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Effect of Smoking on Dental Implant Failure: A Systematic Review

Jaidaa Osama Ismail[1] *Mohamed Amr ElKhashab*[2], *Nagla M.H. Nassouhy*[3] *& Iman Abd-ELWahab Radi*[4]

Abstract

Objectives: The objective of this systematic review is to determine the prognosis of implant treatment in smokers if compared to non-smokers.

Data Sources: Review authors searched 3 electronic databases; Pubmed, Cochrane and Lilacs: 17/11/2018, hand searched 8 journals till December 2018, Grey Literature: 12/11/2018 and snowballing: 12/12/2018.

Eligibility Criteria: Completely or partially edentulous male or female participants who are systematically healthy and who require implant supported prosthesis, whether fixed or removable, were included. Studies that compared implant treatment between smokers and non-smokers, using both delayed insertion and loading protocols were eligible.

Data Collection and Analysis: Review authors extracted data relevant to PECOTS. Besides, confounders and co-interventions were collected and reported. Data was descriptive and statistically analyzed

Results: Nine studies met the inclusion and exclusion criteria; 6 prospective cohort studies and 3 RCTs, including 650 patients. One RCT did not mention the exact number of participants and instead the number of inserted implants was reported. Only 3 studies were included in the meta-analysis.

Conclusions: Implant placement in smokers seems to be possible, in addition to periodontal therapy and strict oral hygiene that might increase the chances of success. Since the quality of evidence is low-very low, results should be taken with cautions.

Keywords: smokers, tobacco smoking, nicotine, oral implantology, dental implants.

1. MSc Student, Prosthodontics department, Faculty of Dentistry, Cairo University, Cairo, Egypt.
2. Lecturer of Prosthodontics, Faculty of Dentistry, Cairo University, Cairo, Egypt.
3. Associate Professor of Prosthodontics, Faculty of Dentistry, Cairo University, Cairo, Egypt.
4. Professor of Prosthodontics, Member of Evidence Based dentistry Center, Head of Fundraising Unit, Head of Central Control Unit, Faculty of Dentistry, Cairo University, Cairo, Egypt.

INTRODUCTION

Implant-retained prostheses have been considered as a common treatment modality associated with high success and survival rates, in addition to increased patient satisfaction. However, multiple risk factors were reported to have an effect on the outcome of osseointegrated implants. Such factors include peri-implant bone quantity and quality, medically compromised patients, osteoporosis, drug consumption and smoking. Smoking in its various forms whether; cigarette, pipe, cigar smoking or smokeless tobacco, has been proven to cause detrimental effects on the oral health ranging from harmless stains, halitosis, alterations in taste sensations to serious major oral diseases such as oral precancerous and cancer lesions.1,2 Periodontal breakdown was also reported by different studies1,3 including; periodontal pockets, attachment loss, alveolar bone loss, gingival recession, furcation defects and subsequent tooth loss. The junctional peri-implant epithelium shows high permeability to nicotine and other exogenous substances, which are therefore present in high concentrations at the bone-implant interface. These substances negatively affect wound closure, angiogenesis and osteogenesis.4

Evidence regarding the effect of smoking on implant failure is, however, still controversial. Unfortunately, previous systematic reviews (SRs)5,6 did not resolve this debate, or even reach a consensus to decide for placing implants in smokers. There were many limitations in those reviews, since they were mostly based on retrospective studies with multiple confounders and different classifications of smoking regarding the frequency and duration of smoking. Therefore, all these factors decrease the creditability and applicability of their findings.

Hence, it seemed necessary to conduct this SR to clarify the effect of smoking on implant therapy, while including prospective studies only and restricting the confounders.

Materials and Methods

This SR was reported following the PRISMA7 (preferred reporting items for systematic reviews and meta-analysis) statement. The review was registered at Removable Prosthodontics Department, Faculty of Oral and Dental Medicine, Cairo University. It was also registered on PROSPERO website (international prospective register of systematic reviews), with a registration date; 21/08/2017and number; CRD42017074902.

Selection Criteria

Randomized clinical trials (RCTs), non-randomized clinical trials (NRCTs), and prospective cohort studies, with follow up period at least 1 year, were included. Completely or partially edentulous male or female participants who are systematically healthy and who require implant supported prosthesis, whether fixed or removable, were included. Patients with aggressive periodontitis, bruxing habits, peri-apical pathosis, tumors or low bone density at the site of implantation were all excluded. Patients with history of chemo- or radiotherapy were also excluded. Studies that compared between smokers and non-smokers using different implant sizes and types except zygomatic implants were included. Implants should have been placed at least 8 weeks following extraction. Only studies with delayed loading protocols (at least 3 months in mandible and 4 months in maxilla) were considered eligible. The need for bone or soft tissue grafting and sinus lifting was considered ineligible. Whenever data regarding eligibility criteria or full text were missing and no replies from relevant authors upon 3 e-mails were obtained, the article was considered ineligible.

The primary outcome of this review was implant failure including; implant loss, pain, implant mobility and inflammation. Published articles with no limitation for year of publication were considered within the scope of the review. Only articles published in English language were included.

Search Methodology

Review authors searched 3 electronic databases; Pubmed, Cochrane and Lilacs: 17/11/2018, hand searched 8 journals till December 2018, Grey Literature: 12/11/2018 and snowballing: 12/12/2018. Hand searching was done for International Journal of Prosthodontics, Journal of Clinical Oral Implant Research, Journal of Implant Dentistry, International Journal of Oral and Maxillofacial implants, Journal of Prosthetic Dentistry, European Journal of Oral Implantology, Journal of dental research, Journal of Quintessence international

IR, JOI and NN searched three electronic databases using combined search strategies and hand searched nine journals electronically without date limitation using the keyword "smoking and dental implants". English filter was used in Lilacs database only.

Search strategies developed for PubMed, Lilacs, and Cochrane library databases are shown in appendix 1 (suppl.).

Study Selection

After searching information sources all identified records were imported to a reference manager (Endnote X7.4, 1988-2015 Thomson Reuters, US) to find and remove duplicates. The titles and abstracts of all studies identified by the created search strategies were initially screened by MK and JOI independently and in duplicate to exclude irrelevant studies. Secondary screening was carried out by NN and JOI. Disagreements were resolved by discussion, or the involvement of a third review author (IR).

Data Collection Process

IR and JOI independently and in duplicate extracted the data of included studies using paper based data extraction forms. Before reading the included studies a preliminary data extraction form, containing information about participants, exposure, comparator, outcomes, time points and study design was used. However, IR and JOI read 3 of the included studies, and after discussion they agreed on a pilot data extraction form.

Risk of Bias

IR and JOI assessed the risk of bias for the included studies independently and in duplicate based on the outcome level within and across the studies. The risk of bias of the included RCTs was assessed using ROB28 and for the NRCTs and cohort studies using ROBINS-I9 Cochrane tools for risk of bias assessment.

Data Analysis

IR and JOI planned to carry out a meta-analysis, if there were at least two clinically and methodologically homogenous studies with similar comparisons reporting the same outcome measures, at the same time periods. The unit of analysis was the participants or implants. Mean differences and standard deviations were combined for continuous data, and risk ratios (RR) for dichotomous data, using either fixed-effect or random-effects models. RevMan software was used to perform meta-analysis. The statistical heterogeneity was assessed by I2 and tau2. RevMan software (Review Manager (RevMan) Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) was used to perform the meta-analyses.

IR and JOI planned for subgroup analysis if more than ten studies were included, but this was not possible due to insufficient number of studies. Sub- grouping was planned to study the impact of different types of tobacco smoking, number of cigarettes per day and follow-up period.

RESULTS

By searching the electronic databases, 3782 references were retrieved in addition to 25 references identified through hand searching, which resulted in a total of 3807 article. After duplicates removal, title and abstract screening resulted in excluding 2753 records and 151 articles were eligible for full text reading. The latter resulted in the exclusion of 142 articles and the inclusion of 9 articles in this SR. From these articles, 3 were included in the meta-analysis. Three10–12 of the 9 included studies were interventional parallel RCTs and 613–18 were observational prospective cohort studies.

Description of included studies

Figure 1 shows the number of articles identified at the different stages of the review. Nine10–18 articles were included the in qualitative synthesis, and only 314,16,17 were included in the meta-analysis. 1,479 patients had participated in the 9 included studies, 650 of which were included in this SR. Total number of implants originally placed in the included studies is 5,024, while the number of implants included in this SR is 3,251. The healing protocol was not reported in all of the included studies except in Lambert 200010 and Tinsley 200111 who used sub-merged healing protocol and in Stoker 201212 who used a non-submerged one. Dropouts were only reported in 3 studies.12,14,18 In Penarrochha 2004,18 4 implants failed and were excluded, while in Stoker 2012,12 3 patients died, 4 were inaccessible and 9 had missing clinical parameters. In Balaguer 2015,14 16 patients were not followed up and 4 had incomplete questionnaires. Bone height was not reported in any of the included articles except in Tinsley 2001,11 which mentioned the inclusion of participants with bone height more than 8mm.

Regarding the implant position, 5 studies10,13–15,18 placed their implants in both arches. Stoker 201212 and Tinsley 200111 placed their implants in the mandibular arch only, particularly in the interforaminal area in the latter study. Regarding the flap design, Balaguer 201514 is the only study that mentioned performing full thickness flap in the surgical procedures of implant insertion. Only 2 studies; 1 cohort study and 1 RCT, mentioned the type of the attachment used. Balaguer 201514 used isolated ball attachments or locator system to retain nonsplinted implants and ball or slide attachments to retain bar-splinted implants. In Stoker 2012,12 two implants with ball attachments (2IBA, group I) and Dalla Bona matrices (Cendres et Métaux, Switzerland), or two implants with a single egg-shaped Dolder bar (2ISB, group II) (CMST53012P20, Cendres et Métaux) or four implants with a triple bar (4ITB, group III) were studied. Characteristics of participants, interventions and exposures are reported in details in table 1.

Risk of bias assessment

Risk of bias assessment for cohort studies regarding objective outcomes , 2 studies14,17 were judged at serious risk of bias and the remaining study16 at unclear risk of bias (fig. 2). When considering subjective outcomes, 1 study18 was judged at critical, 113 at serious and 215,16 at unclear risk of bias (fig. 3).

Risk of bias assessment for the three included RCTs10–12 were judged at high risk of bias (fig. 4).

Results of analyses

Implant failure (as described by Albrektsson 1986,19) was reported in 4 studies; 3 cohort studies14,16,17 at an implant level and in 1 RCT11 at a patient level. They are presented in table 24. Three studies11,14,16 showed no significant difference between smokers and non-smokers (P>.05), except Mohanty 201817 who

studied smokers versus periodontitis and reported a significant difference between the 2 groups at a P-value .018, favoring periodontitis.
P-values, which were unavailable, were imputed by RevMan.
Publication bias assessment and subgroup analysis were not possible since less than 10 studies were included in the review.

Quantitative Analysis

The meta-analysis done in this SR was concerned with implant failure outcome, where the relative risk was used to report the effect size between the studied groups.

Combining studies with follow-up periods ≥ 5 years, revealed no significant difference (P= .08) between smokers and non-smokers regarding implant failure at risk ratio (RR) =1.80, 95% CI (0.92, 3.52), heterogeneity; $Chi^2 = 0.56$; $I^2 = 0\%$.

Sensitivity of the results to the combined effect of smoking and periodontitis was analyzed. The latter revealed a shift in the results to a significant difference (P= .002) between smokers and non-smokers, favoring non-smokers, at a RR=1.77, 95% CI (1.24, 2.54), heterogeneity: $Chi^2 = 0.48$; $I^2 = 0\%$.

DISCUSSION

When considering the effect of smoking on implant therapy, it was reported that implant failure in smokers was twice that of non-smokers, and that the failure in smokers was more in the maxilla than in the mandible.10,20,21 Studies1,2,4 have shown that the detrimental effects of smoking were mainly relevant to their effect on the junctional peri-implant epithelium. The latter was reported to have high permeability to nicotine and other exogenous substances such as carbon monoxide and cyanide, clarifying their presence in high concentrations at the bone-implant interface. These substances negatively affect proper wound healing and healthy scar formation,22,23 suggesting that smoking influenced implant survival mainly at the second stage surgery and not during the osseointegration period.24
Relation between smoking and implant failure, however, remained a controversial issue. Some studies25–28 suggested cessation protocol to enhance the success in smokers. A previously published SR and meta-analysis6 reported a significant difference in implant failure between smokers and non-smokers, favoring the non-smoking group [OR=1.96, 95% CI (1.68, 2.30)].The review was critically appraised by Analia Veitz-Keenan,29 who recommended considering the results with cautious due to confounding bias. In an attempt to overcome the previous limitations, a recent SR5 was published in 2018. Unfortunately, nearly the same results and limitations were reported [OR=2.92, 95% CI (1.76 - 4.83)]. Hence, it was mandatory to conduct

this SR to clarify the chances of implant success in smokers.
Implant failure as a composite outcome, composed of; implant loss, stability, pain and inflammation, was chosen because of its effect on the patient, where its consequences usually involve additional procedures and costs, resulting in patient's discomfort and dissatisfaction.30
In this review, a period that exceeds 5 years following implant installation showed an increased risk in smokers in comparison to non-smokers for implant failure [RR=1.8 ,95% CI (0.92,3.52)]. Statistically, no significant difference was found between both groups, proposing that placing implants in smoking patients was safe. The authors explained their findings by the fact that the main effect of smoking could have happened during the soft tissue healing period, with minimal effect on the bone healing phase or the phase of osseointegration.31 Taking a close look at the CIs of both outcomes, it reflects an imprecision in the reported risks, thereby downgrading the grade of evidence and decreasing the applicability of the results.
On the other hand, involving patients with periodontitis shifted the results of implant failure after 5 years of implant installation to significant difference between smokers and non-, with a RR=1.77 [95% CI (1.24, 2.54)]. Periodontitis seems to complicate the risk of implant failure in smoking patients, suggesting that periodontal treatment is a must before placing implants in those patients.
This could be, additionally, due to the increased sample size that was big enough to reveal the significant difference and could increase the suspicion about a β error in the meta-analysis that did not consider the periodontally affected patients.
However, the second explanation sounds more realistic since the meta-analysis of implant failure on a patient level, reflecting the impact of sample size rather than periodontitis on the results.
Smoking was reported to have a statistically significant impact on implant failure by many studies. They claimed that significantly higher implant-success rates in patients, undergoing smoking cessation protocols compared to patients who did not, were observed.32,33
Moreover, the same findings were reported in previous studies25–28 suggesting that early failure of implants was related to smoking and increased with cigarette consumption.
Alfadda,5 in her SR, that was published in 2018, stated that the results favored the non-smokers at an OR=2.92 [95% CI (1.76 - 4.83)]. She attributed her findings to the effect of tobacco chemicals on reducing the vascularity of the peri-implant tissues, thereby compromising the bone healing process and leading to failure.34 The difference in the findings between our and Alfadda's review could be attributed to the

inclusion of systemically affected patients, bone grafted sites and the big sample size in Alfaddah.5 The 2 former factors might confound the effect of smoking on implant failure. This clarifies why the authors of this review excluded those confounders. On the other hand, Konstrom et al.35 found a trivial association between smoking and implant failure. This was further proven by Sverzut et al.,31 who did not report any statistically significant association between smoking and early implant failures, concluding that smoking alone is not considered as a risk factor.
The prevalence of different types of edentulism, requiring dental implants for restoration, could increase the applicability of the results of this review. However, restricting the eligibility criteria in this review to decrease the risk of confounding bias, could have enhanced the internal validity on one side, but negatively affected the external validity on the other side, whereby the results are only applicable to systemically healthy subjects requiring only early or delayed implant placement. Besides, implants should have been placed using delayed loading protocol without bone or soft tissue graft. Therefore, the results should be interpreted with cautions.

CONCLUSION

Implant placement in smokers seems to be possible, in addition to periodontal therapy and strict oral hygiene that might increase the chances of success. Since the quality of evidence is low-very low, results should be taken with cautions.

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TABLE LEGENDS

Table 1. Characteristics of included articles.

Table 2. Results of implant failure in individual studies.

FIGURE CAPTIONS

Figure 1. PRISMA Flow diagram indicating number of studies during different review stages.

Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included cohort studies (objective outcomes) using ROBINS-I.

Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included cohort studies (subjective outcomes) using ROBINS-I.

Figure 4. Risk of bias summary: review authors' judgements about each risk of bias item for each included RCT using ROB2 (subjective and objective outcomes).

Table 1. Characteristics of included articles

Study ID	Age (years)				Gender		Type of edentulism			Settings	Timing of study	Sample size				Implant number		Implant size (mm)	
	Mean/Average			Range	Male	Female	P	C (both arches)	C (1 or 2 arches)			In study	Final in SR						
	T	S	NS	T									T	S	NS	S	NS	length	diameter
Al-Aali 2018[13]	44.05	44.5	43.6	S (39-51) NS (35-49)	56	0	56	-	-	Saudi Arabia	2013-2018	56	56	29	27	86	91	10-14	4.1
Balaguer 2015[14]	55.9±9.5			23–80	43	52	-	-	95	Spain	1996-2007	115	95	18	77	85	275	10 in Md& 10 in Mx	3.3
Galindo- Moreno 2005[15]	49.77			20-68	93	92	109	76	-	Spain	1997-2001	185	185	63	122	NR	NR	mean 12.92	mean 3.91
Karoussis 2003[16]	NR			NR	NR		53	-	-	Switzerland	NR	53	53	12	41	28	84	NR	NR
Mohanty 2018[17]	NR			NR	48(28 S)	56(24 S)		NR		NR	NR	208	104	52	52	126	144	NR	NR
Penarrocha 2004[18]	44.2			14 – 68	16	26	42	-	-	NR	1996-1999	42	42	16	26	47	61	>12 in 75 cases, 12 in 26 cases and <12 in 7 cases	4.8 in 12 cases, 4.1 in 91 cases and 3.3 in 5 cases
Lambert 2000[10]	NR			<30 - 89	NR			NR		USA	1991-1995	662				854	496	NR	NR
Stoker 2012[12]	59.8			NR	28	66	-	94	-	Netherland	1991-2001	110	94	35	59	96	160	NR	NR
Tinsley 2001[11]	NR			37 - 80	18	30	-	-	48	NR	1990-2000	48	21	7	14	NR	NR	8,10,13 &15	3.25 &4.0
Total	50.74			14-89	302	322	260	170	143			1479	650	232	418	1322	1311		

Table 1. Characteristics of included studies (continued)

Study ID	Implant system/ design	Implant surface treatmen	Type & material of prosthesis	Follow-up (years)	Outcomes	Measuring device
Al-Aali 2018[13]	NR	Moderately rough surfaces	NR	5	Crestal bone loss	Digital intraoral x-ray
					PD / BoP	Periodontal probe
Balaguer 2015[14]	Straumann Tissue Level	NR	Implant supported overdenture	μ=7.9 (3-13.25)	Implant survival (pain, mobility or infection)	Binary
Galindo-Moreno 2005[15]	Branemark System, Nobel Biocare (threaded cylindrical)/ IMTEC Corporation, Ardmore (threaded cylindrical)/Calcitek (cylindrical)	246 Machined CPT 195 TPS coated 73 HA coated	Fixed prostheses, overdentures, and single crowns	3	Peri-implant marginal bone loss	Digital panoramic X-rays
					Gingival health	PI & GI
Karoussis 2003[16]	Hollow screw of the ITI Dental Implant System	NR	Single crowns or fixed partial dentures	10	Changes in bone height	Digital intraoral x-ray
					Implant survival rate/ Implant success / Clinical success/ Biologic complications	Binary
					mPI / mBI / DIM/ PD / BoP	Hu-Friedy PGF-GFS periodontal probe
					PAL	periodontal probe
Mohanty 2018[17]	NR	NR	NR	8-10	Implant loss	Binary
					Mobility, bone loss, peri-implantitis	NR
Penarrocha 2004[18]	Solid, threaded ITI implants	Sandblasted, large grit, acid-etched	PFM crowns/ fixed prostheses	1	Peri-implant bone loss	Conventional/digital periapical, panoramic radiographs
Lambert 2000[10]	NR	HA/ non-HA coated	NR	3	Implant failure	Binary
Stoker 2012[12]	ITI/Bonefit ,(Straumann) (hollow-screw, hollow-cylinder/solid screw)	Plasma sprayed (TPS)	Implant Supported mandibular overdenture	μ=8.3	Marginal bone loss	Peri-apical radiograph
					Peri-implantitis	Binary
					PI / BI / PD	Periodontal probe
Tinsley 2001[11]	Calcitek Integral (cylindrical titanium alloy core)	50–70 mm layer of dense highly crystalline HA	Screw-retained fixed prosthesis + metal reinforced removable overdenture	4-6	Marginal bone height	Periapical radiograph/ Orthopantomogram/Scanogram
					Implant survival /success	Binary
					PI / GI / Pocket depth measurements	calibrated periodontal probe
					Technical complications, maintenance, cost-effectiveness	NR

BI: bleeding index, BoP: bleeding on probing, C: completely edentulous, cig: cigarette, CPT: commercially pure titanium, DIM: distance between the implant shoulder and the mucosal margin (recession scored as negative value), GI: gingival index, HA: hydroxyapatite, mBI: modified bleeding index, mm: millimeter, NR: not reported, NS: non-smokers, μ: mean, P: partially edentulous, PAL: probing attachment level, PD: probing depth, (m)PI: (modified) plaque index, S: smokers, SR: systematic review, T: total, TPS: titanium plasma spray, μ: average.

Table 2. Results of implant failure in individual studies.

	Study ID (variable name) / Time		5 years			8yrs			10 years		
			S (AR)	NS (AR)	P	S (AR)	NS (AR)	P	S (AR)	NS (AR)	P
Implant level	Balaguer 2015[14]					6/85	8/275	0.161			
	Karoussis 2003[16]	*Total*							10/28	19/84	0.197
		No periodontitis							5/18	14/73	0.455
		Periodontitis							5/10	5/11	0.835
	Mohanty 2018[17] *(S Vs Periodontitis)*								34/126	22/144	0.018
Patient level	Tinsley 2001[11]		2/7	3/14	0.725						

Figure 1. PRISMA Flow diagram indicating number of studies during different review stage

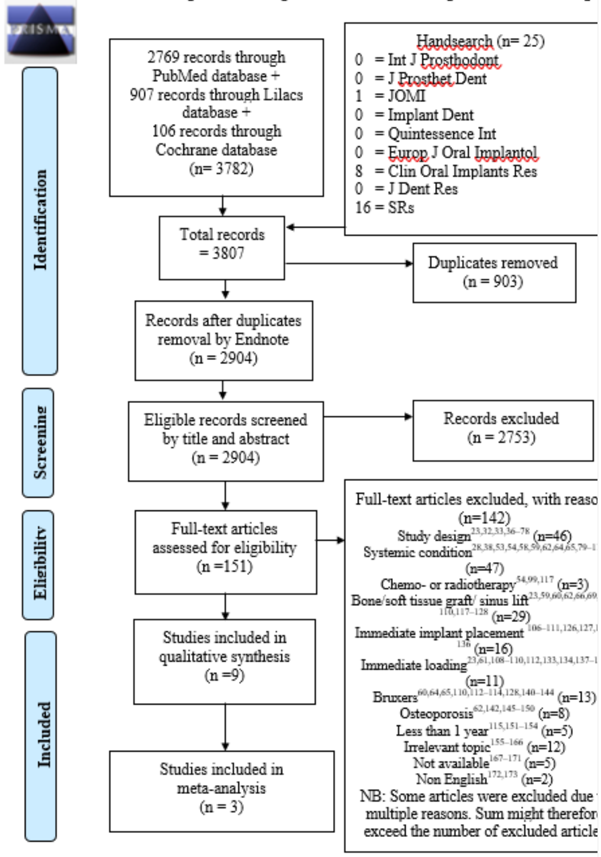


Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included cohort studies (objective outcomes) using ROBINS-I.

Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included cohort studies (subjective outcomes) using ROBINS-I.

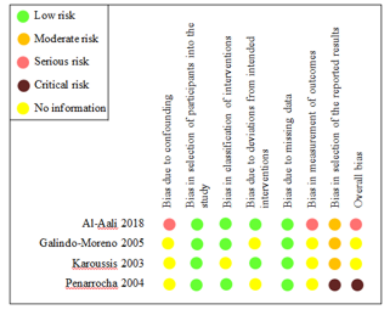
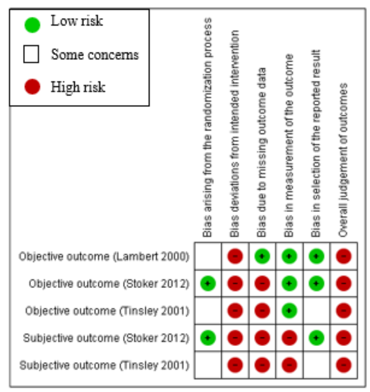


Figure 4. Risk of bias summary: review authors' judgements about each risk of bias item for each included RCT using ROB2 (subjective and objective outcomes).



Appendix 1

Appendix 1A. Search strategy developed for Pubmed database

Item	Primary Term	Synonym 1	Synonym 2	Synonym 3	Synonym 4	Synonym 5	Synonym 6	Synonym 7	Synonym 8	Synonym 9
Exposure	Smoking	Tobacco	Nicotine	Effect smoking	Smoking effects	Tobacco smoking	Cigarette smoking	Cigar smoking	Cigarette smokers	Smokers/ non-smokers
Population	Dental implant/ implants	Oral implant/ implants	Oral implantation	Dental implantation	Oral implanting	Dental implanting	Dental implants, single tooth [Mesh]	Dental implants [Mesh]	Prostheses &implants [Mesh]	Osseointegration [Mesh]
	Peri-implantitis [Mesh]	Prostheses &implants [Mesh]	Prostheses retention [Mesh]	Dental implantation [Mesh]						

Appendix 1B. Search strategy developed for Lilacs database

Item	Primary Term	Synonym 1	Synonym 2	Synonym 3	Synonym 4	Synonym 5	Synonym 6	Synonym 7	Synonym 8	Synonym 9	Synonym 10
Exposure	Smoking	Tobacco	Nicotine smoking	Pipe smoking	Cigar smoking	Tobacco smoking	Cigarette smoking	Smoker	Cigarette smoker	Cigar smoker	Tobacco smoker
Population	Dental implant/ implants	Oral implant/ implants	Oral implantation	Dental implantation	Oral implanting	Dental implanting	Dental implant$	Oral implant$			

Appendix 1C. Search strategy developed for Cochrane Library database

Item	Primary Term	Synonym 1	Synonym 2	Synonym 3	Synonym 4	Synonym 5	Synonym 6	Synonym 7	Synonym 8
Exposure	Smoking	Tobacco	Nicotine	Tobacco smoking	Cigarette smoking	Cigar smoking	Smokers	Non-Smokers	Cigarette smokers
Population	Dental implants	Oral implant/ implants	Oral implantation	Dental implantation	Oral implanting	Dental implanting			

Words within each row were combined using "OR" and the rows were combined together using "AND"