

Periodontal status in cannabis smokers. A systematic review

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Abstract

Aim: To assess the periodontal status in cannabis smokers in comparison with non-cannabis smokers

Methods: Electronic databases were searched as well as hand searches performed. Eligible studies followed the Population Exposure Comparison Outcome Study (PECOS) structure: P: dentate humans, E: cannabis smoking, C: non-cannabis smoking, O: Primary outcomes: periodontitis case definition, clinical attachment loss, probing depth; Secondary outcomes: bleeding on probing/ gingival inflammation, plaque index and calculus; S: observational studies. Qualitative analyses of the studies was done. Quality of cohort studies was assessed with the Newcastle-Ottawa scale and cross-sectional studies were assessed using a modified Newcastle-Ottawa scale.

Results: 2661 records were screened, of which 14 articles were included. Data from a cohort study showed that highly exposed participants were at higher risk of clinical attachment loss progression. Six cross-sectional studies reported worse gingival or periodontal conditions in cannabis smokers. Nevertheless, one did not find such association, neither did three case series. Three studies were of high, two of moderate and six were of low quality.

Conclusion: Based on the available data, frequent cannabis smoking could be detrimental for periodontal tissues and this could be dose-dependent. Studies including long-term cannabis smokers, and stratified for Periodontal Diseases' etiologic factors and risk factors/indicators are needed.

Keywords: *Cannabis, periodontal diseases, epidemiology, substance abuse*

Introduction

One of the most consumed recreational drugs is cannabis (European Monitoring Centre for Drugs and Drug Addiction, 2018) with 183 million consumers in 2014–2015; additionally, this was the most seized drug in that period of time. Monitoring the repercussions of new policies related to cannabis provides an important knowledge flow to the international community (Oficina de las Naciones Unidas contra la Droga y el Delito, 2017).

Recreational cannabis is commonly consumed by smoking. Cannabis products may be consumed to prevent and control a number of medical conditions (Russo, 2011; Burstein, 2015). The number of countries/states legalizing recreational use of cannabis is on the rise, though little is known of any possible harm to periodontal tissues (Mofidi *et al.*, 2019).

Plaque induced gingivitis and periodontitis are highly prevalent diseases. Severe periodontitis is the major cause for tooth loss (Tonetti *et al.*, 2017) and affects approximately 11% of the world population (Kassebaum *et al.*, 2014). Dry mouth is one of the symptoms described after cannabis consumption (Oficina de las Naciones Unidas contra la Droga y el Delito, 2017) and has been associated with difficulties in self-control of biofilm and increased gingival inflammation (Murakami *et al.*, 2018). Given the high prevalence of periodontal diseases and the number of people smoking cannabis around the world, as well as its implications for public health, it is of importance to study any relationship between cannabis smoking and periodontal disease. Therefore, the objective of this systematic review was to assess the periodontal status in cannabis smokers in comparison with non-cannabis smokers. The focused question was: Are there differences in periodontal status of cannabis smokers as compared to individuals not exposed to cannabis?

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Methods

Eligibility criteria

Studies were eligible if they followed the inclusion criteria based on the Population Exposure Comparison Outcome Study (PECOS) structure: P: dentate humans, E: cannabis smoking, C: non-cannabis smoking, O: Primary outcomes: periodontitis case definition, clinical attachment loss, probing depth; Secondary outcomes: bleeding on probing/ gingival inflammation, plaque index and calculus; S: observational studies.

Search strategy

An electronic search was performed in MEDLINE via PubMed, Cochrane Library, SCOPUS, BVS and SciELO databases up to May 2019. In addition, Google Scholar, Science.gov, Directory of open access journals (DOAJ), University of British Columbia database, ADA center for evidence-based dentistry, Ontario Public Health Association, GreyLit and Open Grey, were consulted for grey literature. Hand searching was also performed. In an attempt to recover all available information, colloquial terms and synonyms of marijuana were used (e.g. “ganja”, “grass”, “shisha”). The full electronic search strategies applied for each database, by topic, are shown in the appendix 1.

Study selection

Two independent reviewers (SP, MM) screened the obtained titles and abstracts, looking for potential studies to be analysed as full texts.

Data extraction

Independently, the same two reviewers (SP, MM) carried out the data extraction using predetermined spreadsheets using the reference items: study design, location, characteristics of the sample, exposure, periodontal diagnosis/case definition, calibration and results.

Quality assessment of the studies

Cohort studies were evaluated with the Newcastle-Ottawa scale (Wells *et al.*, 2000) for observational studies, with a maximum of 9 stars, and cross-sectional studies were assessed using the Newcastle-Ottawa scale modified by Zhao *et al.* (2018), with a maximum of 8 stars (Zhao *et al.*, 2018). If the study obtained ≥ 7 stars was considered of high quality, 6 or 5 indicated a moderate quality and 4 or lower was associated with a low-quality study.

Disagreements between the reviewers (SP, MM) in every step mentioned before were solved by a third, more experienced, reviewer (EA). The protocol was registered in the International Prospective Register of Systematic Reviews, PROSPERO (registration number ID given is CRD42018083575).

Results

The flow diagram of the review process is shown in Figure 1. A total of 2661 articles (2653 from electronic databases and 8 manually identified) were retrieved from electronic databases and additional sources. After duplicates were removed, 2018 records (titles and abstracts) were screened, of which 1949 were excluded for not meeting the inclusion criteria. 69 full text articles were assessed for eligibility. From these, 55 were excluded for a variety of reasons (Table 1) and, finally, 14 articles were included in the quality analysis (Thomson *et al.*, 2008; Thomson *et al.*, 2013; Zeng *et al.*, 2014; Meier *et al.*, 2016; Barrios and Vila, 2009; Garay, 2009; Lopez and Baelum, 2009; Jamieson *et al.*, 2010; Reddy *et al.*, 2012; Kayal *et al.*, 2014; Verástegui and Ruiz 2016; Shariff *et al.*, 2017; Ortiz *et al.*, 2018; Núñez Cuello, 2016). From these articles, results from one cohort study performed in Dunedin, New Zealand, over the course of 38 years were published in 4 publications. (Meier *et al.*, 2016; Thomson *et al.*, 2008; Zeng *et al.*, 2014; Thomson *et al.*, 2013). The characteristics of the included studies are demonstrated in Table 2. Due to lack of homogeneity within the studies, they could not be analysed together and no meta-analysis was performed. From the selected studies, one (comprising four publications) was a prospective cohort study and ten were cross-sectional, of which four were descriptive. Studies were undertaken in Argentina, Australia, Chile, India, New Zealand, Peru (2), Puerto Rico, Saudi Arabia, Dominican Republic and the United States.

Regarding the periodontal status assessment: one study only described the gingival status using the Löe & Silness Gingival Index and the O’Leary Plaque Index (Barrios and Vila, 2009). Three studies described the presence of periodontal pocket, attachment level, gingival recession, bleeding on probing, furcation involvement, tooth mobility and oral hygiene. (Garay, 2009; Verástegui and Ruiz, 2016; Núñez Cuello, 2016) Three used the CDC-AAP definition of periodontal disease (Ortiz *et al.*, 2018; Jamieson *et al.*, 2010; Shariff *et al.*, 2017), another utilized Russell’s Periodontal Index, (Reddy *et al.*, 2012) and the other three used different thresholds for periodontal disease related to the clinical attachment loss (CAL), as one or more sites with $CAL \geq 5$ mm (categorical) and mean CAL (continue) (Meier *et al.*, 2016), $CAL \geq 3$ mm (Lopez and Baelum, 2009), and CAL 1 - 2mm (mild), 3 - 4mm (moderate) and > 5 mm (severe) (Kayal *et al.*, 2014). The latter also assessed bleeding on probing and plaque indices.

In terms of reproducibility, five studies reported having calibrated examiner(s). (Kayal *et al.*, 2014; Ortiz *et al.*, 2018; Shariff *et al.*, 2017; Lopez and Baelum, 2009; Thomson *et al.*, 2013) Exposure to cannabis was assessed in many different ways but always self-reported. No studies reported toxicological assays.

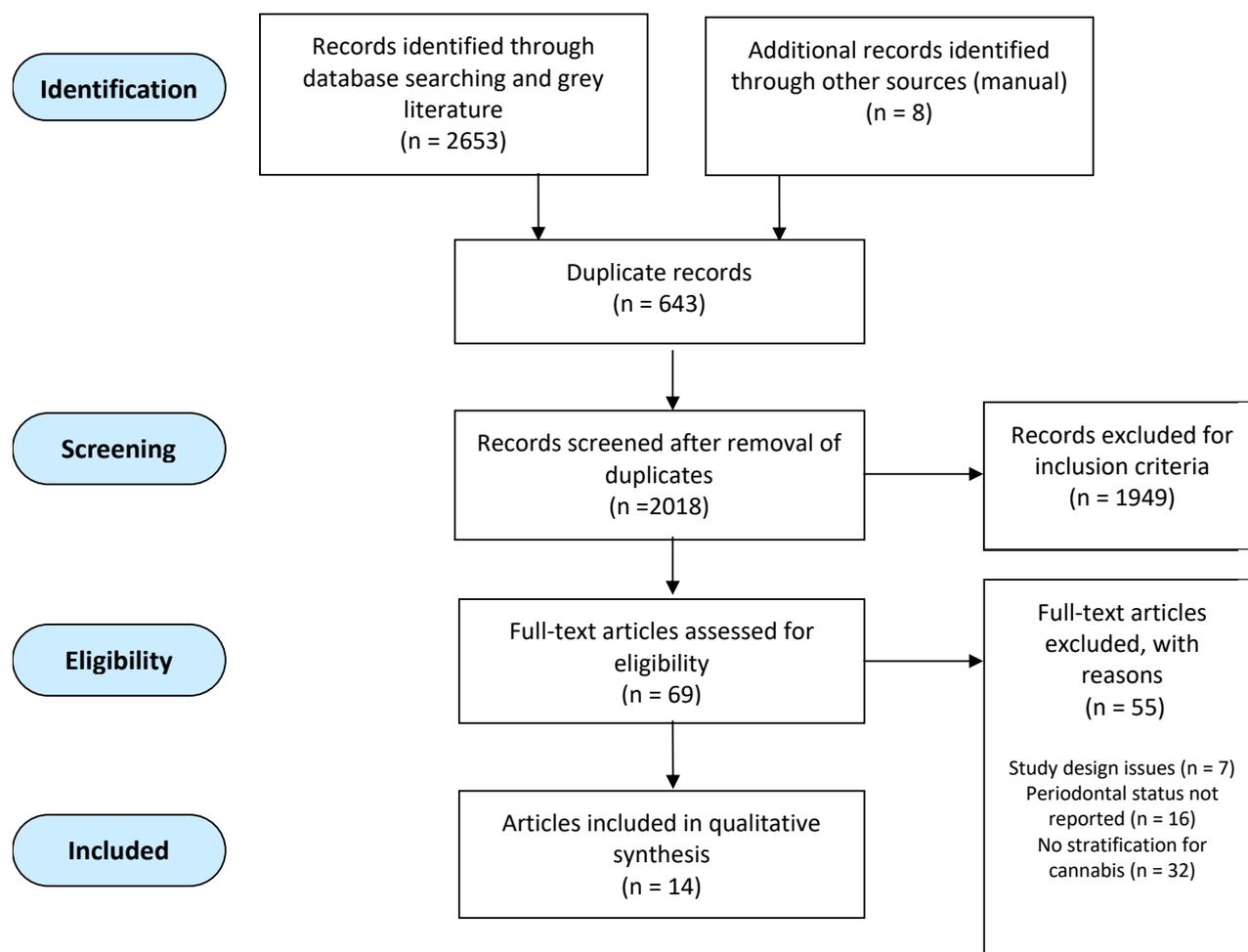


Figure 1. Prisma® flow diagram of the search processes and results.

Table 1. Excluded articles with reasons

| Main reason for exclusion | References |
|---|---|
| Study design | Aston R (1984); Brignardello-Petersen R (2019); Mofidi A <i>et al.</i> (2019); Nesi W (1970); Rawal S (2012); Saini GK (2013); Silvestre FG (1990) |
| Periodontal status analysis missing or inadequately reported | Abuse S (2013); Agrawal A (2009); Aparicio FA (2018); Becart A (1997); Bermeo M (2013); D'Amore MM (2011); Jimenez Polanco M (2011); Marques TC (2015); Osborn M (2003); O'Sullivan E.M. (2012); Parish C (2015); Pedreira RHS (1999); Reece A (2007); Robinson PG (2005); Shekarchizadeh H (2013); Silverstein Steven J. (1973); |
| Inclusion of consumers of multiple drugs, without stratification for cannabis/marijuana | Albini M B (2015); Angelillo IF (1991); Antoniazzi, R P (2016); Arizmendi B (1991); Brezina J (1996); Chaparro-González (2018); Costa SKP (2011); Darling MR (1993); de Brito W (2018); Dedi'c A (2003); Gibson G (2003); Gigena P (2012); Gigena P (2015); Gupta T (2012); Heidari E (2007); Mateos Morenos MV (2013); Molendijk B (1996); Pilinova A (2003); Pourhashemi SJ (2015); Priwe C (2018); Ribeiro EDP (2002); Rodriguez Vazquez C (2002); Rotemberg E (2015); Ruiz Candina H (2015); Sandoval C (1992); Scheutz F (1984); Shapiro SS (1970); Sheridan J (2001); Stolz A (2002); Thavarajah R (2006); Thavarajah R (2008); Vainionpää R (2017) |

The Dunedin Multidisciplinary Health and Development Study (DMHDS) is a large cohort study that has been taking place in New Zealand since 1972-73 and its results have been published in several articles at multiple points throughout the study. Data obtained from the Dunedin Study show that the proportion of cannabis

users decreased with age. Its regular use (weekly or daily) was associated with greater attachment loss (Zeng *et al.*, 2014). In the study by Meier *et al.* (2016) a mean attachment loss, within the whole sample, of 1.61 mm (SD = 0.74) was reported. Also, periodontal disease defined as 1 or more site(s) with 5 mm or more of attachment loss was

Table 2. Characteristics of the included studies

| Study | City, Country | Type of Study | Background | n | % cannabis users/abusers | Sex | Age | Exposure to cannabis categories | Main Outcomes | Main results |
|--|-----------------------|------------------------------|--|-----|--------------------------|----------------|-----------|---|---|---|
| Meier et al. 2016, Zeng et al. 2014, Thomson et al. 2013, 2008 | Dunedin, New Zealand | Prospective Cohort Study | Queen Mary Hospital, birth cohort | 831 | 20.2% high exposure | 51% M 49% F | 38 y | Identification of participants in the highest 20% of exposure (Thomson et al. 2008, 2013) None - less than weekly - weekly - daily (Zeng et al. 2014) Persistent cannabis dependence (26 to 38 y) (Meier et al. 2016) | Combined attachment loss periodontal disease: 1+ site(s) with 5 or more mm of attachment loss | Higher incidence of attachment loss in 20% highest exposure vs. no exposure RR (95% CI): 2.1 (1.2 - 3.8) Higher risk of periodontitis progression in 20% highest exposure vs. 80% less or not exposed RR(95% CI): moderately increased risk of progression 3.5 (1.7 - 7.2); markedly increased risk of progression 2.9 (1.1 - 8.0) Higher attachment loss in weekly (estimate (95%CI): 1.1 (1.0 - 1.1)) and daily users at 32y Higher attachment loss in cannabis-dependent participants RR (95% CI, p): 1.1 (1.0 - 1.2, p=0.046) |
| Barrios and Vila. 2009 | Corrientes, Argentina | Cross-sectional, descriptive | Patients attending to the Chair Clinical Practice of Preventive I FOUNNE | 80 | 50% | 91% M 9% F | 15-30 y | No- mild- moderate- severe consumption of marijuana | Löe & Silness Gingival Index (1963), O'Leary Plaque Index (1972) | GI: excessive consumers 2.5, no consumers 0.9 PI: excessive consumers 48.1%, no consumers 35.6% |
| Garay 2009 (thesis) | Lima, Peru | Case series | Rehabilitation Center Fuente de Agua Viva | 60 | 100% | 60% M 40% F | 18 - 50 y | Frequency: (2+ times / day; 1 -2 times / day; 2+ times / week; 1 -2 times / week);; Marijuana consumption in years | PS; GR; CAL; BoP, tooth mobility, furcation involvement, oral hygiene level | PD ≥ 4mm: 13.3% CAL ≥ 5mm: 6.7% |

Table 2 continued overleaf...

Table 2. Characteristics of the included studies continued....

| | | | | | | | | | | |
|-----------------------------|---------------------------------|-----------------|--|------|----------------|----------------|-----------|--|--|---|
| Lopez <i>et al.</i> 2009 | Santiago, Chile | Cross-sectional | High-school students | 9163 | 6% regular use | 51% M 49% F | 12 - 21 y | Ever use of cannabis (yes / no) Regular use of cannabis (yes / no) | Periodontal disease: CAL \geq 3mm | Multiple logistic regression analyses of the association between having regular use of cannabis, and the presence of CAL \geq 3 mm, for each tobacco smoking status groups (OR (95%CI)): non-smokers: 1.0 (0.3 - 3.4); occasional tobacco smokers: 1.3 (0.5 - 3.3); daily tobacco smokers 0.8 (0.4 - 1.4) |
| Jamieson <i>et al.</i> 2010 | Northern Territory, Australia | Cross-sectional | Aboriginal Birth Cohort, Royal Darwin Hospital | 425 | 32.5% | 48% M 52% F | 16 - 20 y | How much marijuana do you smoke?: (1) never or only tried it once; (2) used to smoke, but not anymore; (3) still smoke sometimes. (2) and (3) were combined to represent a case of consuming marijuana | CDC/AAP Periodontitis case definition | Periodontitis in tobacco smokers (marijuana consumers vs. no consumers) PR(CI): 1.47 (1.03 - 2.11) Periodontitis in non-tobacco smokers (marijuana consumers vs. no consumers) PR(CI): 0.17 (0.01-2.63) |
| Reddy <i>et al.</i> 2012 | Bangalore, India | Cross-sectional | Various deaddiction centres (n=250) General population (n=250) | 500 | 2.8% | 91% M 9% F | 18 - 64 y | Substance abusers according to the International Classification of Diseases 10 (ICD 10) [1] and Diagnostic and Statistical Manual of Mental Disorders (DSM IV), American Psychiatric Association | Oral hygiene index- simplified (OHI-S), Russell's Periodontal Index (RPI) and BoP | Only cannabis abusers: Mean OHI-S: 2.5 Mean RPI: 3.2 Mean BoP: 14% |
| Kayal <i>et al.</i> 2014 | Jeddah, Kingdom of Saudi Arabia | Cross-sectional | Al-Amal Hospital (drug rehabilitation center) | 57 | 66.7% | 100% M | 16 - 64 y | No quantification of cannabis exposed performed | BoP, Silness-Loe PI, Gingival Recession, PD, CAL: mild (1-2 mm), moderate (3-4 mm) or severe (\geq 5mm) | BoP (%): 42.6 \pm 31.4 CAL approx.: severe 14%; moderate 48%; mild 38% |

Table 2 continued overleaf...

Table 2. Characteristics of the included studies continued....

| | | | | | | | | | | |
|------------------------|--|------------------------------|--|------|----------------------|--------------------------|--------------|---|--|--|
| Verastegui et al. 2016 | Chiclayo, Peru | Case series | Pastors of Peru Lambayeque Marijuana Rehabilitation Center | 49 | 100% | 65% M 35% F | 18 - 52 y | Definitive diagnostic of marijuana addiction | BoP, GR, PD, tooth mobility, furcation involvement | BoP: 57.1% PD \geq 4mm: 26.5% GR: 75.5% Tooth mobility: 22.5% Furcation involvement: 14.3% |
| Núñez 2016 (thesis) | San Francisco de Macorís, Dominican Republic | Cross-sectional, descriptive | San Francisco de Macorís, Dominican Republic | 40 | 50% | 43% M 37% F | 18 - 40 y | Exposed group Non-exposed group | PD, CAL, BoP, suppuration, furcation involvement, tooth mobility, O'Leary PI, radiographic marginal bone level | Exposed: Bad OH: 90% BoP: 466 sites PD: 2.6 mm CAL: 2.4mm |
| Shariff et al. 2017 | USA | Cross-sectional | Data from the National Health and Nutrition Examination Survey (NHANES) 2011 to 2012 | 1938 | 26.8% FRC | 50.7% M 48.3% F | 30 - 59 y | FRC users Non-FRC | CDC/AAP periodontitis case definition | Severe Periodontitis in FRC (non-tobacco smokers) vs. non-FRC: aOR (CI: 95%): 1.9 (1.1 - 3.2) |
| Ortiz et al. 2018 | San Juan, Puerto Rico | Cross-sectional | San Juan Overweight Adults Longitudinal Study (SOALS) | 735 | 2.7% Frequent use | 27.6% M 72.4% F | 40 - 70 y | No use or once in lifetime Occasional use, Frequent marijuana use | CDC/AAP periodontitis case definition | Severe Periodontitis in FRC vs. no use of cannabis: aOR (95% CI) 2.9 (1.1 - 7.9) |

Exp.: exposed, BoP: bleeding on probing, OH: oral hygiene, PD: probing depth, GR: gingival recession, CAL: clinical attachment loss, M: males, F: females, y= years, AAP/CDC: Centers for Disease Control and Prevention - American Academy of Periodontology, FRC= frequent recreational cannabis use, GI: gingival index, PI: plaque index, RR: relative risk, OR: odds ratio, PR: prevalence ratio, aOR: adjusted odds ratio.

shown in 18% of females and in 28% of males. Among cannabis users, after adjusting for tobacco pack-years, childhood health and socioeconomic status, brushing and flossing, and alcohol dependence, a greater clinical attachment loss (continuous variable) was seen. This association was significant either for cannabis joint-years or persistent cannabis dependence. However, when the categorical periodontal disease definition was considered such association with joint-years was not seen, though there was an association between periodontal disease and persistent cannabis dependence.

Meier *et al* (2016) also reported poorer oral hygiene habits in cannabis users than in non-users. For tooth brushing, the Pearson correlation was $r = -0.9$ ($p < 0.001$) and $r = -0.26$ ($p < 0.001$) for the associations with cannabis joint-years and with persistent cannabis dependence respectively. For teeth flossing $r = -0.13$ ($p < 0.001$) and $r = -0.15$ ($p < 0.001$), for the associations with cannabis joint-years and with persistent cannabis dependence respectively. In addition to this, Thomson *et al* (2013) reported that participants at all ages from 15 to 38 in the highest 20% of exposure (with calculated mean (18, 21, 26, 32 and 38 years of age) of 41 or more occasions of cannabis use during the previous year) were at higher risk of attachment loss progression, being in the “moderately increasing” or “markedly increasing” trajectory groups.

Before treatment, Barrios and Vila (2009) observed higher gingival inflammation in cannabis consumers than in non-consumers. The mean Gingival Index in low, moderate and severe consumers was 1.3, 2 and 2.5 respectively, while in non consumers they found a mean Gingival Index index of 0.9. The mean Plaque O’Leary index score in moderate (38.9%) and severe (48.1%) consumers was higher than in low (24.4%) and non-consumers (35.6%). Criteria for including subjects in subgroups of consumers were not reported.

Garay (2009) found that 13.3% of marijuana users had periodontal pocket (probing depth ≥ 4 mm), of which almost half had consumed marijuana more than two times daily and the other half less frequently. 60% of participants had mild clinical attachment level (CAL), 33.3% moderate, and 6.7% severe. In the latter category poor oral hygiene was present. Regarding tooth mobility and furcation involvement, percentages of individuals with such conditions were 3.3% and 3.4% respectively. Based on the Greene and Vermillion Oral Hygiene Index, it was reported that 63.3% had fair oral hygiene and 36.7% had poor hygiene, none of participants had good oral hygiene. Gingival bleeding was present in 48.3% of the subjects.

Lopez and Baelum (2009) studied a sample of high school students from the full list of high schools in the Province of Santiago, Chile. They found 4.5% of the study population with presence of CAL ≥ 3 mm. Additionally, 18.9% of the individuals were in the “ever

use of cannabis” group and 6.0% in the “regular use of cannabis” group. After the multiple logistic regression analysis, results did not show association between either “ever use of cannabis” or “regular use of cannabis” and CAL ≥ 3 mm, regardless the tobacco-smoking category considered.

Jamieson *et al* (2010) demonstrated a significant difference in prevalence of periodontal disease among those exposed and non-exposed to cannabis. They observed in an Australian Aboriginal population, which was made up of marijuana consumers ($n = 169$), a prevalence of moderate and severe periodontal disease of 32.5% (95% CI= 25.5 – 39.5); while in non-marijuana consumers ($n = 256$) the prevalence of periodontal disease was 22.7% (95% CI= 17.6 – 27.8). The association was statistically significant ($p < 0.05$). In tobacco smokers, marijuana use was associated with a 1.5-fold increase of the prevalence of periodontal disease when compared to non-marijuana smokers. Despite this, among tobacco non-smokers there were 13 marijuana users, none of them with periodontal disease.

When comparing a group of 250 substance abusers (study group) vs. another group of 250 non-substance abusers (control group), Reddy *et al* (2012) found a mean value of Russell’s Periodontal Index in the study group of 3.68 (± 1.40 SD) and in the control group of 2.59 (± 0.81 SD) which was significant ($p < 0.001$). However, Russell’s Periodontal Index was strongly correlated with the OHI-S (Greene & Vermillion) ($r = 0.721$) in the control group but not in the study group, where the correlation with oral hygiene was moderate ($r = 0.479$). When the comparison was done within substance abusers subgroups, no significant differences were found. The subgroup of individuals who only consumed cannabis ($n = 7$) had a mean Russell’s Index of 3.186 and a mean OHI-S of 2.514. Additionally, another subgroup of people who consumed alcohol, tobacco and cannabis ($n = 10$) showed a mean Russell’s Index of 3.950 and an OHI-S (Greene & Vermillion) score of 2.960.

Kayal *et al* (2014) found, in 38 individuals exposed to cannabis, a mean Silness & Loe Plaque Index of 1.8 ± 0.7 and a mean percentage of bleeding sites of $42.5\% \pm 31.4$. These results compared to those obtained from other drug (heroin, cocaine, alcohol and amphetamines) consumers were not significantly different. When analysing results on CAL of cannabis users, all participants had some degree of CAL, 38% (approx.) had mild CAL (1 - 2mm), 48% (approx.) had moderate CAL (3 - 4mm) and 14% (approx.) had severe CAL (≥ 5 mm). Additionally, the authors reported data on mean CAL discerned by drug consumed (amphetamines, heroin and cocaine) but no results on mean CAL with respect to cannabis consumers were reported. The authors were contacted by e-mail to request the information on clinical attachment level of cannabis smokers, with no answer. Plaque

and gingival indices were significantly associated with the severity of periodontal condition.

Verástegui and Ruiz (2016) described that 26.5% of marijuana consumers had periodontal pocket, 75.5% had gingival recession, 22.5% had tooth mobility and 14.3% had furcation involvement. CAL was not taken into consideration because the categories were not well defined. In addition to this, they found gingival bleeding in 57.1% of marijuana consumers. Data regarding biofilm control was not reported.

In the study performed by Nuñez Cuello (2016) individuals exposed to cannabis had higher O'Leary plaque index levels and more bleeding on probing sites than those non-exposed. While in the exposed group the mean probing depth and the mean CAL were 2.63 mm and 2.39 mm respectively, in the non-exposed group these values were 2.46 mm and 2.03 mm respectively.

Shariff *et al.* (2017) analysed the distribution of periodontitis, as defined by the Centers for Disease Control and Prevention/American Academy of Periodontology (CDC/AAP), in a population of 1938 individuals. From these, 974 subjects were in the “ever used recreational cannabis” category and 465 were “frequent recreational cannabis” (FRC) users. In the FRC group they found a mean attachment loss of 1.8mm, while in non-FRC that value was of 1.6 mm ($p = 0.004$). They performed two different models, one included the whole sample (model 1), and the other exclusively included the 1118 participants who had never smoked tobacco (model 2). After controlling for age, sex, race/ethnicity, family income, systemic conditions, substance use (alcohol and smoking) and periodontal treatment they found in model 1 an aOR of 1.4 (95% CI: 1.1 - 1.9; $p = 0.07$) for severe periodontitis among “frequent recreational cannabis” users. In model 2 after controlling for the same covariates, they obtained an OR of 1.9 (95% CI: 1.1 - 3.2; $p = 0.03$).

The study performed by Ortiz *et al.* (2018) in Puerto Rico, included 2.7% of all participants who were “frequent users” of marijuana and 23.8% were classified in the “occasional” marijuana users group. With respect to periodontal status data of the sample, 39.5% had moderate periodontitis and 20.1% had severe periodontitis. After adjustment for sex, age, healthcare coverage, current smoking status, binge drinking, oral sex partners, oral HPV infection, and dental visits, indicated in the multivariable analysis that frequent marijuana users had increased odds of periodontitis (OR = 2.93, 95% CI = 1.08 - 7.96) when compared to nonusers.

Quality assessment of the included studies is shown in Tables 3 and 4. Three of them were of high quality (Meier *et al.*, 2016; Lopez and Baelum, 2009; Shariff *et al.*, 2017), two showed moderate quality (Jamieson *et al.*, 2010; Ortiz *et al.*, 2018) and six were of low quality (Barrios and Vila, 2009; Kayal *et al.*, 2014; Verástegui, 2016; Garay, 2009; Reddy *et al.*, 2012; Nuñez Cuello, 2016).

Discussion

The present study was undertaken in order to understand the possible role of exposure to cannabis smoking on periodontal health. Therefore, a systematic review, using contemporary guidelines (MOOSE), (Stroup *et al.*, 2000) was conducted. The results indicate a possible worsening of periodontal health in cannabis smokers.

At first, the authors intended to verify possible differences in periodontal microbiological profile of cannabis smokers and non-smokers. However, the search strategy retrieved no studies evaluating microbiological parameters. There is a clear difference between how cannabis is consumed and how it is studied, studies concerning the effects of cannabis compounds on different parts of the body present controversial results, as many benefits were reported (Russo, 2011). Animal-model studies demonstrated an anti-inflammatory response to cannabidiol (Sacerdote *et al.*, 2005; Napimoga *et al.*, 2009), while from another it is reported that cannabis inhalation could adversely affect periodontal tissues (Nogueira-Filho *et al.*, 2011). Recently, Liu *et al.* (2019) demonstrated that stimulation of cannabinoid receptors type 2 (CB2) was associated with cell adhesion and increased migration of periodontal ligament fibroblasts. This suggests a potential effect of cannabinoids on periodontal wound healing and regeneration (Liu *et al.*, 2019). Also, it was described that CB2 could participate in the modulation of the inflammatory response within periodontal tissues (Abidi *et al.*, 2018).

The use of cannabis might be by means of smoking or, in some cases, by other applications, such as ingestion or topical application, for recreational or medical purposes. The greatest interest in terms of periodontal diseases is how the use of smoked cannabis might affect periodontal tissues. The number of countries/states that have legalized recreational cannabis is increasing (European Monitoring Centre for Drugs and Drug Addiction, 2018), though little is known about any specific harm on periodontal tissues so far. How tobacco smoking affects the periodontal support has been extensively studied (Leite *et al.*, 2018) and most cannabis users also smoke tobacco (Agrawal *et al.*, 2012). Cannabis has been compared to tobacco in relation to carcinogenic risk, reporting that the former does not show carcinogenic properties (Melamede, 2005), but this is still controversial. (Fischer *et al.*, 2017)

As a clear controversy exists regarding the implications in general health and specifically regarding the eventual periodontal damage caused by cannabis consumption, a thorough search of the literature is warranted. The search of the literature and retrieval of articles was performed taking into consideration the existing studies, i.e., not only comparative studies were included (according to PECOS strategy), but studies reporting periodontal conditions of cannabis users

Table 3. Quality Assessment of cross sectional studies included (Newcastle-Ottawa scale modified by D. Zhao *et al.* (2018)).

| | SELECTION (max. 4*) | | | | COMPARABILITY (max. 2*) | OUTCOME (max. 2*) | | Total stars (max. 8*) |
|-----------------------------|-------------------------------------|----------------|------------------------------|--------------------------|----------------------------|--------------------------|-------------------------|--------------------------|
| | Representativeness of the sample | Sample size | Ascertainment of exposure | Non- response rate | | Assessment of outcome | Statistical analysis | |
| Lopez and Baelum 2009 | * | * | - | * | ** | * | * | 7 |
| Garay <i>et al.</i> 2009 | - | - | - | - | - | * | - | 1 |
| Barrios and Vila 2009 | - | - | - | - | - | * | - | 1 |
| Jamieson <i>et al.</i> 2010 | * | - | - | * | ** | * | * | 6 |
| Reddy <i>et al.</i> 2012 | - | - | * | - | * | * | * | 4 |
| Kayal <i>et al.</i> 2014 | - | - | - | - | * | * | - | 2 |
| Verástegui and Ruiz 2016 | - | - | - | - | - | * | - | 1 |
| Núñez 2016 | - | - | - | - | - | - | - | 0 |
| Shariff <i>et al.</i> 2017 | * | * | - | * | ** | * | * | 7 |
| Ortiz <i>et al.</i> 2018 | - | * | - | * | ** | * | * | 6 |

Table 4. Quality assessment of the cohort study included (Newcastle-Ottawa scale)

| Study | SELECTION (max. 4*) | | | | COMPARABILITY (max. 2*) | OUTCOME (max. 3*) | | | Total stars (max. 9*) |
|--|--|--|------------------------------|--|----------------------------|--------------------------|--|---|--------------------------|
| | Representativeness of the exposed cohort | Selection of the non- exposed cohort | Ascertainment of exposure | Demonstration that outcome of interest was not present at start of study | | Assessment of outcome | Was follow- up long enough for outcomes to occur | Adequacy of follow up of cohorts | |
| Thomson <i>et al.</i> , 2008, 2013, Zeng <i>et al.</i> , 2014, Meier <i>et al.</i> , 2016, | * | * | * | * | ** | * | * | * | 9 |

were also accepted. Recently, the Joint Workshop for Classification of Periodontal and Peri-Implant Diseases and Conditions (Caton *et al.*, 2018) did not consider that the published evidence was sufficient to include any category related to cannabis. This does not mean cannabis could not have a role, but it is a clear demonstration of the lack of studies up to date.

Two systematic reviews have been published investigating the association between cannabis use and periodontal disease, concluding that there could be a relationship between cannabis exposure and periodontal breakdown (Baghaie *et al.*, 2017; Chisini *et al.*, 2019). One of the systematic reviews (Chisini *et al.*, 2019) was restricted to periodontitis. The uniqueness

of the present systematic review is that the inclusion criteria were less strict, leading to an increased number of included studies, trying to shed more light onto the existing information. In addition, in the present review, one study and two theses were that considered only marginal gingival parameters (Barrios and Vila, 2009; Garay, 2009; Núñez Cuello, 2016). The other systematic review on this topic (Baghaie *et al.*, 2017) evaluated the association between oral health and substance abuse which included any drug abuse.

This systematic review included 14 articles, from 11 different studies. These 11 studies were qualitatively analysed. In spite of being studies with large sample sizes, three had reduced number of cannabis consumers (Lopez and Baelum, 2009; Meier *et al.*, 2016; Ortiz *et al.*, 2018; Thomson *et al.*, 2008; Thomson *et al.*, 2013; Zeng *et al.*, 2014). Regarding sample characteristics, four studies took place in drug rehabilitation centres/clinics (Verástegui and Ruiz, 2016; Garay, 2009; Reddy *et al.*, 2012; Kayal *et al.*, 2014), one at a university dental clinic (Barrios and Vila, 2009), and another obtained data from an overweight adult population (Ortiz *et al.*, 2018). Also, it has to be noted that in the study carried out by Lopez and Baelum (2009), the participants were between 12 and 21 years old, with the majority of the individuals from 15 to 17 years.

These aspects are a clear demonstration of the great variability in study designs, which prevent merging of data in a meta-analysis. Even though 11 different projects were included, the qualitative analysis points to a number of studies with important limitations (Garay, 2009; Barrios and Vila, 2009; Kayal *et al.*, 2014; Reddy *et al.*, 2012; Verástegui and Ruiz, 2016; Núñez Cuello, 2016). The most qualified data in the present study comes from the Dunedin Multidisciplinary Health and Development Study in New Zealand. The important characteristic of such a project is that it is a longitudinal study. The four publications from this longitudinal study indicate that cannabis use is related to clinical attachment loss in 32-year-old or older subjects (Zeng *et al.*, 2014), and that clinical attachment loss has a higher progression rate in the 20% of individuals who use more cannabis (Thomson *et al.*, 2013).

Another study that deserves comment is that by Barrios and Vila (2009), which looked at plaque and gingival inflammatory status. In this study, individuals exposed to cannabis presented a higher degree of gingival inflammation, despite the absence of differences in plaque. A longitudinal approach would allowed better conclusions in terms of causality. On one hand, it could be supposed that exposure to cannabis leads to a pro-inflammatory status. On the other, it is known that cannabis exposure might be associated with poorer lifestyle (Kayal *et al.*, 2014; Meier *et al.*, 2016).

In summary, 3 of the 10 studies that analysed occurrence of periodontitis under a cross-sectional design demonstrated worse periodontal conditions in cannabis smokers when compared to cannabis non-smokers (Shariff *et al.*, 2017; Ortiz *et al.*, 2018; Reddy *et al.*, 2012). Another study, found an increased prevalence of periodontitis in cannabis smokers when tobacco smokers were considered (Jamieson *et al.*, 2010). However, when only tobacco non-smokers were taken into consideration, such association between cannabis and periodontitis was not seen. Additionally, Lopez and Baelum (2009) did not find such worsened conditions in adolescents. In accordance with this, Garay (2009) failed in associating smoking marijuana to periodontitis, since only 13.3% of marijuana users had periodontal pockets. Similar results were obtained in another study performed in a Peruvian drug rehabilitation centre. None of the Peruvian studies had a non-exposed control group or controlled for confounding factors (Garay, 2009; Verástegui and Ruiz, 2016). Another study analysed the periodontal status in multidrug consumers and found some form of periodontitis in all of them. It has to be noted that the severity of the disease was related to oral hygiene, evidenced by high plaque levels in subjects who had advanced forms of periodontitis (Kayal *et al.*, 2014). Núñez Cuello (2016), concluded subjects exposed to cannabis have worse periodontal conditions. Although, differences in probing depth (0.17 mm) and clinical attachment level (0.36 mm) between groups do not seem to be clinically relevant.

Inconsistencies between studies regarding the exposure to cannabis were seen. Apart from being self-reported, these inconsistencies could lead to the real level of consumption being masked; categories were unspecific with respect to the history, frequency, and quantity of drug consumed. Also, it should be noted that is difficult to know the exact composition of the “joints” smoked by the participants, as users sometimes consume only the psychoactive part of the plant, and other times consume other parts of the plant as well or even mix cannabis with tobacco. In addition to this, there were differences in periodontitis case definition. In three studies (Jamieson *et al.*, 2010; Shariff *et al.*, 2017; Ortiz *et al.*, 2018) the widely accepted AAP/CDC periodontitis case definition was utilized. Although, in the DMHDS periodontal disease was defined as 1 or more site(s) with 5 mm or more of attachment loss. This could overestimate the prevalence of the disease given causes for attachment loss other than periodontitis, such as gingival recession or cervical decay. Case definitions for epidemiological purposes that use the consensus reports of workgroups of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions could be useful for interstudy comparisons in the future (Chapple *et al.*, 2018; Papanou *et al.*, 2018; Berglundh *et al.*, 2018)

To conclude, based on the available data, frequent cannabis smoking could be detrimental for periodontal tissues and this could be dose-dependent. Nevertheless, it is desirable to investigate this topic further. Larger sampled longitudinal studies including long-term cannabis smokers, and stratified for periodontitis etiologic factors and risk factors/indicators, specifically age, bio-film control and tobacco, are needed to support this asseveration. Also is important to better report the quantity, frequency, time of consumption, and composition of the “joints” in detail, as well as how these aspects relate to the periodontal status. Regarding the periodontal health/disease case definition, it is desirable to use the case definitions reported by the latest reports about the Classification of Periodontal and Peri-implant Diseases and Conditions.

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References

- Abidi AH, Presley CS, Dabbous M, Tipton DA, Mustafa SM and Moore BM. Anti-inflammatory activity of cannabinoid receptor 2 ligands in primary hPDL fibroblasts. *Archives of Oral Biology* 2018; **87**:79-85.
- Agrawal A, Budney AJ and Lynskey MT. The co-occurring use and misuse of cannabis and tobacco: a review. *Addiction* 2012; **107**:1221-1233.
- Baghaie H, Kisely S, Forbes M, Sawyer E and Siskind DJ. A systematic review and meta-analysis of the association between poor oral health and substance abuse. *Addiction* 2017; **112**:765-779.
- Barrios CE and Vila VG. Estado de Salud Bucodental en Consumidores de Marihuana. *Revista de la Facultad de Odontología* 2009; **11**:30-35.
- Berglundh T, Armitage G, Araujo MG, *et al.* Peri-implant diseases and conditions: Consensus report of workgroup 4 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. *Journal of Clinical Periodontology* 2018; **45 Suppl 20**:S286-S291.
- Burstein S. Cannabidiol (CBD) and its analogs: a review of their effects on inflammation. *Bioorganic & Medicinal Chemistry* 2015; **23**:1377-1385.
- Caton JG, Armitage G, Berglundh T, *et al.* A new classification scheme for periodontal and peri-implant diseases and conditions - Introduction and key changes from the 1999 classification. *Journal of Periodontology* 2018; **89 Suppl 1**:S1-S8.
- Chapple ILC, Mealey BL, Van Dyke TE, *et al.* Periodontal health and gingival diseases and conditions on an intact and a reduced periodontium: Consensus report of workgroup 1 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. *Journal of Clinical Periodontology* 2018; **45 Suppl 20**:S68-S77.
- Chisini LA, Cademartori MG, Francia A, *et al.* Is the use of Cannabis associated with periodontitis? A systematic review and meta-analysis. *Journal of Periodontal Research* 2019; **54**:311-317.
- European Monitoring Centre for Drugs and Drug Addiction. Monitoring drug use in recreational settings across Europe: conceptual challenges and methodological innovations. Technical report. Luxembourg: Publications Office of the European Union, 2018.
- Fischer B, Russell C, Sabioni P, *et al.* Cannabis use guidelines: A Comprehensive update of evidence and recommendation. *American Journal of Public Health* 2017; **107**:e101-e112. .
- Garay R. Consumo de marihuana y características clínicas en el tejido periodontal en pacientes de un centro de rehabilitación. (DDS thesis) E.A.P de Odontología, Universidad Nacional Mayor de San Marcos. Lima, Perú. 2009
- Jamieson LM, Gunthorpe W, Cairney SJ, Sayers SM, Roberts-Thomson KF and Slade GD. Substance use and periodontal disease among Australian Aboriginal young adults. *Addiction* 2010; **105**:719-726.
- Kassebaum NJ, Bernabe E, Dahiya M, Bhandari B, Murray CJ and Marcenes W. Global burden of severe periodontitis in 1990-2010: a systematic review and meta-regression. *Journal of Dental Research* 2014; **93**:1045-1053.
- Kayal RA, Elias WY, Alharthi KJ, Demyati AK and Mandurah JM. Illicit drug abuse affects periodontal health status. *Saudi Medical Journal* 2014; **35**:724-728.
- Leite FRM, Nascimento GG, Scheutz F and Lopez R. Effect of smoking on periodontitis: A systematic review and meta-regression. *American Journal of Preventive Medicine* 2018; **54**:831-841.
- Liu C, Qi X, Alhabeil J, Lu H and Zhou Z. Activation of cannabinoid receptors promote periodontal cell adhesion and migration. *Journal of Clinical Periodontology* 2019; **46**:1264-1272.
- Lopez R and Baelum V. Cannabis use and destructive periodontal diseases among adolescents. *Journal of Clinical Periodontology* 2009; **36**:185-189.
- Meier MH, Caspi A, Cerda M, *et al.* Associations between cannabis use and physical health problems in early midlife: A longitudinal comparison of persistent cannabis vs tobacco users. *JAMA Psychiatry* 2016; **73**:731-740.
- Melamede R. Cannabis and tobacco smoke are not equally carcinogenic. *Harm Reduction Journal* 2005; **2**:21.

- Mofidi A, Fang D and Flores-Mir C. Cannabis and periodontal harm: How convincing is the association? *Oral Diseases* 2019; **25**:350-352
- Murakami S, Mealey BL, Mariotti A and Chapple ILC. Dental plaque-induced gingival conditions. *Journal of Clinical Periodontology* 2018; **45 Suppl 20**:S17-S27.
- Napimoga MH, Benatti BB, Lima FO, et al. Cannabidiol decreases bone resorption by inhibiting RANK/RANKL expression and pro-inflammatory cytokines during experimental periodontitis in rats. *International Immunopharmacology* 2009; **9**:216-222.
- Nogueira-Filho GR, Todescan S, Shah A, Rosa BT, Tunes Uda R and Cesar Neto JB. Impact of cannabis sativa (marijuana) smoke on alveolar bone loss: a histometric study in rats. *Journal of Periodontology* 2011; **82**:1602-1607.
- Núñez Cuello AM. Efecto del consumo de cannabis con relación al estado periodontal en pacientes con edades de 18 a 40 años en San Francisco de Macorís. (MSc thesis) Pontificia Universidad Católica Madre y Maestra (PUCMM), Santo Domingo, República Dominicana. 2016; 7-65
- Oficina de las Naciones Unidas contra la Droga y el Delito, Informe Mundial sobre las Drogas, 2017 (ISBN: 978-92-1-148291-1, eISBN: 978-92-1-060623-3, publicación de las Naciones Unidas, núm. de venta S.17.XI.6)
- Ortiz AP, Gonzalez D, Ramos J, Munoz C, Reyes JC and Perez CM. Association of marijuana use with oral HPV infection and periodontitis among Hispanic adults: Implications for oral cancer prevention. *Journal of Periodontology* 2018; **89**:540-548.
- Papapanou PN, Sanz M, Buduneli N, et al. Periodontitis: Consensus report of workgroup 2 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. *Journal of Clinical Periodontology* 2018; **45 Suppl 20**:S162-S170.
- Reddy S, Kaul S, Agrawal C, et al. Periodontal status amongst substance abusers in Indian population. *ISRN Dentistry* 2012; **2012**:460856.
- Russo EB. Taming THC: potential cannabis synergy and phytocannabinoid-terpenoid entourage effects. *British Journal of Pharmacology* 2011; **163**:1344-1364.
- Sacerdote P, Martucci C, Vaccani A, et al. The non-psychoactive component of marijuana cannabidiol modulates chemotaxis and IL-10 and IL-12 production of murine macrophages both in vivo and in vitro. *Journal of Neuroimmunology* 2005; **159**:97-105.
- Shariff JA, Ahluwalia KP and Papapanou PN. Relationship between frequent recreational cannabis (marijuana and hashish) use and periodontitis in adults in the United States: National Health and Nutrition Examination Survey 2011 to 2012. *Journal of Periodontology* 2017; **88**:273-280.
- Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis of observational studies in epidemiology (MOOSE) group. *JAMA* 2000; **283**:2008-2012.
- Thomson WM, Poulton R, Broadbent JM, et al. Cannabis smoking and periodontal disease among young adults. *JAMA* 2008; **299**:525-531.
- Thomson WM, Shearer DM, Broadbent JM, Foster Page LA and Poulton R. The natural history of periodontal attachment loss during the third and fourth decades of life. *Journal of Clinical Periodontology* 2013; **40**:672-680.
- Tonetti MS, Jepsen S, Jin L and Otomo-Corgel J. Impact of the global burden of periodontal diseases on health, nutrition and wellbeing of mankind: A call for global action. *Journal of Clinical Periodontology* 2017; **44**:456-462.
- Verástegui EA and Ruiz JL. Características Clínicas en el Tejido Periodontal de Internos Consumidores de Marihuana del Centro de Rehabilitación los Pastores del Perú Lambayeque. *Revista Salud & Visa Sipiense* 2016; **3**:32-40.
- Wells GA, Shea B, O'Connell D, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality if nonrandomized studies in meta-analyses. Available from: URL: http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm [cited in May 2020]
- Zeng J, Williams SM, Fletcher DJ, et al. Reexamining the association between smoking and periodontitis in the dunedin study with an enhanced analytical approach. *Journal of Periodontology* 2014; **85**:1390-1397.
- Zhao D, Khawaja AT, Jin L, Li KY, Tonetti M and Pelekos G. The directional and non-directional associations of periodontitis with chronic kidney disease: A systematic review and meta-analysis of observational studies. *Journal of Periodontal Research* 2018; **53**:682-704.

Appendix 1. Search strategy

| Search strategy- indexed data bases | | |
|--|---|--|
| DATA BASE | TERMINOLOGY | RESULT |
| Search strategy topic 1: Periodontal disease prevalence in cannabis smokers | | |
| BVS LILACS CUMED BBO - odontología (Brasil) IBECS (España) | ((“Enfermedades periodontales/EP” OR ((enfermedad\$ AND periodontal\$) AND (preval\$ OR epidemiol\$))) AND (preval\$ OR (enferm\$ OR patolog\$))) AND (((encuesta\$ OR transversal\$ OR (casos AND controles) OR Cohorte\$ OR preval\$ OR epidemiol\$) AND (preval\$ OR frecuen\$)) AND (fuma\$ AND (Cannabis OR (Marijuana OR Mariguana OR Hashish OR Hachis OR Bange OR Ganga OR Shisha OR weed OR pot OR hash OR “BC Bud” OR Ganja OR grass OR doobs OR haschisch OR “wacky baccy” OR “mary jane” OR gage OR chronic OR tea OR leaf OR stuff OR blow OR black OR dope OR maría OR hierba OR grifa OR hachís))) | 35 LILACS (22) CUMED (9) BBO - odontología (Brasil) (7) IBECS (España) (3) |
| Scielo | ((“Enfermedades periodontales/EP” OR ((enfermedad\$ AND periodontal\$) AND (preval\$ OR epidemiol\$))) AND (preval\$ OR (enferm\$ OR patolog\$))) AND (((encuesta\$ OR transversal\$ OR (casos AND controles) OR Cohorte\$ OR preval\$ OR epidemiol\$) AND (preval\$ OR frecuen\$)) AND (fuma\$ AND (Cannabis OR (Marijuana OR Mariguana OR Hashish OR Hachis OR Bange OR Ganga OR Shisha OR weed OR pot OR hash OR “BC Bud” OR Ganja OR grass OR doobs OR haschisch OR “wacky baccy” OR “mary jane” OR gage OR chronic OR tea OR leaf OR stuff OR blow OR black OR dope OR maría OR hierba OR grifa OR hachís))) | 15 |
| MEDLINE (Pubmed) | ((“Periodontal diseases/Epidemiology”[Mesh] OR ((periodontal* AND disease*) AND (preval* OR epidemiol*))) AND ((preval* OR (disease* OR pathol*))) AND (smoke* AND (Cannabis OR (Marijuana OR Mariguana OR Hashish OR Hachis OR Bange OR Ganga OR Shisha OR weed OR pot OR hash OR “BC Bud” OR Ganja OR grass OR doobs OR haschisch OR “wacky baccy” OR “mary jane” OR gage OR chronic OR tea OR leaf OR stuff OR blow OR black OR dope OR maría OR hierba OR grifa OR hachís))) AND (((survey* OR cross* OR (case AND control) OR case-control OR cohort* OR preval* OR epidemiol*) OR cross-sectional OR “cross sectional” OR cross*) AND (preval* OR frecuen*)) | 83 |
| Cochrane Library | #1 MeSH descriptor: [Periodontal Diseases] explode all trees #2 (periodontal* and disease*) and (preval* or epidemiol*) #3 preval* or (disease* or pathol*) #4 smoke* and (Cannabis or Marijuana or Mariguana or Hashish or Hachis or Bange or Ganga or Shisha or weed or pot or hash or “BC Bud” or Ganja or grass or doobs or haschisch or “wacky baccy” or “mary jane” or gage or chronic or tea or leaf or stuff or blow or black or dope or maría or hierba or grifa or hachís) #5 (survey* or cross* or (case and control) or case-control or cohort* or preval* or epidemiol* or cross-sectional or “cross sectional” or cross*) and (preval* or frecuen*) #6 (#1 or #2) and #3 and #4 and #5 | 24 (13 rev 1 protocols 10 trials) |
| SCOPUS | ((“Periodontal diseases/Epidemiology” [mesh] OR ((periodontal* AND disease*) AND (preval* OR epidemiol*))) AND ((preval* OR (disease* OR pathol*))) AND (smoke* AND (cannabis OR (marijuana OR mariguana OR hashish OR hachis OR bange OR ganga OR shisha OR weed OR pot OR hash OR “BC Bud” OR ganja OR grass OR doobs OR haschisch OR “wacky baccy” OR “mary jane” OR gage OR chronic OR tea OR leaf OR stuff OR blow OR black OR dope OR maría OR hierba OR grifa OR hachís))) AND (((survey* OR cross* OR (case AND control) OR case-control OR cohort* OR preval* OR epidemiol*) OR cross-sectional OR “cross sectional” OR cross*) AND (preval* OR frecuen*)) | 110 |

Appendix 1. Continued overleaf...

Appendix 1. Search strategy continued...

| Search strategies topic 2: Prevalence of other oral diseases in cannabis smokers | | |
|---|--|---|
| BVS LILACS IBECS (España) BBO odontología (Brasil) CUMED MedCarib | (Cannabis OR (Mariguana OR Marijuana OR Hashish OR Hachis OR Bange OR Ganga OR Shisha OR weed OR pot OR hash OR "BC Bud" OR Ganja OR grass OR doobs OR haschisch OR "wacky baccy" OR "mary jane" OR gage OR chronic OR tea OR leaf OR stuff OR blow OR black OR dope OR maría OR hierba OR grifa OR hachís)) AND (((encuesta\$ OR transversal\$ OR (casos AND controles) OR Cohorte\$ OR preval\$ OR epidemiol\$)) AND (preval\$ OR frecuen\$)) AND fuma\$ AND ((Enfermedad\$ OR patología\$) AND (Oral\$ OR bucal\$ OR boca\$) AND (preval\$ OR epidemiol\$)) | 69 LILACS (40) IBECS (España) (18) BBO - odontología (Brasil) (11) CUMED (9) MedCarib (2) |
| Scielo | (Cannabis OR (Mariguana OR Marijuana OR Hashish OR Hachis OR Bange OR Ganga OR Shisha OR weed OR pot OR hash OR "BC Bud" OR Ganja OR grass OR doobs OR haschisch OR "wacky baccy" OR "mary jane" OR gage OR chronic OR tea OR leaf OR stuff OR blow OR black OR dope OR maría OR hierba OR grifa OR hachís)) AND (((encuesta\$ OR transversal\$ OR (casos AND controles) OR Cohorte\$ OR preval\$ OR epidemiol\$)) AND (preval\$ OR frecuen\$)) AND fuma\$ AND ((Enfermedad\$ OR patología\$) AND (Oral\$ OR bucal\$ OR boca\$) AND (preval\$ OR epidemiol\$)) | 14 |
| MEDLINE (Pubmed) | (cannabis OR (marijuana OR hashish OR hachisu OR bange OR ganga OR shisha OR weed OR pot OR hash OR "BC Bud" OR ganja OR grass OR doobs OR hashish OR "wacky baccy" OR "mary jane" OR gage OR chronic OR tea OR leaf OR stuff OR blow OR black OR dope OR maria OR hierbas OR griffa OR hachisu)) AND ((survey* OR cross* OR (case AND control) OR case-control OR cohort* OR preval* OR epidemiol* OR cross-sectional OR "cross sectional" OR cross*) AND (preval* OR frecuen*)) AND (smoke* AND ((disease* OR pathol* OR patol*) AND (Oral* OR buccal* OR mouth*) AND (preval* OR epidemiol*))) | 171 |
| Cochrane Library | #1 cannabis or (marijuana or mariguana or hashish or hachisu or bange or ganga or shisha or weed or pot or hash or "BC Bud" or ganja or grass or doobs or hashish or "wacky baccy" or "mary jane" or gage or chronic or tea or leaf or stuff or blow or black or dope or maria or hierbas or griffa or hachisu) #2 (survey* or cross* or (case and control) or case-control or cohort* or preval* or epidemiol*) #3 cross-sectional or "cross sectional" or cross* #4 preval* or frecuen* #5 smoke* and (disease* or pathol* or patol*) #6 Oral* or buccal* or mouth* #7 preval* or epidemiol* #8 (#1 and (#2 or #3) and #4) and #5 and #6 and #7 | 196 157 revs 13 protocols 25 trials 1 special edition |
| Search strategies topic 3: Periodontal status in cannabis smokers | | |
| BVS LILACS BBO - odontología (Brasil) | (Manifest\$ AND (bucal\$ OR oral\$) OR (estado\$ OR manifestacion\$ OR diagnos\$)) AND ((clínic\$ OR exam\$) OR (estado\$ AND periodont\$)) AND ("estado periodontal" OR ((estado\$ OR status\$ OR diagnos\$) AND periodont\$)) AND (fuma\$ AND Cannabis OR Mariguana OR Marijuana OR Hashish OR Hachis OR Bange OR Ganga OR Shisha OR weed OR pot OR hash OR "BC Bud" OR Ganja OR grass OR doobs OR haschisch OR "wacky baccy" OR "mary jane" OR gage OR chronic OR tea OR leaf OR stuff OR blow OR black OR dope OR maría OR hierba OR grifa OR hachís) | 6 LILACS (6) BBO - odontología (Brasil) (2) |

Appendix 1. Continued overleaf...

Appendix 1. Search strategy continued...

| | | |
|---|--|---|
| Scielo | (Manifest\$ AND (bucal\$ OR oral\$) OR (estado\$ OR manifestacion\$ OR diagnos\$)) AND ((clínic\$ OR exam\$) OR (estado\$ AND periodont\$)) AND (“estado periodontal” OR ((estado\$ OR status\$ OR diagnos\$) AND periodont\$)) AND (fuma\$ AND Cannabis OR Mariguana OR Marijuana OR Hashish OR Hachis OR Bange OR Ganga OR Shisha OR weed OR pot OR hash OR “BC Bud” OR Ganja OR grass OR doobs OR haschisch OR “wacky baccy” OR “mary jane” OR gage OR chronic OR tea OR leaf OR stuff OR blow OR black OR dope OR maría OR hierba OR grifa OR hachís) | 0 |
| MEDLINE (Pubmed) | ((Manifest* OR health*) AND ((bucc* OR oral*) OR ((state* OR manifest* OR diagnos*) AND (clinic* OR exam*))) OR ((stage* OR state* OR phase*) AND periodon*)) AND (“periodontal status” OR “periodontal health” OR ((status OR diagnos*) AND periodon*)) AND (smoke* AND (cannabis OR marijuana OR marijuana OR hashish OR hachisu OR bange OR ganga OR shisha OR weed OR pot OR hash OR “BC Bud” OR ganja OR grass OR dobos OR hashish OR “wacky baccy” OR “mary jane” OR gage OR chronic OR tea OR leaf OR stuff OR blow OR black OR dope OR maria OR hierbas OR griffa OR hachisu))) AND “Periodontal disease” | 51 |
| Cochrane Library | #1 Manifest* or health* #2 (bucc* or oral*) or ((state* or manifest* or diagnos*) and (clínic* or exam*)) #3 (stage* or state* or phase*) and periodon* #4 (“periodontal status” or “periodontal health” or ((status or diagnos*) and periodon*)) #5 smoke* and (Cannabis or Mariguana or Marijuana or Hashish or Hachis or Bange or Ganga or Shisha or weed or pot or hash or “BC Bud” or Ganja or grass or doobs or haschisch or “wacky baccy” or “mary jane” or gage or chronic or tea or leaf or stuff or blow or black or dope or maría or hierba or grifa or hachís) #6 Periodontal and disease* #7 (#1 and (#2 or #3)) and #4 and #5 and #6 | 36 19 revs 1 protocol 16 trials |
| Search strategies topic 4: Subgingival microbiological profile in cannabis smokers with and without periodontal diseases | | |
| BVS LILACS BBO - odontología (Brasil) IBECS (España) CUMED | ((microb\$ OR bacter\$ OR perfil\$) AND (subgingiv\$ OR placa\$ OR biofilm\$ OR biopelic\$ OR bacteriana\$)) AND (subgingi* OR gingiv* OR periodont* OR oral) AND (Tetrahidrocannabinol OR dronabinol OR Cannabi\$ OR (Mariguana or Hashish or Marijuana or Hachis or Bange or Ganga or Shisha or weed or pot or hash or “BC Bud” or Ganja or grass or doobs or haschisch or “wacky baccy” or “mary jane” or gage or chronic or tea or leaf or stuff or blow or black or dope or maría or hierba or grifa or hachís))) fuma\$ | 31 LILACS (26) BBO - odontología (Brasil) (9) IBECS (España) (2) CUMED (1) |
| Scielo | ((microb\$ OR bacter\$ OR perfil\$) AND (subgingiv\$ OR placa\$ OR biofilm\$ OR biopelic\$ OR bacteriana\$)) AND (subgingi* OR gingiv* OR periodont* OR oral) AND (Tetrahidrocannabinol OR dronabinol OR Cannabi\$ OR (Mariguana or Marijuana or Hashish or Hachis or Bange or Ganga or Shisha or weed or pot or hash or “BC Bud” or Ganja or grass or doobs or haschisch or “wacky baccy” or “mary jane” or gage or chronic or tea or leaf or stuff or blow or black or dope or maría or hierba or grifa or hachís))) fuma\$ | 11 |

Appendix 1. Continued overleaf...

| | | |
|---|---|---|
| MEDLINE (Pubmed) | ((microb* OR bacter* OR profile*) AND (subgingiv* OR Plaque* OR biofilm* OR film)) AND (cannabis OR (marijuana OR marijuana OR hashish OR hachisu OR bange OR ganga OR shisha OR weed OR pot OR hash OR "BC Bud" OR ganja OR grass OR dobos OR hashish OR "wacky baccy" OR "mary jane" OR gage OR chronic OR tea OR leaf OR stuff OR blow OR black OR dope OR maria OR hierbas OR griffa OR hachisu) AND smoke*) | 130 |
| Cochrane Library | #1 microb* or bacter* or profile* #2 subgingiv* or Plaque* or biofilm* or film #3 (Cannabis or Mariguana or Marijuana or Hashish or Hachis or Bange or Ganga or Shisha or weed or pot or hash or "BC Bud" or Ganja or grass or doobs or haschisch or "wacky baccy" or "mary jane" or gage or chronic or tea or leaf or stuff or blow or black or dope or maría or hierba or grifa or hachís) #4 smoke* #5 #1 and #2 and #3 and #4 | 82 30 rev 3 protocols 49 trials |
| Search strategies topic 5: outcomes: clinical attachment loss, probing depth, gingival index/bleeding on probing, plaque index, bone loss) | | |
| BVS LILACS (58) IBECs (España) (14) CUMED (2) BBO - odontología (Brasil) (1) | (Inserción AND Periodontal) AND (Indice\$ OR perdida OR profundidad\$ OR sonda\$ OR gingiva\$ OR sangra\$ OR placa OR reabsorción OR inflama\$ OR placa\$) AND (Cannabis or (Mariguana or Marijuana or Hashish or Hachis or Bange or Ganga or Shisha or weed or pot or hash or "BC Bud" or Ganja or grass or doobs or haschisch or "wacky baccy" or "mary jane" or gage or chronic or tea or leaf or stuff or blow or black or dope or maría or hierba or grifa or hachís)) | 74 LILACS (58) IBECs (España) (14) CUMED (2) BBO - odontología (Brasil) (1) |
| Scielo | (Inserción AND Periodontal) AND (Indice\$ OR perdida OR profundidad\$ OR sonda\$ OR gingiva\$ OR sangra\$ OR placa OR reabsorción OR inflama\$ OR placa\$) AND (Cannabis or (Mariguana or Marijuana or Hashish or Hachis or Bange or Ganga or Shisha or weed or pot or hash or "BC Bud" or Ganja or grass or doobs or haschisch or "wacky baccy" or "mary jane" or gage or chronic or tea or leaf or stuff or blow or black or dope or maría or hierba or grifa or hachís)) | 54 |
| MEDLINE (Pubmed) | ((Attach* AND periodontal) AND (Index* OR loss OR depth OR probe* OR probing OR bleeding OR gingiv* OR plate OR resorpt* OR inflamm*)) AND ((cannabis OR (marijuana OR marijuana OR hashish OR hachisu OR bange OR ganga OR shisha OR weed OR pot OR hash OR "BC Bud" OR ganja OR grass OR dobos OR hashish OR "wacky baccy" OR "mary jane" OR gage OR chronic OR tea OR leaf OR stuff OR blow OR black OR dope OR maria OR hierbas OR griffa OR hachisu)))) AND smok* AND index AND (survey* OR cross* OR (case AND control) OR case-control OR cohort* OR preval* OR epidemiol* OR cross-sectional OR "cross sectional" OR cross*) | 172 |
| Cochrane Library | #1 Attach* and periodontal* #2 Index* or loss or depth or probe* or probing or bleeding or gingiv* or plate or resorpt* or inflamm* #3 (Cannabis or Mariguana or Marijuana or Hashish or Hachis or Bange or Ganga or Shisha or weed or pot or hash or "BC Bud" or Ganja or grass or doobs or haschisch or "wacky baccy" or "mary jane" or gage or chronic or tea or leaf or stuff or blow or black or dope or maría or hierba or grifa or hachís) and smok* and index #4 (survey* or cross* or (case and control) or case-control or cohort* or preval* or epidemiol* or cross-sectional or "cross sectional" or cross*) #5 (#1 and #2) and #3 and #4 | 40 20 revs 2 protocols 18 trials |

Search strategies - Grey literature

| DATABASE | TERMINOLOGY | RESULT |
|---|--|---------------------|
| Directory of open access journals (DOAJ) | <p>("Cannabis periodontal") https://doaj.org/search?source=%7B%22query%22%3A%7B%22query_string%22%3A%7B%22query%22%3A%22Cannabis%20Periodontal%22%2C%22default_operator%22%3A%22AND%22%7D%7D%2C%22from%22%3A0%2C%22size%22%3A10%7D ("Marijuana periodontal") https://doaj.org/search?source=%7B%22query%22%3A%7B%22query_string%22%3A%7B%22query%22%3A%22Marijuana%20Periodontal%22%2C%22default_operator%22%3A%22AND%22%7D%7D%2C%22from%22%3A0%2C%22size%22%3A10%7D</p> | 3 3 |
| Google Scholar (2009-2019) | <p>(Cannabis OR marijuana) periodontal (observational OR observacional) (smoking OR fuma OR tobacco OR tabaco) https://scholar.google.es/scholar?q=%28Cannabis+OR+marijuana%29+periodontal+%28observational+OR+observacional%29+%28smoking+OR+fuma+OR+tobacco+OR+tabaco%29&hl=es&as_sdt=0%2C5&as_ylo=2009&as_yhi=2019</p> | First 995 from 2720 |
| University of British Columbia | <p>("Cannabis Periodontal observational") http://ubc.summon.serialssolutions.com/search?spellcheck=true&sq=Cannabis+Periodontal%20observational</p> | 44 |
| GreyLit | <p>(marijuana health) http://www.greylit.org/library/search#wt=json&facet=true&q=marijuana+health&q.op=AND&fl=id&qt=dismax&sort=createddesc&page=1&per_page=10&start=0&qf=full_text&facet.field=publisher&facet.field=full_subjects</p> | 37 |
| Open Grey | <p>(Marijuana) http://www.opengrey.eu/search/request?q=Marijuana</p> | 37 |
| ADA center for evidence-based dentistry | <p>(Marijuana) http://ebd.ada.org/en/search-results#q=Marijuana&sort=relevancy&f:adasites=[ADA%20Center%20for%20Evidence-Based%20Dentistry%20(EBD)] (Cannabis)</p> | 20 |
| Science.gov (Información científica federal de USA) | <p>("Marijuana AND) periodontal") https://www.science.gov/scigov/desktop/en/results.html</p> | 108 |
| Ontario Public Health Association | <p>"Marijuana periodontal" http://www.opha.on.ca/Utility-Pages/Search-Results.aspx?searchtext=Marijuana+Periodontal&searchmode=anyword "Cannabis Periodontal" http://www.opha.on.ca/Utility-Pages/Search-Results.aspx?searchtext=Cannabis+periodontal&searchmode=anyword</p> | 3 17 |