Prevalence and risk factors for perianal and/or anal canal condyloma in HIV-infected patients in the era of HAART

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Abstract

Background: HIV-infected patients (pts) are at increased risk of developing ano-genital cancer. Condylomas are presumed to be precursor lesions for cancer. However, there are few data on the prevalence and of risk factors for perianal and/or anal canal condyloma in the general HIV-infected population.

Methods: Screening for anal condyloma was systematically proposed to 516 consecutive out-pts, followed in a university hospital in Paris. Perianal and systematic endoanal examinations with an anoscopy were realised. For each pts, HIV-risk factors, sexual behaviors, previous history of genital condyloma and/or sexually transmitted diseases, CD4 cell count, CD4 nadir, and HIV-RNA were collected.

Results: The 473 (92%) examined pts, consisted of 200 homosexual men, 123 heterosexual men, 150 women of whom 27 (18%) had a history of anoreceptive intercourse; 27% of pts were CDC stage C, 76% were receiving HAART, HIV-RNA was < 50 copies/ml in 60%, mean (±SD) CD4 cell count and nadir were 484 (±274) /mm3 and 220 (±186) /mm3. Overall, 108 (23%) pts had histologically-confirmed anal condyloma (36%, 15% and 11% of the respective populations), including 51 (47%) pts with only endoanal localisation. Histologic examination revealed cervical intraepithelial neoplasia of grade I in 59 pts, of grade II in 10 pts and of grade III in 2 pts and an invasive endoanal cancer in 1. Among homosexual men, condyloma were independently associated with the mean number of incidents of sexual intercourse per month (OR= 1.03; Confidence Interval 95% (1.01-1.06)), history of gonococcia or syphilis (OR=0.54 (0.29-0.99)), and history of previous anal condyloma (OR=2.05 (1.07-3.92). Among heterosexual men, independent risk factors were a history of previous penis condyloma (OR=26.8 (2.3-309.6)), and unprotected sexual intercourses (OR=7.5 (2.1-26.3)). Among women, independent risk factors were CD4 cell count below 200/mm3, (OR=8.9 (1.5-51.6)), receptive anal intercourses (OR 6.7 (1.7-25.8)) and history of previous anal condyloma (OR=25.4 (3.4-188.2)).

Conclusion: In the HAART era, systematic screening revealed a high rate of anal condyloma not only in homosexual men but also in heterosexual men and women, with sexual behavior, history of condyloma and level of immunodepression identified as risk factors. Anal examination should be proposed systematically to at-risk populations

Background

Increase in the incidence of epidermoid anal cancer (EAC)

- High rate among HIV-positive homosexual men
- Putative precursor lesion: anal squamous intraepithelial lesion (ASIL)
- Evidence that ASIL and EAC are linked with some Human Papillomavirus (HPV)
- High rate of anal HPV detection AND cytological dysplasia in HIV-infected homosexual men

Condyloma: visible macroscopic lesion of HPV infection

- Also associated with ASIL and with progression towards anal cancer
- Macroscopically detectable, easily treatable
- Screening for condyloma may represent efficient and non-expensive way of preventing occurrence of anal Cancer
- However, prevalence of condyloma in general HIV-infected population during HAART era is unknown

Methods

- **Screening for anal condyloma** systematically proposed to randomly determined sample of out-pts coming for clinical visit as part of regular HIV follow-up during a 12-month period
- **Data collected:**
  - **For all pts**, **whether accepting the screening or not:**

    Sex, age, geographic origin, HIV-risk factors, mean time of seropositivity, CDC stage, CD4 count and nadir, HIV-RNA level, current antiretrovirals

  - **In pts refusing screening:**

    Reason for refusal (lack of time, condyloma already monitored, unwillingness)

  - **In pts accepting screening:**

    Standardized semi-directive questionnaire: previous sexual transmitted diseases, history of genital and anal condyloma, sexual activities and practices (anal sexual intercourse, N of sexual intercourse per month, number of sexual partners per year, use of condom)

- Anal examination:
  - immediately following the consultation and performed by the same experienced proctologist
  - ocular inspection of anal margin and anal canal examination (anoscopy).
  - all suspected condyloma confirmed histologically
- In males, external genital organs also examined

- Histological classification:
  Dysplasia categorized as
    - low grade dysplasia ((LSIL)
      = anal intraepithelial neoplasia (AIN) of grade I-II)
    - high grade dysplasia (HSIL) (AIN III)

- Multivariate logistic regression analysis of data

Results

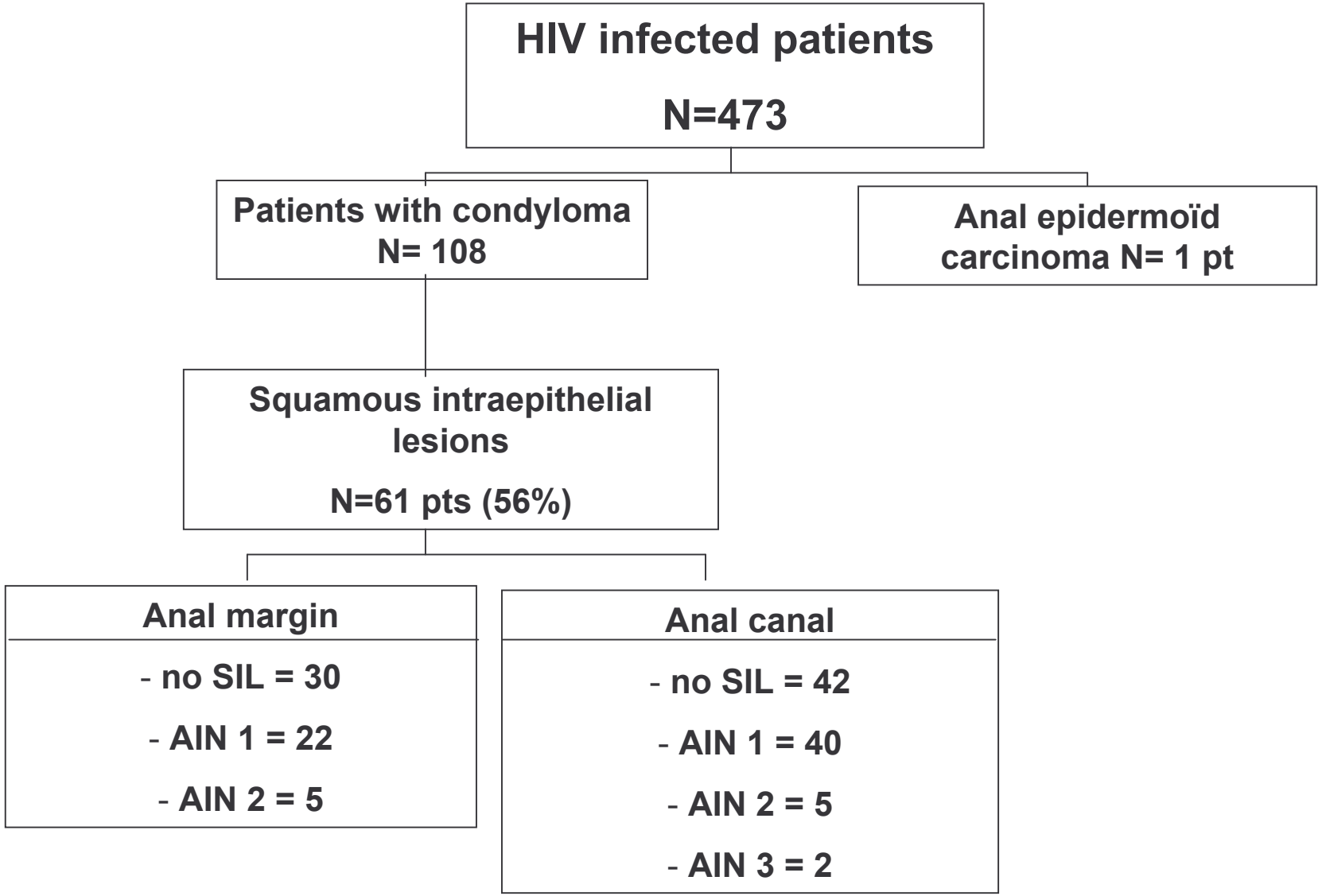
- Anal examination proposed to 516 HIV-infected pts
- 473 pts (92%) accepted screening
- Reasons for refusal in the 43 remaining pts
  - condyloma already monitored: 7 pts
  - lack of time: 13 pts
  - unwillingness: 23 pts

  Pts who refused screening: similar to those who accepted except for higher proportion of IV-drug addiction (23% vs 7%)(p=0.003)
- 108 pts with anal condyloma (23%)
  - 36.5% (73/200) in homosexual men
  - 14.6% (18/123) in heterosexual men
  - 11.3% (17/150) in women
- 1 pt with anal epidermoïd carcinoma

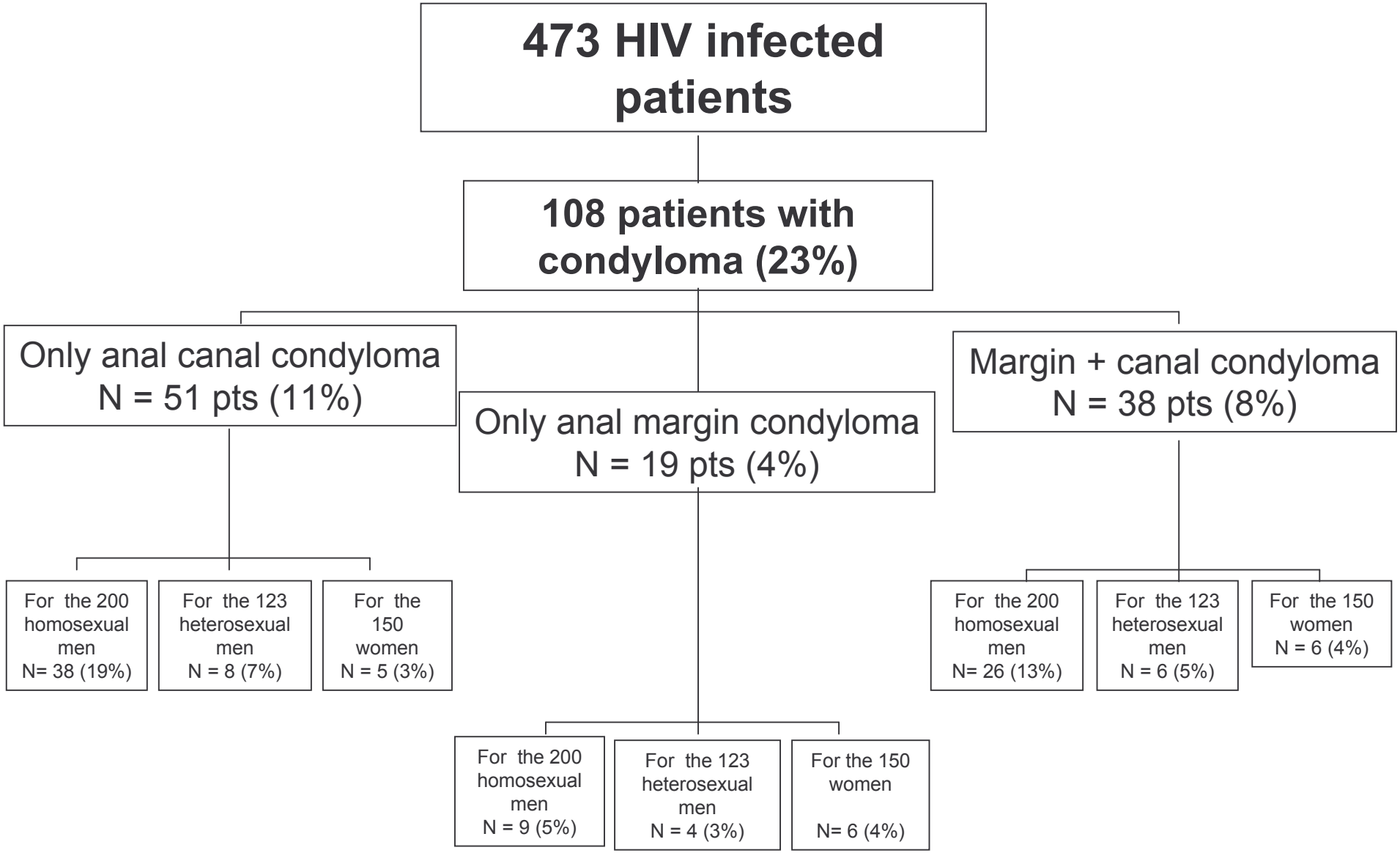
Characteristics of the screened population (n = 473)

Median age (range)	40 (20-78)
Men / Women, n (%):	323 (68%) /150 (32 %)
Geographic origins: Europe, n (%) Black Africa, n (%) others, n (%)	229 (48.4 %) 149 (31.5 %) 95 (20,1%)
Suspected HIV transmission risk factors: Homosexuality, n (%) Injection drug user, n (%) Heterosexuality, n (%) Blood transfusion, n (%) Unknown, n (%)	192 (40.6 %) 37 (7.8 %) 215 (45.4 %) 7 (1.5 %) 28 (5.9 %)
CDC stage C, n (%):	131 (27.7 %)
Median CD4+ cell count and nadir (range), x 10^6 cells/L	454 (3-1749) ; 196 (0-1238)
Patients with HIV RNA level < 50 log copies/ml, n (%)	284 (60 %)
Mean plasma HIV RNA level (range), (log copies/ml)	3.7 (1.4-7.7)
Patient receiving antiretroviral therapy, n (%)	363 (76.7 %)
History of gonorrhoea and syphilis, n (%)	141 (29.8 %) ; 76 (16.1 %)
Sexual practice: • Median sexual intercourse during a month, n (range) • Median sexual partners during a year, n (range) • Pts with unprotected sexual intercourse, n (%) • Women with receptive anal intercourse, n (%) • Men with receptive anal intercourse, n (%) • Heterosexual men, n (%)	 3 (0-250) 1 (0-2000) 104/432 (24 %) 27/150 (18 %) 200 (42%) 123 (26 %)

Histological classification of condyloma according to localization



Condyloma localization according to sexual practices



Condyloma associated factors in homosexual men

	Anal condyloma	No condyloma	Univariate analysis p
Geographic origins Europe North Africa Black Africa Others	 56/73 4/73 1/73 12/73	 105/127 2 /127 5 /127 15 /127	0.18
HIV seropositivity > 10 years, pts (%)	36/73 (49%)	59/127 (46%)	0.09
Nadir CD4+ < 200 x 10^6 /L, pts (%)	31/72 (43%)	55/126 (44%)	0.67
Previous AIDS-defining event, pts (%)	16/73 (22%)	39/127 (31%)	0.18
Pts receiving antiretrovirals (%)	60/73 (82%)	107/127 (84%)	0.71
HIV RNA level < 50 log copies/ml, pts (%)	45/73 (62%)	45/126 (36%)	0.71
CD4+ cell count < 200 x 10^6 cells/L, pts (%)	7/73 (10%)	7/127 (6%)	0.18
History of anal condyloma, pts (%)	27/73 (37%)	29/127 (23%)	0.032
History of genital condyloma, pts (%)	4/73 (5%)	12/127 (9%)	0.32
History of gonorrhoea or syphilis, pts (%)	33/73 (45%)	75/127 (59%)	0.058
Median sexual intercourse / month	2 (2-12)	4 (1-9)	0.058
Median sexual partners / year	4 (1-12)	1 (1-10)	0.24
Unprotected sexual intercourse , pts (%)	17/69 (25%)	34/118 (29%)	0.54

Condyloma associated factors in heterosexual men

	Anal condyloma	No condyloma	Univariate analysis p
Geographic origins Europe North Africa Black Africa Others	 9/18 (50%) 6/18 (33%) 2/18 (11%) 1/18 (6%)	 30/105 (29%) 15/105 (14%) 49/105 (47%) 11/105 (10%)	0.007
HIV seropositivity > 10 years, pts (%)	6/18 (33%)	32/105 (30%)	0.31
Nadir CD4+ < 200 x 10^6 /L, pts (%)	14/18 (78%)	65/104 (63%)	0.53
Previous AIDS-defining event, pts (%)	9/18 (50%)	33/105 (31%)	0.12
Pts receiving antiretrovirals (%)	12/18 (67%)	84/105 (80%)	0.22
HIV RNA level < 50 log copies/ml, pts (%)	9/18 (50%)	66/105 (63%)	0.30
CD4+ cell count < 200 x 10^6 cells/L	7/18 (39%)	47/105 (45%)	0.023
History of anal condyloma, pts (%)	3/18 (17%)	1/104 (1%)	0.01
History of genital condyloma, pts (%)	3/18 (17%)	1/104 (1%)	0.01
History of gonorrhoea or syphilis, pts (%)	6/18 (33%)	36/105 (34%)	0.94
Median sexual intercourse / month	4 (0-10)	3 (0-7)	0.94
Median sexual partners / year	1 (1-1)	1 (1-1)	0.58
Unprotected sexual intercourse, pts (%)	7/16 (44%)	10/97 (10%)	0.002

Condyloma associated factors in women

	Anal condyloma	No condyloma	Univariate analysis p
Geographic origins Europe North Africa Black Africa Others	 4/17 1/17 9/17 3/17	 25/133 18/133 83/133 7/133	0.22
HIV seropositivity > 10 years, pts (%)	6/17 (35%)	31/133 (23%)	0.60
Nadir CD4+ < 200 x 10^6/L, pts (%)	12/17 (71%)	63/133 (47%)	0.24
Previous AIDS-defining event, pts (%)	6/17 (35%)	28/133 (21%)	0.22
Pts receiving antiretrovirals (%)	9/17 (53%)	91/133 (68%)	0.20
HIV RNA< 50 log copies/ml, pts (%)	6/17 (35%)	77/133 (58%)	0.078
CD4+ < 200 x 10^6/L, pts (%)	5/17 (29%)	16/133 (12%)	0.05
History of anal condyloma, pts (%)	5/17 (29%)	5/133 (4%)	0.0018
History of genital condyloma, pts (%)	6/17 (35%)	13/133 (10%)	0.0095
History of gonorrhoea or syphilis, pts (%)	2/17 (1%)	15/133 (11%)	1.0
Median sexual intercourse /month	1 (0-4)	1 (0-4)	0.8
Median sexual partners / year	1 (0-1)	1 (0-1)	0.6
Unprotected sexual intercourse , pts (%)	3/13 (23%)	33/119 (28%)	1.0
Receptive anal intercourse, pts (%)	7/13 (54%)	20/122 (16%)	0.0045

Condyloma independent associated factors

Multivariate analysis OR [95% confidence interval]

	Homosexual men	Heterosexual men	Women
Geographic origins			
HIV seropositivity > 10 years			
Nadir CD4+ < 200 x 10^6/L			
Previous AIDS-defining event			
Antiretrovirals			
HIV RNA< 50 log copies/ml			
CD4+ < 200 x 10^6/L			8.88 [1.52-51.56] (p=0.050)
History of anal condyloma	2.05 [1.07-3.92] (p=0.029)		25.45 [3.44-188.22] (p=0.001)
History of genital condyloma		26.76 [2.31-309.58] (p=0.008)	
History of gonorrhoea or syphilis	0.54 [0.29-0.99] (p=0.046)		
Median sexual intercourse /month	1.03 [1.01-1.06] (p=0.028)		
Median sexual partners / year			
Unprotected sexual intercourse		7.47 [2.11-26.30] (p=0.001)	
Receptive anal intercourse	NA	NA	6.70 [1.73-25.84] (p=0.006)

Conclusion

- High prevalence of anal condyloma in this HIV-infected population during the HAART era
  - particularly in the sub population previously unsuspected to be at risk (women and heterosexual)
  - even without receptive anal intercourse
  - despite a high proportion of pts with HIV-RNA < 50 copies/ml
- Results concordant with the virological detection of HPV in those different HIV-infected populations
- Anoscopy necessary for detection of almost half of condyloma cases
- High prevalence of dysplasia
- Identified risk factors are different according to the populations (sexual behavior, history of condyloma, level of immunodepression)

- Anal examination should be proposed systematically to at-risk populations
- However, our study does not provide evidence as to whether screening for condyloma is clinically beneficial
- Comparative evaluation of clinical benefit of screenings for condyloma, anal HPV and cytological dysplasia should be performed