Published in final edited form as:

Sex Transm Infect. 2012 February ; 88(1): 45–50. doi:10.1136/sextrans-2011-050231.

HIV shedding in the oral cavity: an assessment of HIV type, immunovirologic, demographic and oral factors

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Abstract

Objective—To quantify the prevalence and burden of HIV type 2 (HIV-2) and HIV-1 RNA in the oral cavity of antiretroviral therapy-naïve HIV-infected Senegalese individuals and to identify correlates of oral HIV viral loads.

Design—A cross-sectional study of 163 HIV-1 and 27 HIV-2-infected antiretroviral therapy-naïve Senegalese adults.

Methods—Participants received clinical and oral exams and provided blood and oral wash samples for viral load and plasma CD4 count ascertainment. Logistic and interval regression models were used to identify univariate and multivariable associations between presence and level of oral HIV RNA and various immunovirologic, local and demographic factors.

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An additional table is published online only. To view this file please visit the journal online (<http://sti.bmj.com/content/88/1.toc>).

Competing interests: None.

Ethics approval: University of Washington Institutional Review Board, University of Dakar Institutional Review Board and the Senegalese National AIDS committee.

Contributors: PBP provided the statistical analysis and was the primary writer of this manuscript, which was the topic of her thesis in epidemiology at the University of Washington. SEH provided assistance in the study concept and design, supervised the data analysis and helped to draft the manuscript. GSG provided assistance with the study design, data analysis and interpretation and helped to draft the manuscript. CFN and AG oversaw study procedures, oral exams and specimen collection at the dental clinic. CWC was principal investigator of the study and provided funding for the project. PSS was the head of the outpatient infectious disease clinics at the Fann University Hospital in Dakar, from which study patients were referred and enrolled. QF heads the laboratory in Seattle where study viral loads were quantified. NBK provided assistance in the study concept and design and provided funding for the project. All authors assisted in drafting the manuscript and have approved the final submitted version.

Provenance and peer review: Not commissioned; externally peer reviewed.

Results—Presence of detectable oral HIV RNA was less common in HIV-2-infected compared with HIV-1-infected study participants (33% vs 67%, OR 0.25, 95% CI 0.11 to 0.59). HIV type was no longer associated with oral shedding of HIV when plasma viral load was considered. Detection of oral HIV RNA was associated with increased plasma viral load in both HIV-1-infected and HIV-2-infected individuals (HIV-1, OR 1.89, 95% CI 1.24 to 2.61; HIV-2, OR 1.93, 95% CI 1.1 to 3.39). Oral HIV-1 detection was also associated with periodontal disease (OR 3.02, 95% CI 1.16 to 7.87).

Conclusions—Oral shedding of HIV-2 RNA is less common than HIV-1 RNA, a likely consequence of lower overall viral burden. Both systemic and local factors may contribute to shedding of HIV in the oral cavity.

Introduction

Shedding of HIV-1 and/or HIV-2 has been demonstrated in cervicovaginal fluid, semen, breast milk and anal–rectal mucosa.^{1–6} While research has suggested that the virus is inactivated by inhibitory salivary factors, there is evidence that HIV-1 RNA is present at low levels in the oral cavity. The presence of oral HIV RNA may simply reflect systemic burden of the infection or may be a site of viral replication.

As with other anatomic compartments, HIV-1 DNA and RNA in the oral cavity are not detected in all infected individuals, HIV-1 RNA detection rates ranging from 42% to 100% and proviral DNA typically ranging from 0% to 50%.^{347–12} Consistently across studies, salivary HIV-1 is positively associated with plasma HIV-1 viral load with Pearson's correlation coefficients ranging from 0.21 to 0.51.⁴⁷¹¹ Other factors commonly associated with plasma HIV levels, such as blood CD4 count, antiretroviral therapy (ART) and stage of disease, are inconsistently associated with oral shedding of HIV-1.⁹¹³¹⁴ Associations between oral HIV-1 and dental parameters and/or oral lesions revealed similarly inconsistent associations.^{9–1215}

To our knowledge, all studies looking at oral shedding of HIV are limited to HIV-1-infected participants. Compared with HIV-1, HIV-2 is characterised by reduced transmissibility, lower plasma and genital tract viral loads, slower decline in CD4 T cell counts and slower disease progression.¹²¹⁶¹⁷ The current study aimed to evaluate the difference in oral shedding of HIV between HIV-1-infected and HIV-2-infected individuals in Senegal, West Africa. Among these patients, we also evaluated potential immunovirologic, periodontal and demographic factors associated with oral HIV shedding.

Methods

Study setting and participants

Between September 1994 and July 1998, ART-naïve HIV-1-positive and HIV-2-positive men (18 years) and women (15 years) presenting to either the University of Dakar outpatient infectious disease clinic or an STD clinic in Mbour were asked to participate in a study of oral manifestations of HIV and in a subset of subjects, oral HIV shedding. Of 786 persons testing positive for HIV-1 and 150 testing positive for HIV-2, 163 HIV-1 and 27 HIV-2 individuals provided at least one oral wash sample. We excluded patients who were

infected with both types of HIV. The study was conducted according to procedures approved by the University of Washington Institutional Review Board, University of Dakar Institutional Review Board and the Senegalese National AIDS committee.

Data collection

Consenting participants were interviewed to obtain information regarding demographic characteristics, sexual behaviours and a standard medical history. Fifteen millilitres of peripheral blood was collected to determine the number of CD4 cells per microlitre of blood and qualitative and quantitative assays used to detect the number of HIV-1 and HIV-2 RNA copies per millilitre of blood as described previously.¹⁸

An examiner trained in Oral Medicine at the University of Dakar Dental Clinic examined the oral cavity of each study participant. Information on plaque index, gingival index, probing depth and clinical attachment loss was collected. Additionally, the examiner presumptively diagnosed the following types of oral pathology: candida pharyngitis, candida oesophagitis, perleche (angular cheilitis), hairy leukoplakia, other leukoplakia, ulcerations, oral herpes, aphthous ulcer, condyloma, Kaposi's sarcoma, other cancers, geographic tongue and other lesions. Periodontal disease was defined as the presence of linear gingival erythema, necrotising gingivitis and/or necrotising periodontitis. HIV-associated lesions were defined as presence of candida pharyngitis, angular cheilitis, candida oesophagitis, hairy leukoplakia, Kaposi's sarcoma, oral herpes and/or aphthous ulcers.

Subjects were given a small container containing 10 ml of sterile physiologic saline, instructed to swish the saline around the mouth and spit the saline back out into a sterile tube. Oral washes were collected from all patients and specimens centrifuged at 2000 rpm for 10 min at 4°C. The supernatant was decanted into a sterile tube from which 200 µl was added to 600 µl of lysis reagent containing 800 copies of either HIV-1 or HIV-2 IQS RNA. The samples were ethanol precipitated and the RNA pellet was suspended in 400 µl of specimen diluent.

Quantitative and qualitative HIV-1 and HIV-2 RNA ascertainment in the plasma and oral supernatant were performed using PCR-based assays developed at Roche Molecular Systems (Pleasanton, California, USA) as described previously.²¹⁸¹⁹ The amount of HIV RNA in each sample was calculated from the ratio of the total optical density at 450 nm for the HIV-specific well to the total optical density for the IQS-specific well and the input number of IQS copies and expressed as the number of HIV copies per millilitre of supernatant. The quantitative and qualitative HIV-1 assays provided reliable HIV RNA quantification at levels greater than 400 HIV RNA copies and 200 copies/ml, respectively, with a minimum detection limit of 80 and 40 copies/ml, respectively. The quantitative and qualitative HIV-2 assays provided reliable HIV-2 RNA quantification at levels >200 HIV RNA copies and 100 copies/ml, respectively, with a minimum detection limit of 40 and 20 copies/ml, respectively. All specimens were shipped to Seattle for laboratory analyses.

Statistical analysis

In this analysis, complete cases were used to describe the patient characteristics by HIV type and to assess the association between HIV type and oral HIV viral load in the oral

supernatant using a χ^2 test of association and trend test. For all other analyses, missing values for plasma viral load, CD4 count, presence of periodontal disease, presence of HIV-related oral disorders and WHO-defined HIV disease stage were imputed based on the following set of covariates: HIV type, age, sex, smoking status, alcohol use, presence of gingival tattoos, presence of oral HIV RNA and non-imputed values of plasma viral load, CD4 count, presence of periodontal disease, presence of HIV-related oral disorders and WHO-defined HIV disease stage when non-missing. The range of imputed CD4 count and plasma viral load were set to match the range of non-imputed values.²⁰ Imputation model regression coefficients were estimated using a bootstrapped posterior predictive distribution, relaxing the assumption of multivariate normality on the distribution of regression coefficients. Ten data sets were created using Imputation by Chained Equations to multiply impute the missing values for model covariates.^{20,21}

Regression analyses were performed on each of the 10 imputed data sets and regression coefficients averaged across the 10 to generate final coefficient estimations. Univariate logistic and interval regression models were used to estimate the ORs and slope coefficients (β) of presence and mean of log-transformed oral HIV RNA, respectively, associated with immunovirologic markers of HIV progression (CD4 cell counts and log₁₀ plasma HIV RNA), oral local factors (periodontal disease and HIV-associated oral lesions) and demographic factors (age, sex and WHO-defined HIV disease stage). We created separate models for HIV-1 and HIV-2 because we believed that associations could differ by two types. We also adjusted the above analysis for log₁₀ plasma viral load, the correlate of oral shedding identified, a priori, to be a potential confounding factor in all other associations. Interval regression was used instead of linear regression to accommodate non-censored, interval censored and left censored oral HIV viral load data due to the assay detection limits.²² Robust SEs were used in both modelling techniques to relax the assumption of normal SEs in CI and p value calculations.

The midpoint of the detection range was imputed in subjects with oral and plasma HIV RNA levels below the limits of quantification or detection for the calculation of correlation coefficients, graphical displays and modelling in the case of plasma HIV RNA. Viral loads were transformed to their log₁₀ values to satisfy the assumption of normality. In the case of multiple oral viral load measurements for a given individual, the earliest collection date was used in the analysis. In the case of non-contemporaneous collection of labs (plasma and CD4 counts) and oral exams, the data obtained on the date nearest the date of the oral viral load ascertainment were used.

All analyses were conducted using SAS V.9.1 and STATA V.10.1 with statistical significance criteria set at $p = 0.05$.

Results

Compared with HIV-2-infected persons at baseline, persons with HIV-1 tended to be younger (median age 33 vs 38, $p=0.03$) and were less likely to be female sex workers (16.9% vs 46.6%, $p<0.01$) (table 1). Furthermore, compared with those with HIV-2 infection, participants with HIV-1 were more likely to have plasma viral loads >10000

copies/ml (74.5% vs 22.2%, $p<0.0001$) and CD4 counts <200 cells/ μ l (49.1% vs 29.6%, $p<0.01$). Of the 142 HIV-1-infected patients and 19 HIV-2-infected patients with oral pathology data available, respectively, 21.7% and 3.7% were diagnosed as having linear gingival erythema, 4.4% and 0.6% as having necrotising gingivitis and 6.8% and 0.6% as having necrotising periodontitis. The median number of days between collection of oral samples (for oral viral loads) and blood samples (CD4 cell count and plasma viral load) as well as between oral sample collections and oral exams did not differ by HIV type. The oral sample was collected on the same day as blood for 58.9% of HIV-1 patients and 76.0% of HIV-2 patients and oral sample collected on the same day as the oral exam for 89.0% of HIV-1 patients and 95.0% of HIV-2 patients.

Presence of detectable oral HIV RNA was less common in HIV-2-infected compared with HIV-1-infected study participants (33% vs 67%, $p=0.001$) (table 2). Complete case logistic regression revealed that the odds of detection were 75% lower in HIV-2-infected compared with HIV-1-infected patients (OR 0.25, 95% CI 0.11 to 0.59). However, this difference did not persist after adjustment for log plasma viral load (OR 0.92, 95% CI 0.29 to 2.95). Median levels of oral HIV RNA were significantly lower in HIV-2-infected (median: 0–20, IQR 0–20, 49) compared with HIV-1-infected patients (median: 40–80, IQR 0–40, 718, $p<0.01$).

We imputed values for the missing data for independent variables. The percent missing values by HIV type were as follows: CD4 cell count (HIV-1: 15.3%, HIV-2: 7.4%), plasma viral load (HIV-1: 14.1%, HIV-2: 18.5%), periodontal disease (HIV-1: 12.9%, HIV-2: 29.6%), HIV-related oral lesion (HIV-1: 10.4%, HIV-2: 25.9%) and WHO disease stage (HIV-1: 8.0%, HIV-2: 7.4%). HIV type, age and sex did not have any missing values.

Logistic regression was applied to the 10 imputed data sets to assess predictors of detection of oral RNA. Among HIV-1-infected participants, groups of patients with increased $\log_{10}$ plasma HIV RNA, presence of periodontal disease and WHO disease stage 3, compared with stage 1, were all significantly associated with detection of oral HIV in univariate analyses (table 3). Among HIV-2-infected participants, $\log_{10}$ plasma HIV RNA level was significantly associated with detection and the risk estimate was similar, although slightly higher, to the risk estimate for HIV-1. Similar to HIV-1, there was a trend towards increased odds of oral RNA detection among the group of HIV-2-infected patients with higher levels of WHO-defined disease. However, periodontal disease had an inverse relationship, albeit not significant, with oral RNA detection among HIV-2 individuals. No other factors were significantly associated with detection of oral HIV-2. HIV-1-infected and HIV-2-infected patients with lower CD4 cell counts tended to have more oral RNA detected; however, the trend was not statistically significant when modelling CD4 count linearly, linearly with log transformation, nor categorically (which was the best-fitting model).

In analyses adjusting for $\log_{10}$ plasma HIV RNA, periodontal disease remained associated with oral RNA among HIV-1-infected (OR 2.79, 95% CI 1.08 to 7.24) but not among HIV-2-infected patients (OR 0.43, 95% CI 0.03 to 7.5). After adjustment for periodontal disease, $\log_{10}$ plasma HIV RNA remained significantly associated with oral RNA detection

in both HIV-1-infected (OR 1.74, 95% CI 1.18 to 2.58) and HIV-2-infected patients (OR 1.98, 95% CI 1.08 to 3.62).

Interval regression was applied to the 10 imputed data sets to evaluate the association of viral, systemic, local and demographic factors with the quantity of HIV oral HIV RNA (table 3). Similar to associations with presence of oral RNA, plasma viral load and periodontal disease were each associated with oral HIV viral load among HIV-1-infected persons, whereas only plasma viral loads were associated with oral viral loads among HIV-2-infected persons. After adjustment for $\log_{10}$ plasma viral load, the set of HIV-1-infected patients with periodontal disease had a mean oral RNA level that was 0.42 $\log_{10}$ higher, on average, than HIV-1-infected patients without periodontal disease ($\beta=0.42$, 95% CI 0.09 to 0.75). While there was a trend towards higher levels of oral RNA among patients with WHO-defined disease stage levels greater than 1, this positive association was only statistically significant among HIV-2 patients comparing stage 4 with stage 1 both in univariate and $\log_{10}$ plasma-adjusted models (adjusted $\beta=1.73$, 95% CI 0.93 to 2.53). All regression results using imputed data sets did not differ substantially from those using a complete case analysis (table 4, web only file).

For both HIV-1-infected and HIV-2-infected persons with non-missing values of plasma viral loads and detection limit midpoints used, plasma and oral viral loads were moderately correlated (Pearson's correlation coefficients: 0.33, $p<0.001$ vs 0.46, $p<0.05$) (figure 1). Using simple linear regression, $\log_{10}$ plasma HIV RNA was positively associated with $\log_{10}$ oral HIV RNA (HIV-1: $\beta=0.26$, 95% CI 0.13 to 0.39; HIV-2: $\beta=0.20$, 95% CI 0.02 to 0.38). When considering correlation coefficients using each of the 10 imputed data sets, coefficients ranged from 0.29 to 0.34 for HIV-1 and 0.36 to 0.46 for HIV-2.

Discussion

The present study is the first known assessment of oral HIV RNA shedding in HIV-2-infected individuals. In 67% of 163 HIV-1-infected and 33% of 27 HIV-2-infected ART-naïve individuals, oral shedding of HIV was detected. The detection percentage of HIV-1 found in the present study is within the range presented among HIV-1-infected individuals in other studies (38–100%) that included participants both on and off ART.^{347–1024} Without considering other factors related to oral shedding, the current study found that detection was less common and levels of oral RNA lower in HIV-2-infected compared with HIV-1-infected individuals, a finding similar to differences in shedding in seminal and cervicovaginal fluids between the two virus types.¹²²⁵ However, when considering plasma viral load, we found that HIV type was no longer independently associated with oral RNA. Therefore, differences in oral shedding between the two virus types may be a consequence of plasma viral load differences rather than fundamental difference between the two retroviruses.

We found that plasma viral loads were associated with detection and levels of oral HIV-1 and HIV-2. This association has been described across studies of HIV-1 oral shedding and observed with HIV-1 and HIV-2 shedding in other bodily fluids.²⁴⁹²⁶ We found plasma and oral viral loadstobe moderately correlated in both HIV-1-infected and HIV-2-infected

individuals with levels in plasma being consistently greater than levels in the oral wash. Lower levels in the oral cavity may be due to oral factors that inhibit HIV replication such as mucins, thrombospondin and secretory leucocyte protease inhibitors.^{827–30}

We found that HIV-1-infected patients with periodontal disease were more likely to have oral HIV detected than those without periodontal disease, an association that persisted after adjustment for log₁₀ plasma viral load. We did not find this association in HIV-2-infected individuals, which may be the result of a small sample size or indicative of a different mechanism in HIV-2 individuals. Periodontal disease, and specifically linear gingival erythema, was also shown to be associated with HIV-1 oral shedding in previous studies.⁹²⁴ The independent associations of higher plasma viral loads and periodontal disease shedding with oral HIV-1 suggest that the mechanism by which HIV-1 enters the saliva is likely multifocal, involving local and factors.

Unlike some studies of salivary and oropharyngeal HIV-1 RNA shedding, we did not find evidence of an association between CD4 cell count and oral HIV-1 or HIV-2 RNA.¹³²⁴ Importantly, these studies were conducted in patients who were on and off ART, and presumably all patients with CD4 counts <200 were on ART. Because the data in the present study were collected before widespread use of ART, all patients were ART-naïve and may represent the association between CD4 count and oral HIV in the absence of ART.

The present study was limited by its small sample size cross-sectional design. Despite the small sample of 27 HIV-2-infected patients, we did confirm that plasma viral load is associated with HIV-2 oral shedding. Because we analysed single evaluations of oral shedding and oral physical exams, we were not able to account for fluctuation in shedding and other biologic measures over time and we cannot infer the direction of causality between the factors of interest and oral shedding of HIV. Also, in some cases, measures of viral loads, labs and oral exams were not collected contemporaneously further complicating associations found between factors. However, in sensitivity analyses, including days between collection of oral viral loads and labs and days between oral viral loads and exams as covariates in the model did not alter the findings.

Despite these limitations, the present study was strengthened by the use of quantitative and qualitative assays to measure HIV RNA, decreasing the lower limit of detection. Further the regression technique used to model the dependent variable of oral HIV viral loads did not require imputations below detection limits. While we did impute values within detection ranges for plasma viral loads below the detection limits, cases of undetectable virus were much less common in the plasma (0.7% and 22.7% for HIV-1 and HIV-2, respectively) compared with the saliva (33.3% and 66.7% in HIV-1 and HIV-2, respectively). Furthermore, multiple imputation did not lead to conclusions that differed substantially from complete case analysis.

In summary, the present study confirms findings that plasma viral load and periodontal disease are associated with HIV-1 oral shedding and extends the plasma–oral shedding association to HIV-2-infected patients. The presence of oral HIV RNA shedding and the accessibility of the oral cavity for research and specimen collection over other sites of viral

shedding make the oral cavity a particularly important site for research. Future studies addressing the mechanisms of oral HIV shedding may act as a model for understanding how local factors influence viral replication and harbouring.

Acknowledgments

The authors would like to thank Deana Rich, Elise Reay-Ellers, Dr Mame B Diouf, Macoumba Touré, Dr Mame A Faye Niang, Habibatu Agne and Dr Awa M Coll-Seck for study coordination and supervision of study procedures and data management in Senegal. In addition, Dr Aissatou Diop, Dr Pierre Ndiaye, Marie Pierre Sy and Mame Dieumbe Mbengue-Ly provided patient care and recorded patient information. Shirley Kwok, Rich Respass, Kelly Lagassic and Jane Kuypers developed the assays and conducted the qualitative and quantitative testing of study samples for HIV-1 and HIV-2 RNA and DNA. Dr Penelope Leggott and Dr Paul B Robertson provided expertise regarding the design of oral examination study forms. Alison Starling developed study forms and was the data manager in Seattle.

Funding: This study was supported by grants from the National Institutes of Health (AI37466, CA62801, DE011372).

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Key messages

- Detection of oral HIV RNA was less common and levels of oral RNA lower in HIV-2-infected compared with HIV-1-infected individuals.
- When considering plasma viral load, we found that HIV type was no longer independently associated with oral RNA.
- Both systemic and local factors are associated with shedding of HIV RNA in the oral cavity.

Figure 1.
Log₁₀ copies of oral HIV RNA versus Log₁₀ copies of plasma HIV RNA, by HIV type.

Table 1
Patient demographics by HIV status

Characteristic	HIV serologic status		p Value
	HIV-1 (n=163) n (%) [*]	HIV-2 (n=27) n (%) [*]	
Male	92 (56.4)	12 (44.4)	0.25
Age (range 18–59)			
18–24	19 (11.8)	1 (4.0)	0.03 [†]
25–29	30 (18.6)	3 (12.0)	
30–34	41 (25.5)	4 (16.0)	
35–44	51 (31.7)	11 (44.0)	
45+	20 (12.4)	6 (24.0)	
Median (IQR)	33 (28–40)	38 (31–44)	
Marital status			
Single	30 (18.8)	3 (11.1)	0.10
Monogamously married	59 (36.9)	13 (48.2)	
Polygamously married	19 (11.9)	2 (7.4)	
Divorced/separated	28 (17.5)	6 (22.2)	
Widowed	24 (15.0)	3 (11.1)	
Alcohol user	18 (11.3)	3 (11.5)	0.97
Smoker	36 (22.5)	8 (29.6)	0.42
Female sex worker [‡]	12 (16.9)	7 (46.6)	0.003
Periodontal disease [§]	44 (31.0)	6 (31.6)	0.96
HIV-related oral lesion [¶]	39 (26.7)	2 (10.0)	0.10
Plasma HIV RNA copies/ml			
Below qualitative detection [‡]	1 (0.7)	5 (22.7)	<0.0001 [†]
Below level of quantification [§]	1 (0.7)	2 (9.1)	
Quantification limit [¶] to 999	2 (1.4)	6 (27.3)	
1000 copies/ml to 9999	14 (10.0)	3 (13.6)	
10 000	122 (87.1)	6 (27.3)	
Median (IQR)	123 717 (24 609– 444 608)	310 (20–40 ^{**} to 19511)	
Days between collection of oral and blood samples			
Median (IQR)	0 (0–27)	0 (0–0)	0.38
Days between oral viral load and oral exams			
Median (IQR)	0 (0–0)	0 (0–0)	0.48
CD4 count cells/ μ l			
>500	18 (13.0)	10 (40.0)	0.001 [†]
200–500	40 (29.0)	7 (28.0)	
<200	80 (58.0)	8 (32.0)	
Median (IQR)	169.5 (72–350)	438.0 (170–634)	

Characteristic	HIV serologic status		p Value
	HIV-1 (n=163) n (%) [*]	HIV-2 (n=27) n (%) [*]	
HIV disease stage ^{††}			
1	25 (16.7)	9 (36.0)	0.11
2	39 (26.0)	4 (16.0)	
3	79 (52.7)	11 (44.0)	
4	7 (4.7)	1 (4.0)	

^{*} Column percentages may not add up to 100% because of missing values.

[†] p Values based on the categorical version of variable are presented unless p value of continuous version differed.

[‡] <40 copies/ml; HIV-2: <20 copies/ml of HIV-2.

[§] HIV-1: 40–80 copies/ml; HIV-2: 20–40 copies/ml.

[¶] HIV-1: >80 copies/ml; >40 copies/ml of HIV-2.

^{**} Value within range rather than single value.

^{††} Based on WHO staging system.²³

Table 2
Univariate Detection and Quantification of oral viral loads by HIV type

	HIV type		p Value
	HIV-1 (N=163)	HIV-2 (N=27)	
Detection of oral HIV RNA*			
Below detection limit (DL) [†]	54 (33.3)	18 (66.7)	0.001
Detectable [‡]	108 (66.7)	9 (33.3)	
Quantification of oral HIV RNA [§]			
Below qualitative DL [†]	54 (33.3)	18 (66.7)	0.002
Qualitative DL to quantitative DL [¶]	28 (17.2)	1 (3.7)	
Above quantitative DL** to	48 (29.5)	8 (29.6)	
999 copies/ml			
1000 copies/ml to 9999 copies/ml	30 (18.4)	0	
10 000 copies/ml	1 (0.6)	0	
Median ^{††} (IQR)	40–80 (0–40 to 718)	0–20 (0–20 to 49)	

* Excluded one HIV-1-infected participant who did not have qualitative assay (percentages out of 162).

[†] HIV-1: <40 copies/ml; HIV-2: <20 copies/ml of HIV-2.

[‡] HIV-1: >40 copies/ml of HIV-1 or >20 copies/ml of HIV-2.

[§] Excluded one HIV-1-infected participant who did not have quantitative assay (qualitative reading: 40 copies/ml) and patient missing qualitative assay (percentages out of 161).

[¶] HIV-1: 40–80 copies/ml; HIV-2: 20–40 copies/ml.

^{**} HIV-1: >80 copies/ml; >40 copies/ml of HIV-2.

^{††} Range provided in cases of detection limits.

Table 3
Immunovirologic, systemic and local correlates of oral RNA detection and oral viral load using multiple imputation

	Univariate OR* (95% CI)		Univariate $\beta^{\dagger}$ (95% CI)	
	HIV-1	HIV-2	HIV-1	HIV-2
Immunovirologic factors				
CD4 cell count (cells/ μ l)				
Above 500	Ref	Ref	Ref	Ref
200–500	0.99 (0.31 to 3.14)	2.94 (0.33 to 25.97)	0.08 (–0.47 to 0.63)	0.48 (–0.49 to 1.46)
Below 200	1.16 (0.41 to 3.27)	2.44 (0.28 to 21.19)	0.18 (–0.29 to 0.64)	0.58 (–0.46 to 1.61)
Log ₁₀ plasma HIV RNA	1.80 (1.24 to 2.61)	1.93 (1.1 to 3.39)	0.37 (0.21 to 0.53)	0.30 (0.11 to 0.48)
Oral local factors				
Periodontal disease				
Presence	3.02 (1.16 to 7.87)	0.56 (0.04 to 7.08)	0.51 (0.17 to 0.85)	–0.27 (–1.34 to 0.80)
HIV oral lesion				
Presence	1.57 (0.66 to 3.71)	2.16 (0.11 to 44.08)	0.33 (–0.05 to 0.71)	0.61 (–1.01 to 2.22)
Demographic factors				
Age				
18–29	Ref	Ref	Ref	Ref
30–39	1.00 (0.46 to 2.19)	2.14 (0.16 to 28.45)	0.01 (–0.36 to 0.39)	0.21 (–1.22 to 1.65)
40+	1.00 (0.42 to 2.38)	1.13 (0.08 to 16.3)	–0.01 (–0.41 to 0.40)	–0.20 (–1.61 to 1.21)
Sex				
Male	Ref	Ref	Ref	Ref
Female	0.53 (0.27 to 1.02)	1.0 (0.19 to 5.16)	–0.25 (–0.57 to 0.06)	–0.13 (–0.98 to 0.73)
HIV disease stages				
1	Ref	Ref	Ref	Ref
2	1.66 (0.60 to 4.63)	1.00 (0.19 to 5.16)	0.31 (–0.24 to 0.85)	0.13 (–0.88 to 1.15)
3	2.86 (1.12 to 7.30)	3.19 (0.16 to 62.52)	0.53 (0.06 to 1)	0.62 (–0.26 to 1.49)
4	6.22 (0.66 to 58.75)	4.02 (0.34 to 46.95)	0.65 (–0.1 to 1.4)	1.77 (1.33 to 2.21)

* Dependent variable detection of oral RNA.

[†] Dependent variable quantity of oral RNA (log₁₀ copies per millilitre).

Achieving statistical significance ($p > 0.05$) are in bold.

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