Significance of Peri-implant Keratinized Mucosa on Implant Health: An Umbrella Systematic Review with Evidence Mapping and a Quantitative Meta-Meta-Analysis

Jacob Martin Zimmer[1], DDS, Hamoun Sabri[1,2] DMD, PgC, Lorenzo Tavelli[2,3] DDS, MS, PhD, Asfandyar Tariq Sheikh[1] BDS, Khushboo Kalani[1] BDS, Khoa Huang[1] DDS, Hom-Lay Wang[1], DDS, MSD, PhD, and Shayan Barootchi[1,2] DMD, MS

[1]Department of Periodontics and Oral Medicine, University of Michigan School of Dentistry, Ann Arbor, MI, USA
[2] Center for Clinical Research and Evidence Synthesis in Oral Tissue Regeneration (CRITERION), Ann Arbor, MI, Boston, Massachusetts, USA
[3] Division of Periodontology, Department of Oral Medicine, Infection, and Immunity, Harvard School of Dental Medicine, Boston, Massachusetts, USA

Background:

Keratinized mucosa width (KMW) around implants, is highlighted as one important factor influencing the long-term implant success. Studies suggest that an "adequate" KMW is associated with improved clinical parameters and reduced complications and adverse events[1,2]. In such manner, higher prevalence of peri-implant diseases, discomfort in brushing[3], and an increase in plaque accumulation and mucosal inflammation[4,5,6] have been reported. When it comes to esthetics, it has been reported that a lack of KM on the facial aspect of implants, results in an increased vulnerability to esthetic complications[7,8]. Regarding to changes in peri-implant marginal bone level, the evidence is scarce and inconclusive[9]. While individual studies provide insights, systematic reviews and meta-analyses have been inconclusive due to methodological differences.

Aim:

To conduct a comprehensive umbrella review, including a meta-meta-analysis, to synthesize existing evidence and critically evaluate the significance of keratinized mucosa width (KMW) in peri-implant health, while also assessing the consistency and heterogeneity among previous systematic reviews on this topic.

Figure 1. Implants #3, #4, and #5 width insufficient keratinized mucosa with (KMW) on the buccal aspect.

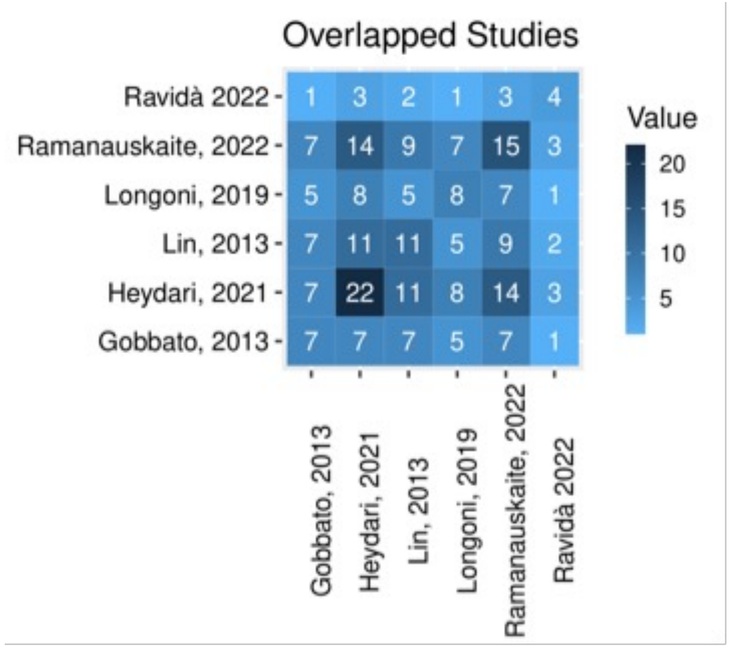

Figure 2. Overlapping graph depicting the number of common original studies between included meta-analyses into this study with a head-to-head fashion.

Significance of Peri-implant Keratinized Mucosa on Implant Health: An Umbrella Systematic Review with Evidence Mapping and a Quantitative Meta-Meta-Analysis

Jacob Martin Zimmer[1], DDS, Hamoun Sabri[1,2] DMD, PgC, Lorenzo Tavelli[2,3] DDS, MS, PhD, Asfandyar Tariq Sheikh[1] BDS, Khushboo Kalani[1] BDS, Khoa Huang[1] DDS, Hom-Lay Wang[1], DDS, MSD, PhD, and Shayan Barootchi[1,2] DMD, MS

[1]Department of Periodontics and Oral Medicine, University of Michigan School of Dentistry, Ann Arbor, MI, USA
[2] Center for Clinical Research and Evidence Synthesis in Oral Tissue Regeneration (CRITERION), Ann Arbor, MI, Boston, Massachusetts, USA
[3] Division of Periodontology, Department of Oral Medicine, Infection, and Immunity, Harvard School of Dental Medicine, Boston, Massachusetts, USA

Methods:

A comprehensive search strategy was developed and executed across multiple databases. Eligible studies were screened, and data were extracted. Methodological quality was assessed using AMSTAR-2, and the strength of evidence was evaluated with GRADE criteria. A meta-meta-analysis using Hedge's g as the effect size measure was performed to query the outcomes of implant therapy in patients with (control) and without (case) adequate KMW of ≥2 mm. A regression analysis was built to explore the impact of follow-up periods on specific outcomes.

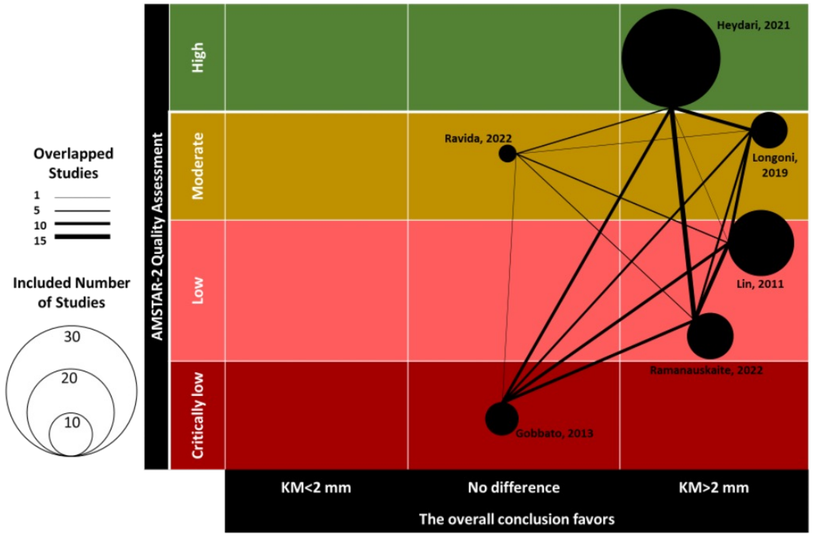

Figure 3. Evidence network map of systematic reviews and meta-analyses describing the impact of wide versus narrow width of keratinized mucosa on peri-implant health outcomes. Each node represents the corresponding article, size of which matches the number of included original studies. The network graph depicts the overlapped number of studies between each meta-analysis.

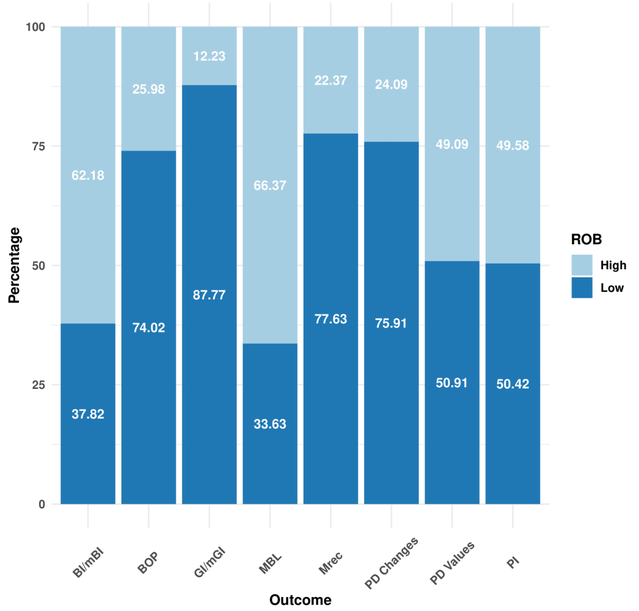

Figure 4. Bar charts presenting a comparison between the data for each outcome included in this meta-meta-analysis, in terms of the risk of bias of the original (source) study.

Significance of Peri-implant Keratinized Mucosa on Implant Health: An Umbrella Systematic Review with Evidence Mapping and a Quantitative Meta-Meta-Analysis

Jacob Martin Zimmer[1], DDS, Hamoun Sabri[1,2] DMD, PgC, Lorenzo Tavelli[2,3] DDS, MS, PhD, Asfandyar Tariq Sheikh[1] BDS, Khushboo Kalani[1] BDS, Khoa Huang[1] DDS, Hom-Lay Wang[1], DDS, MSD, PhD, and Shayan Barootchi[1,2] DMD, MS

[1]Department of Periodontics and Oral Medicine, University of Michigan School of Dentistry, Ann Arbor, MI, USA
[2] Center for Clinical Research and Evidence Synthesis in Oral Tissue Regeneration (CRITERION), Ann Arbor, MI, Boston, Massachusetts, USA
[3] Division of Periodontology, Department of Oral Medicine, Infection, and Immunity, Harvard School of Dental Medicine, Boston, Massachusetts, USA

Results:

Ten systematic reviews were included in this study, published between 2012 and 2023. Significant effect sizes were found for mucosal recession (MRec), gingival index (GI)/modified gingival index (mGI), modified plaque index (mPI) and marginal bone loss (MBL). Specifically, narrow keratinized mucosa width (<2 mm) was associated with increased MRec (eOR = 4.05, p = 0.03), higher GI/mGI scores (eOR = 3.131, p = 0.001), elevated mPI scores (eOR = 5.34, p = 0.005) and greater MBL (eOR = 1.852, p = 0.0007). No significant associations were observed for bleeding on probing (BOP), pocket depth changes, or pocket depth values. Follow-up time did not significantly affect these outcomes.

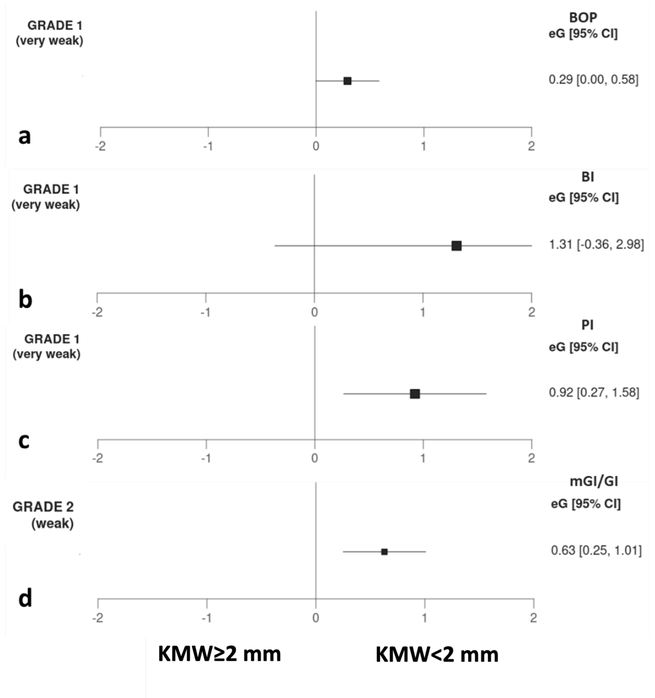

Figure 4. Forest plot, strength of evidence and equivalent Hedge's g (eG) of meta-analysis results on BOP, BI, PI and GI/mGI.

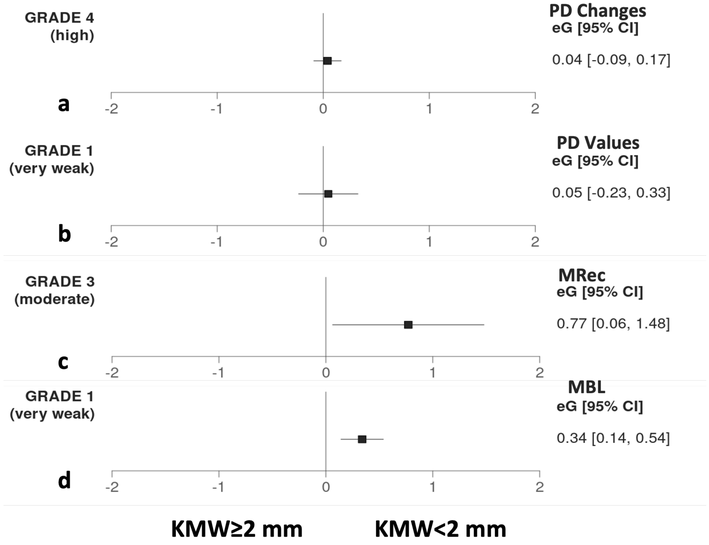

Figure 5. Forest plot, strength of evidence and equivalent Hedge's g (eG) of meta-analysis results on PD changes, PD values, MRec and MBL.

Significance of Peri-implant Keratinized Mucosa on Implant Health: An Umbrella Systematic Review with Evidence Mapping and a Quantitative Meta-Meta-Analysis

Jacob Martin Zimmer[1], DDS, Hamoun Sabri[1,2] DMD, PgC, Lorenzo Tavelli[2,3] DDS, MS, PhD, Asfandyar Tariq Sheikh[1] BDS, Khushboo Kalani[1] BDS, Khoa Huang[1] DDS, Hom-Lay Wang[1], DDS, MSD, PhD, and Shayan Barootchi[1,2] DMD, MS

[1]Department of Periodontics and Oral Medicine, University of Michigan School of Dentistry, Ann Arbor, MI, USA
[2] Center for Clinical Research and Evidence Synthesis in Oral Tissue Regeneration (CRITERION), Ann Arbor, MI, Boston, Massachusetts, USA
[3] Division of Periodontology, Department of Oral Medicine, Infection, and Immunity, Harvard School of Dental Medicine, Boston, Massachusetts, USA

Conclusion:

Inadequate keratinized mucosa width (<2 mm) correlated with increased mucosal recession, higher gingival index (GI)/modified gingival index (mGI), plaque index/modified plaque index (mPI) PI/mPI scores, and greater marginal bone loss (MBL).

GRADE Class	Hedge's g Value [95% CI]	eOR [95% CI]	P value	N of studies	N of Total Implants	I^2	Egger P value	Low ROB %	power
PD Values									
Very weak	0.047[-0.232, 0.327]	1.09 [0.657, 1.808]	0.739	12	1974	87.535	**0.046**	50.91	Low es = 99.1; Med. es = 100; Large es = 100
BOP									
Very weak	0.292[-0.001, 0.584]	1.697 [0.999, 2.883]	0.0505	5	635	57.458	0.34	74.02	Low es = 71.1; Med. es = 100; Large es = 100
mBI									
Very weak	1.309[-0.363, 2.981]	10.746 [0.518, 222.946]	0.125	11	2023	98.104	**0.03**	37.82	Low es = 99.2; Med. es = 100; Large es = 100
GI/mGI									
Weak	0.629[0.252, 1.007]	3.131 [1.58, 6.208]	**0.001**	10	1550	87.77	**0.03**	87.77	Low es = 96.6; Med. es = 100; Large es = 100
MRec									
Moderate	0.771[0.064, 1.479]	4.05 [1.123, 14.612]	**0.03**	9	1529	94.11	0.5	77.63	Low es = 96.3; Med. es = 100; Large es = 100
PD Changes									
High	0.04[-0.088, 0.168]	1.075 [0.852, 1.357]	0.541	9	1461	26.242	0.87	75.91	Low es = 95.8; Med. es = 100; Large es = 100
PI									
Very Weak	0.924[0.267, 1.58]	5.34 [1.624, 17.563]	**0.005**	18	3096	97.147	**0.03**	50.42	Low es = 100; Med. es = 100; Large es = 100
MBL									
Very Weak	0.34[0.142, 0.537]	1.852 [1.294, 2.65]	**0.0007**	8	1368	61.292	0.4	33.63	Low es = 93.8; Med. es = 100; Large es = 100

Table 1. Summary of meta-meta-analysis on impact of KMW <2 mm (factor) on different clinical outcomes. **Abbreviations: eOR:** equivalent odds ratio, **N:** number, **ROB:** risk of bias, **ES:** effect size

eOR: the value of the pooled effect size expressed in equivalent Odds ratio (eOR) and the 95% CI around the pooled effect size expressed in eOR. **P value**: the p-value of the pooled effect size. **I^2**: the inconsistency value (calculated only if the number of studies in the meta-analysis is equal or larger to 2). **Egger P value**: the p-value of the Egger's test for publication bias (calculated only if the number of studies in the meta-analysis is equal or larger to 3). **Power**: The power to detect a small effect size (SMD = 0.2), a moderate effect size (SMD = 0.5) and a large effect size (SMD = 0.8) at an alpha of 0.05 based on the number of cases and controls included in the meta-analysis. **ROB**: percentage of included patients to the analysis from studies with low risk of bias.

Significance of Peri-implant Keratinized Mucosa on Implant Health: An Umbrella Systematic Review with Evidence Mapping and a Quantitative Meta-Meta-Analysis

Jacob Martin Zimmer[1], DDS, Hamoun Sabri[1,2] DMD, PgC, Lorenzo Tavelli[2,3] DDS, MS, PhD, Asfandyar Tariq Sheikh[1] BDS, Khushboo Kalani[1] BDS, Khoa Huang[1] DDS, Hom-Lay Wang[1], DDS, MSD, PhD, and Shayan Barootchi[1,2] DMD, MS

[1]Department of Periodontics and Oral Medicine, University of Michigan School of Dentistry, Ann Arbor, MI, USA
[2] Center for Clinical Research and Evidence Synthesis in Oral Tissue Regeneration (CRITERION), Ann Arbor, MI, Boston, Massachusetts, USA
[3] Division of Periodontology, Department of Oral Medicine, Infection, and Immunity, Harvard School of Dental Medicine, Boston, Massachusetts, USA

References:

1. Del Amo FSL, Yu SH, Sammartino G, et al. Peri-implant soft tissue management: Cairo opinion consensus conference. *International Journal of Environmental Research and Public Health* 2020;17.
2. Perussolo J, Souza AB, Matarazzo F, Oliveira RP, Araújo MG. Influence of the keratinized mucosa on the stability of peri-implant tissues and brushing discomfort: A 4-year follow-up study. *Clinical oral implants research* 2018;29:1177-1185.
3. Perussolo J, Matarazzo F, Dias DR, Oliveira RP, Araújo MG. The effect of brushing discomfort on peri-implant health in sites exhibiting inadequate keratinized mucosa width: A cross-sectional study. *Clinical oral implants research* 2022.
4. Chung DM, Oh TJ, Shotwell JL, Misch CE, Wang HL. Significance of keratinized mucosa in maintenance of dental implants with different surfaces. *J Periodontol* 2006;77:1410-1420.
5. Brito C, Tenenbaum HC, Wong BK, Schmitt C, Nogueira-Filho G. Is keratinized mucosa indispensable to maintain peri-implant health? A systematic review of the literature. *J Biomed Mater Res B Appl Biomater* 2014;102:643-650.
6. Schrott AR, Jimenez M, Hwang JW, Fiorellini J, Weber HP. Five-year evaluation of the influence of keratinized mucosa on peri-implant soft-tissue health and stability around implants supporting full-arch mandibular fixed prostheses. *Clinical Oral Implants Research* 2009;20:1170-1177.
7. Tavelli L, Barootchi S, Majzoub J, et al. Prevalence and risk indicators of midfacial peri-implant soft tissue dehiscence at single site in the esthetic zone: A cross-sectional clinical and ultrasonographic study. *Journal of Periodontology* 2022;93:857-866.
8. Monje A, González-Martín O, Ávila-Ortiz G. Impact of peri-implant soft tissue characteristics on health and esthetics. *J Esthet Restor Dent* 2023;35:183-196.
9. Oliveira CAB, Pereira VL, Dos Santos JN, Araujo NS, Cury PR. Influence of keratinized mucosa on peri-implant diseases: a retrospective cohort study in humans. *Oral Maxillofac Surg* 2023.

First Author, Year	Type of Study (SR/ SRMA)	Protocol Registered (Y/NR) Registry #, Funding (Y/N)	Focused question	Searched Databases	Language restriction	Type of included trials	Included Subjects (Human/ Animal/ Both)	Included Number of Studies (Total/ SR/ MA)	Threshold of thin Vs thick KM	Outcomes	Risk of Bias Assessment (Yes/No), (tools used)	Risk of Bias (HIGH/MOD/ LOW)	Was focused question(s) answered?	Conclusion	Favors
Longoni, 2019	SRMA	Y, CRD42018091806, N	NA	PM, Cochrane, and OpenGrey	N	CS, Cohort	Human	SR: 15, MA: 8	>2mm	(GI/mGI), (PI/mPI), (BoP, mBI).	Yes, modified Newcastle-Ottawa scale	5 low, 3 Mod	N	No definitive conclusion due to the lack of standardized and well-designed studies.	Inconclusive
Lin, 2013	SRMA	N, Y	Does minimal KM width around dental implants have benefits on the health of peri-implant soft and hard tissues?	PM, Ovid, EMBASE, WOS, and Cochrane Central	English	CS, longitudinal (prospective or retrospective)	Human	11	>2mm	BOP, BI, mPI ,GI,mGI,PD, MR ,BL AL.	Yes, Kahn K, 2001	3 mod, 8 high	Y	Lack of KM around endosseous implants is associated with more plaque accumulation, tissue inflammation, MRec, and AL.	KMW>2 mm
Brito, 2013	SR	N, NR	Is KM around the dental implant necessary to maintain proper health of peri-implant tissues?	Cochrane Library, MEDLINE, EMBASE, and Virtual Health Library	English	CS, longitudinal	Human	7	1mm and >2mm	PI, GI, PD, BOP, MRec, BL	Yes, Feldmann I, 2006	4 mod, 3 high	Y	Adequate KT zone can be critical. But, more studies needed to see significance of KT around implants.	Inconclusive
Ramanauskaite, 2022	SRMA	Y, CRD42020211773., N	Effect of reduced KT width with implant sites with a KT width ≥ 2 mm, on the prevalence of peri-implant diseases, soft- and hard-tissue stability?	PM, Cochrane, and Embase	N	CS, case–control, cohort, CCTs, RCTs,longitudinal studies, and case series (prospective or retrospective)	Human	SR: 22, MA :15	<2mm	PPD,PI,mPI,mBI, BOP,MBL	Yes, Newcastle-Ottawa Scale,	13 high, 8 low	Y	Reduced KM levels cause more peri-implantitis, plaque, soft-tissue inflammation, recession, MBL, discomfort.	KMW>2 mm
Wennström, 2012	SR	N, N	Need for KM around implants to maintain health and tis-sue stability?	PM	N	CS and longitudinal	Both	19	<2mm	AL, MRec, BL	N	-	Y	Need for certain amount of KM around implants to maintain health and tissue stability is limited	Inconclusive
Heydari, 2021	SRMA	Y IR.BUMS.REC.1398.359., N	what is the effect of KT on peri-implant health status indices?	PM, Scopus, Embase, WOS, Cochrane	N	CS and longitudinal (prospective or retrospective)	Human	22	<2mm	BL, PD, mBI, BOP, GI, mGI, PI, mPI, and MRec	Y, Newcastle-Ottawa Modified Scale	18 high quality, 4 MOD quality	Y	At least 2 mm of KT around implants is critical for healthy peri-implant tis-sues.	KMW>2 mm
Iorio-Siciliano, 2020	SR	Y #105191, Y	Is the presence of KM a prerequisite to avoid Marginal Recession?	Medline, Embase and Cochrane Oral Health Group	English	Cohort (Prospective)	Human	2	<2mm	MRec, mPI, mBI, PD, and suppuration.	Y, Newcastle-Ottawa Scale,	2 MOD quality	Y	Although no strong evidence was found, the presence of KM was associated with less MRec.	Inconclusive
Ravidà 2022	SRMA	Y, CRD42021233756, N	Whether lack of a prespecified (2 mm) amount of keratinized mucos width (KMW) is a risk factor for peri-implant diseases?	MEDLINE, Scopus, Web of Science, and the Medicine Grey Literature Report.	N	RCT, CCT or non-CCT	Human	9	2mm	PD, MRec, AL, mGI, MBL, PROMs, disease prevalence	Y, Rob-1, Newcastle Ottawa scale	1 Mod, 1 high, 7 low	Y	No increase in MBL, REC, and PD compared to implants with ≥2 mm KMW. But, increased mPI, more discomfort after brushing.	KMW>2 mm
Mahardawi, 2023	SRMA	Y, CRD42022319868, Y	Does the lack of KM around dental implants lead to a higher risk of peri-implantitis?	Medline and Scopus	N	CS, cohort, and case–control (prospective or retrospective)	Human	22 SR, 16 MA	2mm, 1mm or presence/absence	prevalence of peri-implantitis	Y, Newcastle-Ottawa Scale	12 high quality, 10 medium quality	Y	Lack of keratinized mucosa is a risk factor that increases the prevalence of peri-implantitis.	KMW>2 mm
Gobbato, 2013	SRMA	N, NR	Effect of KMW on clinical parameters of peri-implant health and stability?	Web of Knowledge , MEDLINE, National In-stitutes of Health	N	observational and CS (Prospective)	Human	8 SR, 7 MA	<2mm	PD, BOP, mBI, GI, PI, mPI, SR	N	-	Y	< 2 mm is associated with clinical parameters of inflammation.	KMW>2 mm

Table 2. General characteristics of the included systematic reviews with or without meta-analysis. **Abbreviations: SR:** systematic review, **SRMA:** systematic review and meta-analysis, **Y:** yes, **NR:** not reported, **N:** no, **KM:** keratinized mucosa, **MOD:** moderate, **NA:** not available, **PM:** PubMed, **CS:** cross-sectional, **MA:** meta-analysis, **WOS:** web of science, **AL:** attachment loss, **RCT:** randomized controlled trials, **CCT:** controlled clinical trials.