

# Influence of Diabetes on the Survival Rate and Marginal Bone Loss of Dental Implants: An Overview of Systematic Reviews

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We aimed to conduct an analysis of the systematic reviews (SRs) in literature about the implant survival rate (ISR) and marginal bone loss (MBL) in diabetic and nondiabetic patients. This work was registered in The International Prospective Register of Systematic Reviews (CRD42018095314) and was developed following Preferred Reporting Items for Systematic Reviews and Meta-Analyses and the Cochrane Library Handbook. A search was performed on PubMed, Cochrane, Scopus, Embase, and LILACS. The PICO (problem/patient/population, intervention/indicator, comparison, outcome) question was "Do the survival rates of dental implants and marginal bone loss differ between diabetic and nondiabetic patients?" A total of 130 articles were retrieved. After eliminating repetitions, 118 were reviewed. Finally, 6 SRs were included. All the reviews indicated that there is no effect of diabetes on the ISR; however, a negative effect of the disease can be observed in MBL. Analysis of the quality of the studies was performed using the assessment of SRs in dentistry (Glenny Scale) and Assessing the Methodological Quality of Systematic Reviews (AMSTAR 2). Glenny Scale showed a moderate to high quality of the included studies. In contrast, AMSTAR 2 pointed out a critically low level for 4 studies, with no study fulfilling the criteria for high quality. It may be concluded that there is no effect of diabetes on the ISR; however, a negative effect of the disease can be observed on MBL.

**Key Words:** dental implant, diabetes, systematic review, overview

## INTRODUCTION

Dental implant therapy is a successful rehabilitation modality.<sup>1</sup> Advances in the design, surface characteristics, and surgical protocols make implant rehabilitation an effective treatment alternative for edentulous areas, with a survival rate of 97.2% and 95.2% in the 5- and 10-year periods, respectively.<sup>2</sup> However, risk factors such as diabetes may compromise osseointegration or adversely affect peri-implant biological health maintenance.<sup>2</sup>

Diabetes Mellitus is a metabolic disorder that promotes hyperglycemia and may increase the rate of systemic complications caused by micro- and/or macroangiopathy. Diabetes

presents in two major forms namely, Type 1 (insulin-dependent), which is associated with autoimmune destruction of pancreatic  $\beta$ -cells and accounts for 5% to 10% of cases of the disease, and Type 2 (non-insulin dependent) that is characterized by insulin resistance, accounting for 90% to 95% of the cases.<sup>3</sup> According to the World Health Organization,<sup>4</sup> more than 422 million people around the world have been affected by diabetes. Thus, this high incidence necessitates better understanding of the disease and the impact on oral rehabilitation with dental implants, because diabetic patients frequently present with periodontal disease and tooth loss, along with slower response to infections, and prolonged healing time.

In recent years, several systematic reviews (SRs)<sup>5-10</sup> have been published correlating the presence of diabetes to the survival rate of rehabilitations with dental implants. However, these studies did not follow standard eligibility criteria in the selection of studies, publication periods, outcomes, and conclusions.

The above-mentioned factors are fundamental to the design of SRs as tools in clinical decision-making based on scientific evidence.<sup>11</sup> The present overview aimed to compile and evaluate SRs in literature that reported data on the

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<https://doi.org/10.1563/aaid-joi-D-19-00087>

proposed theme. The purpose of this overview on rehabilitation with dental implants in diabetic patients is to perform a quantitative and qualitative analysis of previously published SRs with the null hypotheses that diabetes does not influence dental implant survival rate and marginal bone loss.

## MATERIALS AND METHODS

This overview of SRs has been developed according to other works already developed in the literature<sup>12,13</sup> following the Cochrane guidelines and manual for overviews of reviews and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist.<sup>14</sup> It is registered in the International Prospective Register of Systematic Reviews (PROSPERO) database as CRD42018095314. The PICO (problem/patient/population, intervention/indicator, comparison, outcome) question was, "Do the survival rates of dental implants and marginal bone loss differ between diabetic and nondiabetic patients?" The Population was patients undergoing oral rehabilitation with dental implants; the Intervention was diabetic patients who were referred for rehabilitation with dental implants; the population was Compared to nondiabetic patients rehabilitated with dental implants; and we analyzed the Outcomes of survival rate of implants (primary outcome) and marginal bone loss (secondary outcome).

The selection of SRs was based on the PICO question and reviews in accordance with the following eligibility criteria. Inclusion criteria: SRs in literature. Exclusion criteria: (1) literature reviews; (2) clinical case reports and case series; (3) clinical studies (randomized controlled trials [RCT], prospective, retrospective).

The search was performed in the PubMed, Cochrane, Scopus, Web of Science, and LILACS databases. The search was carried out by two independent researchers (J.S.M., J.M.L.G.) for studies completed up to July 2018. The keywords used were a combination of free terms and MeSH terms (Supplemental Material; <https://doi.org/10.1563/aaid-joi-D-00087.S1>) The researchers (J.S.M., J.M.L.G.) also carried out a manual search of the most relevant journals in implantology and periodontology (Supplemental Material; <https://doi.org/10.1563/aaid-joi-D-00087.S1>).

One author (J.S.M.) collected relevant information from the articles and a second author (C.A.A.L.) evaluated all the information collected. A careful analysis was performed to check for disagreements among the authors. Any such disagreements were resolved through discussion with a third author (E.P.P.) until consensus was reached.

The included studies were assessed for risk of bias using the Assessing the Methodological Quality of Systematic Reviews (AMSTAR 2) scale. This tool developed by Shea et al<sup>15</sup> is composed of 16 questions that analyze the methodology of SRs. In this scale, the final methodological analysis of the review is not designated through scores, but by accurate and comprehensive summary of the results of the available studies that address the question of interest.

The SRs were designated as high risk of bias when they did not have any weakness or had noncritical weakness; moderate risk of bias when they had more than one weakness but no critical flaws; low risk of bias when they had a critical flaw and may not provide an accurate and comprehensive summary of the available studies that address the question of interest; and

critically low risk of bias when they had more than one critical flaw and should not be relied on to provide an accurate and comprehensive summary of the available studies.

The use of the Glenny et al<sup>16</sup> scale was applied to analyze the included studies. The scale consists of a set of 15 items that evaluate the structure of the topics covered, formulation of a specific question (PICO), and interpretation of the data. Scoring is performed as follows: each item with a "yes" answer is assigned 1 point, and the total score obtained can range from 0 to 15 points. A score of 10 to 15 indicates high quality; 5 to 9 points, average quality; and 0 to 4 point, low quality.

An analysis was also carried out to verify whether the SRs were delineated according to PRISMA,<sup>14</sup> as well as whether there was a registry of these SRs on specific platforms. In addition, the bias scales used in the SRs and the types of studies included were evaluated. The outcomes analyzed were (1) implant survival rate (ISR), and (2) marginal bone loss (MBL).

The kappa statistic (k) was used to determine interreader agreement during the database article selection process. Due to heterogeneity between the studies, meta-analysis was not performed.

## RESULTS

The search strategy is described in Figure 1. A total of 130 articles were found in the databases. After duplicate studies were excluded, the titles and abstracts were reviewed to match the eligibility criteria. Ten articles were selected for full reading of the text and 6 studies were selected for analysis in this overview. The reasons for exclusion from the studies are listed in Figure 1.

The characteristics of the SRs are described in Table 1, and the results of scales describing quality assessment of the SRs (Glenny and AMSTAR 2) are described in Tables 2 and 3. The SRs included in this overview were published between 2009 and 2017. Within the SRs, the number of studies evaluated ranged from 7 to 22 studies, the majority of which were of prospective and retrospective in nature. Three reviews included RCTs<sup>5,8,10</sup> and one included an experimental study.<sup>7</sup> Only one SR was registered in PROSPERO<sup>6</sup> and five<sup>6,8,10</sup> used the PRISMA checklist as a guide for structuring the systematic review. The most common risk bias scales used in the SRs were GRADE and NOS (Newcastle-Ottawa Scale). Two studies did not assess the risk of bias.<sup>7,8</sup> One study performed the search in only one database (PubMed/Medline).<sup>7</sup> The other studies conducted the searches in at least three databases.

The methodological quality of the included studies was assessed by Glenny and AMSTAR 2. The AMSTAR 2 is a major revision of the original AMSTAR instrument,<sup>15</sup> rating overall confidence in the results of the review as high, moderate, low, and critically low. The reliability index of included studies ranged from moderate in one study,<sup>5</sup> low in one study,<sup>6</sup> and critically low in four studies.<sup>7-10</sup> The details of analysis of the reviews completed using the AMSTAR 2 scale are listed in Table 2.

The Glenny et al<sup>16</sup> scale scores between 9 and 15 (moderate to high quality); all SRs included at least 9 items. It should be noted that some revisions did not make it clear whether the article peer review process was carried out by two reviewers; however, in relation to the selection of articles performed by at

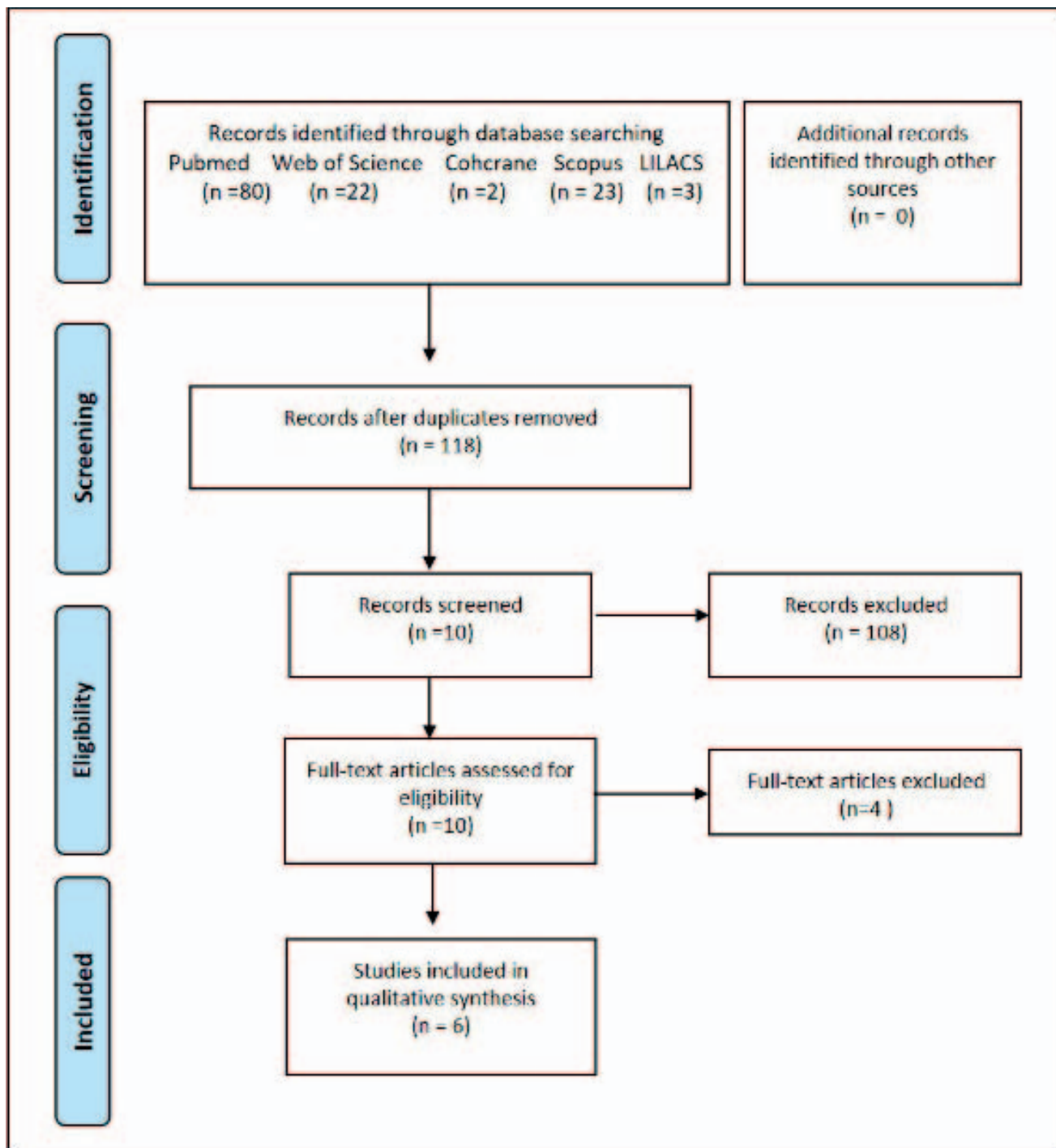


FIGURE 1. Flowchart.

least two reviewers, this point was contemplated by further studies. The aspects that showed the greatest deficiency of information were related to the possible search for unpublished data, with only 50% of the reviews contemplating (Table 3), searching in all languages, the quality of articles evaluated by more than one reviewer.

The agreement between the examiners (J.R.S.M., J.M.L.G.) was verified in the selection of studies in the databases:

PubMed (0.89), Cochrane (1.0), Scopus (0.86), Web of Science (0.95), and LILACS (1.0), obtaining a high degree of agreement among examiners.

**DISCUSSION**

The present study was based on two null hypotheses. The first null hypothesis, which stated that there is no influence of

TABLE 1  
Characteristic of the included studies\*

Study	Registration	Guide	Quality Assessment	Included Studies	Study Design	Databases	Conclusion	AMSTAR 2	Glenny	Type of Study
Monje et al <sup>6</sup>	Yes	PRISMA AMSTAR	NOS	7	Prospective, cross-sectional, retrospective	Medline (Ovid), Embase (Ovid), Web of Science, Cochrane Library, SciVerse	DM/hyperglycemia is associated with higher risk of peri- implantitis	Low	15	MA
Moraschini et al <sup>5</sup>	No	PRISMA AMSTAR	GRADE	14	RCT, prospective, retrospective	PubMed/Medline, Cochrane Library, Web of Science, Embase, gray literature	DM did not influences the implant failure rates	Moderate	14	MA
Naujokat et al <sup>9</sup>	No	PRISMA	USGHRQMGC	22	Prospective, cross-sectional, retrospective	PubMed, Embase, AWMF online, National Guideline Clearinghouse, Guidelines International Network, Cochrane Library	Patients with poorly controlled diabetes suffer from impaired osseointegration, elevated risk of peri- implantitis, and higher level of implant failure	Critically low	14	SR
Arbildo et al <sup>10</sup>	No	PRISMA	JADAD CMQ	3	RCT, CCT, prospective	PubMed, Scielo and RedALyC	Survival rate of dental implants in well- controlled diabetic patients is similar to non-diabetic patients	Critically low	14	MA
Chrcanovic et al <sup>8</sup>	No	PRISMA	NR	14	RCT, retrospective	PubMed, Web of Science, Cochrane Oral Health Group Trials Register	DM did not influences the implant failure rates	Critically low	15	MA
Javed et al <sup>7</sup>	No	NR	NR	18	In vivo (humans and animals)	PubMed/Medline	DM controlled individuals did not influences the implant failure rates	Critically low	9	SR

\*USGHRQMGC indicates US Agency for Healthcare Research and Quality Methods Guide for Comparative; NOS, Newcastle-Ottawa Scale; RCT, randomized controlled trial; NR, Not related; MA meta-analyses; SR, systematic review; CCT, controlled clinical trial; CMQ, checklist for measuring quality.

diabetes on ISR was accepted, because four of the six included studies did not show any difference between diabetic and nondiabetic patients. However, the second null hypothesis, which stated that there is no influence of diabetes on MBL was

rejected, because four of the six studies included showed a negative change in marginal bone level in diabetic patients. Liu et al<sup>17</sup> stated that diabetes can negatively influence the health of individuals by increasing the chances of postoperative

TABLE 2  
Glenny Scale

Questions	Chrcanovic et al <sup>8</sup>	Monje et al <sup>6</sup>	Moraschini et al <sup>5</sup>	Naujokat et al <sup>9</sup>	Javed et al <sup>7</sup>	Arbildo et al <sup>10</sup>
Q1: Did review address a focused question?	1	1	1	1	1	0
Q2: Did authors look for appropriate papers?	1	1	1	1	1	1
Q3: Do you think authors attempted to identify all relevant studies?	1	1	1	1	1	1
Q4: Search for published and unpublished literature	1	1	0	1	0	0
Q5: Were all languages considered?	1	1	1	0	1	0
Q6: Was any hand-searching carried out?	1	1	1	1	0	0
Q7: Was it stated that the inclusion criteria were carried out by at least two reviewers?	1	1	1	1	1	1
Q8: Did reviewers attempt to assess the quality of the included studies?	1	1	1	1	0	1
Q9: If so did they include this in the analysis?	1	1	1	1	0	1
Q10: Was it stated that the quality assessment was carried out by at least two reviewers?	1	1	1	1	0	1
Q11: Are the results given in a narrative or pooled statistical analysis?	1	1	1	1	1	1
Q12: If the results have been combined was it reasonable to do so?	1	1	1	1	1	1
Q13: Are the results clearly displayed?	1	1	1	1	1	1
Q14: Was an assessment of heterogeneity made and reasons for variation discussed?	1	1	1	1	0	0
Q15: Were results of review interpreted appropriately?	1	1	1	1	1	1
Total	15	15	14	14	9	10

TABLE 3  
AMSTAR 2 Scale\*

Study	Instrument Items							8: Included Studies (Adequate Details)
	1: PICO	2: Review Methods†	3: Study Selection	4: Search Strategy†	5: Duplicate Study Selection	6: Duplicate Data Extraction	7: List of Excluded Studies†	
Monje et al <sup>6</sup>	Y	Y	Y	PY	Y	Y	N	Y
Moraschini et al <sup>5</sup>	Y	PY	N	PY	Y	Y	Y	Y
Naujokat et al <sup>9</sup>	Y	PY	N	N	N	N	N	PY
Arbildo et al <sup>10</sup>	Y	N	N	PY	Y	Y	N	PY
Chrcanovic et al <sup>8</sup>	N	N	N	PY	Y	N	N	PY
Javed et al <sup>7</sup>	N	N	N	N	Y	N	N	N

\*Y indicates yes; PY, partial yes; N, no.

†Critical domain.

infection, increasing the length of the healing period, and directly affecting bone metabolism. Also, the historical duration of the disease in each patient could be implicated in the increased risk of microvascular complications, which contributes to the failure of implants by directly affecting the osseointegration period.<sup>8,18,19</sup> According to a study by Javed et al,<sup>7</sup> diabetes was one of the contraindications for rehabilitation with dental implants, requiring metabolic control prior to the procedure. However, the observations of the present overview reported that implant failure was not influenced by the systemic condition of the patient.

Glycemic control is a critical variable in selection of patients for implant rehabilitation.<sup>20</sup> Monje et al<sup>6</sup> stated that individuals with high glycemic level have higher risk of developing peri-implantitis, which may lead to a decrease in the longevity of dental implants.<sup>6</sup> However, optimal glycemic control facilitates an increase in osteoblast production and function, thereby favoring osseointegration.<sup>20</sup> This observation is in consensus with that reported by Alasqah et al,<sup>21</sup> who stated that optimal diabetes control was associated with better periodontal parameters, including marginal bone loss.

One study<sup>22</sup> reported that the presence of diabetes increased the incidence of marginal bone loss. These data were verified in the results of the present overview and were biologically attributed to an increase in proinflammatory cytokines such as interleukins in the crevicular groove and bone. The findings support the hypothesis that bone exhibits an inflammatory response to diabetes.<sup>23</sup> The inflammatory response may lead to an increase in osteoclasts, which would justify the increased rate of bone loss.<sup>7</sup> The studies reviewed did not assess the weight of diabetic and nondiabetic patients. However, it is important to highlight that several new studies<sup>24–26</sup> have assessed the influence of body weight of diabetic individuals on oral health and have demonstrated that an increase in patient weight may result in poor outcomes of periodontal conditions, which may influence MBL.<sup>27</sup>

SRs evaluating the ISR and MBL using the Glenny scale reported a good quality score. However, the AMSTAR 2 scale did not report any study of high quality level, with most studies being designated low and/or critically low quality levels. The

Glenny scale is an instrument that assigns scores to the domains analyzed, whereas in AMSTAR 2, there is no such quantification, which may be responsible for the divergence in results obtained.<sup>28,29</sup> Shea et al<sup>15</sup> recommended that the process of assessing the quality of studies should be based on identification of critical domains, as the use of scores may mask shortcomings of the studies, and decrease confidence in the results of an SR. In addition, greater requirement of details in the methodology of SRs can be observed when evaluated by AMSTAR 2 (Table 3).

The quality of SRs can be improved by recording the data on its own platform (ie, PROSPERO), or by using a guide for the development of revisions (ie, PRISMA) focused beyond question (PICO), among other items. Among the SRs assessed, the chief data missing in the studies was the existence of a registration protocol. A registration tool, such as PROSPERO, has been available since February 2011 and allows free search of subjects in order to maintain transparency in the execution of SRs. Of the seven studies included in the present overview, one was published prior to implementation of the PROSPERO tool.<sup>7</sup> The other six studies were published after 2011 however, only one was registered with PROSPERO. The reason for registration was that SRs often provide an evidence base on which health and social care decisions are made in order to ensure thoroughness of data and have a low risk of bias.

In the use of systematic and explicit methods to identify, select, and critically appraise relevant research, and collect and analyze data from the studies included in the review of the studies analyzed, only one<sup>7</sup> did not use PRISMA as a construction tool for the systematic review, being justified by what was accomplished in the year of release of this protocol. Thus, it is evident that the general concepts and topics covered by PRISMA are relevant to any systematic review.<sup>14</sup>

Another important finding was the search for already consolidated databases—PubMed and the Cochrane Library being the most accessed—with a limited number of searches in databases of clinical studies, as well as in gray literature. This fact was analyzed in item 4 of the Glenny scale and was not scored in 50% of the studies analyzed. These findings reinforce the need for adjustments to be developed in future studies, in order to minimize the risk of bias.

TABLE 3  
Extended

Instrument Items								
9: Assess Risk of Bias†	10: Report on the Sources of Funding	11: Methods for Statistical Analysis	12: Impact of Risk of Bias in Individual	13: Risk of Bias in Individual Studies	14: Heterogeneity Satisfactory	15: Investigation of Publication Bias†	16: Report of Conflict of Interest	Rating Overall Confidence
PY	N	Y	Y	Y	Y	Y	Y	Low
Y	Y	Y	Y	Y	N	Y	Y	Moderate
PY	Y	NM	NM	N	N	NM	Y	Critically low
Y	N	NM	NM	N	Y	NM	N	Critically low
Y	Y	N	N	Y	N	N	Y	Critically low
N	N	NM	NM	N	N	NM	Y	Critically low

The results of this overview should be interpreted with caution since there are factors that are heterogeneous between the studies and are subject to an increased risk of bias. It can be observed that the absence of SRs with only the inclusion of controlled and randomized clinical trials may be a risk factor for bias. Randomized controlled trials delineated according to CONSORT (Consolidated Standards of Reporting Trials) with accurate calculation of the sample size should be undertaken. In addition, better interpretation of the data would be possible if the studies included questions such as type of implant, location of the implant, type and duration of diabetes, glycemic control, and type of prosthetic restoration.

An overview of SRs is a new approach to evaluate and synthesize the results of multiple SRs in a single document that can be used to guide health care providers and policy makers, and is considered the best level of scientific evidence.<sup>30</sup> However, the limitations of this type of study lie in the fact that there is no detailed analysis of the primary studies and conclusions are based on the data recovered from the existing SRs.<sup>30</sup>

However, to validate the data obtained, it is of fundamental importance that overview studies be based on registration protocols, as well as on a checklist of indispensable items (PRISMA) for their construction. Another important measure is the consultation with scales such as AMSTAR 2 and Glenny during a systematic review so that it is already developed considering the items necessary to reach a maximum evaluation of the quality of the evidence produced.

#### CONCLUSION

Based on the observations in the present overview, it can be concluded that there is no effect of diabetes on the survival rate of implants; however, a negative effect of the disease can be observed on MBL, affecting the osseointegration. The Glenny scale showed moderate to high quality of the included studies. On the other hand, AMSTAR 2 pointed out a critically low level for four studies and did not report any study with high quality.

#### ABBREVIATIONS

AMSTAR 2: Assessing the Methodological Quality of Systematic Reviews  
CCT: controlled clinical trial

CONSORT: Consolidated Standards of Reporting Trials

ISR: implant survival rate

k: kappa statistic

MA: meta-analyses

MBL: marginal bone loss

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

PROSPERO: Prospective Register of Systematic Reviews

RCT: randomized controlled trials

SR: systematic review

#### NOTE

This manuscript has no conflict of interest.

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