Is weight gain associated with the incidence of periodontitis? A systematic review and meta-analysis


Abstract
Aim: This study aimed to conduct a systematic review assessing the effects of weight gain on the incidence of periodontitis in adults.

Methods: Electronic searches in four databases were performed up to and including February 2015. Only prospective longitudinal studies assessing the association between weight gain and the incidence of periodontitis in adults were eligible to be included in this study. All studies should state a clear description of nutritional status (Body Mass Index; Waist Circumference) as well as the case definition of periodontitis. Pooled relative risks (RR) for becoming overweight and obese on the incidence of periodontitis were estimated by meta-analysis. Quality was assessed with the Newcastle–Ottawa scale for cohort studies.

Results: Five articles were included in this review and meta-analysis with 42,198 subjects enrolled. Subjects who became overweight and obese presented higher risk to develop new cases of periodontitis (RR 1.13; 95%CI 1.06–1.20 and RR 1.33 95%CI 1.21–1.47 respectively) compared with counterparts who stayed in normal weight.

Conclusions: A clear positive association between weight gain and new cases of periodontitis was found. However, these results are originated from limited evidence. Thus, more studies with longitudinal prospective design are needed.

Body weight tends to remain stable in most adult individuals for long periods of time (Jequier & Tappy 1999). In this context, it is possible to assume that regulatory processes coordinate the dietary fuel supply with energy requirements with the intention of maintaining a stable body mass and adipose reservoir (Schwartz et al. 1999). However, when an unbalance between caloric intake and energy expenditure occurs, the body may excessively accumulate fat leading to overweight and further to obesity (Martinez et al. 1999). According to the World Health Organization recommendation, subjects whose Body Mass Index (BMI) is between 25 and 29.9 are considered overweight, whereas those whose BMI is equal or greater than 30 are considered obese (WHO 2000).

Obesity can be defined as a systemic disease characterized by excessive body fat accumulation that can lead to adverse impacts on health conditions (Kopelman 2000, WHO 2000). Its prevalence has risen not only in high-income but also in medium- and low-income countries, con-
suming large amounts of health care resources (WHO 2000, Specchia et al. 2014). Several reports have demonstrated the adverse effects of obesity on chronic health outcomes, such as diabetes, cardiovascular disease, infectious diseases and cancer (Falagas & Kompoti 2006, Kahn et al. 2006, Van Gaal et al. 2006, Friedman 2009).

Amongst the most prevalent chronic diseases, periodontitis is a destructive condition affecting the supporting structures of the teeth, which develops through an inflammatory process mainly induced by the presence of a microbial biofilm (Van Dyke & van Winkelhoff 2013). It is beyond dispute that besides the role played by periodontopathogens, the quality of the host immune response is also responsible for the transition from health to disease (Cekici et al. 2014). The interplay between immune system and periodontal bacteria challenge determines not only the establishment but also the severity of disease progression (Cekici et al. 2014). As periodontitis presents itself in cycles of progression and latency, when an unbalance in this interplay occurs, it is expected a greater susceptibility for active destruction. This, in turn, is affected by other systemic risk factors (Montero et al. 2011).

Previous reports have demonstrated a positive association between fat accumulation and periodontitis (Al-Zahrani et al. 2003, Han et al. 2010). Different mechanisms have been proposed to explain this possible association. Essentially, macrophage infiltration driven by cell apoptosis at the core of the excessive adipose tissue may induce a generalized chronic low-grade inflammation, with those becoming obese and overweight being more susceptible to infectious diseases than their counterparts who are normal weight (Falagas & Kompoti 2006). Considering the infectious nature of periodontitis, it is expected that a similar relationship between obesity and periodontitis may exist, such as found between obesity and other infectious diseases, like respiratory and skin infections (Falagas & Kompoti 2006).

Systematic reviews exploring the association between obesity/overweight and periodontitis have corroborated the positive association between those conditions (Chaffee & Weston 2010, Suvan et al. 2011, Moura-Grec et al. 2014). Nevertheless, even with those reviews the effects of changes in the nutritional status, especially weight gain, on periodontal disease are not evident, leaving a gap in the literature. Furthermore, no information about development of new cases of periodontitis is addressed in those reports, thus, the role of weight gain in the establishment of periodontal disease is not clear. Studying incidence cases is a more appropriate approach to estimate such an association, as prevalence cases could underestimate the magnitude of this association, and result in biased causal effects in variables that change with time (Heaton et al. 2014).

We previously hypothesized that individuals experiencing more weight gain will present with higher risk of developing periodontitis, than those with less or without weight gain on the basis of the evidence from cross-sectional studies reporting relationship between nutritional status and periodontitis and the occurrence of cumulative inflammatory condition caused by fat accumulation (Nascimento et al. 2014). However, the cross-sectional studies suffer with issues of temporality while longitudinal studies are able to address this. Considering the limitations of cross-sectional studies and the lack of conclusive evidence from longitudinal studies on this relationship, this study conducted a systematic review of prospective longitudinal studies assessing the effects of weight gain, with individuals becoming overweight or obese, on the incidence of periodontitis in adults.

Methods

Review questions

1. Is weight gain leading to overweight associated with the incidence of periodontitis in adults?
2. Is weight gain leading to obesity associated with the incidence of periodontitis in adults?

Inclusion and exclusion criteria

Original prospective observational studies which assessed the association between weight gain and incidence of periodontitis in adults aged 18 or older were included in this systematic review. At least two time points for both exposure and outcome were required to fulfill the inclusion criteria. All studies should state a clear description of nutritional status, such as Body Mass Index, Waist Circumference, as well as the case definition for periodontitis. In each study, the case definition for periodontitis determined by the authors was respected. Case-control, cross-sectional studies, longitudinal retrospective studies, animal studies, in-vitro studies, letters to the editor and reviews were excluded.

Search strategy

An electronic search was conducted without initial date restriction up to and including February 2015 in PubMed via Medline, Embase, Web of Knowledge and Scopus to identify studies that prospectively analysed the effect of weight gain during time on the incidence of periodontitis in adults after follow-up. An initial search was conducted on PubMed with the following MeSH and free terms: “(‘Periodontal diseases’ [Mesh] OR ‘Periodontitis’ [Mesh]) AND ‘Chronic Periodontitis’ [Mesh]) OR ‘Obesity’[Mesh] OR ‘Over-weight’[Mesh] OR ‘Obesity, Abdominal’[Mesh] OR ‘Body Fat Distribution’[Mesh] OR ‘Abdominal Fat’[Mesh] OR ‘Intra-Abdominal Fat’[Mesh] OR ‘Waist Circumfererce’[Mesh]) OR ‘Waist-Hip Ratio’[Mesh]) OR ‘Body Mass Index’[Mesh] OR ‘Weight Gain’ [all] OR ‘Weight Changes’ [all] OR ‘Nutritional Status’ [all] OR ‘Body composition’ [all]). The search was conducted in a second time with the inclusion of specific filters for prospective studies in the search strategy. Strategies used for specific databases are detailed in the Appendix S1. No language restrictions were applied in any search.

All references were managed in the software EndNote X7 (Thomson Reuters, New York, NY, USA). Duplicate references were excluded. Titles, abstracts and key words were screened based on the inclusion and exclusion criteria by two reviewers independently (GGN and FRML). Lists were
compared and in case of disagreement, a consensus was reached by discussion. Assessment of the full articles identified in the initial screening was performed by the same two reviewers. In addition to the electronic search, a hand search was performed in the reference list of all included studies by the same reviewers. Predefined data collection worksheets were employed for the assessment of each selected publication. This systematic review followed the PRISMA statements (Moher et al. 2009).

**Data extraction and quality assessment**

After the first screening, the following data were sought from articles with potential to be included in the review: author’s name, country where the study was conducted, sample size and its main characteristics, subjects enrolment, follow-up period, classification criteria for periodontitis, clinical examination data collected, parameters to determine the incidence of periodontitis, definition and assessment of nutritional status, and presence and type of adjustment.

In addition, to conduct meta-analysis, effect measures (Relative Risk – RR) with respective 95% Confidence Intervals (95%CI) were also recorded. Authors were contacted to clarify any queries on the study methodology or result. Data were extracted by the same two reviewers. Cases of disagreement were discussed until a consensus was reached.

The specific version of the Newcastle–Ottawa scale for cohort studies was used to assess the quality of included studies (Wells et al. 2001). The scale comprises eight items distributed in three dimensions: (a) selection of study groups; (b) comparability of study groups; (c) assessment of outcome and adequacy of follow-up (Appendix S2). Each item scored 1 point, except for one (Comparability dimension) that could score at most 2 points. Thus, total score could range from 0 to 9 points. Studies with 7–9 points (approximately 80% or more of the domains satisfactorily fulfilled) were arbitrarily considered to be of high quality, whereas studies with 5–6 points were classified as moderate quality and studies with less than 5 points were of low-methodological quality (Zangrando et al. 2015). Finally, the overall quality of evidence was estimated according to the GRADE guideline (Guyatt et al. 2008). Papers were evaluated by the same two referees independently and disagreements were decided by consensus after discussion.

**Statistical analysis**

Two different meta-analyses were conducted considering the review questions: (1) association between becoming overweight and the incidence of periodontitis; (2) association between becoming obese and the incidence of periodontitis. Only adjusted results were included in the analysis, once two reports did not present the crude effect size. For each model, a combined relative risk effect was obtained with fixed- and random-effect models. If heterogeneity was present ($p < 0.05$) the random-effect model was employed (DerSimonian & Laird 1986). One study presented missing data; however, after contacting authors, values to be included in the meta-analysis were provided. As the effect measure presented by the authors was odds ratio, a conversion into relative risk was needed. For this, data were converted according to the formula proposed by Zhang and Yu:

$$RR = \frac{odds\ ratio}{1 - risk_0 + risk_0 \times odds\ ratio}$$

where, $risk_0$ is the risk of having a positive outcome in the control or unexposed group (Zhang & Yu 1998). As different relative risk measures were used, a sensitivity analysis was performed to verify the influence of these results in the pooled effect for both exposures. All analyses were conducted using Stata 12.0 software (StataCorp., College Station, TX, USA).

**Results**

Electronic database search revealed 1,398 articles. From those, 471 were duplicated and subsequently removed. A total of 927 articles were included for title and abstract evaluation. Figure 1 displays the flow chart of studies selection. From those, 12 articles were included for full text review. Further seven of those 12 were excluded after full text appraisal conducted independently by two reviewers. Table 1 presents main reasons for exclusions of those seven papers.

Therefore, five studies fulfilled the criteria to be included in this review and meta-analysis. The study of Morita et al. (2011) was included twice in the analyses, as it presented results stratified by gender. Table 2 displays the main findings of included studies. The samples enrolled in the studies that fulfilled all inclusion criteria totalled 42,198 study participants. According to the Newcastle–Ottawa scale included studies scored as follows: 6 (Ekuni et al. 2014) indicating a moderate methodological quality; 7 (Morita et al. 2011, Jimenez et al. 2012); 8 (Saxlin et al. 2010); and 9 (Gorman et al. 2012b), indicating high methodological quality (Fig. 2). The overall quality of evidence applying the GRADE approach was moderate for both meta-analyses (Table S1).

All studies were conducted in high-income countries, with one in Finland (Saxlin et al. 2010), two in Japan (Morita et al. 2011, Ekuni et al. 2014) and two in the United States of America (Gorman et al. 2012b, Jimenez et al. 2012). One study used self-reported data for periodontal disease (Jimenez et al. 2012), whereas the others used clinical measures: probing depth (Saxlin et al. 2010, Morita et al. 2011, Gorman et al. 2012b, Ekuni et al. 2014), clinical attachment loss and alveolar bone loss (Gorman et al. 2012b) and Community Periodontal Index (Ekuni et al. 2014). For nutritional status assessment, the Body Mass Index was used in all articles, however, one used the self-reported measure (Jimenez et al. 2012). All studies also presented adjusted results for sociodemographic, behavioural and oral health variables.

**Results**

Meta-analysis considering the effects of weight gain on the incidence of periodontitis showed that subjects who became overweight had greater risk to develop new cases of periodontitis (RR 1.13; 95% CI 1.06–1.20) (Fig. 3) as well as those who became obese (RR 1.33 95% CI 1.21–1.47) compared with counterparts who stayed normal weight for the same period (Fig. 4). In both
analyses, heterogeneity was not significant \((p > 0.05)\); therefore the fixed-effect model was employed. The omission of any study would not modify the association for both exposures as indicated by Figs 5 and 6.

## Discussion

The present findings demonstrated that individuals who became overweight or obese presented higher risk to develop new cases of periodontitis than those who stayed normal weight in the same period. These findings support our previous hypothesis that fat accumulation could play a role in the development of periodontal disease and obesity has been demonstrated across many reports (Al-Zahrani et al. 2003, Dalla Vecchia et al. 2005, Kongstad et al. 2009, Han et al. 2010). Most of them used a cross-sectional design, which prevented establishing temporal relationships between the presumed exposures and outcome. As a consequence, the actual association between those conditions remains unclear. Prospective longitudinal studies are reliable sources of evidence, with temporal inferences able to be determined (de Castilhos et al. 2012). Hence, to the best of authors’ knowledge, this is the first systematic review with meta-analysis analysing only prospective longitudinal studies exploring the association between weight gain and its effects on the incidence of periodontitis.

Given the results, some mechanisms linking weight gain with periodontitis could be addressed. First, the white adipose tissue works as an endocrine organ, responsible for secreting different types of specific cytokines: adipocytokines, such as resistin, leptin and adiponectin; as well as non-specific cytokines such as interleukins and tumour necrosis factors (Kershaw & Flier 2004, Tilg & Moschen 2006). Furthermore, as adipose tissue volume expands during weight gain some adipocytes could initiate apoptosis due to hypoxia, caused mainly by the constraint of blood vessels responsible for cellular nutrition (Neels & Olefsky 2006). This situation also leads to recruitment of macrophages especially around dead adipocytes, exacerbating the inflammatory framework in an upregulation feedback (Neels & Olefsky 2006). The combination of these situations promotes a chronic generalized low-grade inflammation that alters the host immune innate response threshold making obese and overweight subjects more susceptible to infectious diseases than normal weight ones (Falagas & Kompoti 2006, Morgan et al. 2010). In addition, it is suggested that lipopolysaccharide (LPS) of gram-negative periodontal bacteria could lead to hepatic dyslipidaemia and insulin resistance (Pischon et al. 2007). As the inflammation framework seems to be exacerbated by the increase in fat accumulation, it is expected that subjects with higher fat accumulation would present worse prognosis facing an infectious challenge, such as periodontitis, compared to those less obese, corroborating our findings.

Evidence suggests that other mechanisms rather than the biologic might play a role in this association. Given that both conditions, obesity/overweight and periodontitis, are chronic diseases, it is expected that they share common risk factors, such as low socioeconomic position (Thomson et al. 2012, Adair et al. 2013). As subjects from a disadvantaged background present higher prevalence rates of obesity and overweight (Adair et al. 2013) and periodontitis, a consistent social pattern is observed. Thomson and colleagues (Thomson et al. 2012) also stated that at least part of the socioeco-
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<th>Study and country</th>
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<th>Definition of Periodontal Disease</th>
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<td>Saxlin et al. (2010), Finland</td>
<td>396 dentate, healthy subjects (non-diabetics and non-smokers) aged 30–60-yo enrolled in the Health 2000 Survey</td>
<td>4 years later</td>
<td>Probing Depth: Healthy &lt;4 mm; PD ≥4 mm</td>
<td>Full-mouth examination; 4 sites per tooth. Five dentists at baseline and one at follow-up</td>
<td>Number of teeth with new &gt;4 mm deepened pockets at follow-up; change in periodontal pocket (no change, increase or decrease)</td>
<td>BMI was classified as follow: eutrophic &lt;25, overweight ≥25 to ≤30; obese &gt;30</td>
<td>Subjects who were PD healthy at baseline, obesity (IRR 1.3; 0.7–2.1) and overweight (IRR 1.2; 0.7–1.8) had no effect on incidence of PD after adjustment; Among subjects who presented PD at baseline, obesity (IRR 1.1; 0.8–1.7) and overweight (IRR 1.0; 0.7–1.4) had no effect on the incidence of PD after adjustment, as well as, in the change in periodontal pockets’ depth.</td>
<td>Results adjusted for gender, age (continuous variable), education, presence of dental plaque, dental attendance pattern, toothbrushing frequency, periodontal treatment and number of teeth.</td>
<td>Data regarding only Probing on depth, without any reference to BoP or CAL.</td>
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Table 2. (continued)

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<td>Morita et al. (2011), Japan</td>
<td>3590 (2787 men and 803 women) employed subjects aged 21–69-yo that attended annual statutory health checkups. Only subjects periodontally health at baseline were enrolled in the study.</td>
<td>Assessment of obesity and PD at baseline and 5 years later</td>
<td>Probing Depth: Health &lt;4 mm; PD ≥4 mm</td>
<td>Partial-mouth examination: 10 teeth from 6 sextants; the highest score of the 6 dental sextants was used as the patient’s periodontal disease score</td>
<td>Number of new teeth with PD ≥ 4 mm.</td>
<td>BMI was classified as follow: &lt;22; 22–24.9, 25–29.9, and ≥30</td>
<td>Analyses stratified by gender. In men: incidence of PD was associated with BMI 25–30 after adjustments (HR 1.30; 1.11–1.53); in women: incidence of PD was associated with BMI 25–30 (HR 1.70; 1.15–2.55) and ≥30 (HR 3.24; 1.32–7.94) after adjustments</td>
<td>Results adjusted for age, smoking status, and clinical history of diabetes mellitus</td>
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<td>Gorman et al. (2012b), United States of America</td>
<td>1038 medically healthy, non-Hispanic, white males enrolled in the VA Dental Longitudinal Study since 1969</td>
<td>Baseline assessment of obesity and PD between 1969–1972. (Data regarding CAL were collected only in 1981–1985 assessment). Dental examinations occurred every 3 years.</td>
<td>Alveolar Bone Loss (ABL) ≥40% or PD or CAL ≥5 mm</td>
<td>Full-mouth examination; 6 sites per tooth. ABL: radiographic distance between CEJ and root apex</td>
<td>Two or more teeth advance to PD definition. Lost teeth were considered if tooth presented ABL=20%, &gt;3 CAL/PD &lt;5 at all prior examination</td>
<td>BMI was classified as follow: eutrophic: &lt;25, overweight ≥25 to ≤30; obese &gt;30, WC was classified as follow: ≤102; &gt;102, Waist-height ratio: ≤50%; &gt;50%</td>
<td>After adjustment, obesity (BMI &gt;30) was associated with incidence of PD ≥ 5 (HR 1.40; 1.02–1.91); CAL ≥ 5 (1.52; 1.05–2.21) and ABL ≥ 40% (1.60; 1.07–2.38). High WHtR (≥50%) was associated with incidence CAL ≥ 5 (HR 1.41; 1.01–1.97)</td>
<td>All models adjusted for age, cigarette use, education beyond high school, number of decayed or filled surfaces, treatment for periodontal disease in past year, prophylaxis in past year, and diabetes diagnosis</td>
<td>Sample size composed only by men. No information about date when last assessment was conducted</td>
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<td>Jimenez et al. (2012), United States of America</td>
<td>36,910 healthy male participants of the Health Professionals Follow-Up Study (HPFS) who were free of periodontal disease at baseline</td>
<td>Baseline: 1986; Last assessment: 2006</td>
<td>Self-reported PD: “Have you been professionally diagnosed with periodontal disease with bone loss?”</td>
<td>–</td>
<td>New cases of self-reported PD</td>
<td>Self-reported weight, height, WC and WHR: BMI was classified as follow: eutrophic &lt;25, overweight ≥25 to ≤30; obese &gt;30, WC &gt;40 and WHR &gt;0.95 were considered elevated</td>
<td>After adjustments, overweight (HR 1.09; 1.01–1.17) and obese (1.30; 1.16–1.45) presented higher incidence of PD. WC was not associated with incidence of PD after adjustments. WHR ≥ 0.99 was associated with incidence of PD (HR 1.24; 1.07–1.43).</td>
<td>BMI: Adjusted for age, smoking, race, physical activity, fruit and vegetable intake, alcohol consumption, dental profession, and diabetes status at baseline and number of teeth. WC and WHR: Adjusted for age, smoking, race, physical activity, fruit and vegetable intake, alcohol consumption, dental profession, and diabetes status</td>
<td>Self-reported measures; sample composed only by workers</td>
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<td>Ekuni et al. (2014), Japan</td>
<td>224 university students healthy (non-diabetics and non-smokers)</td>
<td>Baseline: 2009; last assessment: 2012</td>
<td>Probing Depth: Healthy ≤4 mm; PD ≥4 mm</td>
<td>10 indices teeth; 6 sites per tooth</td>
<td>Number of new teeth with PD ≥ 4 mm</td>
<td>BMI was classified as follow: eutrophic &lt;25, overweight ≥25 to ≤30; obese &gt;30</td>
<td>After adjustment, neither overweight (OR 0.52; 0.05–5.10) nor obese (OR 4.48; 0.44–27.67) presented higher incidence of PD</td>
<td>BMI: Adjusted by: Gender, age and oral health behaviours at baseline, and changes in BMI (increase and decrease)</td>
<td>Data provided by the author after contact. Data converted in RR measures as described in the Methods section</td>
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ABL, alveolar bone loss; BMI, Body Mass Index; BoP, bleeding on probing; PD, pocket depth; CAL, clinical attachment loss; HRR, hazard risk ratio; IRR, incidence risk ratio; OR, odds ratio; WC, waist circumference; WHtR, waist-height ratio; WHR, waist-hip ratio.
ymi variation in periodontitis could be influenced by this association. This relationship, however, seems to vary during the life-course, once prevalence rates of obesity increase since early life, whereas an unfavourable periodontal status is more evident in adulthood. The differences in effects of socioeconomic positions on this association between the high and lower – middle income countries could not be highlighted as all the selected studies were from higher income countries. Furthermore, considering that it is quite evident that the patterns of inequalities are different between these two distinct groups of countries, the effects may vary significantly (Lima-Costa et al. 2012).

Some methodological details should be addressed. Morita et al. (2011) used a different cut-off point of BMI to assess overweight and obesity, modified according to their sample. In the study of Gorman et al. (2012b) just data regarding probing depth were used. Even with the limitations of this measure, it was also used for three studies included in this analysis. All studies considered incidence as the development of disease in sites/teeth that were free of disease at baseline. In three of them (Saxlin et al. 2010, Morita et al. 2011, Jimenez et al. 2012), only periodontally health subjects were included at baseline, whereas in the remaining, subjects with periodontitis at baseline were enrolled; in those, incidence was considered the increment of cases from baseline assessment. The small number of studies that fulfilled the inclusion criteria precluded the statistical and the visual assessments for publication bias. The Egger’s test has several limitations when the number of included studies is lower than 20 (Egger & Smith 1998); and the interpretation of a funnel-plot with a small number of studies could misrepresent the actual findings.

Our results however should be considered in the context of some limitations. First, only a few number of studies fulfilled the inclusion criteria defined for this review, and almost all of them presented positive results. Thus, it is not possible to define if longitudinal prospective studies exploring this association have not been conducted, or if studies with negative results have not been published. Second, it was just possible to perform pooled analyses with data regarding probing depth. Even though it is a useful measure to detect periodontal disease, the clinical attachment loss should be preferred, as it is more reliable measure to diagnosis disease. Third, one included study (Jimenez et al. 2012) presented...
only self-reported data for nutritional status so as for periodontal disease with possible recall bias. Even with previous reports validating the self-reported nutritional status (Rimm et al. 1990) and periodontitis (Joshi-pura et al. 2002) used by the authors, it is unclear the impact of such measures on the association between both conditions. This fact impacted negatively on the overall quality of the evidence estimated with the GRADE approach. Fourth, one study (Ekuni et al. 2014) evaluated periodontitis using the Community Periodontal Index, which could have misrepresented the incidence of periodontitis. However, after contacting the authors, data regarding probing depth were provided, which allowed us to include this study in the analyses. Last, the young age of participants enrolled in the study of Ekuni et al. (2014) and the considerable short follow-up period of the studies could have underestimated the magnitude of such association, as many cases of periodontitis could have taken longer period until a clinical sign was observed. Also, in a young population, the incidence of periodontitis is low due to the chronicity of this disease.

Regardless of the limitations, it is worth pointing out some strengths of our review. Initially, as only prospective studies were included, the temporal effects of weight gain on the incidence of periodontitis could be observed. As aforementioned, to the best of authors’ knowledge, no previous systematic review explored this topic previously, supporting in a very explicit way the actual impact of weight gain on the incidence of periodontal disease. The pooled estimates obtained with the meta-analyses showed a positive association between weight gain and periodontitis development, corroborating the findings of almost all the included studies. Even though some studies did not present a statistically significant association in their individual results, the positive association was achieved in the meta-analyses due to the increased sample size. Second, the use of incident cases as outcomes rather than prevalent ones should also be highlighted, as use of the latter could underestimate the actual association (Heaton et al. 2014). Third, the meta-analyses conducted presented pooled results from high-quality articles totalling more than 40,000 people enrolled. These facts could counterbalance the low number of studies included in the review providing a strong evidence of this association, not only due to the number of subjects but also to the quality of results. Even though the study of Ekuni et al. (2014) was classified as moderate risk of bias, this study presented low weight in the analyses (0.28% in the overweight model and 0.08% in the obesity model), not influencing our results as demonstrated by the sensitivity analyses. Fourth, all combined results were originated from adjusted analyses. These results were controlled by potential confounders and mediators of the relationship between weight gain and periodonti-

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tis, such as diabetes and smoking. It may reduce the likelihood of bias providing more solid findings. However, confounders such as medication intake and other systemic diseases should be considered in future cohort studies, since it remains unclear the role played by those in the relationship between weight gain and periodontitis. Finally, the sensitivity analysis estimated the effect of omitting each study in the combined result, supporting the relevance of our findings. This analysis justifies our methodological option to pool studies with distinct relative risk measures as well as to include the study with self-reported data.

The results of our systematic review and meta-analyses clearly demonstrated the effects of weight gain on the incidence of periodontal disease. However, this evidence is originated from limited studies identified after extensive and careful searches. Our findings also suggest that further studies with prospective design exploring this association are needed with further follow-up periods not only in high-income countries, but especially in those low- and middle-income, where the prevalence of obesity and periodontitis is greater. As those conditions share key risk factors, their prevention should be based on a common risk factor approach (Sheiham & Watt 2000), which seems to be more rational than focusing on only one specific condition. Also, clinicians should be aware of the role played by weight gain on the development of new cases of periodontitis, as it seems to be a risk factor for the establishment of such condition.

Acknowledgements
The authors are grateful to the Coordination for the Improvement of Higher Education Personnel (CAPES) for the scholarship provided to GGN (#BEX 13810/13-8) and to the National Counsel of Technological and Scientific Development (CNPq) for the scholarship provided to FRML (#BEX 229279/2013-9).

References

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Principal findings: A relationship between weight gain and incidence of periodontal disease was demonstrated. Thus, subjects who became obese and overweight presented higher risk than those who were normal weight to develop periodontitis. In addition, those who became obese were at higher risk of having periodontitis than overweight subjects.

Practical implications: Clinicians should be aware of the role played by weight gain on the development of periodontitis.