The conclusions and recommendations of systematic reviews can be used by clinicians to incorporate scientific evidence into their daily practices and by decision makers (such as professional medical societies and other organizations) to develop clinical practice guidelines and determine the best place to allocate resources. However, systematic reviews are often appraised as of poor or uncertain quality, and their recommendations could be based on methodological flaws identified in various stages of the review.

Numerous tools have been created to critically appraise or assess the methodological quality of systematic reviews. Although these tools have been used in several studies, their limitations led to the creation of the Risk of Bias in Systematic Reviews (ROBIS) tool, a robust assessment resource.

**ABSTRACT**

**Statement of problem.** Although dental implant treatment has a high success rate, patient-related factors may cause implant failure. In this context, smoking is associated with adverse effects on implant osseointegration. In spite of systematic reviews addressing this topic, the risk of bias in these reviews must be assessed to inform readers whether the studies were conducted with methodological rigor and whether their recommendations are viable in daily clinical practice.

**Purpose.** The purpose of this umbrella systematic review was to assess the risk of bias of systematic reviews regarding dental implant placement in smokers.

**Material and methods.** Systematic review articles with meta-analysis regarding dental implant placement in smokers were eligible for this study. The following were excluded: articles in which implant survival or failure rate was not the primary outcome; articles in which implant survival or failure rate was not related to smokers; and duplicated articles. The search was performed by 2 independent reviewers on MEDLINE (PubMed), Scopus, Web of Science, LILACS, DARE-Cochrane, and SIGLE via OpenGrey. Non-peer-reviewed literature was sought on SIGLE via OpenGrey without language restrictions. Reviewers read titles and/or abstracts to select potential eligible studies, and articles initially selected were read fully. A third reviewer was consulted in cases of disagreement. References of the selected articles were also screened to identify articles of potential interest. The last search was performed on April 29, 2017. Risk of bias assessment was performed with the Risk of Bias in Systematic Reviews (ROBIS) tool.

**Results.** Of the initial 2539 results, 6 systematic reviews with meta-analysis were eligible for the umbrella review (kappa=0.90; very good agreement). All studies were published in the last 11 years. One meta-analysis (16.7%) presented low risk of bias, 3 (50.0%) were assessed as of unclear risk of bias, and 2 (33.3%) received a score of high risk of bias according to the assessment with the ROBIS tool, which also indicated that the criteria most commonly not met were study eligibility criteria and identification and selection of studies.

**Conclusions.** Five of the 6 included meta-analyses had a risk of bias (high or unclear). Therefore, their conclusions and recommendations required careful review. Future meta-analyses must focus especially on study eligibility criteria and identification and selection of studies. (J Prosthet Dent 2018; - - - - - -)
Clinical Implications

Meta-analyses represent the highest scientific evidence available, and their recommendations affect important clinical decisions. Readers and decision makers must be aware of which meta-analyses are of dubious risk of bias and which are of low risk of bias with sound conclusions and safe recommendations for daily clinical practice to avoid unmerited cost and preserve patient health.

Although dental implant treatment has a high success rate, patient-related factors may cause implant failure. In this context, in spite of conflicting scientific evidence, smoking is generally associated with adverse effects on implant osseointegration, which could lead to marginal bone loss or even implant failure.13–15

Although systematic reviews have addressed this topic, risk of bias in these reviews must be assessed to inform readers whether these studies were performed with methodological rigor and whether their recommendations are viable in daily clinical practice. Therefore, the present umbrella review was conducted to answer the following focused question: What is the risk of bias in systematic reviews regarding dental implant placement in smokers?

MATERIAL AND METHODS

The protocol of the present study was registered at the International Prospective Register of Systematic Reviews (PROSPERO—http://www.crd.york.ac.uk/PROSPERO) with the registration number CRD42017060832.

An umbrella systematic review was conducted to assess the risk of bias in systematic reviews regarding dental implant placement in smokers. Umbrella systematic reviews are tertiary studies that have secondary studies, namely systematic reviews and meta-analyses, as the analytic unit, without, however, using a meta-analysis as a statistical tool. Therefore, this work did not need the approval of an ethics committee, and informed consent was not requested.

Systematic review articles with meta-analysis regarding dental implant placement in smokers were eligible for the study. The following were excluded: articles in which implant survival or failure rate was not the primary outcome; articles in which implant survival or failure rate was not related to smokers; and duplicated articles (articles found on more than one database).

The search was performed on MEDLINE via PubMed (from 1966 to 2017), Scopus (from 1996 to 2017), Web of Science (from 1945 to 2017), LILACS (from 1982 to 2017), DARE-Cochrane (up to 2017), and SIGLE via OpenGrey (from 1980 to 2017). Non-peer-reviewed literature was sought on SIGLE via OpenGrey. The following search strategy was used in MEDLINE (via PubMed): systematic[sb] AND “Dental Implants”[MeSH]. This strategy comprises all systematic reviews regarding dental implants. These terms were combined or not to form proper search strategies on the different databases. The last search was performed on April 29, 2017.

The search for eligible studies was conducted by 2 reviewers (O.B.d.O-N. and F.J.C.d.L.). These reviewers read titles and/or abstracts to select potentially eligible studies. Articles initially selected were read fully. References of the selected articles were also screened to identify articles of potential interest. Any disagreements between the reviewers were resolved by discussion to establish a consensus. A third reviewer (F.T.B.) was consulted in situations where disagreement persisted. Although language restrictions were not established, all included articles were published in the English language.

After the final selection of eligible articles, the same reviewers (O.B.d.O-N. and F.J.C.d.L.) performed the risk of bias assessment using the ROBIS tool, which is composed of a 3-phase questionnaire focusing on several aspects of the conduct of a systematic review.3 Phase 1 assesses the relevance of the research question; phase 2 identifies concerns with the review process and is subdivided into 4 domains as follows: study eligibility criteria, identification and selection of studies, data collection and study appraisal, and synthesis and findings; and phase 3 represents the overall risk of bias in the review. Signaling questions in phases 2 and 3 helped identify specific concerns regarding possible bias in the review.3

The assessment of the relevance of the research question (phase 1) is optional and was not performed in the present study. The signaling questions from phase 2 were answered by reviewers as “yes,” “probably yes,” “probably no,” “no,” and “no information.” Then, each domain of phase 2 was judged as “high,” “low,” or “unclear” regarding the level of concern about bias. Finally, in phase 3, the reviewers assessed the overall risk of bias of the review as “high,” “low,” or “unclear.” Any disagreements between O.B.d.O-N. and F.J.C.d.L. were resolved by means of discussion to reach consensus. A third reviewer (F.T.B.) would have been consulted to break the tie if any disagreement had persisted; however, a consensus was reached for all assessments.

The risk of bias of the meta-analyses was the primary outcome of this research. Secondary outcomes were effect measures of the meta-analyses regarding implant failure and marginal bone loss, follow-up period range, and patient age range.
A sample size calculation was not performed because the present research was an umbrella review. The Cohen kappa analysis was performed to measure the level of agreement between the reviewers on the selection of eligible studies. The risk of bias of the systematic reviews (primary outcome) was described according to the ROBIS assessment as “high,” “low,” or “unclear.” Effect measures of the meta-analyses regarding implant failure and marginal bone loss were described as relative risk, odds ratio, risk ratio, mean difference, or standard mean of difference with its respective confidence interval (CI); follow-up period range was described in months; and patient age range was reported in years.

RESULTS

The initial search yielded 2539 results: 760 on MEDLINE via PubMed, 774 on Scopus, 542 on Web of Science, 200 on LILACS, 174 on DARE-Cochrane, and 89 on SIGLE (via OpenGrey). Of these, 2510 were excluded by only reading the titles and abstracts. The 29 remaining articles were read fully, of which 15 articles were excluded as duplicates, and 8 articles were excluded for the reasons listed in Figure 1.15–20 Finally, 6 systematic reviews with meta-analysis were eligible for the umbrella review (kappa=0.90; very good agreement).21–26

All studies were published in the past 11 years. Hinode et al21 were the first authors to publish a meta-analysis on the theme, and Moraschini et al26 were the most recent. The characteristics of the included studies are summarized in Supplemental Table 1.

Assessments regarding phase 2 from the ROBIS tool indicated that 25% of all assessments were judged as high risk of bias, 50% as unclear risk of bias, and 25% as low risk of bias with 66.7% of the last percentage pertaining to the study of Chambrone et al.24 Domains 1 and 2 from phase 2 had 16.7% of judgments as low risk of bias, 33.3% as high risk of bias, and 50% as unclear risk of bias. Domain 3 had 50% as low risk of bias, 16.7% as high risk of bias, and 33.3% as unclear risk of bias. Domain 4 had 16.7% as low risk of bias, 16.7% as high risk of bias, and 66.7% as unclear risk of bias. The percentages of low risk of bias from domains 1, 2, and 4 were obtained solely from the study by Chambrone et al.24 Hinode et al21 and Strietzel et al22 did not obtain any score of low risk of bias, and the study by Strietzel et al22 had the highest number of assessments as high risk of bias (75%).

Regarding phase 3 from the ROBIS tool (the overall risk of bias), 1 meta-analysis presented low risk of bias, 3 were assessed as unclear risk of bias, and 2 received a score of high risk of bias according to the assessment with the ROBIS tool. All data regarding the assessment with the ROBIS tool are available in Figures 2 and 3.

The follow-up period ranged from zero to 240 months, and the patients’ age ranged from 12 to 88 years.
All studies performed a meta-analysis on implant failure in smokers and showed significant statistical difference (Table 1). Regarding marginal bone loss, only 2 studies performed a meta-analysis on this outcome and showed that the insertion of dental implants in smokers statistically affects marginal bone loss (Table 2).

**DISCUSSION**

According to the findings, 5 of the 6 included meta-analyses showed a nonreliable risk of bias (high or unclear), and only 1 meta-analysis was assessed as low risk of bias (Fig. 2).

Domains 1 and 2 obtained the worst results from phase 2 of ROBIS (Figs. 2, 3). The 4 main factors that influenced these results were the absence of a registered protocol by most authors, which made impossible the comparison about what was planned a priori and what was performed and reported; the search for eligible studies in electronic databases was negatively influenced by 2 factors: a search strategy with a range not as thorough as it should have been and the absence of a database specifically to search for non-peer-reviewed literature; eligibility criteria were often ambiguous; and the design of the included studies in several systematic reviews was not correctly planned, which led to weakened results and consequently flawed recommendations and conclusions.

Domain 3 obtained the best overall results from phase 2 of the ROBIS tool (Figs. 2, 3). Authors were often thorough in minimizing errors in data collection, assessing the methodological quality of the included studies, and presenting sufficient data regarding the characteristics of eligible studies.

International guidelines such as the Preferred Reporting Items for Systematic Reviews and Meta-Analyses

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PRISMA) statement may help authors improve the quality of the reporting of the systematic review.27 However, a systematic review can be well reported and still can be assessed as of high risk of bias or low methodological quality, aspects that are related to the quality of a review.3,5,28

All studies showed statistically significant differences in meta-analyses regarding implant failure (Table 1). However, these results were influenced by factors such as heterogeneity of the primary studies and the type of primary studies included in the systematic reviews. The study by Chambrone et al24 seems to be the only properly conducted study, with solid conclusions based on robust findings obtained after thorough planning and execution. The overall meta-analysis of their study indicated that patients who smoke are at a higher risk of implant failure than patients who do not (risk ratio=1.87; 95% CI, 1.35 to 2.58; P<.001; 7 studies; 3326 implants). Nevertheless, the subgroup analysis of prospective studies revealed no statistical differences regarding implant failure in smokers versus nonsmokers (risk ratio=1.55; 95% CI, 0.91 to 2.65; P=.11; 3 studies; 2342 implants). Because this is the only reliable meta-analysis of the theme, with solid evidence and safe recommendations, implant placement in smokers will remain a controversial topic until further meta-analysis can prove otherwise.

Moreover, the findings from the studies by Chrcanovic et al25 (mean difference=0.32; 95% CI, 0.21 to 0.43; P<.001) and Moraschini et al26 (standard mean of difference=0.49; 95% CI, 0.07 to 0.90; P=.02) indicate that smoking significantly affects marginal bone loss (Table 2). These studies, however, were assessed as unclear risk of bias, and their findings must be carefully reviewed.

Meta-analyses represent the highest scientific evidence available, and their recommendations affect important clinical decisions worldwide.1,9 Readers and decision makers must be aware of which meta-analyses are of dubious risk of bias and which are of low risk of bias with sound conclusions and safe recommendations for daily clinical practice to maintain costs and preserve patient health.

Based on the assessment with the ROBIS tool, most of the current systematic reviews with meta-analysis of dental implant placement in smokers presented satisfactory results on data collection and study appraisal and unsatisfactory results on study eligibility criteria and identification and selection of studies. Therefore, future meta-analyses addressing the focused theme should be planned and conducted to overcome these flaws.

To the best of the authors’ knowledge, this is the first systematic review of systematic reviews regarding dental implant placement in smokers. The findings provide no statistical confirmation or solid scientific evidence to support the theory that patients who smoke are at a higher risk of implant failure than patients who do not; however, surgeons must be aware that patients who smoke might present higher marginal bone loss than patients who do not.

**CONCLUSIONS**

Based on the findings of this umbrella systematic review, the following conclusions were drawn:

1. Five of the 6 included meta-analyses were of dubious risk of bias (high or unclear), and their conclusions and recommendations must be carefully reviewed.
2. Future meta-analyses on the focused theme should be conducted with low risk of bias. The expected improvements must focus especially on study eligibility criteria and identification and selection of studies.

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**Table 1. Individual results of the 6 included meta-analyses regarding implant loss**

<table>
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<th>Effects Model</th>
<th>Outcome</th>
<th>Effect Measures</th>
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<td>Value (%)</td>
<td>P</td>
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<td>.26</td>
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**Table 2. Individual results of the 6 included meta-analyses regarding marginal bone loss**

<table>
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<th>Study ID</th>
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</thead>
<tbody>
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<td>Value (%)</td>
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<tr>
<td>Moraschini et al, 2016</td>
<td>t²</td>
<td>98</td>
</tr>
</tbody>
</table>

NP, not performed. NR, not reported. *Outcomes of effect measures regarding marginal bone loss.
Although patients who smoke might present higher marginal bone loss, scientific evidence is not currently available to establish a relation between cigarette smoking and an increased risk of implant failure.

REFERENCES


