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Linha de pesquisa:

Epidemiologia, etiopatogenia e repercussão das doenças da cavidade bucal e estruturas anexas.

Dissertação:

ESTADO PERIODONTAL EM FUMANTES DE CANABIS

Mestranda:

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PORTO ALEGRE 2019

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ESTADO PERIODONTAL EM FUMANTES DE CANABIS

Dissertação apresentada ao Programa de Pós-Graduação em Odontologia da Universidade Federal do Rio Grande do Sul como requisito parcial para obtenção do título de Mestre em Odontologia, área de concentração em Clínica Odontológica/Periodontia.

Orientador: Prof. Dr. Cassiano Kuchenbecker Rösing

Porto Alegre - 2019

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DEDICATÓRIA

A mis padres, Rosario y Jorge, por quienes siento profundo orgullo y admiración, modelos a seguir en lo personal y en lo profesional.

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Ao meu colega e amigo Sebastian Pérez, pela sua enorme generosidade.

APRESENTAÇÃO

Esta dissertação é parte dos requisitos para obtenção do grau de Mestre em Odontologia, com área de concentração em Clínica Odontológica/Periodontia pelo Programa de Pós-Graduação em Odontologia da Universidade Federal do Rio Grande do Sul.

A participação de docentes da Universidad de la Republica (UDELAR), do Uruguay é fruto de uma colaboração entre a Universidade Federal do Rio Grande do Sul e da referida Universidade uruguaia, que se iniciou há mais de 10 anos e tem por objetivo a qualificação de docentes da UDELAR a partir da realização de um Programa Acadêmico. Mais de 20 titulações já ocorreram desse convênio e a presente dissertação é fruto do amadurecimento da colaboração, contando já com o auxílio de titulados da própria UDELAR na tutoria da mestranda.

A dissertação segue as normas da Universidade Federal do Rio Grande do Sul, sendo composta por elementos pré e pós-textuais, Introdução e Considerações Finais, em Português e de um artigo em língua inglesa a ser submetido no periódico Oral Diseases.

Sumário

Resumo

Antecedentes: A gengivite induzida por placa e a periodontite, são patologias muito prevalentes e a canabis é a droga psicoativa mais consumida. O número de países que legalizam a utilização recreativa da canabis é cada vez maior, porém, sabe-se pouco sobre algum possível efeito nos tecidos periodontais. Pela alta prevalência das doenças periodontais e o grande número de fumantes de canabis no mundo, passa a ser de fundamental importância estudar qualquer possível relação em profundidade.

Objetivo: Avaliar o estado periodontal em fumantes de canabis e compará-lo com o de não fumantes da droga.

Métodos: Os estudos elegíveis foram: estudos de coorte, caso-controle, transversais e série de casos. Assim como, estudos coincidentes com a seguinte estrutura: Population, Exposure, Comparison, Outcome (PECO); P: humanos dentados, E: fumantes de canabis, C: não fumantes de canabis, O: desfechos primários: definição de caso de Periodontite, perda de inserção clínica, profundidade da sondagem. Desfechos secundários: sangramento à sondagem/ inflamação gengival, índice de placa e cálculo. Foi feita uma busca eletrônica até maio de 2019 nas seguintes bases de dados: MEDLINE via PubMed, Cochrane Library, SCOPUS, BVS, LILACS e SciELO. Acrescente-se: Google Scholar, Science.gov, GreyLit, Open Grey e outras, além de uma busca manual.

Resultados: Foram revisados 2661 artigos, do quais 14 foram incluídos na análise qualitativa. Um dos estudos é prospectivo (de coorte) e dez são transversais, dos quais quatro são descritivos. Dados a partir do estudo de coorte evidenciam que os participantes que estão dentro do 20% de maior exposição tinham um risco superior de progressão de perda de inserção clínica (PIC). Três estudos de desenho transversal, que analisaram a ocorrência de periodontite, demostraram piores condições periodontais em fumantes de canabis, quando comparados com não fumantes da droga. Ao considerar fumantes de tabaco, um quarto estudo encontrou maior prevalência de periodontite em fumantes de canabis. O quinto estudo que avaliou o estado periodontal em consumidores de multi-drogas, reportou que todos os participantes tinham alguma forma de periodontite. Porém, um sexto estudo não encontrou associação entre o "uso regular da canabis" e PIC ≥3mm, independentemente da categoria de tabaco acessada. Finalmente, outros três

estudos de serie de casos também não detectaram associação entre fumar maconha e a periodontite.

A análise da qualidade dos estudos incluídos com a escala Newcasttle Otawa mostrou que três foram de qualidade alta, dois de qualidade moderada e seis de qualidade baixa.

Conclusão: Com base na evidência disponível, fumar canabis frequentemente pode ser prejudicial para os tecidos periodontais dependendo da dose; porém, é preciso aprofundar mais o conhecimento sobre o tema.

Palavras-chave: Canabis. Doenças e condições Periodontais. Epidemiologia

Abstract

Background: Plaque induced gingivitis and periodontitis are prevalent diseases and cannabis is the most widely consumed psychoactive drug. The countries/states legalizing the use of cannabis is on the rise, though little is known of a possible harm to periodontal tissues. Given the high prevalence of periodontal diseases and the number of people smoking cannabis around the world, it is of paramount importance to deeply study any relationship.

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

Methods: Eligible studies were: cohort studies, case-control studies, cross-sectional studies and case series. Also, those studies matching the following Population Exposure Comparison Outcome (PECO) structure: P: dentate humans, E: cannabis smoking, C: non-cannabis smokers, and O: Primary outcomes: periodontitis case definition, clinical attachment loss, probing depth; Secondary outcomes: bleeding on probing/ gingival inflammation, plaque index, calculus. An electronic search up to May 2019 was performed in MEDLINE via PubMed, Cochrane Library, SCOPUS, BVS, LILACS and SciELO databases. In addition, Google Scholar, Science.gov, GreyLit, Open Grey and other grey literature databases, were consulted and hand searching was also performed.

Results: 2661 records were screened, of which 14 articles were included in the qualitative analysis. One of the studies (comprising 4 articles) is a prospective cohort study and ten are cross-sectional. Data from the cohort study showed that participants at the highest 20% of exposure were at higher risk of clinical attachment loss (CAL) progression. 3 studies that analysed occurrence of periodontitis under a cross-sectional design generically demonstrated worse periodontal conditions in cannabis smokers when compared to non-cannabis smokers. Another study found an increased prevalence of periodontitis in cannabis smokers when tobacco smokers were considered. Also, another study analysed the periodontal status in multidrug consumers and found some form of Periodontitis in all of them. However, one did not find evidence for an association between "regular cannabis use" and CAL≥3mm, irrespective of the tobacco-smoking category considered. Additionally, 3 case series failed in associating smoking marijuana to periodontitis. Quality assessment of the included studies with the Newcasttle Otawa Scale showed that three of them were of high quality, two of moderate quality and six of low quality.

Conclusion: Based on the available data, frequent cannabis smoking could be detrimental for periodontal tissues and this could be dose-dependent; nevertheless, is desirable to deepen the knowledge on this topic even further.

Key words: Cannabis. Periodontal Diseases and Conditions. Epidemiology.

Introdução

A canabis é a droga ilícita (dependendo do país ou estado) mais utilizada. Segundo um relatório mundial sobre drogas do Escritorio das Nações Unidas sobre Drogas e Crime, a maior prevalência de consumo descrita vem da África central e ocidental, da América do Norte e da Oceania. (OPS, 2018)

Os produtos da canabis têm origem na planta Cannabis Sativa feminina, com pelo menos 750 compostos conhecidos, dos quais 104 são cannabinoides. Deles, os principais são o 9-tetrahidrocannabinol (THC), o cannabidiol (CBD) e o cannabinol (CBN), sendo o primeiro reconhecido por suas propriedades psicoativas e aparecendo em maior proporção quando a canabis é utilizada com fins recreativos. Dos outros componentes, o CBD, que pode modificar os efeitos psicoativos do THC, (OPS, 2018) é também reconhecido por suas propriedades anti-inflamatórias. (Sacerdote et al., 2005; Napimoga et al., 2009)

A partir de dados obtidos na Austrália, no Canadá e nos Estados Unidos, considera-se que os transtornos por consumo da canabis afetam entre 4% e 8% dos adultos ao longo da vida. A prevalência mundial de dependência de consumo da canabis é de 0.5%, com variações em base à população em estudo. Além disso, o consumo em longo prazo e em quantidades importantes está associado com problemas de saúde. (OPS, 2018, Fischer et al., 2017)

A canabis está legalizada no Uruguai e no Canadá, assim como em vários estados dos Estados Unidos (ex. Oregon). No Uruguai, em Janeiro de 2014 foi publicada a lei N° 19172 para a regulamentação e controle da canabis. Junto à lei, criou-se o Instituto de "Regulación y Control del Cannabis" (IRCCA) com a finalidade de regulamentar a plantação, cultivo, colheita, produção, processamento, armazenamento e distribuição da canabis. O número de pessoas registradas no mercado regulamentado pelo IRCCA em Janeiro de 2019 foi de 43694 entre os quais os meios de aquisição são: farmácias, clubes de associação e cultivadores domésticos. (IRCCA, 2019) A pesquisa da "Encuesta nacional en hogares sobre consumo de drogas" publicada em 2016 apontou que 6,5% da população relevada tinha consumido canabis nos últimos 30 dias. (IRCCA, 2019) No Brasil, 6.8% da

população adulta consumiu canabis pelo menos uma vez na vida e 2.5% consumiram durante o último ano de (2011-2012). (OPS, 2018; Laranjeira et al., 2012)

A forma mais comum de consumo da canabis recreativa é fumada, mas também é consumida mediante ingestão ou vaporização. Quando fumada, pode vir a ser misturada com tabaco. Em relação a isto, fumar canabis, associa-se com riscos para a saúde respiratória, pelos produtos de combustão, que são incrementados em caso de ser misturada com tabaco. (Fischer et al., 2017)

A gengivite induzida por placa e a periodontite, são patologias muito prevalentes. A periodontite severa é a maior causa de perda dentária, e afeta aproximadamente 11% da população mundial. (Tonetti et al., 2017)

Entre os efeitos que seguem ao consumo da canabis fumada, foi descrita a "boca seca" (OPS, 2018), condição que pode ser associada à dificuldade no controle do biofilm dental e maior inflamação gengival. (Murakami et al. 2018)

Considerando a alta prevalência de doença periodontal e as grandes quantidades de pessoas consumidoras de canabis no mundo inteiro, como também o impacto negativo do tabaco sobre os tecidos periodontais, é fundamental estudar em profundidade se há relação entre fumar canabis e as doenças periodontais. Com essa informação disponível seria possível criar estratégias apropriadas de atendimento e recomendações com base na evidência.

Periodontal status in cannabis smokers.

A systematic review

Authors: Mayol M., Pérez S., Andrade E., Bueno L., Rösing C.K.

Abstract

Background: Little is known of a possible harm of smoking cannabis to periodontal tissues. Given the high prevalence of periodontal diseases and cannabis smoking, it is of paramount importance to deeply study any possible relationship among them.

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

Methods: Studies eligible were: cohort studies, case-control studies, cross-sectional studies and case series. An electronic search was performed in MEDLINE via PubMed, Cochrane Library, SCOPUS, BVS, LILACS and SciELO databases. In addition, grey literature databases were consulted and hand searching was performed.

Results: 2661 records were screened, of which 14 articles were included in the qualitative analysis. 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 three case series. Three studies were of high quality, two of moderate quality and six of low quality.

Conclusion: Based on the available data, frequent cannabis smoking could be detrimental for periodontal tissues and this could be dose-dependent; nevertheless, is desirable to deepen the knowledge on this topic even further.

Clinical relevance: The authors recommend to include a cannabis behaviour assessment, past and present, in every medical record of young adult and adult patients.

Key words: Cannabis. Periodontal Diseases and Conditions. Epidemiology. Substance Abuse

Introduction

One of the most consumed recreational drugs is cannabis [1] 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. [2]

Recreational cannabis is commonly consumed by smoking a joint. Cannabis smoking was compared with tobacco smoking, as some smoke by-products might be similar in both cannabis and tobacco, and cannabis combustion temperature is higher than tobacco [3]. In contrast to this, due to their positive properties, cannabis products are consumed to prevent and treat many medical conditions [4, 5]. The number of countries/states legalizing recreational use of cannabis is on the rise, though little is known of a possible harm to periodontal tissues.

Plaque induced gingivitis and periodontitis are highly prevalent diseases. Severe periodontitis is the major cause for tooth loss [6] and affects approximately 11% of the world population [7]. Dry mouth is one of the symptoms described after cannabis consumption [2] and has been associated with difficulties in self-control of biofilm and increased gingival inflammation.[8]

Given the high prevalence of periodontal diseases and the number of people smoking cannabis around the world, as well as their implications on public health, it is of paramount importance to deeply study any relationship.

Objective

The main 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?

Methods

Eligibility criteria

Studies were eligible if they followed these inclusion criteria based on this 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) did the data extraction in 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 [9] for observational studies, with a maximum of 9 stars, and cross-sectional studies were assessed using the Newcastle-Ottawa scale modified by D. Zhao et al. (2018), with a maximum of 8 stars [10]. 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).

3- Results

The flow diagram of the review is presented 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, 2019 records (titles and abstracts) were screened, of which 1949 were excluded for not meeting the inclusion criteria. 70 full text articles were assessed for eligibility. From these, 56 were excluded for a variety of reasons (Table 1) and, finally, 14 articles were included in the quality analysis [11-24]. From these articles, one cohort study performed in Dunedin, New Zealand, over the course of 38 years was published in 4 publications. [11-14]

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. Therefore, their main results will be described in the text.

From the selected studies, one (comprising 4 publications) is a prospective cohort study and ten are cross-sectional, of which four are descriptive. Studies took part in Argentina, Australia, Chile, India, New Zealand, Peru (2), Puerto Rico, Saudi Arabia, Dominican Republic and the United States.

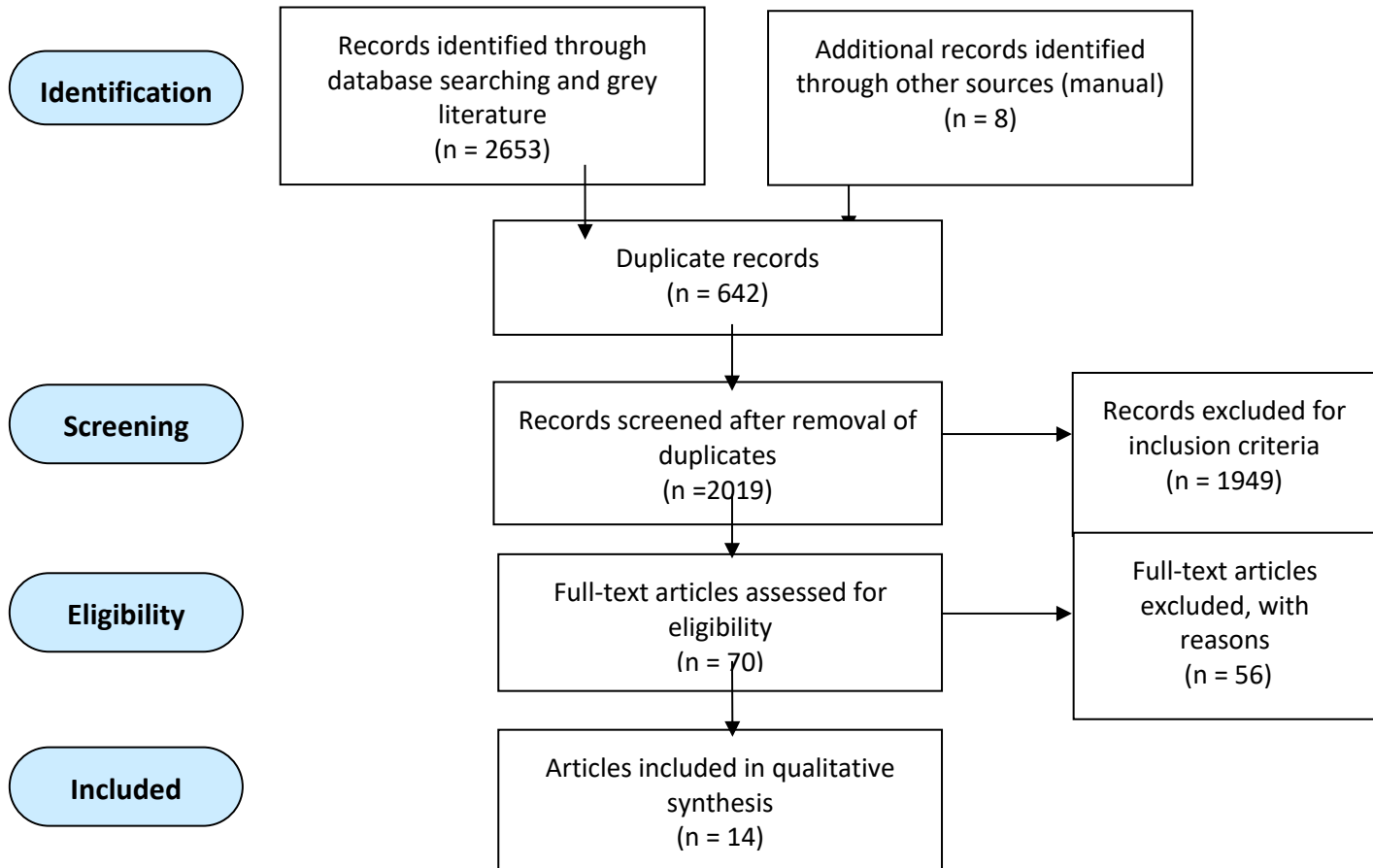Figure 1: Prisma® flow diagram of the search processes and results

Table 1 – Excluded articles with reasons

Main reason for exclusion	References
Study design	Aston R (1984); Brignardello-Petersen 2019; Mofidi et al. 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); Aston R (1984); Brezina J (1996); Chaparro-González (2018); Costa (2011); Darling (1993); Dedi'c A (2003); Ferreira de Brito (2018); Gibson G (2003); Gigena P (2012); Gigena P (2015); Gupta (2012); Heidari (2007); IADR (2017); Mateos Morenos (2015); Molendijk B (1996); Pilinova A (2003); Pourhashemi (2015); Ribeiro EDP (2002);Rodriguez Vazquez C (2002); Rooban Thavarajah (2008); Rooban Thavarajah (2006); Rotemberg E (2015); Ruiz Candina H (2015); Sandoval C (1992); Scheutz F (1984); Shapiro SS (1970); Sheridan J (2001); Stolz A(2002) Vainionpää R (2017)

Regarding the periodontal status assessment: one study only described the gingival status using the Löe & Silness Gingival Index and the O'Leary Plaque Index [15]. Three studies described the presence of periodontal pocket, attachment level, gingival recession, bleeding on probing, furcation involvement, tooth mobility and oral hygiene. [16, 21, 24] Three used the CDC-AAP definition of periodontal disease [18, 22, 23], another utilized Russell's Periodontal Index, [19] and the other three used different thresholds for periodontal disease related to the clinical attachment loss (CAL), as one or more sites with CAL ≥ 5 mm (categorical) and mean CAL (continue) [14], CAL ≥ 3mm [17], and CAL 1-2mm (mild), 3-4mm (moderate) and >5mm (severe) [20]. The latter also assessed bleeding on probing and plaque indices.

In terms of reproducibility, 5 studies reported having calibrated the examiner(s). [12, 17, 20, 22, 23] Exposure to cannabis was assessed in many different ways but always self-reported. No studies reported toxicological assays.

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.[13] In the article published by Meier et al. (2016) a mean attachment loss, within the whole sample, of 1.61 mm (SD=0.74) was reported. [14] Also, periodontal disease defined as 1+ site(s) with 5 or more mm of attachment loss was 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.

Table 2- Characteristics of the 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): 2.15 (1.20-3.85) Higher risk of periodontitis progression in 20% highest exposure vs. 80% lessor 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): 1.063 (1.010 to 1.119) and daily (Estimate (95%CI): 1.147 1.030 to 1.278)) cannabis users at 32y Higher attachment loss in cannabis-dependent participants (RR (95%CI, p): 1.11 (1.01, 1.24, p=0.046))
Barrios et al. 2009	Corrientes, Argentina	Cross-sectional, descriptive	Patients attending to the Chair Clinical Practice of Preventive I FOUNNE 91% males in exposed group	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: excesive consumers2.5, no consumers 0.9 PI: excesive 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 higyene level	PD ≥4mm: 13.3% CAL ≥5mm: 6.7%
Lopez et al. 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 ≥ 3mm	Multiple logistic regression analyses of the association between having regular use of cannabis, and the presence of CAL ≥3 mm, for each tobacco smoking status groups (OR (95%CI)): Non-smokers: 1.03 [0.3;3.4]; Occasional tobacco smokers: 1.27 [0.5;3.3] Daily tobacco smokers 0.77 [0.4;1.4]
Jamieson et al. 2010	Northern Territory, Australia	Cross-sectional	Aboriginal Birth Cohort, Royal Darwin Hospital	425	32.5%	48% M 52% F	16-20y	'how much marijuana do you smoke'? (1) 'never or only tried it once'; (2) 'used to smoke, but not any more'; (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 et al. 2012	Bangalore, India	Cross-sectional	n= 250 various deaddiction centres n= 250 "general population"	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: 2.514 Mean RPI: 3.186 Mean BoP: 14%
Kayal et al. 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 exposure performed	BoP, Silness-Loe PI , Gingival Recession, PD, CAL: mild (1-2 mm), moderate (3-4 mm) or severe (≥ 5mm)	PI: 1.83 ± 0.73 BoP (%) :42.56 ± 31.4 CAL aprox.: severe 14%; moderate 48%; mild 38%
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 ≥ 4mm: 26.5% GR: 75.5% Tooth mobility: 22.5% Furcation involvement: 14.3%

Author	Country	Study design	Setting / Data source	N	Prevalence	Sex	Age	exposed group / non-exposed group	Case definition / Measures	Results
Nuñez 2016 (thesis)	San Francisco de Macoris, Dominican Republic	Cross-sectional, descriptive	San Francisco de Macoris, Dominican Republic	40	50%	43% M 37% F	18 - 40 y	exposed group non-exposed group	PD, CAL, BoP, suppuration, furcation involvement, tooth movility, O Leary PI, radiographic marginal bone level	Exposed: bad OH: 90% BoP: 466 sites PD: 2.63 mm CAL: 2.39mm
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 to 3.2)
Ortiz et al. 2018	San Juan, Puerto Rico	Cross-sectional	San Juan Overweight Adults Longitudinal Study (SOALS)	735	2.7% "Frequent"	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) 2.93 (1.08-7.96)

References: exp.: exposed BoP: Bleeding on Probing. 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

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.[14] 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. [12]

Before treatment, Barrios (2009) observed higher gingival inflammation in marijuana consumers than in non-consumers. Mean Löe & Silness Gingvial Index in low, moderate and severe consumers was 1.3, 2 and 2.5 respectively, while in non consumers they found a mean Löe & Silness index of 0.9. Mean Plaque O´Leary index in moderate (38.9%) and severe (48.1%) consumers was higher than in low (24.4%) and non-consumers (35.6%). [15]

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% of them moderate, and 6.7% severe. In the latter category poor oral hygiene was present in all of them. 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. [16]

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 ≥ 3mm. 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 do not show association between either "ever use of cannabis" or "regular use of cannabis" and CAL≥3mm, regardless the tobacco-smoking category considered. [17]

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% (25.5–39.5); while in non-marijuana consumers (n=256) the prevalence of periodontal disease was 22.7% (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. [18]

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), a significant difference (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. [19]

Kayal et. al. (2014) found, in 38 individuals exposed to cannabis, a mean Silness & Löe Plaque Index of 1.83 ± 0.73 and a mean percentage of bleeding sites of 42.56% ± 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 (≥5mm). 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. [20]

Verástegui (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. [21]

In the study performed by Nuñez Cuello (2016) it was described that 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 2.63mm and 2.39mm respectively, in the non-exposed group these values were 2.46mm and 2.03mm respectively. [24]

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 1.6mm (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 to 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 aOR of 1.9 (95% CI: 1.1 to 3.2; P = 0.03). [22]

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.[23]

Quality assessment of the included studies is shown in Tables 3 and 4. Three of them were of high quality [14, 17, 22], two showed moderate quality [18, 23] and six were of low quality [15, 16, 19-21, 24].

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

Study	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 et al. 2009	*	*	-	*	**	*	*	7
Garay et al. 2009	-	-	-	-	-	*	-	1
Barrios et al 2009	-	-	-	-	-	*	-	1
Jamieson et al. 2010	*	-	-	*	**	*	*	6
Reddy et al 2012	-	-	*	-	*	*	*	4
Kayal et al. 2014	-	-	-	-	*	*	-	2
Verástegui et al. 2016	-	-	-	-	-	*	-	1
Nuñez 2016	-	-	-	-	-	-	-	0
Shariff et al. 2017	*	*	-	*	**	*	*	7
Ortiz et al. 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	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow up of cohorts	
Thomson 2008, 2013, Zeng 2014, Meier 2016,	*	*	*	*	**	*	*	*	9

4- Discussion

The present study was conceived in order to understand the possible role of exposure to cannabis smoking on periodontal health. Therefore, a systematic review, using contemporary guidelines (MOOSE), [25] was conducted. The results indicate a possible worsening of periodontal health in cannabis smokers.

In the beginning, 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.

Cannabis smoking is a habit of different populations and several aspects have been under study, from negative impacts on health [26] to medical benefits. Studies concerning the effects of cannabis compounds on different parts of the body also present controversial results, as many benefits were reported.[4]
One important aspect in these studies is that there is a clear difference between how cannabis is consumed and how it is studied. Animal-model studies demonstrated an

anti-inflammatory response to cannabidiol [27, 28], while from another it is reported that cannabis inhalation could deteriorate periodontal tissues [29]. Recently, Liu et. al. (2019) demonstrated that stimulation of cannabinoids receptors type 2 (CB2) was associated with cell adhesion, thus increased migration of periodontal ligament fibroblasts. This suggests a putative role of cannabinoids on periodontal wound healing and regeneration [30]. Also, it was described that CB2 could participate in the modulation of the inflammatory response within periodontal tissues.[31]

The use of cannabis might be by means of smoking or, in some cases, by other applications, such as ingested or topical, for recreational or medical purposes. The greatest interest in terms of periodontal diseases is how the use of smoked cannabis could affect periodontal tissues.

The number of countries/states that have legalized recreational cannabis is increasing [1], though little is known about any specific harm on periodontal tissues so far. How tobacco smoking affects the periodontal support has been extensively studied [32] and most cannabis users also smoke tobacco [33].

Cannabis was compared to tobacco in relation to carcinogenic risk, reporting that the former does not show carcinogenic properties [34], but this is still controversial. [35]

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 were also accepted. Recently, the Joint Workshop for Classification of Periodontal and Peri-Implant Diseases and Conditions [36] 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 were published associating cannabis and periodontal disease, concluding that there could be a role of its exposure in periodontal breakdown. [37, 38] One of them [38] is 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 was included with only marginal gingival parameters [15] and two theses [16, 24]. The other systematic review on this topic [37] evaluated the association between oral health and substance abuse. Here, studies on any drug abuse were included.

The 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 [11-14, 17, 23]. Regarding sample characteristics, four studies took place in drug rehabilitation centres/clinics [16, 19-21], one at a university dental clinic [15], and another obtained data from an overweight adult population [23]. Also, it has to be noted that in the study carried out by Lopez et al. (2009) [17], the participants were between 12 and 21 years old, with the majority of the individuals matching the age range 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.[15, 16, 19-21, 24]

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 of the study have different approaches and the main results are that cannabis use is related to clinical attachment loss in 32-year-old or older subjects [13], and that clinical attachment loss has a higher progression rate in the 20% of individuals who use more cannabis [12].

Another study that deserves highlight is the study by Barrios, which looked at plaque and gingival inflammatory status. In that study, individuals exposed to cannabis

presented a higher degree of gingival inflammation, despite the absence of differences in plaque. [15] A longitudinal approach would allow 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. [14, 20] This could reflect in persistent worse oral hygiene, not depicted in the single examination performed.

In summary, 3 of the 10 studies that analysed occurrence of periodontitis under a cross-sectional design generically demonstrated worse periodontal conditions in cannabis smokers when compared to cannabis non-smokers.[19, 22, 23] Another study, found an increased prevalence of periodontitis in cannabis smokers when tobacco smokers were considered.[18] However, when only tobacco non-smokers were taken into consideration, such association between cannabis and periodontitis was not seen. Additionally, Lopez et al. (2009) didn't find such worse conditions, in adolescents, when comparing one group to the other. In accordance with this, Garay et al. (2009) failed in associating smoking marijuana to periodontitis, since only 13.3% of marijuana users had periodontal pocket. 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. [16, 21]

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 severer forms of periodontitis.[20]

Nuñez Cuello (2016), in her thesis work concludes that exposed subjects have worse periodontal conditions. Although, differences in probing depth (0.17 mm) and clinical attachment level (0.36 mm) between groups don't seem to be clinically relevant.

Inconsistencies between studies regarding the exposure registration were seen. Apart from being self-reported, those inconsistencies could lead to the actual level of consumption being masked; categories are 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 main studies [18, 22, 23] the widely accepted AAP/CDC periodontitis case definition was utilized. Although, in the DMHDS periodontal disease was defined as 1+ site(s) with 5 or more mm of attachment loss. This could overestimate the prevalence of the disease given causes for attachment loss other than periodontitis, (i.e.: gingival recession or cervical decay).

Case definitions for epidemiological purposes reported on consensus reports of workgroups of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions could be elements in favour of the comparison between future studies. [39-41]

To conclude, based on the available data, frequent cannabis smoking could be detrimental for periodontal tissues and this could be dose-dependent; nevertheless, is desirable to deepen the knowledge on this topic even further. Larger sampled longitudinal studies including long-term cannabis smokers, and stratified for Periodontal Diseases' etiologic factors and risk factors/indicators, specifically age, biofilm control and tobacco, are needed to support this asseveration. Also is important to report 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.
Clinical relevance: The authors recommend to include a cannabis behaviour assessment, past and present, in every medical record of young adult and adult patients.

Compliance with Ethical Standards

Conflict of Interest: The authors declare that they have no conflict of interest.

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Considerações Finais

Nos últimos anos, países como o Uruguai e o Canadá, assim como nove estados dos Estados Unidos (ex. Oregon, Califórnia, Massachussets), legalizaram o uso recreativo da maconha.

Os produtos derivados da planta *Cannabis sativa* vêm sendo utilizados com vários propósitos ao redor do mundo desde épocas antigas. É possível que a utilização com fins recreativos, por seus componentes psicoativos (principalmente THC), seja a mais polêmica por ter associada comorbidades e consequências que prejudicam a saúde de quem a consome em curto e em longo prazos.

Considerando que a canabis recreativa é mais consumida em forma de fumo, que o tabaco é um fator de risco de periodontite e que ambos compartilham produtos de combustão, surge a interrogativa de se a canabis fumada pode influenciar de alguma forma no desenvolvimento da periodontite, em sua progressão ou de alguma forma de doença ou condição periodontal.

Foi realizada uma revisão sistemática com o objetivo de conhecer o estado de saúde/doença periodontal em fumantes de canabis. Foram encontrados 11 estudos nos quais reportam-se parâmetros periodontais de fumantes de canabis, mas com ampla heterogeneidade entre eles, fato que dificulta a comparação direta.

Idealmente são necessários estudos longitudinais com grupo exposto e controle, assim como estratificação adequada para os fatores de risco de doenças periodontais. Também é preciso conhecer a composição do produto da canabis e detalhes sobre a frequência e a quantidade de consumo. Neste aspecto, o Uruguai se encontra em uma posição de vantagem devido às normas de regulamentação com relação à produção, venda, quantidade dispensada por pessoa e registro dos consumidores.

O Artigo 1 da Lei N° 19172 de regulamentação e controle da canabis no Uruguai declara "de interesse público as ações tendentes a proteger, promover e melhorar a saúde pública da população mediante uma política orientada a minimizar os riscos e

reduzir danos no uso da canabis, que promova a devida informação, educação e prevenção sobre as consequências e efeitos prejudiciais vinculados ao consumo (...)".

Desta forma, compete ao Estado Uruguaio e à comunidade científica perante a sociedade, aprofundar no conhecimento sobre eventuais riscos que possam acompanhar o consumo da canabis recreativa.

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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	24 (13 rev 1 protocols 10 trials)

	sectional" or cross*) and (preval* or frecuen*) #6 (#1 or #2) and #3 and #4 and #5	
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
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 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 ((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 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) #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)
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	36 19 revs 1 protocol 16 trials

	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	

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
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)	(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	74 LILACS (58) IBECS

CUMED (2) BBO - odontología (Brasil) (1)	maría or hierba or grifa or hachís))	(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)	("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	3
	("Marijuana periodontal") https://doaj.org/search?source=%7B"query"%3A%7B"query_string"%3A%7B"query"%3A"Marijuana%20Periodontal"%2C"default_operator"%3A"AND"%7D%7D%2C"from"%3A0%2C"size"%3A10%7D	3
Google Schoolar (2009-2019)	(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	First 995 from 2720
University of British Columbia	("Cannabis Periodontal observational") http://ubc.summon.serialssolutions.com/search?spellcheck=true&s.q=Cannabis+Periodontal#!/search?ho=t&fvf=ContentType,Journal%20Article,f&l=en&q=Cannabis%20Periodontal%20observational	44
GreyLit	(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	37
Open Grey	(Marijuana) http://www.opengrey.eu/search/request?q=Marijuana	37
ADA center for evidence-based dentistry	(Marijuana) http://ebd.ada.org/en/search-results#q=Marijuana&sort=relevancy&f:adasites=[ADA%20Center%20for%20Evidence-Based%20Dentistry%20(EBD)] (Cannabis)	2 0
Science.gov (Información científica federal de USA)	("Marijuana AND) periodontal)") https://www.science.gov/scigov/desktop/en/results.html	108
Ontario Public Health Association	"Marijuana periodontal" http://www.opha.on.ca/Utility-Pages/Search-Results.aspx?searchtext=Marijuana+Periodontal&searchmode=anyword	3
	"Cannabis Periodontal" http://www.opha.on.ca/Utility-Pages/Search-Results.aspx?searchtext=Cannabis+periodontal&searchmode=anyword	17