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Association of marijuana use with oral HPV infection and periodontitis among Hispanic adults: Implications for oral cancer prevention

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Abstract

Background: Despite limited data, research suggests that marijuana use is associated with oral HPV infection and periodontitis, two potential oropharyngeal cancer risk factors. We assessed these associations in a Hispanic adult population in Puerto Rico.

Methods: A cross-sectional study of 735 adults assessed marijuana use, determined through an audio computer-assisted self-interview, and periodontitis and self-collection of oral HPV samples following the National Health and Nutrition Examination Survey methodology. The Centers of Disease Control and Prevention/American Academy of Periodontology definition was used for periodontitis. HPV typing was performed using polymerase chain reaction with modified L1 consensus primers (MY09/MY11).

Results: 26.5% of adults reported lifetime use of marijuana, 2.7% were frequent users (lifetime use ≥ 6 times, past year use ≥ 6 times, and past 30-day use ≥ 2 times), 5.7% had oral HPV infection, and 20.1% had severe periodontitis. The multivariate logistic regression analysis showed that frequent marijuana users were more likely to have severe periodontitis (OR=2.91, 95%CI= 1.06 – 7.96) than never/once lifetime users after adjusting for age, sex, healthcare coverage, smoking, binge drinking, number of oral sex partners, and oral HPV infection. However, frequent marijuana use was not associated with oral HPV infection.

Conclusion: Marijuana use was associated with periodontitis, but not with oral HPV infection. Further evaluation of the role of marijuana use in oral HPV infection and periodontitis may inform novel preventive public health strategies, as marijuana users could be at increased risk of oral cancer.

One-sentence summary:

Frequent marijuana use was associated with severe periodontitis, but not with oral HPV infection in an adult Hispanic population.

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Keywords

Periodontitis; marijuana; oral cancer; HPV

Introduction

Marijuana contains more than 60 active ingredients called cannabinoids. The cannabinoid 1-delta-9-tetrahydrocannabinol (THC), the psychoactive component in cannabis, has a depressant effect that may increase susceptibility to infections¹. Cannabinoids also seem to attenuate the production of some inflammatory mediators^{2,3}. In addition, marijuana smoke delivers harmful substances to users, similar to those found in tobacco smoke¹. These substances may impair the immune response and compromise the healing ability of the periodontal tissue, as occurs with tobacco smoking⁴. Consistent with this biological plausibility, recent studies suggest that marijuana use may be associated with oral human papillomavirus (HPV) infection⁵ and periodontitis^{6,7}.

Oral HPV infection has been associated with a subset of oropharyngeal squamous cell carcinomas (OPCs)⁸, being HPV-16 responsible for 87% of HPV-positive OPCs⁹. During 2011–2014, the prevalence of oral HPV infection among adults aged 18–69 years in the U. S. National Health and Nutrition Examination Survey (NHANES) was 7.3% for any type and 4.0% for oncogenic or high-risk (HR) types; men had higher prevalence of oral infection (11.5% for any HPV type and 6.8% for HR types) than women (3.3% for any type and 1.2% for HR types)¹⁰. HPV-related OPC is increasing significantly and is expected to exceed the annual cervical cancers cases by the year 2020 in the United States¹¹. Most common risk factors for oral HPV infection are male gender, high number of sexual partners, and current smoking¹².

Periodontitis is an inflammatory disease that affects the soft and hard structures that support the teeth, in which the gums pull away from the tooth and supporting gum tissues are destroyed¹³. Periodontitis has also been associated with oral cavity, oropharynx, and larynx squamous cell carcinomas¹⁴. During 2009–2012, prevalence of periodontitis in the United States was 46%, with 8.9% of adults aged 30 years or older having severe disease¹⁵. It has also been suggested that periodontitis may facilitate HPV acquisition and persistence¹⁶ and thus may be involved in the etiology of OPCs, supporting the potential role of oral HPV infection and chronic local inflammation in OPC risk. Major common risk factors for periodontitis include age, genetics, smoking, physical inactivity, diet, and obesity¹⁵.

Although some research studies suggest that marijuana use may be a risk factor for both oral HPV infection and severe periodontitis, results are inconclusive. Among 2009–2010 NHANES participants aged 30 to 59 years, oral HPV infection was two-fold (OR:1.92, 95%CI: 1.07–3.44) higher in current (those who had use it at least once in the last 30 days) marijuana users than in never users⁵. However, Gillison et al. found higher prevalence of oral HPV infection in current marijuana users in crude (Prevalence Ratio= 2.87, 95% CI=1.85–4.46), but not in multivariate analysis among adults aged 14 to 69 years¹². Similarly, marijuana use was not independently associated with oral HPV infection in HIV-positive and HIV-negative patients with oral lesions, although marijuana use was defined as

never versus ever use¹⁷. With respect to periodontitis, the U.S. NHANES 2011–2012¹⁸ and a cohort study in New Zealand⁶ reported positive associations between increased cannabis use (marijuana and hashish) and cannabis smoking, respectively, and periodontitis. Nonetheless, a study among young Chilean adolescents showed no association of cannabis use and periodontitis¹⁹, although young individuals have a lower risk of periodontitis and less likely to have had long-term exposure to cannabis. To elucidate the inconsistency in findings, additional studies assessing the association between marijuana use, oral HPV infection, and periodontitis are needed, as identification of modifiable risk factors are necessary to develop adequate preventive strategies for OPC control.

Despite the availability of various studies in this complex area, some of these are limited in sample size and lack of racial diversity, findings are somewhat inconsistent, only some have considered frequency of marijuana use, and most have not focused on marijuana use as the main exposure^{5–7,12,17–19}. Thus, we aimed to assess if there is a positive association between marijuana use and periodontitis, and between marijuana use and oral HPV infection among a sample of Hispanic adults.

Materials and Methods

Study design and study population.

The present study analyzed data from a cross-sectional study that evaluated the association between oral HPV infection and periodontitis. The study group consisted of participants of the San Juan Overweight Adults Longitudinal Study (SOALS), which recruited overweight/obese adults aged 40–65 years in Puerto Rico between 2011 and 2013^{20,21}. The recruitment in the parent study was performed by different strategies (e.g. flyers, mass-media communications, and word of mouth). Exclusion criteria included a history of clinically diagnosed diabetes, less than four natural teeth, a history of conditions that increase the risk of systemic complications during a periodontal exam, and inability to complete study procedures. Participants were also excluded if their fasting, two-hour glucose, or HbA1c levels met the American Diabetes Association thresholds for diabetes at the baseline exam²². SOALS participants who came to the follow-up examination visit between September 2014 and May 2016 were invited to participate in the present study (n=773) and 99.7% accepted to undergo the procedures. A total of 24 participants were excluded from the analysis due to incomplete HPV collection (n=4) or periodontitis evaluation (n=20), seven because of unsatisfactory HPV results in the laboratory (samples negative for β -globin gene amplification), and five due to missing information on marijuana use; the remaining 735 (95% of recruited participants) were included in the present analysis. The study was approved by the Institutional Review Board of the University of Puerto Rico Medical Sciences Campus, and written informed consent was provided by all subjects.

Periodontitis assessment:

Full mouth clinical exams were conducted using a modified version of the NHANES procedures by one examiner (JV) who had been previously trained and calibrated by the reference examiner (Dr. Bruce Dye). Periodontitis was assessed by clinical measurements of probing depth (PD) and clinical attachment loss (AL) at six sites (disto-buccal, mid-buccal,

mesio-buccal, disto-lingual, mid-lingual, and mesio-lingual buccal) for all teeth, excluding the third molars. All measurements were taken with a periodontal probe (Hu-Friedy, Chicago, IL, USA, product number PCP2) and rounded off upwards to the nearest millimeter. The Centers for Disease Control/American Academy of Periodontology (CDC/AAP) working definition was used to define severe periodontitis (2 interproximal sites with AL 6 mm (not on the same tooth) and 1 interproximal site with PD 5 mm), moderate periodontitis (2 interproximal sites with AL 4 mm (not on the same tooth) or 2 interproximal sites with PD 5 mm (not on the same tooth), and no or mild periodontitis (as neither “moderate” nor “severe” periodontitis)²³.

Collection of oral HPV specimens using oral rinse.

After proper orientation by study personnel, participants self-collected oral rinse samples using the NHANES methodology²⁴ for HPV detection and typing; details of oral HPV collection procedures have been described in detail elsewhere²⁵. A 50 mL sterile collection cup filled with 10 mL of mouthwash was given to participants. After removing any gum from their mouths, participants were asked to rinse/gargle the mouthwash for 30 seconds, and spit it into the collection cup. Samples were transferred to a 15 mL tube and centrifuged at 4200 rpm for 10 min. After centrifugation, the supernatant was discarded and the pellet was re-suspended with 10 mL of saline solution [Phosphate Buffer Saline (PBS) 1X]. Samples were then centrifuged for a second time at 4200 rpm for 10 minutes and after discarding the supernatant, the remaining pellet was re-suspended with 1 mL of saline solution (PBS 1X). The re-suspended whole pellet was then transferred to a pre-identified 2.0 mL micro-tube and stored at –80°C until shipment to the HPV Virology Core Laboratory at the University of California in San Francisco.

DNA extraction/HPV Detection and Typing.

HPV typing was performed at UCSF using polymerase chain reaction (PCR) with modified L1 consensus primers (MY09/MY11). After thawing, the samples were processed for DNA using the Gentra Puregene Buccal Cell Kit (QIAGEN) following manufacturer’s instructions. Five microliters of sample were used for PCR amplification using the standard 40 cycle protocol²⁶; PCR is a highly sensitive method for the detection of HPV DNA^{27,28}. PCR products were typed by dot-blot hybridization using 38 type-specific probes, including oncogenic HR HPV types as defined by The International Agency for Research on Cancer (IARC, 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 66)²⁹ and other non-oncogenic types (6/11, 26/69, 30, 32/42, 34, 53, 54, 57/2/27, 61, 62, 67, 68, 70, 71, 72, 73, 81, 82, 83, 84, 85, 86/87, 90/106, 97, 102/89, and 2 separate mixtures: mix1 (7/13/40/43/44/55/74/91) and mix2 (3/10/28/29/77/78/94). A sample was considered HPV positive if it was positive for the consensus probes or any specific HPV type probes. Controls consisted of amplification of solution containing all the above components except for sample DNA, or DNA from cell lines with and without HPV.

Assessment of marijuana use:

Participants completed an audio computer-assisted self-interview to gather information on drug use. Marijuana use was defined as no use (never/once in lifetime), occasional use, and frequent use. Frequent marijuana use was defined as having consumed marijuana 26 times

during the lifetime, 6 times during the past year, and 2 times during the past 30 days; the remaining participants were classified as occasional users.

Assessment of potential confounders:

Demographic, clinical, and behavioral characteristics were collected by the parent study using face-to-face interviews, and sexual behaviors were collected using an audio computer-assisted self-interview. These variables were collected given their relevance as risk factors for oral HPV infection¹² and/or periodontitis¹⁵. Covariates included gender (male, female), age (41–54, 55 years), education (<12, ≥12 years), income (<\$20,000, ≥\$20,000), and health insurance (private, public, none). Clinical characteristics included obesity [obese if body mass index (BMI) ≥30 kg/m², non-obese if BMI <30 kg/m²]³⁰, abdominal obesity (at risk if waist circumference in men >102 cm and if waist circumference in women >88 cm, not at risk if below these thresholds)³⁰, impaired glucose metabolism (fasting glucose ≥100 mg/dl, 2-hour post load glucose ≥140 mg/dl, or HbA1c ≥5.7%)²², dental visits in the past three years (yes, no), and periodontal treatment in the past three years (yes, no). Behavioral characteristics included current smoking (yes/no), binge drinking (5 or more drinks on a single occasion for men or 4 or more drinks on a single occasion for women in the last 30 days), and lifetime number of oral sex partners (0–5, ≥6).

F. Statistical analysis.

Frequency distributions were used to describe sociodemographic, clinical, and behavioral characteristics of study participants. Contingency tables, chi-square statistics, and Fisher's exact test were used to describe the associations of marijuana use and other covariates with oral HPV infection and periodontitis severity. Separate multivariable logistic regression models were fitted to evaluate the associations of marijuana use with oral HPV infection and severe periodontitis. The models were adjusted by covariates significantly associated ($p < 0.05$) in the bivariate analysis to both oral HPV infection and periodontitis and other relevant variables in the literature. The statistical package Stata for Windows, version 14 (Stata Corporation, College Station, TX) was used for data management and statistical analyses.

Results

Univariate analysis.

Mean age of participants was 53.4 ± 6.6 years, 72.4% were women, and 18.4% were current smokers (Table 1). Overall, 26.5% of study participants had ever consumed marijuana during their lifetime and 10.1% had consumed it on at least 26 occasions. Less than 10% reported marijuana use at least twice (7.1%) during the past 12 months and past 30 days (3.9%). Overall, 2.7% were frequent marijuana users, and 5.7% of persons had oral HPV infection. According to the CDC/APP definition²³, 39.5% had moderate periodontitis and 20.1% had severe periodontitis.

Bivariate analyses.

Although age was not associated with oral HPV infection in bivariate analysis, men (10.3%) had higher prevalence of oral HPV infection as compared to women (3.9%) ($p=0.001$), as well as did persons with no health care coverage (12.7%) as compared to those with private

(4.1%) and public (6.6%) health insurance ($p=0.026$). Prevalence of oral HPV infection was also higher among persons with severe periodontitis (11.5%) as compared to those with moderate (4.1%) or none/mild (4.4%) disease ($p=0.003$). Among lifestyle characteristics, persons with at least 6 lifetime number of oral sex partners had higher prevalence of oral HPV infection (12.3%) as compared to their counterparts (4.0%) ($p<0.001$). Meanwhile, the prevalence of oral HPV infection increased from 4.1% among non-users to 10.0% among frequent marihuana users, respectively ($p=0.006$).

For periodontitis, men had higher prevalence of moderate (45.6% vs. 37.1%) and severe (30.4% vs. 16.2%) periodontitis as compared to women ($p<0.001$). Adults in the older age group also had higher prevalence of moderate and mild periodontitis than their counterparts ($p<0.001$). Lower education and lower annual income were also positively associated with severity of periodontitis ($p<0.05$). Participants without health insurance (29.1%) and with public health insurance (27.2%) had higher prevalence of severe periodontitis than persons with private health care coverage (13.6%) ($p<0.001$). The prevalence of severe periodontitis was also higher in persons with oral HPV infection (40.5%) than in those without infection (18.9%). Current smoking, binge drinking and having 6 lifetime number of oral sex partners were all positively associated with periodontitis severity in bivariate analyses ($p<0.05$). Finally, the prevalence of severe periodontitis increased from 17.0% among non-marihuana users, to 25.7% in occasional users, to 55.0% among frequent users ($p<0.001$).

Multivariable analysis.

Although occasional marijuana users were more likely to have oral HPV infection as compared to non-users in bivariate analysis, no significant association was observed between marijuana use and oral HPV infection was observed in multivariable analysis adjusting for sex, age, healthcare coverage, oral sex partners and periodontitis (Table 3). On the other hand, occasional (OR=1.69, 95% CI=1.12–2.53) and frequent (OR=5.95, 95% CI=2.40–14.77) marihuana users had significantly increased odds of severe periodontitis. However, only frequent marijuana users had increased odds of periodontitis (OR=2.91, 95% CI=1.06–7.96) as compared to non-users after adjusting for sex, age, healthcare coverage, current smoke, binge drinking, oral sex partners, oral HPV infection, and dental visits (Table 3).

Discussion

This study evaluated the association of marijuana use with oral HPV infection and periodontitis in a Hispanic adult population. Overall, 5.7% of the study population had oral HPV infection, 20.1% had severe periodontitis, 23.8% were occasional marihuana users, and 2.7% were frequent users. Our results evidenced an association between marijuana use and severe periodontitis, but not with oral HPV infection. The lack of statistical association between marijuana use and oral HPV infection in multivariable models adjusting for HPV risk factors, including gender and number of oral sex partners¹², highlights the relevance of these other known risk factors, rather than marijuana consumption, on oral HPV infection. Although our definition of marijuana consumption is limited in its determination of frequency of use throughout the life course, which may have an impact on study findings, our study result is consistent with other previous studies. A study of young adults aged 19–

35 years that evaluates ever illegal drug use, including cannabis³¹, in which the authors suggested that the absence of a statistically significant association may be attributed to the low prevalence of oral HPV infection in the study sample (4.0%) and lack of statistical power. Two previous studies in Puerto Rico did not find an association between marijuana use and oral HPV infection among drug users³² and men from an STI clinic³³, although frequency of marijuana use was not assessed in these analyses. However, the analysis performed in adults aged 30 to 59 years using the 2009–2010 NHANES data found that current marijuana use was independently associated with oral HPV infection⁵. Similarly, a hospital-based case-control study reported an association between oral HPV-16 infection and current marijuana use (OR=4.7, 95% CI: 1.3–17.0)³⁴ among patients diagnosed with HPV-16 – positive head and neck squamous cell carcinomas.

According to the CDC/APP definition²³, 39.5% of study participants had moderate periodontitis and 20.1% had severe periodontitis. Meanwhile, a strong association (close to 3-fold) between frequent marijuana use and severe periodontitis was evidenced, even after adjusting for various confounders, including tobacco, age, and other periodontitis risk factors. This result is consistent with the NHANES 2011–12 cross-sectional study (n=1,938) among adults in which the authors reported that frequent users of cannabis (marijuana and hashish) at least once per month for the last 12 months had higher odds of having severe periodontitis in comparison to their counterparts¹⁸. Similarly, a prospective cohort study in New Zealand⁶ found that young individuals in the some exposure of cannabis group (RR=1.47, 95%CI: 0.87–2.47) and in the high exposure group (>40 times, RR=2.15, 95%CI: 1.20–3.85) had increased risk of periodontitis compared to those in the no exposure group, independent of tobacco consumption⁶.

The mechanism in which the use of marijuana affects the risk of HPV is unclear. It is known that the virus can lodge in the surface of the mouth, the linings of the lips or the tongue³⁵. A possible route of transmission for HPV can be through sharing a rolled cigarette or pipe in a group setting³⁵. Meanwhile, various mechanisms have been proposed for the potential link between marijuana and periodontitis. First of all, it is known that cannabis users have lesser oral health than the general population, including less healthy gingiva^{36,37}. Some of the acute symptoms that cause the marijuana use in the mouth are irritation of the oral epithelium, which is one of the symptoms of periodontal disease. Additionally, chronic use of marijuana may produce a chronic inflammation of the oral epithelium, which can progress to neoplasia³⁶. In addition, THC, the most potent cannabinoid in cannabis, has an immunosuppressive effect through the cannabinoid receptor type 2 found in immune cells³⁸. THC can potentially propagate change of oral microbiota altering the immune response³⁸. Gingival enlargement occurs mainly in the marginal and papillary part of the mouth³⁹, possibly due to smoke accumulation³⁹. Research has also found that frequent marijuana use could lead to cytokine suppression in periodontitis, supporting the potential local immunosuppressant role of marijuana use⁴⁰. In addition, animal models have shown that marijuana smoke may affect alveolar bone by increasing bone loss in rats with ligature-induced periodontitis⁴¹. Further research of the biological mechanisms of this association are warranted.

Given the increased acceptance and legalization of marijuana use worldwide, further understanding of the beneficial therapeutic and detrimental effects on human health is of great relevance. In fact, researchers have suggested that changing patterns of marijuana legalization world-wide have led to a need to conduct further studies assessing the association between marijuana use and cancer risk⁴². With respect to oropharyngeal cancer, marijuana use has been reported as a potential risk factor for this malignancy⁴³. Although our results did not evidence an association between marijuana use and oral HPV infection, a strong association was observed between marijuana use and periodontitis. Given that periodontitis has been suggested as a potential risk factor for oropharyngeal cancer^{40,43}, our study results may have implications for oral cancer prevention, as marijuana users may need periodontitis screening and treatment as a way to prevent oral cancer risk among them. Thus, longitudinal well-powered studies on these associations are warranted to better conclude on the links and potential interactions of these risk factors (marijuana use, periodontal disease, and oral HPV infection) with oropharyngeal cancer risk.

Our study has several limitations. First, marijuana use and frequency was based on self-report, which is often under-reported and subject to recall bias. Marijuana was defined in terms of frequency of use, but we did not collect amount of marijuana consumed, route of consumption (inhaled vs. oral), and duration of use and time when they quit. Also, a temporal association between marijuana use and periodontal disease and oral HPV infection could not be established because of the cross-sectional nature of the study. Also, the low prevalence of frequent marijuana use and oral HPV infection limited the statistical power of this study to detect a significant association between marijuana use and oral HPV infection. In addition, given that many marijuana users were ever smokers, analysis of the association among never smokers was not performed due to the limited sample size. Finally, the lack of uniformity in defining marijuana use across studies may lead to conflicting results and limits comparability of study findings.

Conclusion

Despite these limitations, we conclude that marijuana use was strongly associated with severe periodontitis in this Hispanic adult population, but not to oral HPV infection. Further evaluation of the role of frequent marijuana use in oral HPV infection and periodontitis, as well as on the interaction of these factors on OPC risk, may inform novel preventive public health strategies, as marijuana users could be a potential target for oral health screening and intervention efforts³⁸.

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Table 1.

Demographic, clinical, and behavioral characteristics of the study population (n=735).

Characteristics	n (%)
Sex	
Male	204 (27.6)
Female	531 (72.4)
Age (years)	
40–54	435 (59.2)
55–70	300 (40.8)
<i>Mean 53.4 (± 6.6 SD)</i>	
Education	
12 years	400 (54.4)
>12 years	335 (45.6)
Family income	
<\$20,000	392 (53.5)
\$20,000	341 (46.5)
Healthcare coverage	
Private	390 (53.1)
Public	290 (39.4)
None	55 (7.5)
General obesity	
Not obese	268 (36.5)
Obese	467 (63.5)
Abdominal obesity	
Not at risk	119 (16.2)
At risk	616 (83.8)
Impaired glucose metabolism	
No	334 (45.5)
Yes	400 (54.5)
Oral HPV infection	
No	693 (94.3)
Yes	42 (5.7)
Periodontitis	
None/Mild	297 (40.4)
Moderate	290 (39.5)
Severe	148 (20.1)
Periodontal treatment during the past 3 years	

Characteristics	n (%)
No	586 (80.6)
Yes	141 (19.4)
Dental care visit during the past 3 years	
No	72 (9.8)
Yes	663 (90.2)
Current smoking	
No	599 (81.6)
Yes	135 (18.4)
Binge drinking	
No	626 (85.2)
Yes	109 (14.8)
Lifetime number of oral sexual partners	
0–5	580 (79.1)
6	154 (20.9)
Marijuana use [*]	
No use	540 (73.5)
Occasional	175 (23.8)
Frequent	20 (2.7)

* Marijuana use was defined as no use (never/once in lifetime), occasional use, and frequent use. Frequent use was defined as having consumed marijuana 26 times during the lifetime, 6 times during the past year, and 2 times during the past 30 days; the remaining participants were classified as occasional users.

Table 2. Factors associated with oral HPV infection and periodontitis in the study population (n=735).

Characteristics	Oral HPV Infection			Periodontitis		
	Negative	Positive	p-value	None/mild	Moderate	Severe
	n (%)	n (%)		n (%)	n (%)	p-value
Sex [‡]						
Male	183 (89.7)	21 (10.3)	0.001	49 (24.0)	93 (45.6)	62 (30.4) <0.001
Female	510 (96.1)	21 (3.9)		248 (46.7)	197 (37.1)	86 (16.2)
Age (years)						
41–54	407 (93.6)	28 (6.4)	0.310	203 (46.7)	149 (34.3)	83 (19.1) <0.001
55–70	286 (95.3)	14 (4.7)		94 (31.3)	141 (47.0)	65 (21.7)
Education						
12 years	378 (94.5)	22 (5.5)	0.784	128 (32.0)	171 (42.7)	101 (25.3) <0.001
>12 years	315 (94.0)	20 (6.0)		169 (50.5)	119 (35.5)	47 (14.0)
Family income						
<\$20,000	365 (93.1)	27 (6.9)	0.148	126 (32.1)	159 (40.6)	107 (27.3) <0.001
\$20,000	326 (95.6)	15 (4.4)		169 (49.6)	131 (38.4)	41 (12.0)
Healthcare coverage [‡]						
Private	374 (95.9)	16 (4.1)	0.026	182 (46.7)	155 (39.7)	53 (13.6) <0.001
Public	271 (93.4)	19 (6.6)		98 (33.8)	113 (39.0)	79 (27.2)
None	48 (87.3)	7 (12.7)		17 (30.9)	22 (40.0)	16 (29.1)
General obesity						
Not obese	252 (94.0)	16 (6.0)	0.821	103 (38.4)	106 (39.6)	59 (22.0) 0.563
Obese	441 (94.4)	26 (5.6)		194 (41.5)	184 (39.4)	89 (19.1)
Abdominal obesity [‡]						
Not at risk	109 (91.6)	10 (8.4)	0.167	44 (37.0)	50 (42.0)	25 (21.0) 0.703

Characteristics	Oral HPV Infection				Periodontitis			
	Negative		Positive		None/mild		Moderate	
	n (%)		n (%)	p-value	n (%)		n (%)	p-value
At risk	584 (94.8)		32 (5.2)		253 (41.1)		123 (20.0)	
Impaired glucose metabolism								
No	320 (95.8)		14 (4.2)	0.103	150 (44.9)		66 (19.8)	0.051
Yes	372 (93.0)		28 (7.0)		146 (36.5)		82 (20.5)	
Oral HPV infection								
No	--		--	--	284 (41.0)		131 (18.9)	0.003
Yes	--		--		13 (31.0)		17 (40.5)	
Periodontitis								
None/Mild	284 (95.6)		13 (4.4)	0.003	--		--	--
Moderate	278 (95.9)		12 (4.1)		--		--	
Severe	131 (88.5)		17 (11.5)		--		--	
Periodontal treatment during the past 3 years								
No	554 (94.5)		32 (5.5)	0.670	236 (40.3)		118 (20.1)	0.941
Yes	132 (93.6)		9 (6.4)		59 (41.8)		28 (19.9)	
Dental care visit during the past 3 years								
No	65 (90.3)		7 (9.7)	0.123	24 (33.3)		23 (32.0)	0.031
Yes	628 (94.7)		35 (5.3)		273 (41.2)		125 (18.8)	
Current smoking [‡]								
No	567 (94.7)		32 (5.3)	0.351	256 (42.7)		98 (16.4)	<0.001
Yes	125 (92.6)		10 (7.4)		40 (29.6)		50 (37.0)	
Binge drinking [‡]								
No	592 (94.6)		34 (5.4)	0.428	268 (42.8)		114 (18.2)	0.001
Yes	101 (92.7)		8 (7.3)		29 (26.6)		34 (31.2)	

Oral HPV Infection				Periodontitis			
Characteristics	Negative	Positive	p-value	None/mild	Moderate	Severe	p-value
Lifetime number of oral sexual partners [‡]							
0-5	557 (96.0)	23 (4.0)	<0.001	249 (42.9)	221 (38.1)	110 (19.0)	0.029
6	135 (87.7)	19 (12.3)		48 (31.2)	69 (44.8)	37 (24.0)	
Marijuana use [*]							
No use	518 (95.9)	22 (4.1)	0.006	239 (44.3)	209 (38.7)	92 (17.0)	<0.001
Occasional	157 (89.7)	18 (10.3)		56 (32.0)	74 (42.3)	45 (25.7)	
Frequent	18 (90.0)	2 (10.0)		2 (10.0)	7 (35.0)	11 (55.0)	

* Marijuana use was defined as no use (never/once in lifetime), occasional use, and frequent use. Frequent use was defined as having consumed marijuana 26 times during the lifetime, 6 times during the past year, and 2 times during the past 30 days; the remaining participants were classified as occasional users.

[‡]Variables associated to frequent marijuana use. **Boldface** figures denote statistical significance (p<0.05).

Table 3.

Logistic regression models for the associations of marijuana use with oral HPV infection and severe periodontitis.

Marijuana use [±]	Oral HPV Infection [*]			Severe periodontitis [‡]		
	OR _{crude} (95% CI)	OR _{adjusted} (95% CI)	Reference	OR _{crude} (95% CI)	OR _{adjusted} (95% CI)	Reference
	Reference	Reference	Reference	Reference	Reference	Reference
No use						
Occasional	2.70 (1.41–5.16)[‡]	1.61 (0.78–3.34)		1.69 (1.12–2.53)[‡]	1.06 (0.66–1.70)	
Frequent	2.62 (0.57–11.98)	0.93 (0.18–4.73)		5.95 (2.40–14.77)[‡]	2.90 (1.06–7.93)[‡]	

^{*} Oral HPV infection: full model was adjusted by sex, age, healthcare coverage, oral sex partners and periodontal disease;

[‡] Severe periodontitis: full model was adjusted by sex, age, healthcare coverage, current smoke, binge drinking, oral sex partners, oral HPV infection, and dental visit (past 3 years).

[‡] p<0.05

[±] Marijuana use was defined as no use (never/once in lifetime), occasional use, and frequent use. Frequent use was defined as having consumed marijuana 26 times during the lifetime, 6 times during the past year, and 2 times during the past 30 days; the remaining participants were classified as occasional users.