

## Obesity and periodontitis: systematic review and meta-analysis

Obesidade e periodontite: revisão sistemática e meta-análise

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**Abstract** *The scope of this study was to conduct a systematic review of the studies on the association between obesity and periodontitis. The methods applied included a literature search strategy and selection of studies using inclusion and exclusion in accordance with the criteria for characteristics of the studies and meta-analysis. The research was conducted in the PubMed, Embase and Lilacs databases through 2010. Selected papers were on studies on humans investigating whether or not obesity is a risk factor for periodontitis. Of the 822 studies identified, 31 studies met the inclusion criteria and were included in this meta-analysis. The risk of periodontitis was associated with obesity (or had a tendency for this) in 25 studies, though it was not associated in 6 studies. The meta-analysis showed a significant association with obesity and periodontitis (OR = 1.30 [95% Confidence Interval (CI), 1.25 - 1.35]) and with mean Body Mass Index (BMI) and periodontal disease (mean difference = 2.75). Obesity was associated with periodontitis, however the risk factors that aggravate these diseases should be better clarified to elucidate the direction of this association. Working with paired samples and avoiding confusion factors may contribute to homogeneity between the studies.*

**Key words** *Obesity, Overweight, Periodontal diseases, Periodontitis*

**Resumo** *O objetivo deste estudo foi realizar uma revisão sistemática sobre a associação entre obesidade e periodontite. Os métodos aplicados incluíram uma estratégia de busca na literatura, seleção dos estudos por meio dos critérios de inclusão e exclusão de acordo com as características dos estudos e meta-análise. A busca foi realizada nas bases de dados PubMed, EMBASE e LILACS até 2010. Os artigos selecionados foram sobre estudos em humanos, investigando se a obesidade é um fator de risco para periodontite. Dos 822 estudos identificados inicialmente, 31 atendiam aos critérios de inclusão e foram incluídos na meta-análise. O risco da periodontite esteve associado com obesidade (ou teve uma tendência para isso) em 25 estudos, sendo que 6 não encontraram esta associação. A meta-análise mostrou uma associação significativa entre obesidade e periodontite. (OR = 1,30 [95% Intervalo de Confiança (IC); 1,25 – 1,35]) e entre o Índice de Massa Corporal (IMC) médio e doença periodontal (diferença nas médias = 2,75). Obesidade esteve associada à periodontite, entretanto os fatores de risco que agravam essas doenças devem ser melhor esclarecidos para elucidar a direção dessa associação. Trabalhar com amostras pareadas e evitar fatores de confusão podem contribuir para a homogeneidade entre os estudos.*

**Palavras-chave** *Obesidade, Sobrepeso, Doenças periodontais, Periodontite*

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## Introduction

The prevalence of obesity is increasing worldwide<sup>1</sup>. Obesity, defined as a Body Mass Index (BMI)  $\geq 30$  kg/m<sup>2</sup>, and overweight (BMI  $\geq 25$  kg/m<sup>2</sup>) are becoming a worldwide epidemic estimated to involve 1.7 billion people in developed and developing countries<sup>2</sup>, being considered a public health problem<sup>3</sup>. According to the WHO Global Info-base, the prevalence of obesity among american adults in 2010 was 44.2% in men and 48.3% in women, and the global obesity epidemic keeps to increase<sup>4</sup>.

This disease is so common among the world population that it is becoming the most important contributors to ill health<sup>5</sup>. This is a complex and multi-factorial disease arising from excessive storage of fat, resulting from the interaction of social, behavioral, cultural, psychological, metabolic and genetic factors<sup>5</sup>. Obesity causes or exacerbates a large number of health problems, both independently and in association with other diseases (comorbidities)<sup>3</sup>. These diseases may be type 2 diabetes, hypertension, hypoventilation, sleep apnea, venous stasis, tumor, regenerative joint disease, and others<sup>6</sup>.

Overweight and obesity have been suggested to be associated with periodontitis, because obesity may have some effects on systemic health by affecting the host susceptibility to periodontitis due to inflammatory mediators<sup>7</sup>. Periodontitis is a common chronic inflammatory oral disease of the adult population characterized by a gingival inflammatory response against a pathogenic bacterial microflora, resulting in alveolar bone loss and eventually tooth loss<sup>8</sup>. The link between periodontitis and obesity may have relevant public health implications because both diseases are important risk factor for cardiovascular diseases<sup>9-11</sup>.

However this association is not entirely clear in the literature because there are controversies on finding of the studies. Obesity have been associated with periodontitis in some studies<sup>12-15</sup> and not in others<sup>16-18</sup>. For these reasons the present study aimed to review systematically the studies on the association between overweight/obesity and periodontitis.

## Materials and Methods

### Search Strategy and Study Selection

The methods applied in this review included a literature search strategy, inclusion and exclusi-

on criteria for selecting the studies, selection process and data extraction and quantitative data synthesis.

The Cochrane Library revealed no systematic review on association between obesity and periodontal disease in adults. Subsequently, we searched PubMed (Medline), Embase and LILACS using the following combinations of keywords in English, Spanish and Portuguese: Obesity OR body weight OR Body mass index OR overweight OR abdominal fat OR obese AND periodontal diseases OR gingivitis OR periodontitis OR alveolar bone loss.

### Inclusion and exclusion criteria for selecting studies

The inclusion criteria were human studies with subjects up 15 years old, written in English, Spanish and Portuguese, investigating whether or not obesity is a risk factor for periodontitis. Those papers that were published until 2010 were selected.

Excluded were those case reports describing periodontal conditions in obese, ecological studies, experimental animal studies and reviews. In addition, published studies showing repeated results from the same original study were excluded. Studies that had inadequate or unclear scoring systems for the measurement of periodontal disease and nutritional status were excluded. Periodontal measures were classified as adequate when clinical measures were based on periodontal pocket depths (PPD) and/or clinical attachment loss (CAL) measures or based on Community Periodontal Index (CPI) or alveolar bone loss (Alveolar Bone Score - ABS) assessed using radiographs or tooth mobility. Nutritional status was classified as adequate when it was assessed through Body mass index (BMI) or Waist Circumference (WC).

### Selection process and data extraction

Two reviewers (P.G.M.G. and C.A.P.C) independently retrieved and evaluated the articles for eligibility. The extraction of information from studies was conducted by the first and a third reviewer (J.A.M.), and the information included number of patients, the range and the mean of age, gender (n), country of the sample, method of periodontal disease evaluation, method of nutritional status evaluation and the main results. Any discrepancies between reviewers were discussed with a fourth reviewer (S.H.C.S.P.) and resolved by consensus. We recorded general study characteristics in Table 1.

**Table 1.** Characteristics of the included studies ( $n = 31$ ).

Reference (Author, year)	Subjects (n)	Age range	Mean age (years)	Percent female (%)	Country	Method of periodontal evaluation and criteria
Al-Zahrani et al., 2003 <sup>19</sup>	13.665	≥ 18	NR	52.7	USA	PPD ≥ 4 mm and CAL ≥ 3 mm
Borges et al., 2007 <sup>20</sup>	318	≥ 30	57.0	55.0	Brazil	CPI scores 3 and 4
D'Aiuto et al., 2008 <sup>21</sup>	13.677	> 17	NR	NR	USA	PPD ≥ 4 mm
Dalla Vecchia et al., 2005 <sup>22</sup>	706	30-65	NR	53.4	Brazil	CAL ≥ 5 mm
Dumitrescu; Kawamura, 2010 <sup>12</sup>	79	19-69	NR	60.8	Norway	PPD > 6mm
Ekuni et al., 2008 <sup>23</sup>	618	18-24	21.4	52.1	Japan	CPI scores 3 and 4
Furuta et al., 2010 <sup>24</sup>	2.225	18-19	18.6	43.2	Japan	PPD ≥ 4 mm
Genco et al., 2005 <sup>7</sup>	12.367	NR	43.5	53.1	USA	CAL ≥ 1.5 mm
Haffajee; Socransky, 2009 <sup>25</sup>	695	18-86	46.8	49.6	USA	PPD ≥ 4 mm
Han et al., 2009 <sup>13</sup>	1.046	15-84	40.8	54.5	South Korea	CPI scores 3 and 4
Khader et al., 2009 <sup>14</sup>	340	18-70	NR	50.6	Jordan	PPD ≥ 4 mm and CAL ≥ 3 mm
Kongstad et al., 2009 <sup>17</sup>	1.504	20-95	52.8	53.9	Denmark	CAL ≥ 3 mm
Kumar et al., 2009 <sup>26</sup>	513	18-54	32.6	NR	India	CPI scores 3 and 4
Kushiyaama et al., 2009 <sup>18</sup>	1.070	40-70	NR	73.7	Japan	CPI score 4
Li et al., 2009 <sup>27</sup>	208	37-78	61.1	54.8	China	CAL ≥ 3 mm
Linden et al., 2007 <sup>28</sup>	1.362	60-70	64.2	0.0	UK	PPD ≥ 5 mm
Lundin et al., 2004 <sup>29</sup>	32	13-24	17.8	65.6	Sweden	PPD ≥ 4 mm
Machado et al., 2005 <sup>30</sup>	60	> 20	43.9	43.3	Brazil	PPD ≥ 5 mm
Morita et al., 2009 <sup>31</sup>	2.478	24-60	43.3	18.2	Japan	CPI scores 3 and 4
Pitiphat et al., 2008 <sup>32</sup>	121	20-67	40.5	73.6	Thailand	PPD ≥ 5 mm
Saito et al., 2001 <sup>33</sup>	643	NR	45.6	79.6	Japan	PPD ≥ 4 mm
Saito et al., 2005 <sup>34</sup>	584	40-79	56.6	100.0	Japan	PPD ≥ 1.9 mm (quintile)
Saito, 2008 <sup>35</sup>	76	55-59	55.0	100.0	Japan	PPD 3 teeth ≥ 4 mm or 1 tooth ≥ 6 mm
Saxlin et al. 2010 <sup>36</sup>	214	30-59	44.3	58.4	Finland	PPD ≥ 4 mm
Saxlin et al., 2008 <sup>37</sup>	1.297	30-49	NR	60.8	Finland	PPD ≥ 4 mm
Shimazaki et al., 2007 <sup>38</sup>	584	40-79	55.7	100.0	Japan	PPD ≥ 2 mm
Torrungruang et al., 2005 <sup>39</sup>	2.005	50-73	60.0	25.6	Thailand	CAL ≥ 4 mm
Wang et al., 2009 <sup>40</sup>	12.123	35-44	39.5	64.3	Taiwan	CPI scores 3 and 4
Wood et al., 2003 <sup>41</sup>	8.842	≥ 18	NR	51.3	USA	PPD ≥ 3 mm
Wood; Johnson, 2008 <sup>42</sup>	1.098	> 18	NR	NR	USA	PSR scores 3 and 4 (pocket ≥ 3.5 mm)
Borges-Yáñez et al., 2006 <sup>43</sup>	365	> 60	73.0	NR	Mexico	PPD ≥ 6 mm

it continues

Table 1. continuation

Method of nutritional evaluation and criteria to define obesity	Sampling calculation	Were the examiners calibrated for periodontal assessment? (Kappa values)	Main variables controlled	Significant association: obesity and periodontitis
BMI $\geq$ 30Kg/m <sup>2</sup>	#	No	Age, gender, ethnicity, smoking habits, diabetes, schooling, last dental visit	Yes
BMI mean	No	No	Ethnicity, schooling, PCR	Tendency
WC > 102cm (male) or > 88cm (female)	#	Yes*	Age, gender, smoking habits, schooling, ethnicity	Tendency
BMI $\geq$ 30Kg/m <sup>2</sup>	Yes	k = 0.85 to 0.92	Diabetes	Yes
BMI $\geq$ 30Kg/m <sup>2</sup>	No	No	None	Yes
BMI $\geq$ 30Kg/m <sup>2</sup>	No	No	Unclear	Yes
BMI $\geq$ 25Kg/m <sup>2</sup>	No	Yes*	None	Tendency
BMI $\geq$ 27Kg/m <sup>2</sup>	No	No	Diabetes, age, gender, smoking habits, ethnicity, schooling, cholesterol	Yes
BMI $\geq$ 30Kg/m <sup>2</sup>	No	No	Antibiotic therapy, age, gender, smoking habits	Yes
BMI $\geq$ 25Kg/m <sup>2</sup>	No	k = 0.84 to 0.97 (intra); k = 0.62 (inter)	Gender, smoking habits, age, sociodemograph factors, physical activity	Yes
BMI $\geq$ 30Kg/m <sup>2</sup> and WC > 102cm (men) or > 88cm (women)	No	No	Pregnancy, antibiotic therapy, osteoporosis, cancer, age, dental plaque, number of teeth	Yes
BMI $\geq$ 30Kg/m <sup>2</sup>	No	k = 0.52	Age, gender, smoking habits, diabetes, physical activity	No
BMI $\geq$ 30Kg/m <sup>2</sup>	Yes	k = 0.84	Age	Yes
BMI $\geq$ 25Kg/m <sup>2</sup>	No	No	Age, gender, smoking habits	No
BMI $\geq$ 25Kg/m <sup>2</sup> and WC > 90cm (men) or > 80cm (women)	No	No	Antibiotic therapy, age, gender, smoking habits	Tendency
BMI $\geq$ 30Kg/m <sup>2</sup>	No	Yes*	gender, smoking habits, age, diabetes, schooling	Tendency
BMI mean	No	No	smoking habits	No
BMI $\geq$ 30Kg/m <sup>2</sup>	No	No	age, gender	No
BMI $\geq$ 25Kg/m <sup>2</sup>	No	No	age, gender, smoking habits	Yes
BMI mean	No	Yes*	medication, pregnancy, systemic diseases, periodontal therapy	Yes
BMI $\geq$ 30Kg/m <sup>2</sup>	No	k = 0.58 to 0.75	age, gender, social class, diabetes, smoking habits, oral hygien	Yes
BMI mean	No	No	age, dental plaque, smoking habits	Yes
BMI $\geq$ 25Kg/m <sup>2</sup>	No	Yes*	gender	Yes
BMI $\geq$ 30Kg/m <sup>2</sup>	#	k = 0.83	age, gender, schooling, dental plaque, number of teeth	Tendency
BMI > 28.6Kg/m <sup>2</sup> (quintile)	#	k = 0.82	diabetes, smoking habits	Yes
WC > 88cm (women)	No	k = 0.80	age, smoking habits	Yes
BMI $\geq$ 25Kg/m <sup>2</sup>	No	k = 0.72 to 0.90	age, dental plaque, smoking habits, diabetes	No
BMI $\geq$ 25Kg/m <sup>2</sup>	No	k = 0.55 to 0.61 (intra); k = 0.42 to 0.44 (inter)	severe systemic disease	Tendency
BMI mean	#	Yes*	age, gender, ethnicity, smoking habits, diabetes, schooling, last dental visit	Yes
BMI $\geq$ 30Kg/m <sup>2</sup>	No	Yes*	smoking habits	Tendency
BMI $\geq$ 30Kg/m <sup>2</sup>	No	Yes*	age, gender, sociodemograph factors, schooling, smoking habits	No

NR = Not Reported; ABS = Alveolar Bone Score; PPD = Periodontal Pocket Depths; CAL = Clinical Attachment Loss; CPI = Community Periodontal Index; PSR = Periodontal Screening and recording; BMI = Body Mass Index; WC = Waist Circumference; \* Sample of a National Health Examination Survey; \* Clinical calibration was performed, but the results were not reported.

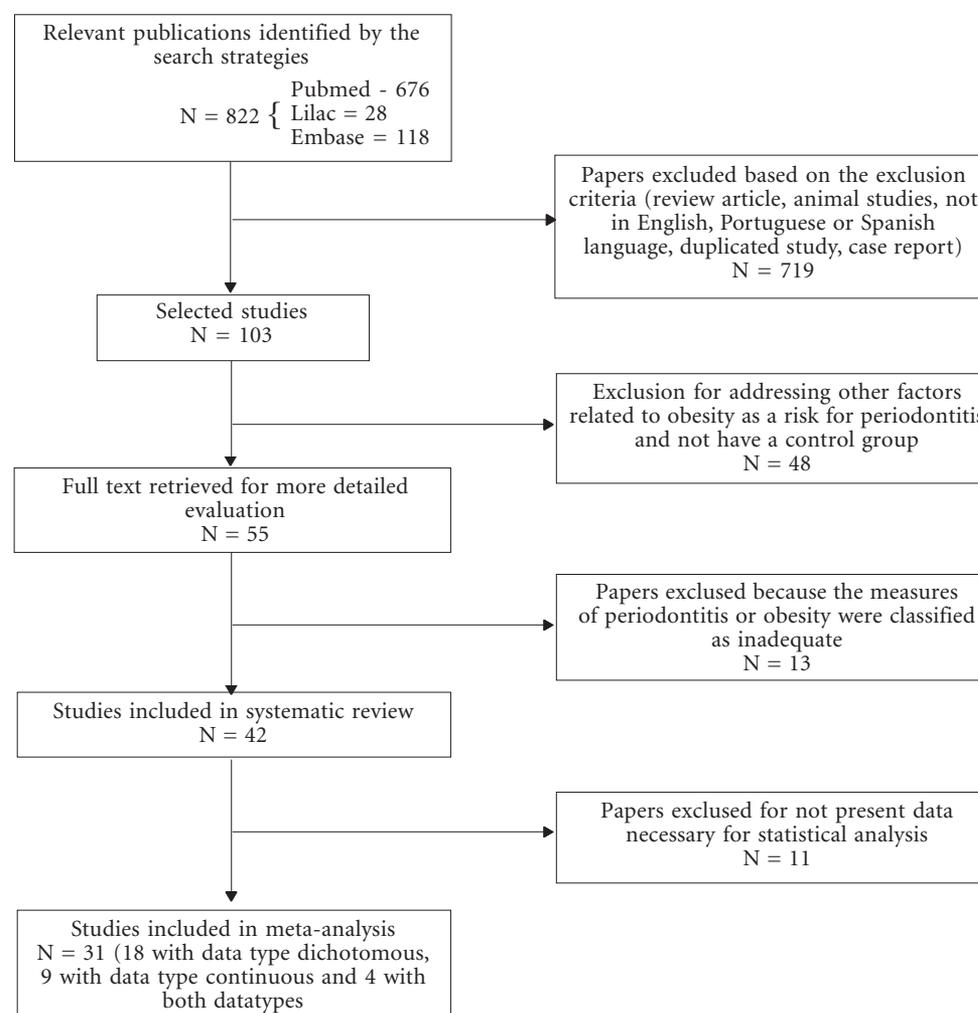
### Data Synthesis and Analysis

A descriptive analysis was performed using frequencies and means. Studies that did not present the results of periodontal measures and of nutritional status were scored as unclear and were excluded of meta-analysis. Studies with data type dichotomous the statistical method used was *Mantel-Haenszel* with odds ratio as effect measure. For this analysis it was considered as event the number of subjects with periodontitis, divided into control group (subjects with normal nutritional status) and experimental group (subjects with overweight and obesity). Studies with data type continuous the statistical method used was *Inverse Variance* with mean difference as effect

measure. Mean and standard deviation of BMI were distributed between control group (without periodontal disease) and experimental group (with periodontal disease). *Review Manager 5.0* computer program was used.

### Results

As shown in Figure 1, from a total of 822 identified records by the three search strategies, 103 were manually selected on the basis of their titles and abstracts, with interobserver agreement. A further 72 were excluded, leaving 31 papers for the meta-analysis (Figure 1). All studies were cross-sectional.



**Figure 1.** Flow chart of studies through the review.

The risk of periodontal disease was associated with obesity in 17 studies, it had a tendency for this in 8 studies, and 6 studies had not associated.

The studies that showed the number of participants with events (periodontal disease) and total number of participants in experimental (obese) and control groups (normal weight) were included in dichotomous meta-analysis ( $n = 22$ ; Figure 2). Compared with normal weight, overweight and obesity conferred increased odds of periodontal disease, with an odds ratio (OR) of 1.30 [95% CI, 1.25–1.35].

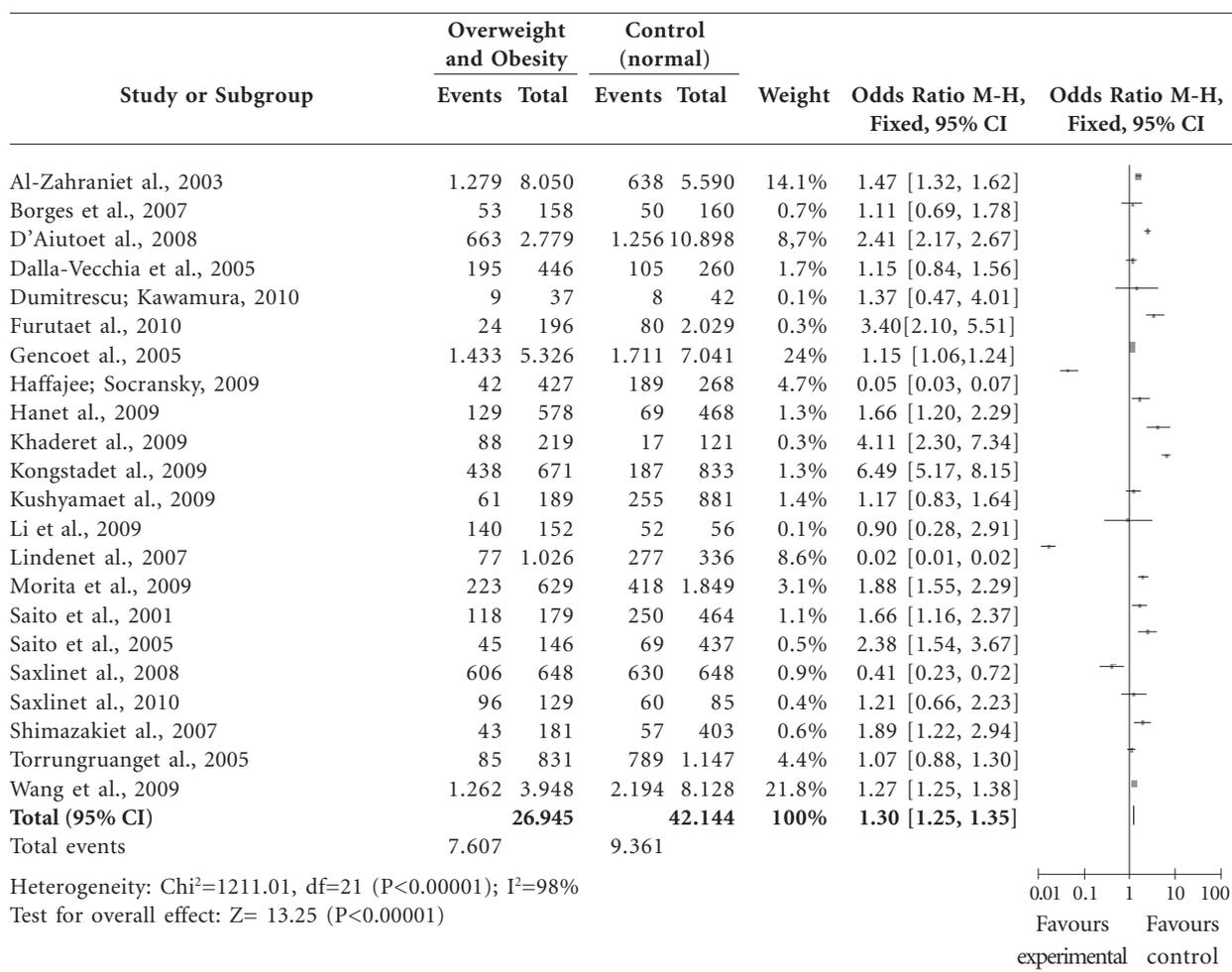
Studies with data of the BMI mean, standard deviation and number of participants in experimental (with periodontal disease) and control groups (periodontally healthy) were included in continuous meta-analysis ( $n = 13$ ; Figure 3).

Meta-analysis showed a significant difference of  $2.74 \text{ kg/m}^2$  [95% CI, 2.70 - 2.79] on BMI mean. Compared with the control group (without disease), the experimental group presenting greater BMI.

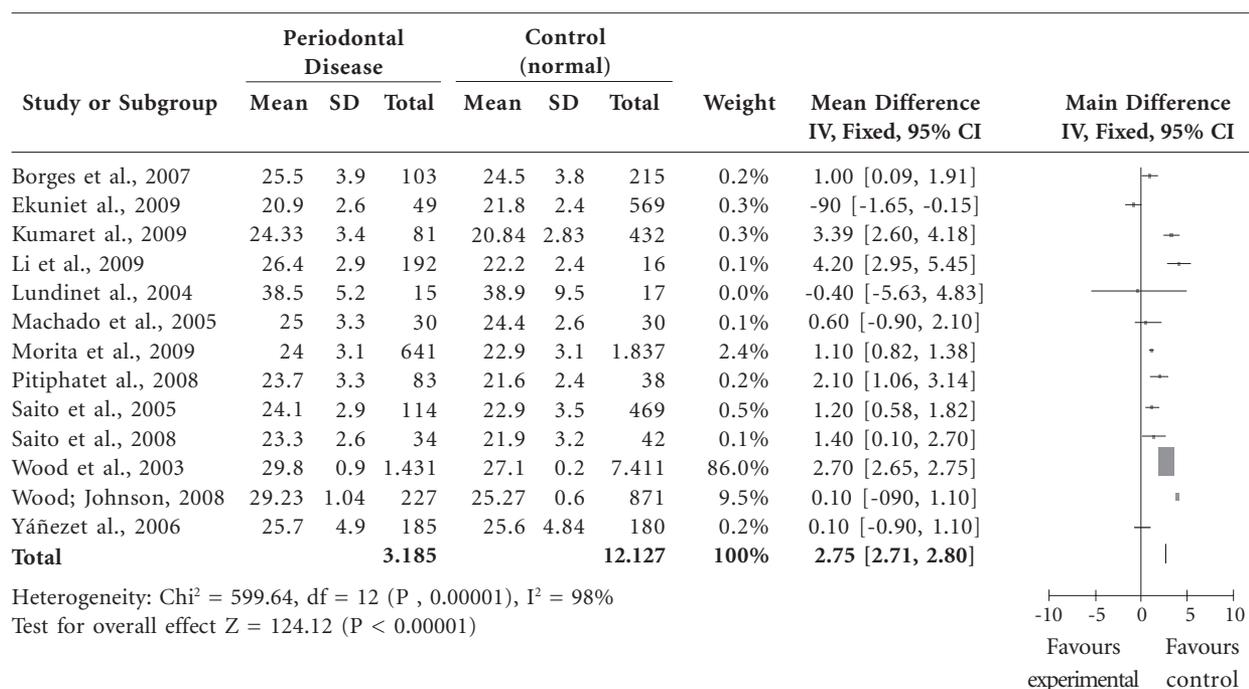
## Discussion

This systematic review was performed to contribute to higher scientific evidence about the association between periodontitis and obesity, and a statistical method (meta-analysis) was incorporated to strengthen the findings.

The weight of the studies took into account mainly the sample size in meta-analysis. Studies with a larger sample, therefore relevant weights, showed an odds ratio of 1.15 or more of disease



**Figure 2.** Subgroup analysis of studies included in meta-analysis. The study results contributing to the meta-analysis were divided into groups (normal weight and overweight/obesity) and fixed-effects ORs were calculated accordingly.



**Figure 3.** Meta-analysis forest plot. Sizes of the boxes are proportional to the weight assigned to each result in calculating of the presence or absence of periodontitis.

occurs among obese, or that individuals with periodontitis presented a difference of 2.70 to 3.96  $\text{Kg/m}^2$  over in BMI compared to periodontally healthy individuals. It points to an association between obesity and periodontitis. The odds of periodontitis in overweight/obesity group was significant statistically. Of the 31 studies, more than 50% ( $n = 17$ ) observed association between overweight or obesity with periodontitis and the other half considered this association equivocal ( $n = 6$ ) or unclear ( $n = 8$ ), because found that body weight weakly predicts the development of periodontal infection, so the evidence for an association between obesity and periodontitis may be insufficient. However, the meta-analysis also showed that mean BMI was lower in the periodontally healthy group. Of the 13 studies that presented data for this analysis, only 4 did not showed great differences in mean BMI between the groups. Therefore, the association between obesity and periodontitis became true again.

Some recent cross-sectional studies have suggested an association between body weight and periodontal disease in young subjects<sup>23,26,44</sup>, however no association was detected in the study of Lundin et al.<sup>29</sup>. Regarding to older subjects, no association was observed in this age group in numerous studies<sup>17,20,27,28,39</sup>, suggesting that other

systemic factors, not the obesity, related to age may contribute to periodontitis, factors that possibly have not been present in elderly Japanese women because in the studies of Saito<sup>35</sup> and Saito et al.<sup>34</sup> reported an association of BMI with periodontal disease.

These conflicting findings occurred probably due the methodological heterogeneity among the studies. In the meta-analysis it was high ( $I^2 = 98\%$ ). Although we have been chosen studies with similar methodologies in obesity and periodontal evaluations, they differ in some aspects, such as sample size, confounder variables control, age range and preliminary calibration, characterizing low homogeneity among them. Some factors determine the quality of the studies, such as sampling calculation, calibration of examiners and adjustment for potential confounders<sup>45</sup>.

It may be noted that only 2 studies performed the sample calculation<sup>22,26</sup> and other 5 studies obtained their sample from a National Survey, which usually is performed the sample calculations, moreover, because it is nationwide study, the sample size is large which makes the data more reliable and relevant. If we analyze just these 7 studies, considering them of better quality, we can confirm that this association is true be-

cause five studies observed association between obesity and periodontitis and only 2 observed a trend of association<sup>21,46</sup>.

The calibration of examiners is important to standardize the periodontal assessment and to obtain reliable results. Despite this, clinical calibration was not performed in 13 papers. Of the 18 studies that performed the calibration, 10 presented the results with *kappa* value. The degree of agreement ranged from moderate to very good<sup>47</sup>. Only 2 found no link between obesity and periodontitis, which evaluated only older population<sup>39</sup> and another study the *kappa* value was 0.52<sup>17</sup>.

The most of the studies adjusted the confounding variables by multivariate statistical analysis, especially regarding to gender, age and smoking status. Few studies reported the influence of sociodemographic factors or physical activity and few bothered to consider the presence of diabetes in the exclusion criteria and the diabetes often coexists with obesity and periodontal infection<sup>48</sup>, but the most excluded the individual that had not received systemic treatment with antibiotics.

Confounding control is of increasing importance as periodontal research addresses the associations between periodontal disease and systemic diseases. This is especially pertinent when dealing with smoking that is a major risk factor for both periodontal disease and systemic diseases<sup>49</sup>. The association between high body weight and periodontitis could be due to common lifestyle characteristics that make subjects more prone to both obesity and periodontitis<sup>46</sup>, for example, an unhealthy dietary patterns with insufficient micronutrients and excess sugar and fat content could thus pose a risk both diseases<sup>19</sup>. As well as obesity can be an indirect predictor of periodontitis because insulin resistance<sup>7</sup> and low social class<sup>43</sup> appeared to mediate this relationship.

All these studies about the link between obesity and periodontitis were cross-sectional or case-control, so prospective studies are needed because it is still unclear how obesity may have an adverse effect on the periodontium. One of the possible mechanisms that explains an association between obesity and periodontitis may include hepatic disorders<sup>50</sup> the fact of the adipose tissue secrete proinflammatory cytokines which may be the molecules linking the pathogenesis of these diseases<sup>7</sup>. The association between BMI and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) in gingival crevicular fluid<sup>29</sup> suggests that TNF- $\alpha$  in this fluid is derived from adipose tissue in obese subjects<sup>51</sup>. In addition, an increase in serum level of interleukin 6 and resistin, both secreted by adipocytes,

has been proposed to be associated with periodontitis<sup>15,35</sup>. Furthermore, Haffajee and Socransky<sup>25</sup> observed an overgrowth of *Tannerella forsythia* in the subgingival biofilms of periodontally healthy obese individuals, that might put them at risk for initiation of periodontitis. It suggests a possible relationship between obesity and periodontitis.

The results of the present systematic review provide evidence that there is an association between overweight/obesity and periodontal infection, nonetheless the strength of the association may be underestimated due the heterogeneity of the studies. Thus, all health professionals, including the dental team, can provide to education, prevention and treatment for obese patients about the risk of periodontal diseases.

## Conclusion

There is a link between obesity and periodontitis, however the risk factors that aggravate these diseases should be clarified to elucidate the direction of this association. Nevertheless, oral health care measures should be implemented to obese patients. Working with paired samples and avoid confounding factors may contribute to the homogeneity of the studies. These suggestions can improve the scientific evidence that might address these concerns.

## Collaborations

PG Moura-Grec was involved in the original conception of the research, carrying out the study (data search, paper selection, extraction of information and meta-analysis) and writing of the manuscript. JA Marsicano contributed at the extraction of information from studies. CAP Carvalho contributed at the evaluation of the articles for eligibility and reviewed the manuscript. SHC Sales-Peres was involved in the original conception of the research, contributed at the extraction information from studies, and reviewed the final version of the manuscript.

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