), Lim et al. (2019), Todisco et al. (2019), Wada et al. (2019), Guarnieri et al. (2018), Matarazzo et al. (2018), Horikawa et al. (2017), Thöne-Mühling et al. (2016), Rokn et al. (2017), Poli et al. (2016), Schwarz et al. (2017), Canullo et al. (2016), Schuldt Filho et al. (2014)
Evaluated the effect of surgical interventions aimed at increasing KT at implant sites	Frisch et al. (2015)

3.3 | Characteristics of the sample

The participants' mean age ranged from 49.9 to 69.85 years. As indicated in eight studies, 3% to 75% of involved patients were current smokers. Eight studies provided information on patients' periodontal health. The proportion of patients with a history of periodontitis ranged from 35.14% to 71% in four studies, whereas in one study, 21.62% of enrolled patients had active periodontal disease. Thirteen studies addressed information on patients' adherence to supportive therapy. In ten of those studies, all patients were enrolled to a

TABLE 2 General and patient-related information

(a) Studies reporting on clinical/radiographic outcomes

Author year	Study design	Follow-up period/implant functioning time Mean (*SD*)	Setting uni/ private	General information			
				No. of patients	No. of implants	Jaw (upper/lower)	Location (anterior/ posterior)
Kungsadalpipob et al. (2020)	Cross sectional	Loading time: 4.4 years (range: 1.5–15.9)	Uni	200	412: KT =0: 32 KT >0: 389	Upper: 181, Lower: 231	Anterior: 81 Posterior: 331
Kabir et al. (2020)	Cross sectional	Loading time: 10.15 (6.31) years; range: 1–31 years	Uni	130	130: KT <2 mm: 74 KT ≥2 mm: 56	Upper KT <2 mm: 29 (42%) KT ≥2 mm: 40 (58%) Lower KT <2 mm: 45 (73.8%) KT ≥2 mm: 16 (26.2%)	Anterior KT <2 mm 20 (52.6%) KT ≥2 mm: 18 (47.4%) Posterior KT <2 mm: 54 (58.7%) KT ≥2 mm: 38 (41.3%)
Grischke et al. (2019)	Cross sectional	Loading time: 7.3 (5.6) years	Uni	52	231: KT <2 mm: 44 (12 patients) KT >2 mm: 187 (40 patients)	NR	Anterior: 14 Posterior: 38
Monje and Blasi (2019)	Cross sectional	5.73 (2.89) years	Private	37	66: KT <2 mm: 26 KT ≥2 mm: 40	45 edentulous gaps: 26—lower jaw, 19—upper jaw	Lower posterior: 43 edentulous gaps, Upper posterior: 17 edentulous gaps, Upper anterior: 2 edentulous gaps
Souza et al. (2016)	Prospective cohort study	Loading time: 58.9 (13.2) months	Uni	80	268: KT < 2 mm: 137 KT ≥ 2 mm: 131	Upper: 129 Lower: 140	NR
Perussolo et al. (2018) (continuum Souza et al. 2016)	Prospective study	4 years	Uni	54 KT <2 mm: 20 KT ≥2 mm: 17 17—exhibited both implant sites (<2 mm and ≥2 mm)	222: KT <2 mm: 90 KT ≥2 mm: 112	Upper: 106%–52.5% implants Lower: 96%–47.5% implants	Upper jaw: 26.7% posterior, 25.7% anterior regions Lower jaw: 41.1% posterior, 6% anterior
Ueno et al. (2016)	Cross sectional	Loading time: 56.6 (38.4) months	Uni	60	89: KT < 2 mm: 32 KT ≥ 2 mm: 57	NR	Premolar and molar regions were included
Esfahanizadeh et al. (2016)	Cross sectional	≥6 months in function	Uni	36	110: KT <2 mm: 62 KT ≥2 mm: 48	NR	Premolar and molar regions were included.
Romanos et al. (2015)	Cross sectional	Loading time: 6.4 (13.7) years	Uni	118	320: KT <2 mm: 199 KT ≥2 mm: 121	NR	NR
Roccuzzo et al. (2016)	Prospective comparative study	10 years	Private	98	87: KT =0: 24 KT >0: 63	Lower	Posterior regions
Ladwein et al. (2015)	Cross sectional	7.78 (1.92) years	Uni	211	967: KT =0: 358 KT >0: 609	KT = 0: Lower: 170 Upper: 188 KT >0: Lower: 248 Upper: 361	KT = 0: Anterior: 97, Posterior: 261 KT >0: Anterior: 222, Posterior: 387

Patient-related information					
Age Mean years	**Gender**	**Systemic condition**	**Smoking status**	**History of periodontitis**	**Maintenance program**
57.3 (range: 18–79)	117/83	18 (9%) patients had diabetes	Former smokers: 10 (10%); Current smokers: 4 (2%)	72 (36%) patients had a history of periodontitis	All participants were placed in a maintenance program
69.85 ± 10.32 years	71/59	Only patients with a history of antibiotic therapy during the last 3 months and lactating mothers were excluded	Smokers: 11 (8%)	History of periodontitis: 92 patients (71%); Periodontitis: 71 patients (55%)	All patients attended maintenance care
67.3 ± 11.2	29/23	Systemically healthy	Non-smokers	Only periodontally healthy patients	All patients enrolled in maintenance care (≥1 time/year)
49.9 ± 12.9	37.6%/32.4%	Systemically healthy	Non-smokers	8 (21.62%) patients had active periodontal disease, 16 (43.24%) history of periodontitis, and 13 (35.14%) periodontally healthy	All patients had erratic compliance (i.e., not attending to a minimum of 2 times of supportive maintenance therapy per year)
52 ± 11.7		Systemically healthy	Heavy smokers (>10 cig./day) excluded	Patients with periodontitis excluded	All patients were enrolled in a maintenance program
55.7 ± 10.7	18/36	Systemically healthy	Heavy smokers (>10 cig./day) excluded	Patients with active periodontal disease excluded	All patients were enrolled in a maintenance program
60.7 ± 12.9	37/23	Systemically healthy	7 Smokers; heavy smokers were (>10 cig./day) excluded	31 (52%) patients had a history of periodontal disease	All patients were enrolled in a maintenance program
57.04 (30–76)	17/19	Systemically healthy	NR	NR	NR
62.6 ± 13.7	55/63	NR	NR	NR	42 (36%) patients were regular compliers 76 (64%) were irregular compliers (hygiene visit every >13 months)
KM = 0:52.8 ± 9.5 KM >0:52.2 ± 10.7	60/38	Systemically healthy	KM =0: 9 (14.3%) Smokers KM >0: 2 (5.7%) Smokers	Severe periodontitis patients excluded	Adherence to supportive therapy: KM =0: 24 (68.6%) KM >0: 52 (82.5%)
54.63 ± 13.58 (at implant insertion)	114/97	NR	NR	NR	NR

(Continues)

TABLE 2 (Continued)

(a) Studies reporting on clinical/radiographic outcomes

Author year	Study design	Follow-up period/implant functioning time Mean (*SD*)	Setting uni/private	General information			
				No. of patients	No. of implants	Jaw (upper/lower)	Location (anterior/posterior)
Boynueğri et al. (2013)	Prospective longitudinal comparative study	1 year	Uni	15	36: KT ≥2 mm: 19 KT <2 mm: 17	Lower	Interforaminal
Crespi et al. (2010)	Prospective longitudinal comparative study	4 years	Uni	29	132: KT <2 mm: 39 KT ≥2 mm: 125	Upper: KT <2 mm: 18, KT ≥2 mm: 114 Lower: KT <2 mm: 21, KT ≥2 mm: 11	Incisors, canines, and premolars
Adibrad et al. (2009)	Cross sectional	Loading time: 25.40 (10.28) months	Uni	27	66: KT <2 mm: 30 KT ≥2 mm: 36	Upper: 24 (36%) Lower: 42 (64%)	NR
Kim et al. (2009)	Cross sectional	12.71 (4.87) months	Uni	100	276: KT <2 mm: 90 KT ≥2 mm: 186	Upper: KT <2 mm: 21, KT ≥2 mm: 101 Lower: KT <2 mm: 59, KT ≥2 mm: 85	Molar and premolar regions
Schrott et al. (2009)	Prospective longitudinal study	5 years	Uni	58	386: KT <2 mm: 40; KT ≥2 mm: 346	Lower	Anterior–posterior
Bouri et al. (2008)	Cross sectional	Loading time: KT <2 mm: 4.10 (2.48) years, KT ≥2 mm: 4.91 (2.76) years	Uni	76	200: KT <2 mm: 90 KT ≥2 mm: 110	NR	NR
Zigdon and Machtei (2008)	Cross sectional	Loading time: 35.24 (16.65) months	Uni	32	63: KT ≤1 mm: 41 KT >1 mm: 22	NR	NR
Chung et al. (2006)	Cross sectional	Loading time: 8.1 (0.23) years	Uni	69	339: KT <2 mm: 84 KT ≥2 mm: 255	Upper: 198 (58.4%), Lower: 141 (41.6%)	Upper: 57—molars, 75—premolars, 35—canines, 31—incisors. Lower: 40—molars, 33—premolars, 24—canines, 44—incisors.
Mericske-Stern et al. (1994)	Prospective longitudinal study	5 years	Uni	33	64: KT <2 mm: 24 KT ≥2 mm: 40	Lower	Interforaminal

(b) Studies reporting only on peri-implant tissue disease

Author year	Study design	Follow-up period/implant functioning time Mean (*SD*)	Setting (Uni/private practice)	General information		
				No. of patients	No. of implants	Jaw (maxilla/mandible)
Ferreira et al. (2015)	Cross sectional	4.02 (1.67) years	Uni	193	725: KT <2 mm: 486 KT ≥2 mm: 238	NR
Roos-Jansåker et al. (2006)	Cross sectional	9–14 years	Uni	218	993: KT = 0: 473 KT >0: 520	NR

Abbreviations: KT, keratinized tissue; NR, not reported; *SD*, standard deviation; Uni, university.

Patient-related information					
Age Mean years	Gender	Systemic condition	Smoking status	History of periodontitis	Maintenance program
NR	8/7	Systemically healthy	Non-smokers only	NR	NR
49.52 (25–67)	11/18	Systemically healthy	Heavy smokers (>10 cig./day) excluded	NR	NR
63.1 ± 6.9	15/12	Systemically healthy	Non-smokers: 22 (18%) Former smokers: 2 (8%) Current smokers: 3 (11%)	NR	All patients enrolled in a regular maintenance care
52.24 ± 10.77	48/52	NR	NR	NR	NR
58.0 ± 9.6	NR	Systemically healthy	55 (75%) smokers and heavy smokers (>10 cig./day) excluded	NR	All patients enrolled in a regular maintenance care
NR	NR	NR	NR	NR	NR
58.6 ± 16.65	18/14	NR	NR	NR	All patients enrolled in a supportive therapy
61.3 ± 13.60	41/28	6 patients had diabetes type 2.	Smokers: 2 (3%) patients	NR	NR
69 ± 7	17/15	NR	NR	NR	All patients enrolled in a supportive therapy

	Patient-related information					
Location (anterior/posterior)	Age Mean years	Gender	Systemic condition	Smoking status	History of periodontitis	Maintenance program
NR	52.67 (14–85)	126/67	NR	NR	NR	NR
NR	NR	NR	Systemically compromised patients included	Smokers included	NR	All patients enrolled in a supportive maintenance program

TABLE 3 Implant and prosthodontic design-related information

Author year	Implant brand/surface	Bone augmentation procedures	Implant placement: immediate/delayed, two–one-stage	Prosthesis design	Loading protocol: immediate/delayed (time to load; months)
(a) Studies reporting on clinical/radiographic outcomes					
Kungsadalpipob et al. (2020)	NR	NR	NR	Fixed prostheses	NR
Kabir et al. (2020)	Straumann and Astra Tech systems	KT <2 mm: 38 (58.5%) KT ≥2 mm: 41.5%	NR	NR	NR
Grieschke et al. (2019)	NR	Yes: 33 patients No: 19 patients	NR	NR	NR
Monje and Blasi (2019)	NR	NR	NR	Screw-retained fixed prostheses	NR
Souza et al. (2016)				Single crowns: 169, fixed-partial prostheses: 83, full-arch fixed prostheses: 16	
Perussolo et al. (2018) (continuum)	NR	NR	NR	Fixed single crowns: 87 Partial prostheses: 91 Fixed full-arch prostheses: 24	NR
Ueno et al. (2016)	63 implants were sand blasted and acid etched, 23 TiUnite, 6—not identified	NR	NR	44—screw-retained restorations, 39—cemented restorations	NR
Esfahanizadeh et al. (2016)	Bone-level implants	No	Delayer, 2 stages	Cemented porcelain-fused-to-metal restorations	NR
Romanos et al. (2015)	Ankylos implants	NR	NR	Single crowns, fixed partial dentures, and removable prostheses	NR
Roccuzzo et al. (2016)	SLA Straumann	No	Delayer, 2 stages	Cemented restorations	NR
Ladwein et al. (2015)	Tissue level Standard Plus/ Standard, Straumann	NR	NR	NR	NR
Boynueğri et al. (2013)	SLA Straumann	NR	Delayed	Overdentures	Early, 2 weeks
Crespi et al. (2010)	Rough surfaced, titanium plasma-sprayed implants Seven, Sweden-Martina	NR	Immediate	Cemented partial or total bridges	Immediate
Adibrad et al. (2009)	NR	NR	NR	Overdentures	NR
Kim et al. (2009)	TiUnite, Implantium, and OssTem	NR	NR	NR	NR
Schrott et al. (2009)	ITI Solid Screw Implants and TPS surface	NR	Delayed, two stages	Full-arch, screw-retained, hybrid-type prostheses	Conventional
Bouri et al. (2008)	NR	NR	NR	NR	NR
Zigdon and Machtei (2008)	Osseotite	NR	NR	Single crowns or fixed partial denture	NR

TABLE 3 (Continued)

Author year	Implant brand/surface	Bone augmentation procedures	Implant placement: immediate/delayed, two-one-stage	Prosthesis design	Loading protocol: immediate/delayed (time to load; months)
Chung et al. (2006)	87 implants—smooth surface (Branemark), 252 implants—modified surfaced of various brands	NR	NR	Fixed prostheses: 250 implants, removable prostheses: 89 implants	NR
Mericske-Stern et al. (1994)	Hollow cylinder ITI	NR	Delayed, one stage	Overdentures	Conventional
(b) Studies reporting only on peri-implant diseases					
Ferreira et al. (2015)	External-hexed cylindric implants	NR	NR	NR	NR
Roos-Jansåker et al. (2006)	NR	NR	Delayed, two stages	NR	Conventional

Abbreviations: KT, keratinized tissue, NR, not reported.

regular maintenance program, whereas one study explicitly included patients not adhering to a regular supportive treatment.

The average implant loading period ranged from 6 months to 14 years. In all but one study, implants with modified surfaces were used. Seven studies lacked information on implant surface or brand. Based on the 14 studies that reported on implant location, 57% of implants were inserted in the lower jaw and 43% were inserted in the upper jaw. As specified in 15 studies, posterior implant locations were more frequent than anterior locations. According to the studies that reported on prostheses designs (n = 15 studies), implants were restored with fixed prostheses (n = 9 studies), removable reconstructions (n = 3 studies), or both prostheses designs (n = 3 studies).

In 16 studies, KT width was measured at the mid-buccal aspect, and two studies provided mean values for the assessed mesial, mid-buccal, and disto-buccal aspects. In the remaining three studies, KT measurements were collected at the mid-buccal and mid-lingual aspects and were either addressed as average values (i.e., including mid-lingual and mid-buccal aspects; Grischke et al. 2019) or reported separately for the two aspects (Mericske-Stern et al. 1994; Schrott et al. 2009). A threshold of <2 mm was used most frequently to define inadequate KM width (n = 16 studies). One study used a cut-off value of 1 mm, and in four studies, the absence of KT (i.e., 0 mm) was defined as a threshold value.

3.4 | Synthesis of results

3.4.1 | Primary outcome

Influence of KT upon peri-implant diseases

Four cross-sectional studies reported on the prevalence of peri-implant diseases relative to KT width (Table 4). There was considerable diversity in the definitions used for the disease, particularly for the threshold values used for MBL for peri-implantitis diagnosis (i.e., >2 mm [Ferreira et al. 2015] and ≥3 mm [Roos-Jansåker et al., 2006, Kungsadalpipob et al. 2020]). One study used definitions introduced by the 2017 World Workshop on the Classification of Periodontal and Peri-implant Diseases and Conditions (Monje & Blasi, 2019).

For implant sites with inadequate KT width (<2 mm in two studies or 0 mm in two studies), peri-implant mucositis and peri-implantitis affected 20.8% to 42% and 10.5% to 44% of implants, respectively. For implant sites with sufficient KT (i.e., ≥2 mm or >0 mm), the corresponding values were 20.5% to 53% (peri-implant mucositis) and 5.1% to 8% (peri-implantitis).

3.4.2 | Secondary outcomes

Considering different study designs, 15 studies (i.e., cross sectional: n = 9 and longitudinal studies: n = 6) that assessed KT width on the buccal aspect and used a threshold of 2 mm (i.e., <2 mm vs. ≥2 mm) were considered for quantitative analysis.

TABLE 4 Association between amount of keratinized tissue (KT) and peri-implant tissue health or disease

Author and year	Amount of KT	Definitions of peri-implant disease	Association between amount of KT and occurrence of peri-implant diseases	Additional comments
Kungsadalpipob et al. (2020)	KT > 0 *n* = 380 implants KT ≤ 0 *n* = 32 implants	Healthy implants: absence of soft-tissue inflammation and bone loss PM: soft-tissue inflammation with bleeding during probing at ≥1 aspect (recorded as mSBI ≥ 2) and no evidence of bone loss after remodeling PI: presence of soft-tissue inflammation with bleeding/suppuration at least 1 aspect of implants and bone loss beyond functional remodeling ≥3 mm	KT ≤ 0 Health: 43.8% implants PM: 31.3% PI: 25% KT >0 Health: 72.6% PM: 20.5% PI: 6.8%	Absence of KT was associated with PI ($p < .005$)
Monje and Blasi (2019)	KT <2 mm *n* = 26 implants KM ≥2 mm *n* = 40 implants	Health, PM, and PI defined according to workgroup 4 of the 2017 World Workshop on the Classification of Periodontal and Peri-implant Diseases and Conditions	KT <2 mm Health: 16% PM: 40% PI: 44% KT ≥2 mm Health: 53.8% PM: 41% PI: 5.1%	All clinical and radiographic parameters were significantly increased when KM was <2 mm
Ferreira et al. (2015)	KT <2 mm *n* = 486 implants KT≥2 mm *n* = 238 implants	PM: PD ≥4 mm + BOP + bone loss <2 mm PI: PD ≥4 mm + BOP/suppuration + bone loss ≥2 mm	KT <2 mm Health: 334/486 (68.7%9 PM: 101/486 (20.8%) PI: 51/486 (10.5%) KT≥2 mm: Health: 156/238 (65.5%) PM: 65/238 (27.3%) PI: 17/238 (7.2%)	Significant association between KT <2 mm and the presence of peri-implant disease
Roos-Jansåker et al. (2006)	KT ≤0 *n* = 473 implants KT >0 *n* = 520 implants	PM: PD≥4 mm + BOP PI: bone loss ≥3 mm threads when comparing with radiograph taken at the final examination with the one taken 1 year after placement of suprastructure + BOP/Suppuration	PM: KT ≤0 201/473 (42%) KM >0 275/520 (53%) PI: KT ≤0 24/468 (5%) KT >0 42/514 (8%)	Presence of KT was associated with PM ($p = .02$)

Abbreviations: BOP, bleeding on probing; MBL, marginal bone loss; PD, probing pocket depth; PI, peri-implantitis; PI, plaque index; PM, peri-implant mucositis.

Influence of KT upon hygienic conditions

Longitudinal studies. According to the data extrapolated from three longitudinal studies with a mean follow-up period ranging from 1 to 5 years, WMD for mPI was −0.30 (95% CI: −0.61 to 0.00; $p = .05$), with considerable heterogeneity existing among the studies ($I^2 = 95\%$; $p < .0001$; Figure 2a).

Cross-sectional studies. The summary of data provided in the three studies revealed WMD for mPI of −0.25 (95% CI: −0.33 to −0.17; $p < .0001$), with irrelevant heterogeneity detected among the studies ($I^2 = 34\%$, $p = .22$; Figure 2b). Based on six studies, WMD for PI was −0.32 (95% CI: −0.64 to 0.00; $p = .05$). The heterogeneity among the studies was considerably high ($I^2 = 93\%$, $p < .00001$; Figure 3).

Influence of KT upon soft-tissue stability

Longitudinal studies. According to the data extracted from two longitudinal studies with 4- to 5-year follow-up periods, the average WMD for mBI was −0.21 (95% CI: −0.65 to 0.23; $p = .36$). Considerably high heterogeneity was found between the studies ($I^2 = 99\%$; $p < .0001$; Figure 4a). The WMD for BOP was −0.12 (95% CI: −0.17 to −0.07; two studies; $p = .00001$), and insignificant heterogeneity was found between the investigations (range of mean follow-up: 1 to 4 years; $I^2 = 0\%$; $p = .89$; Figure 5).

Based on data extrapolated from three studies with a mean follow-up period ranging from 1 to 4 years, WMD for PD was 0.03 mm (95% CI: −0.16 to 0.21; $p = .77$), and high heterogeneity was found ($I^2 = 76\%$; $p = .01$; Figure 6a). The estimated WMD for MR was −0.35 mm (95% CI: −0.81 to 0.11; $p = .13$). The heterogeneity value was 81%, with $p = .02$, indicating significant heterogeneity between the studies the two studies (range of mean follow up: 1 to 4 years; Figure 7a).

Cross-sectional studies. Based on the results from five studies, the average WMD for mBI was −0.22 (95% CI: −0.50 to 0.07; $p = .14$), with considerable heterogeneity existing among the studies ($I^2 = 97\%$; $p < .0001$; Figure 4b).

When the data provided in nine studies were pooled, the estimated WMD for PD was −0.12 mm (95% CI: −0.28 to 0.04; $p = .13$). The heterogeneity among the studies appeared to be high ($I^2 = 79\%$; $p < .0001$; Figure 6b). According to the five studies, the WMD for MR was −0.21 (95% CI: −0.29 to −0.13; $p = .0001$), and irrelevant heterogeneity was detected among the studies ($I^2 = 14\%$; $p = .32$; Figure 7b).

The WMD for Sup was −0.02 (95% CI: −0.07 to 0.03; $p = .47$), with irrelevant heterogeneity existing between the two cross-sectional studies ($I^2 = 0\%$; $p = 1.0$; Figure 8).

Influence of KT upon bone stability

Longitudinal studies. Two longitudinal studies (the range of the mean follow-up period was 1 to 4 years) were included for the evaluation of WMD MBL, which was −0.17 mm (95% CI; −0.30 to −0.05; $p = .007$). Insignificant heterogeneity was found among the studies ($I^2 = 0\%$, $p = .64$; Figure 9a).

Cross-sectional studies. According to five cross-sectional studies, WMD for MBL was −0.33 mm (95% CI: −0.62 to 0.04; $p = .03$). The heterogeneity among the studies was considerably high ($I^2 = 88\%$; $p < .0001$; Figure 9b).

Influence of KT upon PROMs

Five analyses, two of which considered the same patient population (Perussolo et al. 2018; Souza et al. 2016), reported on PROMs (Monje & Blasi, 2019; Roccuzzo et al. 2016; Ueno et al. 2016). Dichotomous (yes/no) grading or visual analogue scale (VAS) was adopted to assess patients' discomfort during brushing. Level of brushing discomfort was significantly higher at sites with <2 mm of KT (Monje & Blasi, 2019; Perussolo et al. 2018; Souza et al. 2016). This was particularly true for implant sites with reduced KT in the posterior regions of the lower jaw compared to the posterior sites in the upper jaw (Perussolo et al. 2018). Likewise, significantly more patients reported pain or discomfort during oral hygiene procedures with insufficient KT at lower posterior implants compared to the control group patients (i.e., KM > 0 mm; 42.9% vs. 0%, respectively; $p < .001$; Roccuzzo et al. 2016). By contrast, in another study, reduced KT width (<2 mm) did not present an impediment to oral hygiene control compared to control sites ($p = .1$; Ueno et al. 2016).

3.5 | Risk of bias

Summarized results of the assessment of risk of bias are presented in Table 6. Based on the Newcastle-Ottawa Scale, 13 studies had an overall high risk of bias (4 to 6 stars) and eight studies (7 to 9 stars) were judged to have a low risk of bias.

4 | DISCUSSION

4.1 | Main findings

The present systematic review evaluated the influence of KT width at implant sites on peri-implant tissue health or disease. In total, 22 publications reporting data from 21 different observational investigations were included, the majority of which were cross-sectional studies ($n = 13$) and the remaining were either longitudinal ($n = 5$ studies) or case–control ($n = 1$ study) analyses.

Basically, the summary of the data provided by the included studies suggests that a reduced amount or a lack of KT (i.e., <2 mm) is associated with compromised peri-implant tissue health compared to implant sites with at least 2 mm of KT. In particular, according to the data extrapolated from cross-sectional studies, peri-implantitis was more frequently detected at dental implants with reduced width of KT (i.e., <2 mm or ≤0 mm) than at those with adequate KT width (i.e., ≥2 mm or >0 mm; 10.5% to 44% and 5.1% to 8%, respectively). Furthermore, implant sites with KT <2 mm yielded higher plaque and bleeding scores compared to the control sites, as shown by the summary of cross-sectional and longitudinal data (mPI: WMD: −0.30;

95% CI: −0.30 to −0.1, $p = .05$ [longitudinal studies]; WMD: −0.25; 95% CI: 9.33 to −0.17, $p < .0001$ [cross-sectional studies]; and WMD BOP: −0.12; 95% CI −0.17 to −0.07, $p = .05$ [longitudinal studies]).

Cross-sectional and longitudinal studies indicated significant differences between the two groups, in terms of MBL, favoring implants exhibiting KT of ≥2 mm (cross-sectional studies: WMD: −0.33; 95%

TABLE 5 Association between KT and clinical and/or radiographic outcomes

Author and year	KT threshold value/ assessment location	Bleeding scores Mean (*SD*) (G1/G2) Mean (*SD*)	Plaque scores Mean (*SD*) (G1/G2) Mean (*SD*)	PD Mean (*SD*) (G1/G2) Mean (*SD*)
Kungsadalpipob et al. (2020)	G1: KT =0; G 2: KT >1 mm Mid-B	mSBI (implant level) 0.25 (0.40)/0.32 (0.46) $p = .446$	mPI 0.18 (0.25)/0.15 (0.35), $p = .073$	2.74 (0.64)/2.83 (0.77) $p = .601$
Kabir et al. (2020)	G1: KT <2 mm; G 2: KT ≥2 mm Mid-B	mBI (implant level) 1.42(0.8)/1.41(0.87) BOP Yes: 70 (58.8%)/49 (41.2%) NO 4 (36.4%)/7 (36.6%)	mPI 0.86(0.94)/0.82(0.75)	3.93(1.93)/3.65(1.38)
Grieschke et al. (2019)	G1: KT <2 mm; G 2: KT >2 mm Mid-B+Mid-L	BOP (implant level) Yes: 24 (54.4%)/122 (65.2%) No: 20 (45.5%)/65 (34.8%) $p = .1214$ BOP (patient level) Yes: 2 (16.7%)/17 (42.5%) No: 10 (83.3%)/23 (57.5%) $p = .1487$	NR	NR
Monje and Blasi (2019)	G1: KT <2 mm; G2: KT ≥2 mm B (mesial, middle, distal)	mBI (implant level) 1.15(0.69)/0.46(0.57) $p = <.001$	PI 1.08(0.86)/0.28(0.41) $p < .001$	4.86 (1.06)/3.65(1.06) $p < .001$
Souza et al. (2016)	G1: KT <2 mm; G 2: KT ≥2 mm Mid-B	BOP (implant level) 63.8(2.93)/51.0(27.2) $p = .033$	PI 0.92(0.52)/0.60(0.51) $p = .008$	2.43(0.65)/2.61(0.41) $p = .582$
Perussolo et al. (2018) (continuum Souza et al)	G1: KT <2 mm; G 2: KT ≥2 mm Mid-B	BOP (implant level) Baseline: 0.55(0.19)/0.44(0.27) 4 years: 0.67(0.21)/0.56(0.26) $p = .039$	mPI Baseline 0.83(0.92)/0.45(0.55) 4 years: 0.91(0.60)/0.54(0.48) $p = .008$	Baseline: 2.30(0.52)/2.43(0.77) 4 years: 2.77(0.68)/2.76(0.75) $p = .188$
Ueno et al. (2016)	G1: KT <2 mm; G 2: KT ≥2 mm B (mesial, middle, distal)	BOP (implant level) 0.21(0.41)/0.06(0.25) $p = .001$	PI 0.24(0.45)/0.13(0.35) $p = .04$	2.66(1.20)/2.21(0.86) $p = .001$
Esfahanizadeh et al. (2016)	G 1: KT <2 mm, G 2: KT ≥2 mm Mid-B	mBI (implant level) 0.822(0.371)/0.50(0.3649 $p = .001$	mPI 0.866(0.364)/0.677(0.252) $p = .002$	2.65(0.339)/2.531(0.366) $p < .05$
Romanos et al. (2015)	G 1: KT <2 mm; G 2: KT ≥2 mm Mid-B	mBI (implant level) 0.39(0.60)/0.12(0.37) $p = <.001$	PI 0.69(0.63)/0.45(0.56) $p = .001$ Regular compliers: 0.53(0.60) /0.38(0.54) Irregular compliers: 0.89(0.62)/0.55(0.58)	NR
Roccuzzo et al. (2016)	G 1: KT =0; G 2: KT >0 Mid-B	BOP (implant level) 33.3(25.2)/23.4(18.4) $p = .23$	PI 37.5(27.6)/21.0(20.2) $p = .03$	2.77(0.70)/3.13(0.59) $p = .08$

CI; −0.62 to 0.04, $p = .03$; longitudinal studies: WMD: −0.17; 95% CI: −0.30 to −0.05, $p = .007$). As suggested by cross-sectional and longitudinal analysis, PD values did not differ between the implant sites with KT <2 mm and those with ≥2 mm. The quantitative summary of cross-sectional studies revealed a significant difference in MR between the two groups, favoring implants with KT ≥2 mm (WMD:

SUP Mean (*SD*) (G1/G2) Mean (*SD*)	MBL Mean (*SD*) (G1/G2) Mean (*SD*)	MR Mean (*SD*) (G1/G2) Mean (*SD*)	PROMs
NR	1.18 (1.43)/0.77(1.04) $p = .490$	0.17(0.45)/0.03(0.26) $p = .05$	NR
NR	NR	NR	NR
NR	NR	NR	NR
0.08(0.20/0.06(0.18) $p = .666$	2.03 (1.65)/0.64(0.93) $p = .001$	NR	Brushing discomfort VAS: 53.8(30.7)/97.0(8.5) $p < .001$
NR	NR	NR	Brushing discomfort VAS: 16.9(21.8)/5.1(9.2), $p = .0014$
NR	Baseline: 1.82(0.83)/1.82(0.75) 4 years: 2.11(1.13)/1.87(0.77) Bone loss: 0.26(0.71)/0.06(0.48) $p < .05$	NR	Brushing discomfort VAS: Baseline and 4 years: G1:51.4% of the patients reported some discomfort At baseline VAS in lower jaw: 24.37(28.31) G2: most of the patients reported no discomfort At baseline in lower jaw: 4.5(8.64), $p = .013$ 4 years: upper and lower jaw: no difference between two groups
0.03(0.18)/0.01(0.08) $p = .17$	NR	0.44(0.71)/0.34(0.69) $p = .25$	Degree of difficulty of brushing (0—easy, 1—ordinary, 2—difficult) 2.19(0.47)/2.09(0.51), $p = .1$
NR	NR	0.230(0.459)/0.10(0.309) $p = .007$	NR
NR	NR	0.27(0.44)/ 0.06(0.23) $p < .0001$	NR
NR	0.50(0.38)/0.34(0.38) $p = .07$	2.08(0.71)/0.16(0.39) $p = .0001$	Presence of discomfort upon hygiene maintenance (1—yes, 0—no) 15 (42.9%)/ 0, $p < .001$

TABLE 5 (Continued)

Author and year	KT threshold value/ assessment location	Bleeding scores Mean (*SD*) (G1/G2) Mean (*SD*)	Plaque scores Mean (*SD*) (G1/G2) Mean (*SD*)	PD Mean (*SD*) (G1/G2) Mean (*SD*)
Ladwein et al. (2015)	G 1: KT =0; G 2: KT >0 Mid-B	BOP (implant level) Distal: 46.1%/35.9% $p < .05$ Buccal: 43.7%/32.1% $p < .05$ Mesial: 57.7%/50.6% $p = .55$	mPI score 0:24.3%/32.8% score 1:19%/36.1% score 2:23.9%/18.1% score 3:32.7%/12–9% $p < .05$	Distal: 3.3(1.4)/3.5(1.5) $p = .21$ Buccal: 2.9(1.3)/2.9(1.3) $p = .81$ Mesial: 3.8(1.6)/3.6(1.5) $p = .28$
Boynueğri et al. (2013)	G 1: KT <2 mm; G 2: KT ≥2 mm Mid-B	BOP (implant level) Baseline: 0.5(0.310)/0.258(0.252) 6 months: 0.383(0.410)/0.467(0.329) 1 year: 0.392(0.356)/0.241(0.304) $p > .05$	PI Baseline: 0.283(0.378)/ 0.120(0.1946) months: 0.20(0.240)/0.283(0.402) 1 year: 0.583(0.532)/ 0.250(0.486) $p < .05$	NR
Crespi et al. (2010)	G 1: KT <2 mm; G 2: KT ≥2mm Mid-B	mBI (implant level) 0.78(0.05)/0.35(0.05) $p = .008$	mPI 1.71(0.12)/1.18(0.09) $p = .005$	2.81(0.41)/2.71(0.34) $p = .531$
Adibrad et al. (2009)	G 1: KT <2 mm; G 2: KT ≥2mm Mid-B	BOP (implant level) 0.49(0.30)/0.38(0.34) $p = .04$	PI 1.87(0.59)/1.20(0.71) $p = .02$	3.11(0.56)/2.98(0.51) $p = .115$
Kim et al. (2009)	G 1: KT <2 mm; G 2: KT ≥2 mm Mid-B	NR	PI (implant level) 0.74(0.91)/0.74(0.83) $p = .943$	2.62(1.55)/2.84(1.80) $p = .328$
Schrott et al. (2009)	G 1: KT <2 mm; G 2: KT ≥2 mm Mid-B+Mid-L	mBI (implant level) buccal: 0.05(0.24)/0.07(0.32) $p = .13$ lingual: 0.13(0.41)/0.22(0.53) $p < .01$	mPI buccal: 0.24(0.54)/0.25(0.56) $p = .38$ lingual: 0.67(0.85)/0.40(0.68) $p = .001$	NR
Bouri et al. (2008)	G 1: KT <2 mm; G 2: KT ≥2 mm Mid-B	NR	PI (implant level) 1.78(0.78)/1.25(0.53) $p < .001$	3.87(0.66)/3.72(0.75), $p = .132$
Zigdon and Machtei (2008)	G 1: KT ≤1 mm, G 2: KT >1 mm Mid-B	BOP (implant level) 0.226(0.347)/0.363(0.295) $p = .031$	NR	2.664(0.776)/3.13(0.868) $p = .04$
Chung et al. 2006	G 1: KT <2 mm; G 2: KT ≥2 mm Mid-B	mBI (implant level) 0.40(0.06)/0.54(0.09) $p > .05$	mPI 1.51(0.09)/1.26(0.05) $p < .05$	2.85(0.06)/2.90(0.05) $p > .05$
Mericske-Stern et al. (1994)	G 1: KT <2 mm; G 2: KT ≥2 mm Mid-B+Mid-L	BI (implant level) Buccal: 0.16(0.1)/0.10(0.3) Lingual: 0.24(0.6)/0.35(0.1) $p > .05$	NR	Buccal: 2.45(1.1)/2.82(0.9) Lingual: 2.88(0.8)/3.06(1.0) $p > .055$

Abbreviations: B, buccal; BOP, bleeding on probing; G1, KT <2 mm; G2, KT≥2 mm; KT, keratinized tissue; L, lingual; MBL, marginal bone loss; MR, mucosal recession; PD, probing pocket depth; PI, plaque index; SBI, sulcus bleeding index; *SD*, standard deviation; SUP, suppuration; VAS, visual analogue scale.

−0.21; 95% CI: −0.29 to −0.13; $p = .0001$). This latter finding, however, was not supported by the meta-analysis based on longitudinal studies (WMD: −0.35; 95% CI: −0.81 to 0.11, $p = .13$). Based on the patient-reported outcomes, implant sites with an absent or reduced KT band (i.e., <2 mm) were more prone to brushing discomfort.

To the authors' knowledge, this is the first analysis evaluating the impact of KT width at implant sites to specify different investigation types (i.e., cross-sectional and longitudinal studies).

4.2 | Agreements and disagreements with previous systematic reviews

4.2.1 | Prevalence of peri-implant diseases

To the authors' best knowledge, no former systematic reviews assessed the impact of KT width on peri-implant buccal aspect on the prevalence of peri-implant diseases, which in turn does not allow

SUP Mean (*SD*) (G1/G2) Mean (*SD*)	MBL Mean (*SD*) (G1/G2) Mean (*SD*)	MR Mean (*SD*) (G1/G2) Mean (*SD*)	PROMs
NR	Vertical bone defect distal: 0.8(1.4)/0.7(1.2) $p = .70$ Mesial: 0.9(1.2)/0.8(1.3) $p = .31$	NR	NR
NR	NR	NR	NR
NR	0.99(0.58)/0.85(0.23) $p = .25$	1.30(0.80)/0.24(0.16) $p = .008$	NR
NR	1.24(0.91)/1.12(0.75) $p = .07$	0.85(0.79)/0.55(0.49) $p = .03$	NR
NR	0.65(0.81)/0.41(0.75) $p = .019$	0.72(0.99)/0.32(0.69) $p = .001$	NR
NR	NR	0.69(1.11)/0.08(0.86) $p = .001$	NR
NR	1.72(1.18)/1.24(0.69) $p < .001$	NR	NR
NR	NR	0.274(0.515)/0.9(0.778) $p = .001$	NR
NR	0.11(0.02)/0.11(0.02) $p > .05$	NR	NR
	NR	NR	NR

for any comparison. Nonetheless, the tendency noted in the present analysis, pointing to higher peri-implantitis prevalence at implant sites with reduced KT width (i.e., <2 mm or 0 mm), may be supported by abundant data from observational clinical studies that identified reduced KT width (i.e., <2 mm) as one factor that increases the risk for biological implant complications (Canullo et al. 2016; Matarazzo et al. 2018; Rokn et al. 2016; Vignoletti et al. 2019; Wada et al. 2019). Furthermore, one retrospective analysis depicted that a KT of ≤1 mm significantly increased the risk for peri-implantitis in patients who were initially suffering from peri-implantitis mucositis, irrespective of the patients' adherence to preventive maintenance care ($p = .001$; Costa et al. 2012). By contrast, other authors failed to show that a lack of or reduced amount of KT in patients who adhere to regular maintenance increases the risk of peri-implant diseases

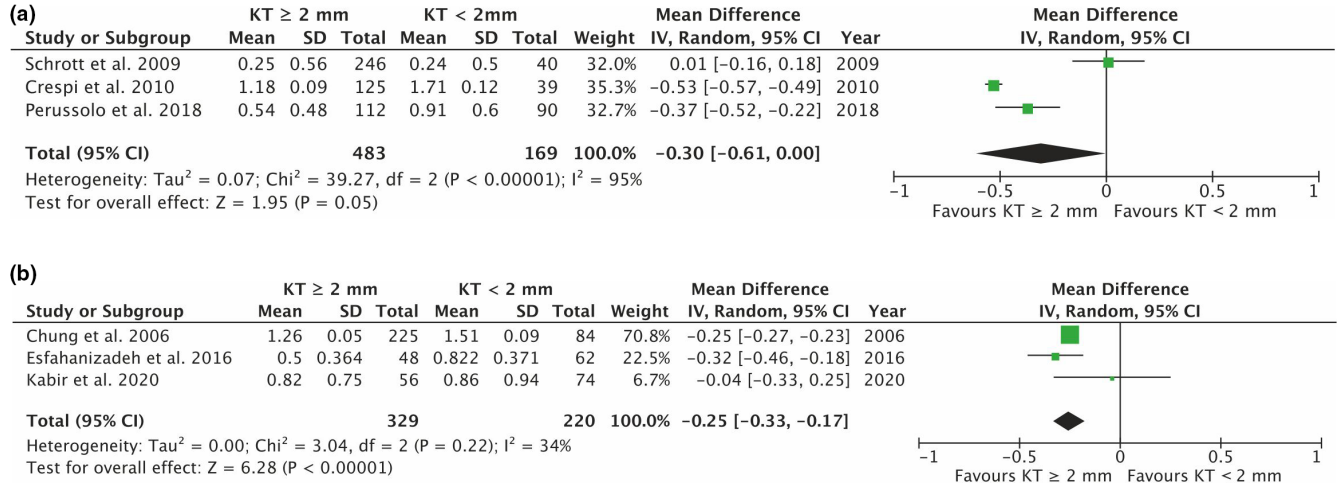

FIGURE 2 (a) Forest plot indicating the weighted mean difference (95%) in modified plaque indices (mPI; longitudinal studies). (b) Forest plot indicating the weighted mean difference (95%) in modified plaque indices (mPI; cross-sectional studies)

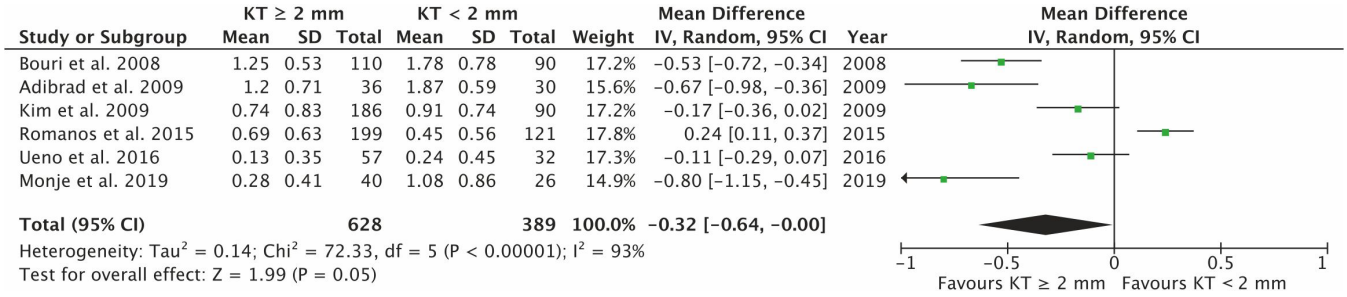

FIGURE 3 Forest plot indicating the weighted mean difference (95%) in plaque indices (PI; cross-sectional studies)

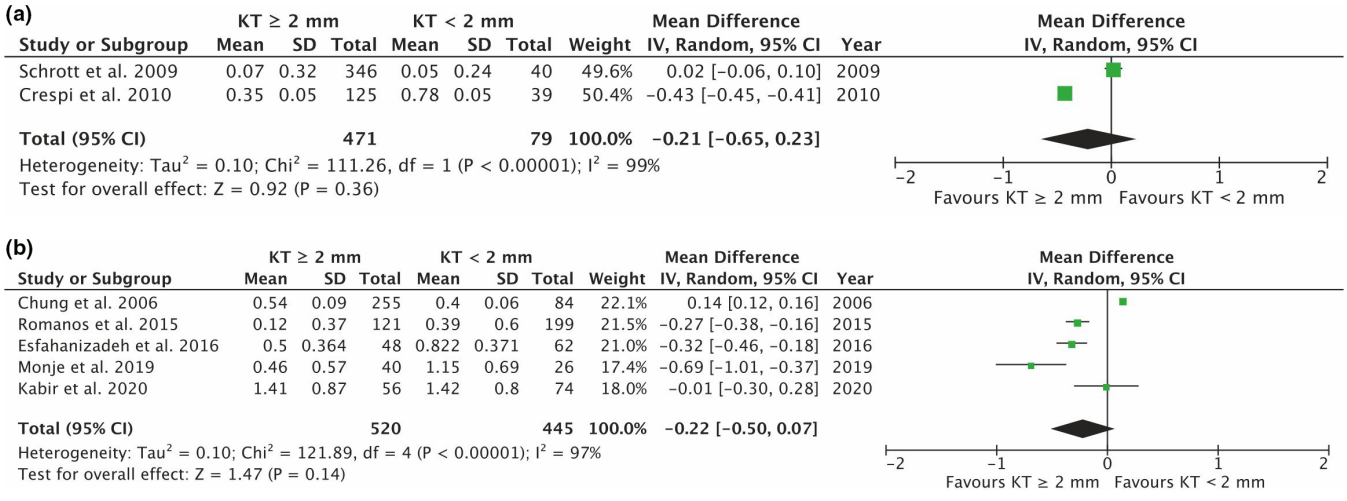

FIGURE 4 (a) Forest plot depicting the weighted mean difference (95%) in modified bleeding indices (mBI; longitudinal studies). (b) Forest plot depicting the weighted mean difference (95%) in modified bleeding indices (mBI; cross-sectional studies)

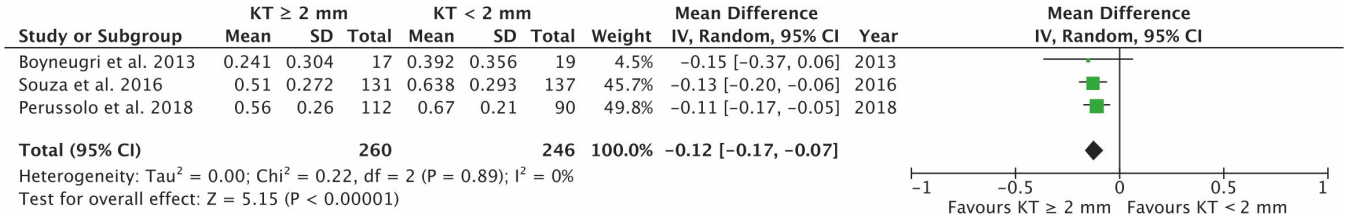

FIGURE 5 Forest plot depicting the weighted mean difference (95%) in bleeding on probing (BOP; longitudinal studies)

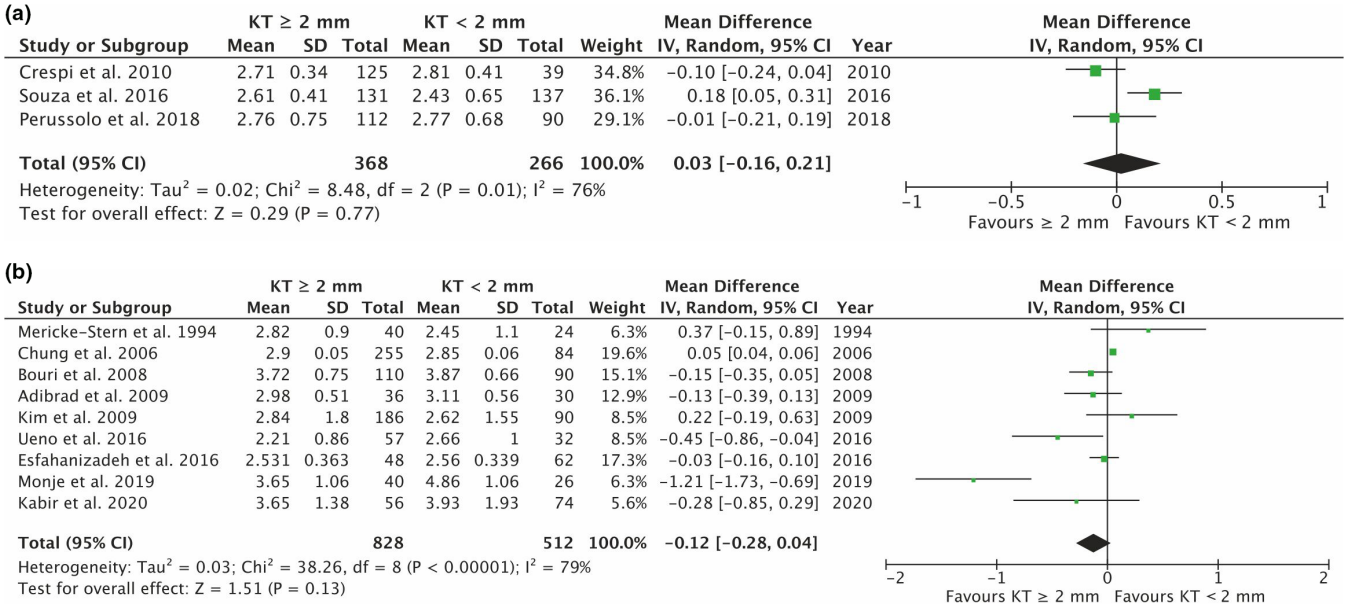

FIGURE 6 (a) Forest plot illustrating the weighted mean difference (95%) in probing depth values (PDs; longitudinal studies). (b) Forest plot illustrating the weighted mean difference (95%) in probing depth values (PDs; cross-sectional studies)

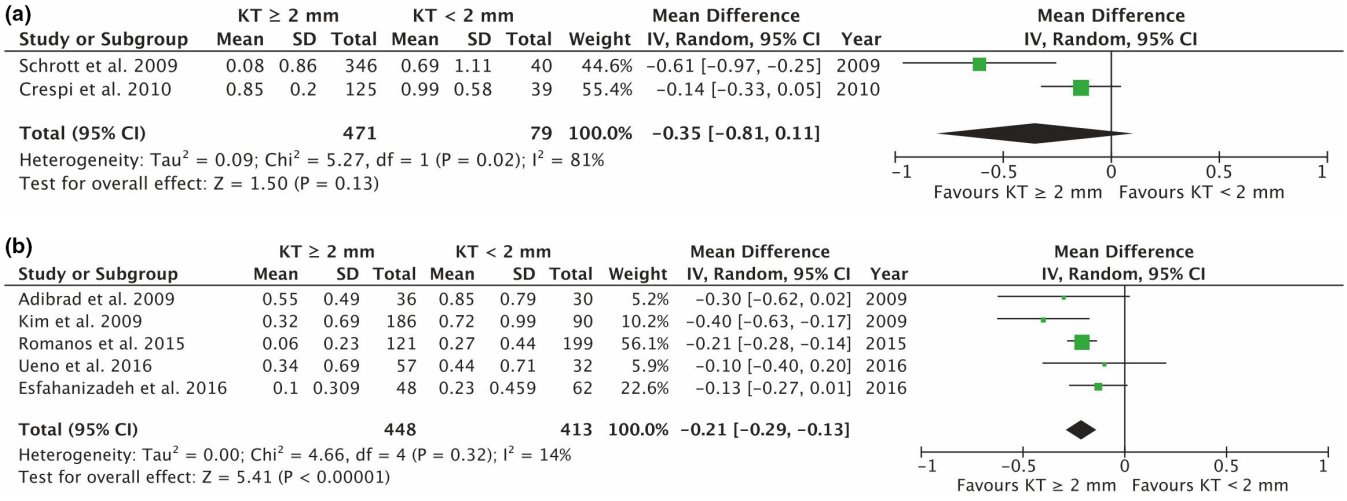

FIGURE 7 (a) Forest plot depicting the weighted mean difference (95%) in mucosal recession (MR; longitudinal studies). (b) Forest plot depicting the weighted mean difference (95%) in mucosal recession (MR; cross-sectional studies)

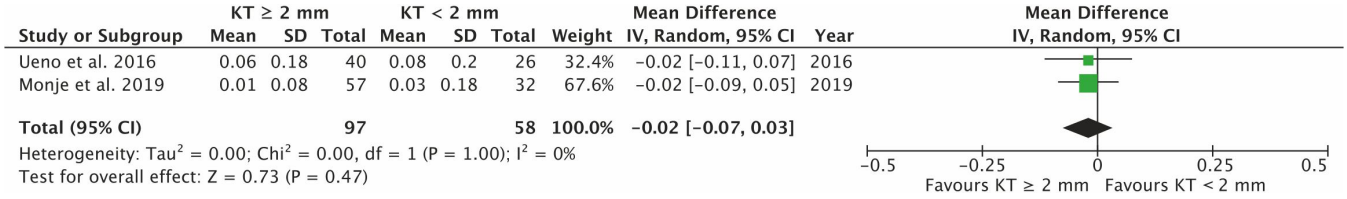

FIGURE 8 Forest plot depicting the weighted mean difference (95%) in suppuration (Sup; cross-sectional studies)

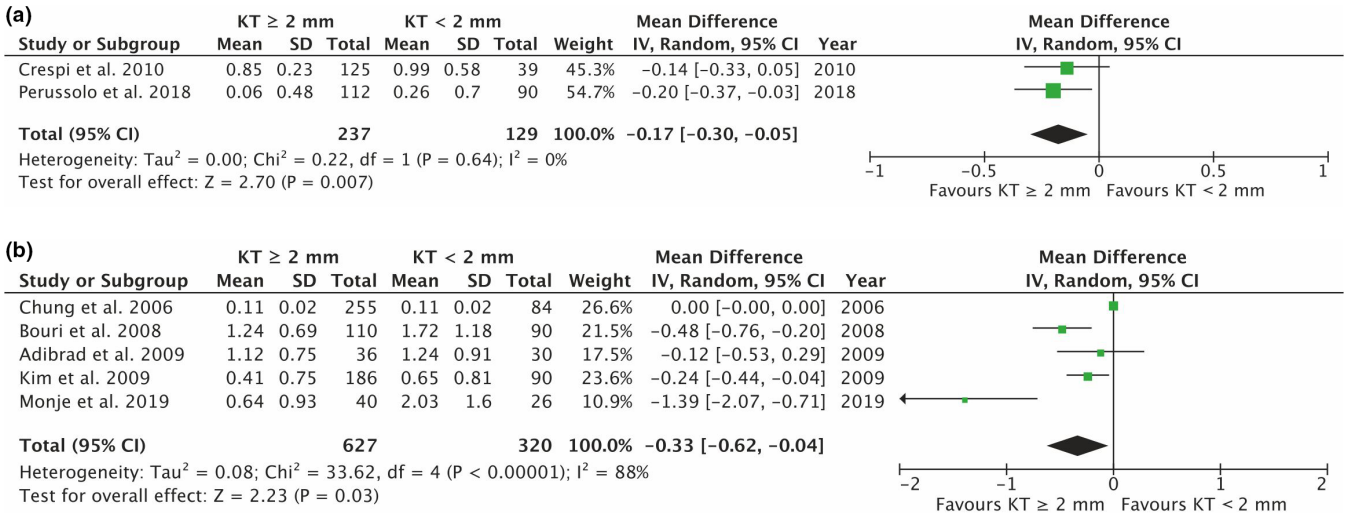

FIGURE 9 (a) Forest plot depicting the weighted mean difference (95%) in marginal bone loss (MBL; longitudinal studies). (b) Forest plot depicting the weighted mean difference (95%) in marginal bone loss (MBL; cross-sectional studies)

(Frisch et al. 2015; Lim et al. 2019). Although the frequency of peri-implant maintenance therapy appears to be directly associated with the occurrence of peri-implant diseases (Monje et al. 2017), with one exception (Monje & Blasi, 2019), none of the included studies reported on the frequency of maintenance therapy or provided information on the patients' compliance with the supportive therapy, which subsequently did not allow for an evaluation of the extent to which the reported prevalence of the diseases may have been influenced by the patients' compliance with supportive therapy.

An important aspect that must be highlighted is the huge diversity in definitions applied to the disease, as the reported disease's prevalence is directly influenced by the definitions used to characterize the pathology (Derks & Tomasi, 2015). Furthermore, the occurrence of peri-implant diseases in the presence of wide and narrow or lacking KT was only investigated by the cross-sectional studies, whereas none of the longitudinal studies reported on the occurrence of either peri-implant mucositis or peri-implantitis. Generally, cross-sectional designs do not permit assessment of the true potential effect of the width of KT on peri-implant tissue health (Sanz et al., 2012); therefore, taken together, the aforementioned findings must be interpreted with caution.

4.2.2 | Hygienic conditions

The current findings suggest significantly higher plaque accumulation at implant sites with reduced KT width, which was subsequently associated with increased BOP values, thus, depicting a correlation between plaque and bleeding scores. The aforementioned findings generally align with results from previous meta-analyses that pointed to significantly higher plaque accumulation and tissue inflammation at implant sites without adequate KT (i.e., <2 mm; Gobbato et al. 2013; Lin et al. 2013). In this context, however, it is very important to remark that both prior meta-analyses pooled different study designs (i.e., cross-sectional and longitudinal studies), as well as different cut-off values used to define adequate and reduced KT width (i.e., 0, 1, and 2 mm). Nonetheless, our findings also agree with the proceedings of the 2018 Worlds Workshop, suggesting that KT's absence or reduced width negatively affects self-performed oral hygiene measures, and, subsequently, increases implants' susceptibility to inflammatory complications (Schwarz, Becker, et al., 2018; Schwarz, Derks, et al., 2018).

4.2.3 | Soft-tissue stability

Although the differences in PD values between the groups were not significant, there was a tendency toward increased PDs at implants with KT >2 mm. This tendency aligns with the findings of former meta-analyses (Gobbato et al. 2013; Lin et al. 2013), and it might be at least partially attributed to the increased physiological vertical peri-implant soft-tissue dimensions in the presence of a wider band of KT. Notably, one recent clinical analysis found that an increase of 1 mm in the thickness of vertical soft-tissue increased peri-implantitis risk by 1.5 times,

TABLE 6 Assessment of the risk of bias for included studies

Assessment of the risk of bias for included cross-sectional and longitudinal clinical studies with the Newcastle-Ottawa scale

	Selection (max 4*)				Comparability (max 2*)	Outcome (max 3*)			
Author	Representativeness of the sample	Selection of non- exposed cohort	Ascertainment of exposure	Demonstration of the outcomes of interest was not present at start of the study	Comparability of cohorts on the basis of the design or analysis	Ascertainment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow up of cohorts	Total
Kungsadalpipo et al. (2020)	*			*	*	*	*	*	6*
Kabir et al. (2020)	*	*		*	*	*	*	*	7*
Grieschke et al. (2019)	*	*		*	**	*	*	*	8*
Monje and Blasi (2019)	*	*		*	**	*	*	*	8*
Perussolo et al. (2018)	*	*		*	*	*	*	*	7*
Souza et al. (2016)	*	*		*	*	*	*	*	7*
Ueno et al. (2016)	*			*	*		*	*	5*
Esfahanizadeh et al. (2016)	*	*		*	*		*		5*
Romanos et al. (2015)	*	*		*	*		*	*	6*
Ladwein et al. (2015)	*	*		*	*	*	*	*	7*
Ferreira et al. (2015)	*			*	*		*	*	4*
Boynueğri et al. (2013)	*			*	*		*	*	5*
Crespi et al. (2010)	*			*	*	*	*	*	6*
Adibrad et al. (2009)	*			*	*		*	*	4*
Schrott et al. (2009)	*		*	*	*	*	*	*	7*
Kim et al. (2009)	*			*	*		*	*	4*
Bouri et al. (2008)	*			*	*		*	*	4*
Zigdon and Machtei (2008)	*			*	*	*	*	*	5*
Chung et al. (2006)	*	*		*	**	*	*	*	8*
Roos-Jansåker et al. (2006)	*			*	*	*	*	*	5*
Mericske-Stern et al. (1994)	*			*	*	*	*	*	6*

Assessment of the risk of bias for included case-series study with the Newcastle-Ottawa scale

	Selection (max 4*)				Comparability (max 2*)	Exposure (max 3*)			
Author	Is the case definition adequate?	Representativeness of the cases	Selection of Controls	Definition of Controls	Comparability of cases and controls on the basis of the design or analysis	Ascertainment of exposure	Same method of ascertainment for cases and controls	Non-Response rate	Total
Roccuzzo et al. (2016)	*	*	*	*	*	*	*	*	8*

thus, affirming that excessive soft-tissue thickness may negatively affect peri-implant tissue health (Zhang et al. 2020). This was confirmed in a study employing the experimental peri-implant mucositis model in humans, as implant sites exhibiting a wider KT were associated with a lower frequency of disease resolution than implants exhibiting a narrow KT (Schwarz, Becker, et al., 2018; Schwarz, Derks, et al., 2018). Nonetheless, the effect of increased KT amount (i.e., >2 mm) on peri-implant tissue health and the threshold value needed to ensure favorable long-term outcomes must be further elucidated.

Interestingly, although quantitative analysis based on cross-sectional studies revealed a significant difference in MR between the two groups, favoring implants with KT ≥ 2 mm, which aligns with findings from a previous meta-analysis (Lin et al. 2013), analysis of longitudinal data failed to identify a statistical difference. This discrepancy may be firstly attributed to the limited number of longitudinal studies investigating MR, as it was only feasible to include two studies reporting on MR over the 1- to 4-year periods. Study design is another crucial element in validating the potential relationship between risk factors and the development of disease (Caruana et al., 2015), suggesting the need for further prospective observational follow-up clinical studies.

4.2.4 | Bone stability

Upon further analysis of the present data synthesis, MBL differed significantly between the two groups, favoring implants with wider KT. This finding corroborates the results of former observation, which over a 4-year period detected significantly more MBL at implants with KT < 2 mm compared to the control sites (Mameno et al. 2020). Consequently, as the previous meta-analysis based on four prospective clinical studies indicates, soft-tissue augmentation for KT gain significantly improved gingival and plaque indices and yielded more stable MBLs, relative to non-augmented sites, thereby confirming that adequate KT at an implant site is associated with superior peri-implant soft- and hard-tissue health and stability (Thoma et al. 2018).

4.2.5 | PROMs

The observed tendency of implant sites with an absent or reduced KT band (i.e., <2 mm) to be more prone to brushing discomfort may be attributed to the fact that, in the absence of KT, a lining mucosa rich in elastic fibers and poor in collagen provides inferior sensory isolation compared to the KT (Berglundh et al. 2007). Interestingly, when the KT band was 2.5 mm, all patients reported maximum comfort (VAS = 100; Monje & Blasi, 2019). Notably, patients' discomfort during oral hygiene measures tended to decrease over time, and differences at the baseline were not detected after 4 years (Perussolo et al. 2018). This latter tendency might be at least partially credited to the patients' adaptation to an uncomfortable experience (Murata & Nakamura, 2017). Contradicting data, however, failed to support an association between reduced KT width and patients' discomfort during brushing or ability to perform oral hygiene measures (Bonino et al. 2018; Ueno et al. 2016). Regardless, this appears to be a subjective outcome to evaluate because it depends on numerous factors, such as patients' pain threshold, strength applied during brushing, implant location, vestibulum depth, mucosal thickness, and other anatomy-related factors that may play important roles.

4.3 | Limitations

Several limitations of the present systematic review must be addressed. First, a majority of the included studies had a cross-sectional design, which does not allow the assessment of the KT amount's actual impact on peri-implant tissue health (Sanz et al., 2012). Second, the studies with various patient-related (e.g., patients' adherence to professionally administered plaque measures, periodontal health, and smoking status) and prosthetic design-related confounding factors were pooled into the analysis, which contributed to the high degree of heterogeneity among the studies. An important aspect, which should be acknowledged, is the reporting on patients' periodontal health, as more than half of the studies (n = 13) did not provide this information, and the remaining studies (n = 8) pooled periodontally healthy patients and those with a history of periodontitis or active periodontal disease. This, in turn, may have affected the investigated outcomes. Furthermore, due to the limited available studies, descriptive analysis on potential influence of KT upon peri-implant diseases was conducted pooling studies that applied different cut-off values to define insufficient KT widths (i.e., 2 and 0 mm), which also might have influenced the interpretation of the results.

5 | CONCLUSIONS

Within these limitations, it was concluded that reduced KT levels at dental implants are associated with increased prevalence of peri-implantitis, plaque accumulation, soft-tissue inflammation, mucosal recession, marginal bone loss, and greater patient discomfort.

5.1 | Clinical implications

Implant sites with the absence of KT or reduced KT width (i.e., <2 mm) appear to be more susceptible to peri-implant tissue inflammation. Hence, in the cases lacking KT, clinicians might consider soft-tissue grafting to increase KT to promote peri-implant soft- and hard-tissue stability.

5.2 | Recommendations for future research

Further prospective clinical studies should investigate the role of the width of KT on the long-term stability and health of peri-implant tissues based on the accepted case definitions.

ACKNOWLEDGEMENTS

The study was self-funded by the authors own departments.

CONFLICT OF INTEREST

All authors stated explicitly that there are no conflicts of interest related to this article.

AUTHOR CONTRIBUTION

Ausra Ramanauskaite contributed to the data acquisition, interpretation and analysis, and manuscript writing; Frank Schwarz contributed to the data acquisition and interpretation, data analysis, and critical revision of the manuscript; and Robert Sader contributed to the critical revision and approval of the manuscript.

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How to cite this article: Ramanauskaite A, Schwarz F, Sader R. Influence of width of keratinized tissue on the prevalence of peri-implant diseases: A systematic review and meta-analysis. *Clin Oral Impl Res*. 2022;33(Suppl. 23):8–31. https://doi.org/10.1111/clr.13766