## Title

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## Journal

Journal Of Clinical Periodontology, 44(1)

## ISSN

0303-6979

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## Publication Date

2017

## DOI

10.1111/jcpe.12646

Peer reviewed

HHS Public Access

Author manuscript

*J Clin Periodontol*. Author manuscript; available in PMC 2018 January 01.

Published in final edited form as:

*J Clin Periodontol*. 2017 January ; 44(1): 2–12. doi:10.1111/jcpe.12646.

# Prevalence of Periodontal Diseases in a Multicenter Cohort of Perinatally HIV-Infected and HIV-exposed and Uninfected Youth

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## Abstract

**Aims—**To compare the prevalence and severity of periodontal diseases between 180 perinatally HIV-infected (PHIV) and 118 perinatally HIV-exposed and uninfected (PHEU) youth in a cross-sectional study conducted at 11 clinical sites in the United States and Puerto Rico from the Adolescent Master Protocol (AMP) study of the Pediatric HIV/AIDS cohort study (PHACS) network.

**Methods—**Several analyses were conducted, employing the current CDC/AAP classification for periodontitis and incorporating a definition of gingivitis based on a bleeding on probing threshold, and analyses based on more detailed whole mouth, intraoral regionally, site-based, and tooth-based criteria of bleeding on probing, plaque levels, pockets depths and clinical attachment levels.

**Results—**After adjusting for plaque control habits, and behavioral and sociodemographic factors, there were no significant differences in periodontal diseases between the PHIV and PHEU youth using any of these criteria. For PHIV youth, there was no significant association between parameters of periodontal disease and current HIV status.

**Conclusions—**While no significant differences in periodontal parameters were noted between the PHIV and PHEU youth, the influence of antiretroviral therapy on merits further exploration in this cohort in a longitudinal study.

## Introduction

Although periodontal disease has been well described in HIV-infected adults, it has not been adequately investigated among children who acquired HIV through perinatal exposure. More

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importantly, perinatally HIV-infected children are living longer into adolescence and young adulthood when periodontal disease begins to emerge as a major health problem regardless of HIV status. Among adults, several forms of periodontal diseases have been found to be associated with HIV including unusual forms of gingivitis, necrotizing gingivitis and periodontitis (Reddy, 2007). Few studies have examined periodontal health in perinatally HIV-infected (PHIV) youth with a full set of periodontal parameters, including a full-mouth assessment of clinical attachment loss (CAL)(Howell et al., 1996, Vaseliu et al., 2005, Magalhaes et al., 2001, Santos et al., 2001). The small number of studies which have been conducted did not include an adequate comparison group of uninfected children. PHIV youth may be at particular risk for disease due to exposure to sugar-containing liquid medications before and during tooth eruption and immunosuppression resulting in chronic gingival bacterial growth.

We previously published our findings comparing caries, mucosal disease, and periodontal disease (using the updated Centers for Disease Control and Prevention/ American Academy of Periodontology (CDC/AAP) classification (Eke et al., 2015, Eke et al., 2012)) between PHIV and perinatally HIV-exposed but uninfected (PHEU) youth (Moscicki et al., 2016). The comparison group of PHEU youth is unique since socioeconomic factors which are known to influence oral health are similar to those of PHIV youth. As classifications of periodontal disease for larger populations, such as the CDC/AAP classification, are based on a few sites with the highest level of specific periodontal parameters, such categorization of periodontal disease may lead to misclassification because only a fraction of periodontal measurements are considered. However, optimal statistical methods for clustered data that allow the inclusion of all measurements on all teeth have been used in the analysis of periodontal data (DeRouen et al., 1995). Thus this paper investigates not only periodontal disease assessed using the well-established CDC/AAP classification, but also detailed full-mouth periodontal parameters, in PHIV as compared to PHEU youth.

## Methods

### Study Design and Population

The Pediatric HIV/AIDS Cohort Study (PHACS) oral health substudy was a cross-sectional observational study that included participants currently enrolled in the PHACS Adolescent Master Protocol (AMP). AMP is a prospective cohort study designed to determine the impact of HIV infection and antiretroviral therapy (ART) on PHIV compared to PHEU youth at 15 clinical sites in the United States and Puerto Rico (Van Dyke et al., 2011). AMP eligibility criteria included perinatal HIV infection or exposure, age 7 to 16 years at enrollment as confirmed by the medical record, and engagement in medical care with available ART history for the PHIV group. Participants enrolled in AMP from March 2007 through October 2009 at 15 US clinical research sites. Regularly scheduled visits included audio-computer assisted structured interviews (ACASI), physical examination, chart reviews for medications and illnesses, and for CD4 counts and viral load assessments. Participants were recruited from 11 AMP sites with an affiliated dental school or dentist from September 2012 to January 2014 after written informed consent was obtained from both participants and their legal guardian, following a protocol approved by the Institutional Review Board of

each participating site and the Harvard T.H. Chan School of Public Health. Exclusion criteria included an inability to sit through a comprehensive oral examination due to acute systemic illness or presence of craniofacial anomalies, or a history of treatment with head or neck radiation (Moscicki et al., 2016).

## Variables and Measures

Standardized dental and periodontal examinations were performed on youth at participating clinical research sites. The clinical periodontal parameters recorded included: 1) Probing depths (PD) measured for each tooth with a UNC probe on six sites rounded down to the nearest millimeter; 2) Distance from the gingival margin (GM) to the cementoenamel junction (CEJ), for for calculation of clinical attachment level (CAL); 3) Bleeding on probing (BOP) on six sites for each tooth recorded as present or absent: 4) Gingival index (GI) measured on six sites around the tooth using the standard GI of Löe and Silness (Loe and Silness, 1963); 5) The modified plaque index (PI) of Silness and Löe (Silness and Loe, 1964) for each buccal and lingual surface of each tooth.

Prior to commencing examination of participants, a periodontist/calibrator (MR) conducted a training at each of the examination centers with each of the participating dentists. The orientation included a demonstration of techniques to measure GI, BOP, PI, GM, and PD. Following this demonstration, each examiner was assessed with the calibrator (MR) on a second participant for PD, GM to CEJ to calibrate CAL, and GI. A minimum concurrence of 90% for both PD and GM position was required. If this level of concurrence was not achieved, the calibrator would review these techniques and conduct a second calibration on another patient until this minimal concurrence was met. All patients were referred for dental care if needed.

While the main outcomes of interest were the periodontal parameters used in the diagnosis of periodontitis and their association with HIV infection, other explored covariates considered to be associated with periodontal diseases included demographics (age, sex, race and ethnicity), caregiver socioeconomic characteristics (education and income), history of sex (ever had sex, ever had oral sex), drinking alcohol in the past 3 months, smoking cigarettes in the past 3 months, oral hygiene behavior (brushing frequency, flossing frequency), dental care (having a source of, cleaning in the last year), meal/snack consumption frequency per day and juice/soda consumption frequency per day. For PHIV participants, the risk factors considered also included HIV disease severity (lifetime CD4+ nadir $< 200$ cells/mm$^3$, current CD4+ $\leq 350$ cells/mm$^3$, current viral load $\geq 400$ copies/mL) and history of AIDS-defining illness.

## Statistical Analyses

Summary statistics for demographics and other characteristics were compared across the two subgroups (PHIV and PHEU) with a Wilcoxon rank-sum test for continuous measures and a Fisher's Exact test for discrete measures.

Based on the periodontal parameters of CAL and PD, periodontitis was first summarized as either absent, mild, moderate, or severe using the CDC/AAP definition (Eke et al., 2015, Eke et al., 2012). Among those with no periodontitis, gingivitis was defined as having BOP on at

least 10% of the sites scored (definition adapted from (Offenbacher et al., 2008)). The extent and severity of periodontal disease of a participant was then measured by number (or percentage) of teeth and percentage of sites, respectively, of assessments exceeding various thresholds of each of the periodontal parameters. These measures were then summarized by HIV infection status using mean, standard deviation, median and quartiles.

The association between HIV infection and the prevalence of periodontal diseases at the tooth surface level was then assessed using two separate parameters: GI ≥ 2 for gingival inflammation, and CAL ≥ 3mm for periodontitis. Taking the association among the multiple sites within each participant into account, Generalized Estimating Equation (GEE) models with a logistic link function were applied with and without adjustment for known risk factors and for the location of the site in the mouth. The analyses were conducted using Proc GLIMMIX of SAS 9.4 (METHOD=RMPL, EMPIRICAL=FIRORES) with a compound symmetry working correlation matrix (Mancl and DeRouen, 2001). Univariable logistic regression models were constructed for each covariate. The multivariable models adjusted for demographics, drinking alcohol, smoking cigarettes, oral hygiene behavior in addition to all other covariates with a p-value < 0.2 in the univariable analyses and a p-value < 0.1 in the final multivariable model after backward selection. The final model also considered the variation among multiple centers using random intercept with participants nested within center.

Another set of analyses was performed using one summary measure per participant to assess the association of HIV infection with the extent of periodontal diseases, for each of two separate parameters: the number of teeth with GI ≥ 2 at any site for gingival inflammation, and the number of teeth with CAL ≥ 3mm at any interproximal site for periodontitis. These tooth counts were corrected for missing teeth by multiplying the ratio of 28 over the number of scored teeth. The unadjusted and adjusted regression analyses were applied directly to the tooth count whose distributions were characterized by an extra proportion of zeros and overdispersion when compared to Poisson distributions. Therefore, zero-inflated negative binomial (ZINB) regression analyses were performed to assess the association of HIV infection and other covariates with the tooth counts.

## Results

### Sample Characteristics

A total of 335 participants enrolled in the PHACS oral health substudy (209 PHIV and 126 PHEU). For the analysis of periodontal parameters, 37 participants were excluded (PHIV: 29, PHEU: 8) either because of the inability to complete the examination (PHIV: 4, PHEU: 1) or because they were currently taking an antibiotic, or had taken one within 90 days before the oral examination (PHIV: 25, PHEU:7). Statistically significant differences between the 180 PHIV and 118 PHEU youth were noted in that the PHIV were older, had greater physical development (Tanner stage), a greater proportion of Hispanics (Table 1), smaller proportion of caregivers being biological parent, annual income of $30,000 or less, and had more sexual experience and marijuana use (Table 2). These differences were similar to previous research from this cohort since the PHIV youth were older and their parents with HIV were more likely to have died of AIDS. There was no significant differences between

the two groups with respect to sex, smoking, use of alcohol, oral hygiene and dental care (Tables 1 and 2). Among the 180 PHIV youth, 29% had a lifetime nadir CD4+ cell count below 200 cells/mm$^3$, 14% had a CD4+ cell count below 350 cells/mm$^3$, and 71% had suppressed viral load (< 400 copies/mL) at the time of the oral examination, or within 3 months prior.

## Periodontal parameters by HIV Status

No significant differences in the prevalence of periodontal disease measured using the modified CDC-AAP classification were observed between the PHIV and PHEU groups (Table 3).

Table 4 shows the distribution patterns for specific periodontal parameters. Without adjusting for confounding factors, both PHIV and PHEU participants demonstrated similar patterns for periodontal parameters that primarily measure clinical inflammation and plaque levels. Specifically, no difference was seen for the overall percent of sites with BOP per participant, percent of teeth with at least one site with BOP per participant, and percent of teeth with at least four sites with BOP per participant. When we examined the severity and extent of higher levels of plaque and gingival inflammation, several differences were found. The mean percent of sites with a PI score = 3 was lower in the PHIV than the PHEU youth (2.81 versus 4.7; $p = 0.04$) and the number of teeth with at least 1 surface with a PI = 3 was also lower in the PHIV than the PHEU youth (1.46 versus 2.25; $p = 0.04$). Similarly, percent of sites with GI = 3 and number of teeth with at least 1 surface with GI = 3 were lower in the PHIV than the PHEU youth. However the actual number of sites per subject with this highest level of PI=3 or GI=3 was relatively small. By contrast, the overall measures of PD and CAL and the severity and extent of higher measures of PD and CAL were similar between the PHIV and PHEU groups (Table 4). Similar distributions patterns were observed for the prevalence of periodontal parameters when utilizing different cut-off levels (Supplementary Table 1).

Further stratified by site or region, the observed proportion of GI scores ≥ 2 among all examined tooth surfaces of the study population was lower for PHIV compared to PHEU youth regardless of sites or regions, with an overall proportion of 13.9% and 18.6%, respectively (Table 5). Regional and site variations for both PHIV and PHEU subjects were also observed, with the highest proportion of GI ≥ 2 on lower anterior teeth and on mesial buccal and distal buccal sites, and the lowest on upper posterior teeth and on lingual sites. The overall observed proportion of CAL ≥ 3mm was similar between the PHIV and PHEU groups, with the highest proportion on mesial buccal surfaces and upper posterior teeth, and lowest proportion on lingual surfaces and anterior teeth. For PD ≥ 4mm, the overall proportion was also similar between the PHIV and PHEU groups with a similar regional distribution pattern (Table 5)

## Univariate and Multivariable analyses

In the unadjusted logistic regression model, PHIV youth had a lower risk of having a GI ≥ 2 compared to PHEU youth (Odds Ratio (OR) = 0.69, 95%CI = 0.48, 1.00) (Table 6). However, in the adjusted logistical regression model incorporating the observed higher

levels of PI in the PHEU group and the influence of variation among centers, the two groups were not different (adjusted OR (aOR) = 1.05, 95%CI = 0.73, 1.50). Other associations with having GI scores ≥ 2 were having juice/soda twice or more per day compared to once or none per day, having a higher PI and lower brushing frequency; flossing frequency was found to have a negative association. The odds of GI scores ≥ 2 showed similar regional variation and site variation with and without adjustment for other covariates. Among PHIV youth, no association was found between having GI scores ≥ 2 and low lifetime nadir CD4+, low current CD4+, or high current viral load in both unadjusted and adjusted analyses. Mild association was observed between having GI scores ≥ 2 and a history of an AIDS-defining illness in adjusted analysis.

No significant association was found between HIV infection and having interproximal CAL ≥ 3mm (Table 7). The regional pattern stayed the same with or without adjustment for other covariates. Significant positive associations were noted between CAL ≥ 3mm and a history of sex and PI. Having a caregiver with some college education was associated with lower odds of interproximal CAL ≥ 3mm with marginal statistical significance; but drinking alcohol and smoking cigarettes were not associated with interproximal CAL ≥ 3mm.

Within the PHIV cohort, no significant association was found between CAL ≥ 3mm and lower CD4+ cell count nadir, low current CD4+ cell count, detectable current viral load or history of an AIDS-defining illness after adjusting for demographics, history of sex, education of caregiver, drinking alcohol and floss frequency, PI, site and region.

ZINB regression analyses on the extent of periodontal diseases confirmed the findings of the GEE analysis. There were no significant associations observed between HIV infection and the number of teeth with GI ≥ 2 at any site. However, these models confirmed that having juice/soda ≥ 2 per day (adjusted mean count ratio (aMR) =1.75, 95% CI=1.26, 2.44) and high percent of teeth with visible plaque (aMR = 1.03, 95% CI=1.01, 1.04) were significantly associated with higher mean number of teeth with GI ≥ 2 at any site (Supplementary Table 2); Additionally, a history of sex (aMR= 2.17, 95% CI=1.34, 3.53). and high percent of teeth with visible plaque (aMR =1.01 per unit, 95% CI=1.00, 1.02) were significantly associated with higher mean number of teeth with any interproximal CAL ≥ 3mm, and caregiver had some college education was associated with lower mean tooth count of interproximal CAL ≥ 3mm (aMR = 0.44, 95% CI=0.29, 0.67) (Supplementary Table 3).

## Discussion

The general findings of the periodontal component of this oral health study were that there were no significant differences in the overall periodontal condition between the PHIV and PHEU groups. The proportion of sites with the high levels of gingival inflammation were lower in the PHIV group when compared to the PHEU group, but was not statistically significant after adjusting for factors such as plaque index and the influence of variation among centers. Nevertheless it is possible that ART may influence the ecology of the oral microbiome and/or secretion of inflammatory cytokines and chemokines. in particular as plaque and gingival inflammation tend to increase in prevalence during puberty. However to date the influence on the lifelong antiretroviral therapies on the bacterial oral microbiome

remains to be determined (Beck et al., 2015, Brito et al., 2008, Goncalves et al., 2007, Navazesh et al., 2005, Ryder et al., 2012).

The first cases of the unusual periodontal diseases and conditions associated with HIV, including linear gingival erythema (LGE), necrotizing ulcerative gingivitis (NUG) and necrotizing ulcerative periodontitis (NUP), were published 3 decades ago (Rosenstein et al., 1989, Winkler et al., 1989, Williams et al., 1990, Masouredis et al., 1992, Riley et al., 1992, EC-Clearinghouse, 1993). Furthermore, several studies demonstrated an association between periodontal disease and low CD4 cell count and progression to AIDS (Glick et al., 1994). Since that time, the prevalence of these conditions seems to have declined in part due to the advent of ART (Patton et al., 2000, Tappuni and Fleming, 2001, Ramirez-Amador et al., 2003, Ferreira et al., 2007, Vernon et al., 2011) and non-ART local and systemic antimicrobial approaches (Ryder et al., 2012). Most of these studies focused on adults, with relatively few on HIV-infected youth. One difficulty in developing such surveys on periodontal conditions in this younger population is that periodontitis in general is a slowly progressing chronic condition that does not manifest itself clinically until adulthood. Therefore, any minor changes in periodontal attachment loss that may start in childhood or adolescence are usually not clinically detectable with conventional periodontal diagnostic approaches. In addition, the classifications for the type and severity of periodontal diseases for adults may not be relevant to children (Lopez and Baelum, 2003, Albandar and Tinoco, 2002). The earliest clinical manifestations of disease may be a simple form of gingival inflammation without measurable CAL. In addition, distinguishing periodontitis from gingivitis by PD measures may be of limited value as increases in PD in this age group may more often reflect gingival enlargement from inflammation, rather than CAL.

Therefore it is understandable that when we used both the current CDC/AAP classification for periodontitis and a separately created definition for gingivitis without periodontitis using a BOP threshold (Offenbacher et al., 2008), there were no significant differences in the prevalence of mild, moderate or severe forms of periodontitis between PHIV and PHEU youth. In addition, direct comparisons using our definition to other studies, which use a range of classification systems, are difficult. However, several general observations can be made. First, the prevalence of gingivitis (including a diagnosis of gingivitis alone or periodontitis) of 80% in this PHIV/PHEU population is comparable to the range of the prevalence of gingivitis from other cross sectional studies in children (Jenkins and Papapanou, 2001). However, the 31% prevalence of mild to moderate forms of periodontitis as defined by the current modified CDC classification was higher than reported in some studies and comparable to other studies (Albandar and Tinoco, 2002, Jenkins and Papapanou, 2001)

When considering the reported lower prevalence of more severe forms of periodontal diseases in these younger populations (Howell et al., 1996, Lopez and Baelum, 2003, Albandar and Tinoco, 2002), several more extensive analysis strategies were employed in this study to determine if there were differences in the extent, severity, distribution, and intraoral geographic clustering of clinical indicators for gingivitis. These included more rigorous analyses of the extent and distribution of clinical measures of inflammation (GI) and attachment loss (CAL) by numbers of affected teeth and numbers of sites, taking into

consideration known sociodemographic, behavioral, clinical, and laboratory findings. Instead of a broad categorization by the number of interproximal sites with attachment loss or deep pockets, we directly analyzed all available data of CAL or GI from all surfaces within the entire dentition. This methodology avoids collapsing or summarizing information to only one measure per participant and makes direct use of each observation from all sites and thus is more sensitive to identify subtle differences across the entire mouth. At the same time, this method recognizes the data collected from the same participant and participants from the same institution are correlated and thus adjusts the statistical comparison to prevent exaggerated differences. These more rigorous analytical approaches did not demonstrate statistical differences between the PHIV and PHEU cohorts for periodontal measures at the time of this survey.

In conclusion, this study found that using both general disease categories and more in depth analysis, that the overall presence of periodontal disease in PHIV youth was similar to our comparison group of HIV –exposed but uninfected youth. The influence of HIV-exposure and ART, whether perinatally or through-out childhood on periodontal health and disease needs further exploration. Furthermore, microbial and inflammatory marker assessments of these two populations may show differences between these groups which in turn may affect clinical manifestations as both of these population groups grow older. Therefore, follow-up studies on the development of periodontal diseases for these PHIV and PHEU groups at selected intervals are warranted in order to assess the long-term effects of HIV infection on the periodontium in the ART era.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

**Conflict of Interest and Source of Funding**

This study was supported by the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development with cofounding from the National Institute of Dental and Craniofacial Research, National Institute on Drug Abuse, the National Institute of Allergy and Infectious Diseases, the Office of AIDS Research, the National Institute of Mental Health, the National Institute of Neurological Disorders and Stroke, the National Institute on Deafness and Other Communication Disorders, the National Heart Lung and Blood Institute, and the National Institute on Alcohol Abuse and Alcoholism, through cooperative agreements with the Harvard T. H. Chan School of Public Health (HD052102, 3 U01 HD052102-05S1, and 3 U01 HD052102-06S3) and the Tulane University School of Medicine (HD052104, 3U01 HD052104-06S1) Data management services were provided by Frontier Science and Technology Research Foundation and regulatory services and logistical support were provided by Westat, Inc. Westat, Inc. provided regulatory services, protocol development support and logistical support but had no additional role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

The following institutions, clinical site investigators, and staff participated in conducting the Pediatric HIV/AIDS Cohort Study Adolescent Master Protocol in 2012, in alphabetical order: Baylor College of Medicine: Ester Yang*, William Shearer, Mary Paul, Norma Cooper, Lynette Harris; Bronx Lebanon Hospital Center: Karen Kemp-Posterman*, Selene Wun*, Murli Purswani, Mahboobullah Baig, Anna Cintron; Children's Diagnostic and Treatment Center: Jennifer Zeni*, Ana Puga, Sandra Navarro, Doyle Patton, Deyana Leon; Children's Hospital, Boston: Man Wai Ng*, Sandra Burchett, Nancy Karthas, Betsy Kammerer; Ann and Robert H. Lurie Children's Hospital of Chicago: Ray Jurado*, Johnny Kuttab*, Ashlee Vorachek*,Ram Yogev, Margaret Ann Sanders, Kathleen Malee, Scott Hunter; Jacobi Medical Center: Victor Badner*, Ronald Garreett*, Andrew Wiznia, Marlene Burey, Molly Nozyce; St. Christopher's Hospital for Children: Susan Chialastri*, Janet Chen, Latreca Ivey, Maria Garcia Bulkley, Mitzie Grant; San Juan Hospital/Department of Pediatrics: Ramon Gonzalez*, Midnela Acevedo-

Flores, Heida Rios, Vivian Olivera; Tulane University Health Sciences Center: Janice Townsend*, Margarita Silio, Medea Jones, Patricia Sirois; University of Colorado Denver Health Sciences Center: Roopa Gandhi*, Elizabeth McFarland, Emily Barr, Robin McEvoy; University of Medicine and Dentistry of New Jersey: Kenneth Markowitz*, Arry Dieudonne, Linda Bettica, Susan Adubato; the authors thank the children and families for their participation in PHACS, and the individuals and institutions involved in the conduct of PHACS. *Participating Dentist

## References

Albandar JM, Tinoco EM. Global epidemiology of periodontal diseases in children and young persons. Periodontol 2000. 2002; 29:153–176. [PubMed: 12102707]

Beck JM, Schloss PD, Venkataraman A, Twigg H 3rd, Jablonski KA, Bushman FD, Campbell TB, Charlson ES, Collman RG, Crothers K, Curtis JL, Drews KL, Flores SC, Fontenot AP, Foulkes MA, Frank I, Ghedin E, Huang L, Lynch SV, Morris A, Palmer BE, Schmidt TM, Sodergren E, Weinstock GM, Young VB. Multicenter Comparison of Lung and Oral Microbiomes of HIV-infected and HIV-uninfected Individuals. Am J Respir Crit Care Med. 2015; 192:1335–1344. [PubMed: 26247840]

Brito A, Escalona LA, Correnti M, Perrone M, Bravo IM, Tovar V. Periodontal conditions and distribution of Prevotella intermedia, Porphyromonas gingivalis and Aggregatibacter actinomycetemcomitans in HIV-infected patients undergoing anti-retroviral therapy and in an HIV-seronegative group of the Venezuelan population. Acta Odontol Latinoam. 2008; 21:89–96. [PubMed: 18841752]

DeRouen TA, Hujoel PP, Mancl LA. Statistical issues in periodontal research. J Dent Res. 1995; 74:1731–1737. [PubMed: 8530733]

EC-Clearinghouse. Classification and diagnostic criteria for oral lesions in HIV infection. EC-Clearinghouse on Oral Problems Related to HIV Infection and WHO Collaborating Centre on Oral Manifestations of the Immunodeficiency Virus. J Oral Pathol Med. 1993; 22:289–291. [PubMed: 8229864]

Eke PI, Dye BA, Wei L, Slade GD, Thornton-Evans GO, Borgnakke WS, Taylor GW, Page RC, Beck JD, Genco RJ. Update on Prevalence of Periodontitis in Adults in the United States: NHANES 2009 to 2012. J Periodontol. 2012; 86:611–622.

Eke PI, Page RC, Wei L, Thornton-Evans G, Genco RJ. Update of the case definitions for population-based surveillance of periodontitis. J Periodontol. 2012; 83:1449–1454. [PubMed: 22420873]

Ferreira S, Noce C, Junior AS, Goncalves L, Torres S, Meeks V, Luiz R, Dias E. Prevalence of oral manifestations of HIV infection in Rio De Janeiro, Brazil from 1988 to 2004. AIDS Patient Care STDS. 2007; 21:724–731. [PubMed: 17949271]

Glick M, Muzyka BC, Salkin LM, Lurie D. Necrotizing ulcerative periodontitis: a marker for immune deterioration and a predictor for the diagnosis of AIDS. J Periodontol. 1994; 65:393–397. [PubMed: 7913962]

Goncalves LS, Soares Ferreira SM, Souza CO, Souto R, Colombo AP. Clinical and microbiological profiles of human immunodeficiency virus (HIV)-seropositive Brazilians undergoing highly active antiretroviral therapy and HIV-seronegative Brazilians with chronic periodontitis. J Periodontol. 2007; 78:87–96. [PubMed: 17199544]

Howell RB, Jandinski JJ, Palumbo P, Shey Z, Houpt MI. Oral soft tissue manifestations and CD4 lymphocyte counts in HIV-infected children. Pediatr Dent. 1996; 18:117–120. [PubMed: 8710712]

Jenkins WM, Papapanou PN. Epidemiology of periodontal disease in children and adolescents. Periodontol 2000. 2001; 26:16–32. [PubMed: 11452904]

Loe H, Silness J. PERIODONTAL DISEASE IN PREGNANCY. I. PREVALENCE AND SEVERITY. Acta Odontol Scand. 1963; 21:533–551. [PubMed: 14121956]

Lopez R, Baelum V. Classifying periodontitis among adolescents: implications for epidemiological research. Community Dent Oral Epidemiol. 2003; 31:136–143. [PubMed: 12641595]

Magalhaes MG, Bueno DF, Serra E, Goncalves R. Oral manifestations of HIV positive children. J Clin Pediatr Dent. 2001; 25:103–106. [PubMed: 11314206]

Mancl LA, DeRouen TA. A covariance estimator for GEE with improved small-sample properties. Biometrics. 2001; 57:126–134. [PubMed: 11252587]

Masouredis CM, Katz MH, Greenspan D, Herrera C, Hollander H, Greenspan JS, Winkler JR. Prevalence of HIV-associated periodontitis and gingivitis in HIV-infected patients attending an AIDS clinic. J Acquir Immune Defic Syndr. 1992; 5:479–483. [PubMed: 1560345]

Moscicki AB, Yao TJ, Ryder MI, Russell JS, Dominy SS, Patel K, McKenna M, Van Dyke RB, Seage GR 3rd, Hazra R. The Burden of Oral Disease among Perinatally HIV-Infected and HIV-Exposed Uninfected Youth. PLoS One. 2016; 11:e0156459. [PubMed: 27299992]

Navazesh M, Mulligan R, Pogoda J, Greenspan D, Alves M, Phelan J, Greenspan J, Slots J. The effect of HAART on salivary microbiota in the Women's Interagency HIV Study (WIHS). Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2005; 100:701–708. [PubMed: 16301151]

Offenbacher S, Barros SP, Beck JD. Rethinking periodontal inflammation. J Periodontol. 2008; 79:1577–1584. [PubMed: 18673013]

Patton LL, McKaig RG, Strauss RP, Rogers D, Eron JJ Jr. Changing prevalence of oral manifestations of human immuno-deficiency virus in the era of protease inhibitor therapy. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2000; 89:299–304. [PubMed: 10710453]

Ramirez-Amador V, Esquivel-Pedraza L, Sierra-Madero J, Anaya-Saavedra G, Gonzalez-Ramirez I, Ponce-de-Leon S. The Changing Clinical Spectrum of Human Immunodeficiency Virus (HIV)-Related Oral Lesions in 1,000 Consecutive Patients: A 12-Year Study in a Referral Center in Mexico. Medicine (Baltimore). 2003; 82:39–50. [PubMed: 12544709]

Reddy J. Control of HIV/AIDS and AIDS-related conditions in Africa with special reference to periodontal diseases. J Int Acad Periodontol. 2007; 9:2–12. [PubMed: 17274234]

Riley C, London JP, Burmeister JA. Periodontal health in 200 HIV-positive patients. J Oral Pathol Med. 1992; 21:124–127. [PubMed: 1583595]

Rosenstein DI, Eigner TL, Levin MP, Chiodo GT. Rapidly progressive periodontal disease associated with HIV infection: report of case. J Am Dent Assoc. 1989; 118:313–314. [PubMed: 2921429]

Ryder MI, Nittayananta W, Coogan M, Greenspan D, Greenspan JS. Periodontal disease in HIV/AIDS. Periodontol 2000. 2012; 60:78–97. [PubMed: 22909108]

Santos LC, Castro GF, de Souza IP, Oliveira RH. Oral manifestations related to immunosuppression degree in HIV-positive children. Braz Dent J. 2001; 12:135–138. [PubMed: 11450684]

Silness J, Loe H. PERIODONTAL DISEASE IN PREGNANCY. II. CORRELATION BETWEEN ORAL HYGIENE AND PERIODONTAL CONDTION. Acta Odontol Scand. 1964; 22:121–135. [PubMed: 14158464]

Tappuni AR, Fleming GJ. The effect of antiretroviral therapy on the prevalence of oral manifestations in HIV-infected patients: a UK study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2001; 92:623–628. [PubMed: 11740479]

Van Dyke RB, Patel K, Siberry GK, Burchett SK, Spector SA, Chernoff MC, Read JS, Mofenson LM, Seage GR 3rd. Pediatric, H. I. V. A. C. S. Antiretroviral treatment of US children with perinatally acquired HIV infection: temporal changes in therapy between 1991 and 2009 and predictors of immunologic and virologic outcomes. J Acquir Immune Defic Syndr. 2011; 57:165–173. [PubMed: 21407086]

Vaseliu N, Carter AB, Kline NE, Kozinetz C, Cron SG, Matusa R, Kline MW. Longitudinal study of the prevalence and prognostic implications of oral manifestations in romanian children infected with human immunodeficiency virus type 1. Pediatr Infect Dis J. 2005; 24:1067–1071. [PubMed: 16371867]

Vernon LT, Babineau DC, Demko CA, Lederman MM, Wang X, Toossi Z, Weinberg A, Rodriguez B. A prospective cohort study of periodontal disease measures and cardiovascular disease markers in HIV-infected adults. AIDS Res Hum Retroviruses. 2011; 27:1157–1166. [PubMed: 21443451]

Williams C, Winkler J, Murray P, Grassi M. HIV-associated periodontitis complicated by necrotizing stomatitis. Oral Surg Oral Med Oral Pathol. 1990; 69:351–355. [PubMed: 2314860]

Winkler J, Murray P, Grassi M, Hammerle C. Diagnosis and management of HIV-associated periodontal lesions. J Am Dent Assoc Nov. 1989 Nov.:25S–34S.

## Clinical Relevance of the Study

**Scientific rationale for the study**

To compare the periodontal health between perinatally HIV-infected (PHIV) and perinatally HIV-exposed and uninfected (PHEU) youth in a multicenter cross-sectional study.

**Principle Findings**

There were no significant differences in periodontal health between PHIV and PHEU youth. For PHIV youth, there was no significant association between parameters of periodontal disease and current HIV status.

**Practical Implications**

In the current HIV treatment era, PHIV youth and PHEU youth have similar levels of periodontal health. However the longer-term effects of antiretroviral treatment need to be monitored.

*J Clin Periodontol*. Author manuscript; available in PMC 2018 January 01.

**Table 1**

Study Population: Demographic, Developmental Covariates, Caregiver Characteristics and Substance Use by HIV Infection Status

| | | HIV Infection Status | | | |
|---|---|---|---|---|---|
| **Characteristic** | | **Infected (N=180)** | **Uninfected (N=118)** | **Total (N=298)** | **P-Value** * |
| Age at OH Visit (years) | N | 180 | 118 | 298 | <.001 |
| | Mean (s.d.) | 16.84 (2.61) | 14.76 (2.53) | 16.02 (2.77) | |
| | Median (Q1, Q3) | 17.26 (14.88, 18.85) | 14.47 (12.51, 16.48) | 16.25 (13.80, 18.39) | |
| | Min, Max | 10.25, 21.71 | 10.63, 20.90 | 10.25, 21.71 | |
| Age Category (years) | 10 to <14 | 30 (17%) | 51 (43%) | 81 (27%) | <.001 |
| | 14 to <17 | 55 (31%) | 46 (39%) | 101 (34%) | |
| | 17 to <19 | 52 (29%) | 12 (10%) | 64 (21%) | |
| | 19+ | 43 (24%) | 9 (8%) | 52 (17%) | |
| Female Sex | | 88 (49%) | 57 (48%) | 145 (49%) | 1.00 |
| Black Race | | 119 (66%) | 67 (57%) | 186 (62%) | 0.11 |
| Hispanic Ethnicity | | 48 (27%) | 50 (42%) | 98 (33%) | 0.006 |
| Maximum Tanner Stage | 1–3 | 23 (13%) | 33 (28%) | 56 (19%) | 0.001 |
| | 4 | 35 (19%) | 28 (24%) | 63 (21%) | |
| | 5 | 122 (68%) | 57 (48%) | 179 (60%) | |
| Caregiver is Biological Parent | | 65 (36%) | 95 (81%) | 160 (54%) | <.001 |
| Caregiver Some College | | 67 (37%) | 36 (31%) | 103 (35%) | 0.26 |
| Caregiver Income <$30,001 | | 93 (52%) | 99 (84%) | 192 (64%) | <.001 |
| Ever Had Sex | | 86 (48%) | 39 (33%) | 125 (42%) | 0.01 |
| Drink Alcohol: Past 3 Months | | 44 (24%) | 20 (17%) | 64 (21%) | 0.15 |
| Smoke Cigarette: Past 3 Months | | 20 (11%) | 6 (5%) | 26 (9%) | 0.09 |
| Use Marijuana: Past 3 Months | | 43 (24%) | 13 (11%) | 56 (19%) | 0.006 |

*P-value by Wilcoxon Test for continuous measures and Fisher's exact test for categorical characteristics

Missing data on 2 participants for caregiver some college, 6 for caregiver income, 6 for ever had sex, 6 for alcohol, 8 for cigarettes, and 6 for marijuana,

**Table 2**

Oral health behavioral characteristics by HIV Infection Status

| | | HIV Infection Status | | | |
|---|---|---|---|---|---|
| **Characteristic** | | **Infected (N=180)** | **Uninfected (N=118)** | **Total (N=298)** | **P-Value*** |
| Brush Frequency (times/day) | <1 | 16 (9%) | 8 (7%) | 24 (8%) | 0.86 |
| | 1 | 69 (38%) | 46 (39%) | 115 (39%) | |
| | ≥2 | 95 (53%) | 64 (54%) | 159 (53%) | |
| Floss Frequency (times/day) | <1 | 154 (86%) | 96 (81%) | 250 (84%) | 0.15 |
| | 1 | 14 (8%) | 17 (14%) | 31 (10%) | |
| | ≥2 | 12 (7%) | 5 (4%) | 17 (6%) | |
| Have Source of Dental Care | | 144 (80%) | 88 (75%) | 232 (78%) | 0.56 |
| Cleaning in Last Year | | 116 (64%) | 73 (62%) | 189 (63%) | 0.62 |
| Juice/Soda Frequency (times/day) | 0–1 | 52 (29%) | 34 (29%) | 86 (29%) | 1.00 |
| | ≥2 | 128 (71%) | 84 (71%) | 212 (71%) | |
| Saliva Volume (mL/min) | Median (Q1, Q3) | 0.72 (0.40, 1.00) | 0.60 (0.40, 1.00) | 0.60 (0.40, 1.00) | 0.08 |
| | Min, Max | 0.06, 3.00 | 0.00, 2.20 | 0, 3 | |
| Plaque Index: % Teeth Any Site >1 | Median (Q1, Q3) | 25.00 (10.71, 47.29) | 32.14 (11.54, 59.26) | 26.42 (10.71, 53.57) | 0.14 |
| | Min, Max | 0, 100 | 0, 100 | 0, 100 | |

*P-value by Wilcoxon ranksum test for continuous measures and Fisher's exact test for binary characteristics.

Missing data on 4 participants for have source of dental care, 1 for cleaning in last year, and 2 for saliva volume.

**Table 3**

Study Population: Periodontal Disease Diagnosis Using the CDC-AAP Case Definition

| Characteristic | | Cohort | | | |
|---|---|---|---|---|---|
| | | Infected (N=180) | Uninfected (N=118) | Total (N=298) | P-Value* |
| Periodontal Disease | None | 37 (21%) | 23 (19%) | 60 (20%) | 0.93 |
| | Gingivitis | 85 (47%) | 60 (51%) | 145 (49%) | |
| | Mild Periodontitis | 30 (17%) | 17 (14%) | 47 (16%) | |
| | Moderate Periodontitis | 28 (16%) | 18 (15%) | 46 (15%) | |

*Fisher's Exact Test

**Table 4**

Summary of Extent and Severity of Periodontal Diseases by HIV Infection Status

| Characteristic | | HIV Infection Status | | | P-Value* |
|---|---|---|---|---|---|
| | | Infected (N=180) | Uninfected (N=118) | Total (N=298) | |
| % Sites BOP | Mean (s.d.) | 21.49 (18.02) | 23.64 (18.61) | 22.34 (18.25) | 0.30 |
| | Median (Q1, Q3) | 15.77 (9.62, 30.95) | 17.86 (9.52, 35.12) | 16.96 (9.52, 31.55) | |
| % Teeth BOP | Mean (s.d.) | 57.32 (27.78) | 60.59 (26.19) | 58.61 (27.17) | 0.34 |
| | Median (Q1, Q3) | 59.99 (39.29, 79.97) | 61.84 (42.86, 83.33) | 60.71 (39.29, 81.48) | |
| % Teeth BOP 4–6 Sites | Mean (s.d.) | 10.00 (17.84) | 12.41 (18.80) | 10.95 (18.23) | 0.13 |
| | Median (Q1, Q3) | 0.00 (0.00, 10.71) | 3.57 (0.00, 18.52) | 3.57 (0.00, 14.81) | |
| % Sites PI ≥1 | Mean (s.d.) | 64.22 (27.91) | 63.17 (25.81) | 63.80 (27.06) | 0.58 |
| | Median (Q1, Q3) | 69.20 (41.07, 89.74) | 68.30 (44.23, 82.14) | 68.75 (42.86, 87.04) | |
| % Sites PI ≥2 | Mean (s.d.) | 18.42 (17.72) | 22.64 (20.45) | 20.09 (18.93) | 0.13 |
| | Median (Q1, Q3) | 12.50 (5.36, 26.36) | 16.96 (7.14, 35.71) | 14.29 (5.36, 30.77) | |
| % Sites PI =3 | Mean (s.d.) | 2.81 (6.77) | 4.71 (9.79) | 3.56 (8.14) | 0.04 |
| | Median (Q1, Q3) | 0.00 (0.00, 1.79) | 0.00 (0.00, 5.36) | 0.00 (0.00, 3.57) | |
| # Teeth Max PI ≥1 | Mean (s.d.) | 21.92 (6.93) | 21.69 (6.75) | 21.83 (6.85) | 0.43 |
| | Median (Q1, Q3) | 24 (19, 28) | 24 (18, 27) | 24 (19, 28) | |
| # Teeth Max PI ≥2 | Mean (s.d.) | 8.54 (7.20) | 9.97 (7.86) | 9.11 (7.49) | 0.16 |
| | Median (Q1, Q3) | 7 (3, 13) | 9 (3, 16) | 7 (3, 15) | |
| # Teeth Max PI =3 | Mean (s.d.) | 1.46 (3.43) | 2.25 (4.39) | 1.77 (3.85) | 0.04 |
| | Median (Q1, Q3) | 0 (0, 1) | 0 (0, 3) | 0 (0, 2) | |
| % Sites GI ≥1 | Mean (s.d.) | 52.43 (36.66) | 52.69 (35.10) | 52.53 (35.99) | 0.94 |
| | Median (Q1, Q3) | 53.87 (16.96, 89.38) | 53.87 (17.26, 85.71) | 53.87 (17.26, 87.50) | |
| % Sites GI ≥2 | Mean (s.d.) | 13.82 (19.35) | 18.76 (23.19) | 15.78 (21.05) | 0.13 |
| | Median (Q1, Q3) | 4.76 (0.00, 20.12) | 4.85 (0.00, 31.55) | 4.76 (0.00, 26.19) | |
| % Sites GI =3 | Mean (s.d.) | 1.43 (4.19) | 3.06 (7.43) | 2.07 (5.74) | 0.009 |
| | Median (Q1, Q3) | 0 (0, 0) | 0.00 (0.00, 1.28) | 0.00 (0.00, 0.60) | |
| # Teeth Max GI ≥1 | Mean (s.d.) | 18.79 (10.21) | 19.49 (9.42) | 19.07 (9.90) | 0.99 |

| Characteristic | | HIV Infection Status: Infected (N=180) | Uninfected (N=118) | Total (N=298) | P-Value* |
|---|---|---|---|---|---|
| | Median (Q1, Q3) | 24 (10, 28) | 24 (14, 27) | 24 (10, 28) | |
| # Teeth Max GI ≥2 | Mean (s.d.) | 7.84 (9.08) | 9.47 (9.74) | 8.49 (9.36) | 0.19 |
| | Median (Q1, Q3) | 4 (0, 14) | 6 (0, 19) | 4.50 (0.00, 17.00) | |
| # Teeth Max GI =3 | Mean (s.d.) | 1.11 (2.91) | 2.02 (4.14) | 1.47 (3.47) | 0.01 |
| | Median (Q1, Q3) | 0 (0, 0) | 0 (0, 2) | 0 (0, 1) | |
| % Sites PD ≥3 | Mean (s.d.) | 22.02 (16.90) | 22.77 (16.84) | 22.32 (16.85) | 0.63 |
| | Median (Q1, Q3) | 19.05 (7.49, 32.14) | 20.14 (10.12, 32.64) | 19.57 (7.74, 32.14) | |
| % Sites PD ≥4 | Mean (s.d.) | 3.57 (5.04) | 4.04 (7.03) | 3.76 (5.90) | 0.73 |
| | Median (Q1, Q3) | 1.19 (0.00, 5.57) | 1.40 (0.00, 5.95) | 1.19 (0.00, 5.59) | |
| # Teeth Max PD ≥3 | Mean (s.d.) | 14.83 (8.24) | 15.48 (7.94) | 15.09 (8.12) | 0.51 |
| | Median (Q1, Q3) | 15 (8, 22) | 16 (9, 23) | 15 (9, 22) | |
| # Teeth Max PD ≥4 | Mean (s.d.) | 3.79 (4.78) | 4.04 (5.18) | 3.89 (4.94) | 0.72 |
| | Median (Q1, Q3) | 2.00 (0.00, 6.50) | 2 (0, 6) | 2 (0, 6) | |
| % Sites CAL ≥2 | Mean (s.d.) | 17.03 (19.40) | 17.24 (17.47) | 17.12 (18.63) | 0.47 |
| | Median (Q1, Q3) | 10.71 (2.68, 23.12) | 14.88 (3.57, 24.40) | 11.46 (2.98, 23.21) | |
| % Sites CAL ≥3 | Mean (s.d.) | 2.91 (6.17) | 2.65 (5.50) | 2.81 (5.91) | 0.63 |
| | Median (Q1, Q3) | 0.00 (0.00, 2.47) | 0.60 (0.00, 2.38) | 0.00 (0.00, 2.47) | |
| # Teeth Max CAL ≥2 | Mean (s.d.) | 11.46 (8.92) | 12.25 (8.48) | 11.78 (8.74) | 0.37 |
| | Median (Q1, Q3) | 11.00 (3.50, 19.00) | 14 (4, 18) | 12 (4, 18) | |
| # Teeth Max CAL ≥3 | Mean (s.d.) | 2.79 (4.88) | 2.65 (4.61) | 2.74 (4.77) | 0.62 |
| | Median (Q1, Q3) | 0.00 (0.00, 3.50) | 1 (0, 3) | 0 (0, 3) | |

*Wilcoxon Test

"% Sites XXX" parameter: percent of all sites examined in the entire dentition of a participant with characteristic XXX.
% Teeth BOP: percent of all teeth with at least one site with BOP per participant
% Teeth BOP 4–6 sites: percent of all teeth with at least four sites with BOP per participant

"# Teeth Max XXX" parameter: the count of teeth of a participant withat least one surface with characteristic XXX"



*J Clin Periodontol*. Author manuscript; available in PMC 2018 January 01.

**Table 5**

Proportion of selected periodontal parameters by site or region and by HIV infection status

| | | GI ≥ 2 Frequency (Proportion) | | CAL ≥ 3 mm Frequency (Proportion) | | PD ≥ 4 mm Frequency (Proportion) | |
|---|---|---|---|---|---|---|---|
| **Group (Total number of tooth surfaces)** | | **PHIV (n=29372)** | **PHEU (n=19099)** | **PHIV (n=29301)** | **PHEU (n=18980)** | **PHIV (n=29306)** | **PHEU (n=19022)** |
| Overall | | 4,083 (13.9%) | 3,555 (18.6%) | 862 (2.94%) | 502 (2.64%) | 1,041 (3.55%) | 755 (3.97%) |
| site | distal buccal | 893 (18.2%) | 764 (24.1%) | 261 (5.34%) | 137 (4.33%) | 351 (7.18%) | 224 (7.06%) |
| | buccal | 563 (11.5%) | 535 (16.9%) | 27 (0.56%) | 28 (0.89%) | 18 (0.37%) | 14 (0.44%) |
| | mesial buccal | 943 (19.3%) | 782 (24.7%) | 224 (4.58%) | 150 (4.74%) | 290 (5.93%) | 244 (7.70%) |
| | distal lingual | 683 (14.0%) | 568 (17.8%) | 173 (3.54%) | 96 (3.04%) | 211 (4.32%) | 149 (4.70%) |
| | lingual | 333 (6.8%) | 369 (11.6%) | 25 (0.51%) | 22 (0.70%) | 14 (0.29%) | 17 (0.54%) |
| | mesial lingual | 668 (13.6%) | 537 (16.8%) | 152 (3.11%) | 69 (2.18%) | 157 (3.21%) | 107 (3.37%) |
| region | lower anterior | 1,294 (20.1%) | 1,160 (27.7%) | 60 (0.93%) | 58 (1.39%) | 91 (1.41%) | 76 (1.81%) |
| | upper anterior | 828 (12.9%) | 610 (14.7%) | 98 (1.53%) | 61 (1.47%) | 106 (1.65%) | 121 (2.92%) |
| | lower posterior | 1,075 (13.0%) | 1,012 (18.8%) | 328 (3.98%) | 192 (3.59%) | 412 (5.00%) | 297 (5.53%) |
| | Upper posterior | 886 (10.7%) | 773 (14.4%) | 376 (4.58%) | 191 (3.60%) | 432 (5.26%) | 261 (4.90%) |

*J Clin Periodontol*. Author manuscript; available in PMC 2018 January 01.

**Table 6**

Surface Level Logistic Regression Models for the Risk of Gingival Index ≥ 2 using GEE Methods*

| Parameter | Level | Unadjusted Univariate Models | | | Adjusted Multivariable Model** (290 participants) | |
|---|---|---|---|---|---|---|
| | | N*** | OR (95% CI) | p-value | aOR (95% CI) | p-value |
| HIV Infected | | 298 | 0.69 (0.48, 1.00) | 0.05 | 1.05 (0.73, 1.50) | 0.81 |
| Age Category (years) | 19+ | 298 | 0.83 (0.48, 1.42) | 0.50 | 1.04 (0.59, 1.81) | 0.90 |
| | 17 to <19 | . | 1.01 (0.61, 1.67) | 0.98 | 0.93 (0.55, 1.59) | 0.80 |
| | 14 to <17 | . | 1.12 (0.69, 1.81) | 0.66 | 1.09 (0.77, 1.54) | 0.64 |
| | 10 to <14 | . | 1 | | 1 | |
| Female Sex | | 298 | 0.88 (0.62, 1.27) | 0.50 | 1.07 (0.81, 1.42) | 0.62 |
| Black Race | | 298 | 1.00 (0.69, 1.45) | 0.98 | 0.70 (0.41, 1.22) | 0.21 |
| Hispanic Ethnicity | | 298 | 1.08 (0.75, 1.57) | 0.67 | 0.83 (0.49, 1.42) | 0.50 |
| Tanner Category | Stage 5 | 298 | 1.18 (0.69, 2.04) | 0.54 | -- | -- |
| | Stage 4 | . | 0.96 (0.53, 1.75) | 0.90 | -- | -- |
| | Stage 1–3 | . | 1 | | -- | -- |
| Caregiver is Biological Parent | | 298 | 1.00 (0.69, 1.43) | 0.98 | -- | -- |
| Caregiver has some College | | 296 | 0.82 (0.54, 1.26) | 0.37 | -- | -- |
| Caregiver Income <$30,001 | | 292 | 0.83 (0.55, 1.26) | 0.38 | -- | -- |
| Sex Ever | | 292 | 0.90 (0.63, 1.30) | 0.59 | -- | -- |
| Oralsex Ever | | 292 | 0.88 (0.61, 1.29) | 0.52 | -- | -- |
| Drink Alcohol: Past 3 Months | | 292 | 1.06 (0.69, 1.62) | 0.78 | 1.30 (0.76, 2.21) | 0.34 |
| Smoke Cigarette: Past 3 Months | | 290 | 0.87 (0.46, 1.64) | 0.67 | 0.81 (0.53, 1.22) | 0.31 |
| Use Marijuana: Past 3 Months | | 292 | 0.76 (0.47, 1.23) | 0.27 | -- | -- |
| Brush Frequency (times/day) | <1 | 298 | 1.92 (1.02, 3.63) | 0.04 | 1.76 (1.12, 2.77) | 0.02 |
| | 1 | . | 1.56 (1.06, 2.28) | 0.02 | 1.02 (0.74, 1.41) | 0.91 |
| | ≥2 | . | 1 | | 1 | |
| Floss Frequency (times/day) | <1 | 298 | 0.81 (0.30, 2.16) | 0.67 | 0.63 (0.43, 0.90) | 0.01 |
| | 1 | . | 1.01 (0.34, 3.01) | 0.99 | 0.68 (0.40, 1.14) | 0.14 |

| Parameter | Level | Unadjusted Univariate Models | | | Adjusted Multivariable Model** (290 participants) | |
|---|---|---|---|---|---|---|
| | | N*** | OR (95% CI) | p-value | aOR (95% CI) | p-value |
| | ≥2 | . | 1 | | 1 | |
| Have No Source of Dental Care | | 294 | 0.95 (0.61, 1.49) | 0.82 | -- | -- |
| No Cleaning in Last Year | | 297 | 1.13 (0.78, 1.64) | 0.52 | -- | -- |
| Meal/Snack Frequency (times/day) ≥5 | | 298 | 1.47 (0.99, 2.19) | 0.06 | -- | -- |
| Juice/Soda Frequency (times/day) ≥2 | | 298 | 1.78 (1.12, 2.83) | 0.01 | 1.90 (1.30, 2.79) | <.001 |
| Saliva Volume (mL/min) | | 296 | 1.00 (0.71, 1.40) | 0.98 | -- | -- |
| PI: 1 vs 0 | | 298 | 1.81 (1.61, 2.04) | <.0001 | 1.70 (1.39, 2.08) | <.0001 |
| PI: 2 vs 0 | | . | 3.78 (3.14, 4.55) | <.0001 | 3.37 (2.26, 5.01) | <.0001 |
| PI: 3 vs 0 | | . | 8.17 (5.72, 11.7) | <.0001 | 7.03 (4.17, 11.8) | <.0001 |
| Site | | 298 | | | | |
| Distal Buccal | | . | 2.73 (2.32, 3.21) | <.0001 | 2.62 (1.68, 4.08) | <.0001 |
| Buccal | | . | 1.66 (1.42, 1.95) | <.0001 | 1.47 (1.13, 1.90) | <.01 |
| Mesial Buccal | | . | 2.87 (2.42, 3.41) | <.0001 | 2.78 (1.72, 4.48) | <.0001 |
| Distal Lingual | | . | 1.93 (1.72, 2.16) | <.0001 | 2.06 (1.20,3.56) | <.01 |
| Mesial Lingual | | . | 1.84 (1.65, 2.06) | <.0001 | 1.95 (1.22, 3.12) | <.01 |
| Lingual | Reference | . | 1 | | 1 | |
| Region | | 298 | | | | |
| Lower Anterior | Teeth 22–27 | . | 2.16 (1.83, 2.56) | <.0001 | 2.10 (1.48, 3.00) | <.0001 |
| Lower Posterior | Teeth 18–21, 28–31 | . | 1.33 (1.18, 1.50) | <.0001 | 1.34 (1.04, 1.74) | 0.03 |
| Upper Anterior | Teeth 6–11 | . | 1.13 (0.96, 1.33) | 0.15 | 1.24 (0.80, 1.93) | 0.33 |
| Upper Posterior | Teeth 2–5, 12–15 | . | 1 | | 1 | |
| **PHIV cohort** | | | | | (n=175)# | |
| CD4+ Nadir < 200 cells/mm$^3$ | | 180 | 1.44 (0.86, 2.41) | 0.16 | 1.30 (0.84, 2.00) | 0.23 |
| Current CD4+ ≤350 cells/mm$^3$ | | 180 | 1.13 (0.63, 2.05) | 0.68 | 1.30 (0.97, 1.74) | 0.08 |
| HIV Viral Load ≥ 400 | | 178 | 1.22 (0.73, 2.01) | 0.45 | 1.13 (0.82, 1.55) | 0.46 |

*J Clin Periodontol*. Author manuscript; available in PMC 2018 January 01.

| Parameter | Level | Unadjusted Univariate Models | | | Adjusted Multivariable Model** (290 participants) | |
|---|---|---|---|---|---|---|
| | | N*** | OR (95% CI) | p-value | aOR (95% CI) | p-value |
| copies/mL | | | | | | |
| History of AIDS-Defining illness | | 180 | 1.21 (0.70, 2.08) | 0.50 | 1.51 (1.04, 2.20) | 0.03 |

*Generalized Estimating Equation method using the assumption that any two surfaces within a participant have the same correlation, and bias-corrected sandwich estimator was used for the covariance matrix of the estimates.

**One final multivariable model include HIV infection, demographics, drinking alcohol, smoking cigarettes, brush and floss frequencies, juice/soda frequency, PI, site and region. The effect of institution was also considered as a random effect (p-value < 0.0001) in the intercept of the model.

***Number of participants in the respective unadjusted analysis. The number of surfaces with gingival index scored for each participant ranges from 123 to 168.

#aOR in PHIV cohort analyses were adjusted for all significant covariates identified in the PHIV and PHEU combined multivariable model above. The sample size of the model for the association with viral load was 173 due to two more missing in viral load.

**Table 7**

Surface Level Logistic Regression Models for the Risk of Interproximal Clinical Attachment Loss at least 3mm using GEE Methods*

| Parameter | Level | Unadjusted Univariate Models | | | Adjusted Multivariable Model** (288 participants) | |
|---|---|---|---|---|---|---|
| | | N*** | OR (95% CI) | p-value | aOR (95% CI) | p-value |
| HIV Infected | | 298 | 1.15 (0.69, 1.93) | 0.59 | 1.05 (0.85, 1.31) | 0.64 |
| Age Category (years) | 19+ | 298 | 1.82 (0.83, 4.02) | 0.14 | 0.78 (0.36, 1.72) | 0.54 |
| | 17 to <19 | . | 1.31 (0.60, 2.84) | 0.50 | 0.54 (0.20, 1.44) | 0.22 |
| | 14 to <17 | . | 1.01 (0.52, 1.98) | 0.98 | 0.71 (0.41, 1.25) | 0.24 |
| | 10 to <14 | . | 1 | | 1 | |
| Female Sex | | 298 | 0.87 (0.52, 1.45) | 0.60 | 1.44 (0.93, 2.23) | 0.11 |
| Black Race | | 298 | 0.66 (0.40, 1.11) | 0.12 | 0.51 (0.19, 1.36) | 0.18 |
| Hispanic Ethnicity | | 298 | 1.27 (0.77, 2.09) | 0.36 | 0.54 (0.15, 1.95) | 0.35 |
| Tanner Category | Stage 5 | 298 | 1.84 (0.77, 4.38) | 0.17 | -- | -- |
| | Stage 4 | . | 1.40 (0.54, 3.67) | 0.50 | -- | -- |
| | Stage 1–3 | . | 1 | -- | -- | |
| Caregiver is Biological Parent | | 298 | 0.91 (0.55, 1.51) | 0.72 | -- | -- |
| Caregiver has some College | | 296 | 0.47 (0.24, 0.93) | 0.03 | 0.58 (0.34, 1.01) | 0.06 |
| Caregiver Income <$30,001 | | 292 | 1.45 (0.77, 2.73) | 0.25 | -- | -- |
| Sex Ever | | 292 | 2.33 (1.41, 3.83) | <.001 | 2.36 (1.50, 3.71) | <.001 |
| Oralsex Ever | | 292 | 2.15 (1.30, 3.55) | <.01 | -- | -- |
| Drink Alcohol: Past 3 Months | | 292 | 1.61 (0.90, 2.90) | 0.11 | 1.11 (0.61, 2.00) | 0.74 |
| Smoke Cigarette: Past 3 Months | | 290 | 1.50 (0.75, 2.98) | 0.25 | 1.00 (0.42, 2.39) | 1.00 |
| Use Marijuana: Past 3 Months | | 292 | 1.25 (0.63, 2.49) | 0.53 | -- | -- |
| Brush Frequency (times/day) | <1 | 298 | 1.05 (0.38, 2.92) | 0.92 | 0.83 (0.36, 1.93) | 0.67 |
| | 1 | . | 0.88 (0.51, 1.51) | 0.63 | 0.98 (0.57, 1.69) | 0.95 |
| | ≥2 | . | 1 | | 1 | |

| Parameter | Level | Unadjusted Univariate Models | | | Adjusted Multivariable Model** (288 participants) | |
|---|---|---|---|---|---|---|
| | | N*** | OR (95% CI) | p-value | aOR (95% CI) | p-value |
| Floss Frequency (times/day) | <1 | 298 | 2.08 (0.77, 5.64) | 0.15 | 1.62 (0.69, 3.77) | 0.27 |
| | 1 | . | 3.60 (1.11, 11.7) | 0.03 | 1.75 (0.67, 4.57) | 0.25 |
| | ≥2 | . | 1 | | 1 | |
| Have No Source of Dental Care | | 294 | 0.64 (0.32, 1.29) | 0.22 | -- | -- |
| No Cleaning in Last Year | | 297 | 0.97 (0.57, 1.63) | 0.90 | -- | -- |
| Meal/Snack Frequency (times/day) ≥5 | | 298 | 0.67 (0.40, 1.13) | 0.13 | -- | -- |
| Juice/Soda Frequency (times/day) ≥2 | | 298 | 0.93 (0.52, 1.69) | 0.82 | -- | -- |
| Saliva Volume (mL/min) | | 296 | 1.00 (0.61, 1.62) | 0.98 | -- | -- |
| PI: 1 vs 0 | | 298 | 1.95 (1.54, 2.48) | <.0001 | 1.74 (1.36, 2.23) | <.0001 |
| PI: 2 vs 0 | | . | 3.14 (2.25, 4.39) | <.0001 | 2.79 (1.80, 4.32) | <.0001 |
| PI: 3 vs 0 | | . | 2.76 (1.70, 4.46) | <.0001 | 2.38 (1.27, 4.46) | <.01 |
| Site | | 298 | | | | |
| Distal Buccal | | . | 1.85 (1.54, 2.21) | <.0001 | 1.74 (1.48, 2.05) | <.0001 |
| Mesial Buccal | | . | 1.73 (1.41, 2.12) | <.0001 | 1.61 (1.36, 1.91) | <.0001 |
| Distal Lingual | | . | 1.23 (1.08, 1.39) | < 0.01 | 1.22 (1.12, 1.32) | < .0001 |
| Mesial Lingual | Reference | . | 1 | | 1 | |
| Region | | 298 | | | | |
| Upper Posterior | Teeth 2–5, 12–15 | | 4.27 (2.81, 6.49) | <.0001 | 4.72 (2.43, 9.17) | <.0001 |
| Lower Posterior | Teeth 18–21, 28–31 | . | 3.80 (2.48, 5.83) | <.0001 | 4.15 (2.25, 7.64) | <.0001 |
| Upper Anterior | Teeth 6–11 | . | 1.44 (1.01, 2.05) | 0.04 | 1.68 (1.32, 2.15) | <.0001 |
| Lower Anterior | Teeth 22–27 | . | 1 | | 1 | |
| **PHIV cohort** | | | | | n = 174# | |
| CD4+ Nadir < 200 cells/mm$^3$ | | 180 | 1.31 (0.68, 2.55) | 0.42 | 0.97 (0.47, 2.01) | 0.94 |



*J Clin Periodontol*. Author manuscript; available in PMC 2018 January 01.

| Parameter | Level | Unadjusted Univariate Models | | | Adjusted Multivariable Model** (288 participants) | |
|---|---|---|---|---|---|---|
| | | N*** | OR (95% CI) | p-value | aOR (95% CI) | p-value |
| Current CD4+ ≤350 cells/mm$^3$ | | 180 | 0.59 (0.24, 1.49) | 0.26 | 1.07 (0.65, 1.78) | 0.79 |
| HIV Viral Load ≥ 400 copies/mL | | 178 | 0.43 (0.22, 0.86) | 0.02 | 0.84 (0.42, 1.69) | 0.63 |
| History of AIDS-Defining Illness | | 180 | 1.49 (0.72, 3.10) | 0.28 | 0.79 (0.49, 1.27) | 0.33 |

*Generalized Estimating Equation method using the assumption that any two surfaces within a participant have the same correlation, and bias-corrected sandwich estimator was used for the covariance matrix of the estimates.

**One final multivariable model include HIV infection, demographics, drinking alcohol, smoking cigarettes, brush and floss frequencies, ever had sex, caregiver had some college education, PI, site and region. The effect of institution was also considered as a random effect (p-value < 0.0001) in the intercept of the model.

***Number of participants in the respective unadjusted analysis. The number of surfaces with clinical attachment loss measured for each participant ranges from 58 to 112.

#aOR for viral load was adjusted for all significant covariates identified in the PHIV and PHEU combined multivariable model with sample size 172. aOR for CD4+ nadir < 200 cells/mm$^3$,for current CD4+ ≤350 cells/mm$^3$ or for History of AIDS-Defining Illness was adjusted for all these covariates except female, brushing frequency and smoking in past 3 months which were selected by less significant results to avoid numerical issues.