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2011  
BOSTON  
FEB 27-MAR 2, 2011



## ABSTRACT

**Background:** An increased prevalence and incidence of high-grade anal intra-epithelial neoplasia (HGAIN or AIN 2-3) caused by persistent high-risk human papillomavirus (HR-HPV) infection among men who have sex with men (MSM) has been shown in recent years. Data from Asia are limited to guide appropriate AIN surveillance and management for at-risk men in the region.

**Methods:** HIV-positive and HIV-negative Thai MSM, aged 18 years and older were enrolled from Dec 2009-Jun 2010. Demographic and sexual behavior data were collected. All received anogenital examination, high resolution anoscopy (HRA) with biopsy of lesions, and anal sample collection in LiquiPrep for anal cytology and HPV typing (Roche LA HPV GT).

**Results:** Among 202 MSM enrolled, 123 were HIV-positive (60.9%) and 79 were HIV-negative MSM (39.1%). Median age was 28 (IQR 23–33) years. Median age at first sex was 18 (IQR 16–20) years and 85% had >5 lifetime sexual partners. Among HIV-positive men, median CD4 count was 343 (IQR 248–455) cells/mm<sup>3</sup>, median plasma HIV RNA was 5.42 (IQR 3.82 to 4.94) log<sub>10</sub> copies/mL, and 11% were taking antiretroviral treatment.

Abnormal anal cytology was found in 7.3%, HIV-positive MSM had a higher prevalence of abnormal anal cytology (10.3% vs. 2.6%,  $p=0.05$ ). HRA-guided biopsies showed AIN 1 in 5%, AIN 2 in 6.4%, and AIN 3 in 8.4%. AIN 1 was diagnosed among 6.5% of HIV-positive and 2.5% of HIV-negative MSM ( $p=0.32$ ). AIN 2-3 was diagnosed among 18% of HIV-positive and 10% of HIV-negative MSM ( $p=0.13$ ).

HIV-positive MSM had a higher prevalence of anal HPV infection (84% vs 41%,  $p<0.001$ ) and HR-HPV infection (58% vs 32%,  $p<0.001$ ) than HIV-negative MSM. The most common HR-HPV type identified was HPV16 (16.1%), followed by HPV51 (11.1%), 68 (9.0%), 39 (8.0%), 58 and 59 (7.5%). HPV16 (22% vs. 7.6%,  $p=0.01$ ), 58 (11% vs. 2.5%,  $p=0.03$ ) and 68 (13% vs. 2.5%,  $p=0.01$ ) were significantly more prevalent among HIV-positive than HIV-negative MSM. HPV16 and 18 were found in 21.9% of HGAIN cases while other HR-HPV types were found in 43.8%.

**Conclusions:** The prevalence of HGAIN is quite alarming given the younger age of our Thai MSM participants compared with cohort participants in the US. HIV-positive MSM had a higher prevalence of any anal HPV infection and HR-HPV infection than HIV-negative MSM. With the exception of HPV type 16, none of the common HR-HPV types identified in Thai MSM are included in the current HPV vaccines.

## INTRODUCTION

- Incidence of anal cancer in MSM has risen sharply in the past decade. Risk in HIV-positive MSM is twice that in HIV-negative MSM.
- High grade anal intraepithelial neoplasia (HGAIN), is a putative precancerous lesion for anal cancer with increased prevalence and incidence in HIV-positive MSM in the HAART era.
- HIV prevalence and incidence among MSM in Bangkok have increased in recent years. (van Griensven F, et al. JAIDS 2010, 53:234-239.)
  - HIV prevalence: 7.3% in 2003 → 28.3% in 2005 → 30.8% in 2007 (1.2% in general population)
  - HIV incidence (aged 15-22 years): 4.1% in 2003 → 6.4% in 2005 → 7.7% in 2007
- Developing countries need data on AIN burden among their MSM population in order to plan how to best screen and treat these lesions.

# High-grade anal intraepithelial lesion among HIV-positive and HIV-negative men who have sex with men

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<sup>3</sup>HIV Netherlands Australia Thailand Research Collaborative

## METHODS

- HIV-positive and HIV-negative Thai MSM, aged 18 years and older were enrolled from the Thai Red Cross Anonymous Clinic (TRC-AC) during December 2009-June 2010. Demographic and sexual behavior data were collected.
- All received anogenital examination, high resolution anoscopy (HRA) with biopsy of lesions, and anal sample collection in LiquiPrep<sup>®</sup> for anal cytology and HPV typing.

### Anal Pap smear

- Anal cytology results were classified using the 2001 Bethesda system as normal, atypical squamous cell of undetermined significance (ASC-US), atypical squamous cells cannot exclude high-grade squamous intraepithelial lesion (ASC-H), LSIL (low-grade squamous intraepithelial lesion), HSIL (high-grade squamous intraepithelial lesion), or carcinoma.



- Ten percent of slides with normal cytology result were randomly checked by histopathologists and all slides with abnormal cytology result were checked by histopathologists.

### HPV genotyping

- HPV DNA amplification was done using AMPLICOR HPV DNA kit.
- HPV typing was done using the LINEAR ARRAY HPV Genotyping Test (LA HPV GT, Roche Molecular Systems, Inc.) which can identify 37 anogenital HPV DNA genotypes including 13 high-risk genotypes which are 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 68.
- The primers for human  $\beta$ -globin gene was also used to ensure proper processing of the samples (cell adequacy, extraction and amplification).

## RESULTS

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### Table 1

Characteristic	Number (n)	Percentage (%)
Normal	10	10.0
ASC-US	10	10.0
ASC-H	10	10.0
LSIL	10	10.0
HSIL	10	10.0
Carcinoma	10	10.0

### Table 2

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# epithelial neoplasia and high HIV-negative Thai men with

lipat Teeratakulpisarn<sup>1</sup>, Stephen Kerr<sup>3</sup>, Surang Triratanachai<sup>4</sup>, Somboon Keelawat<sup>4</sup>, Phanuphak<sup>1,2,3</sup>, Jintanat Ananworanich<sup>2,3</sup>, Joel Palefsky<sup>5</sup> on behalf of the Thai Red Cross Blood Centre, Bangkok, Thailand; <sup>2</sup>South East Asia Research Collaboration with the Thai Red Cross Blood Centre, Bangkok, Thailand; <sup>4</sup>Chulalongkorn University, Bangkok, Thailand, <sup>5</sup>University of Pennsylvania, Philadelphia, PA, USA

## RESULTS

- We enrolled 202 MSM, 123 were HIV-positive (60.9%) and 79 were HIV-negative MSM (39.1%).
- Median age was 28 (IQR 23–33) years (Table 1). Median age at first sex was 18 (IQR 16–20) years and 85% had >5 lifetime sexual partners.
- Among HIV-positive men, median CD4 count was 343 (IQR 248–455) cells/mm<sup>3</sup>, median plasma HIV RNA was 5.42 (IQR 3.82 to 4.94) log<sub>10</sub> copies/mL, and 11% were taking antiretroviral treatment.

**Table 1: Characteristics of HIV-negative and HIV-positive MSM in the TRC-AC cohort**

Characteristic	HIV-negative MSM (N=79)	HIV-positive MSM (N=123)	All MSM (N=202)
Age, median (IQR) in years	26 (22-32)	28 (23-33)	28 (23-33)
Gender, n (%)			
Male	79 (100)	123 (100)	202 (100)
Transgender	0 (0)	0 (0)	0 (0)
Thai ethnicity, n (%)	79 (100)	123 (100)	202 (100)
Marital status, n (%)			
Single	72 (91)	113 (92)	185 (92)
Living together/married	3 (4)	6 (5)	9 (4)
Widowed	-	2 (2)	2 (1)
Don't want to answer	4 (5)	2 (2)	6 (3)
Education, n (%)			
Never	-	1 (1)	1 (0.5)
High school or less	29 (37)	49 (40)	78 (39.5)
Bachelor Degree	45 (57)	69 (56)	114 (56)
Don't want to answer	5 (6)	4 (3)	9 (5)
Occupation, n (%)			
Not working	7 (9)	13 (11)	20 (10)
Student	13 (16)	15 (12)	28 (14)
Office or factory worker	54 (68)	88 (72)	142 (70)
Don't want to answer	5 (6)	7 (6)	12 (6)
Monthly income, n (%)			
<10,000 Baht	27 (34)	32 (26)	59 (29)
10,000 – 20,000 Baht	30 (38)	41 (33)	71 (35)
20,000 – 50,000 Baht	15 (19)	22 (18)	37 (18)
>50,000 Baht	-	5 (4)	5 (3)
Don't want to answer	7 (9)	23 (19)	30 (15)
STI diagnosed in previous year, n (%)	16 (20)	32 (26)	48 (24)

## Anal cytology results

- Abnormal anal cytology from ASC-US and above was found in 7.3% of all MSM.
- HIV-positive MSM had a higher prevalence of abnormal anal cytology (10.3% vs. 2.6%, p=0.05).

# high-risk HPV infection who have sex with men

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 1 with Hawaii, Bangkok, Thailand;  
<sup>5</sup>University of California at San Francisco, California, USA

## HRA and histology results (Table 2)

- Higher proportion of HIV-positive MSM had abnormal HRA (69% vs. 37%,  $p < 0.001$ ).
- Histology identified AIN I in 5% (6.5% in HIV-positive vs. 2.5% in HIV-negative MSM,  $p = 0.32$ ).
- HGAIN (AIN II and III) were identified in 6.4% and 8.4%, respectively. The prevalence of AIN II-III was 18% in HIV-positive and 10% in HIV-negative MSM ( $p = 0.13$ ). Abnormal anal cytology was found in 9.7% of HGAIN cases.

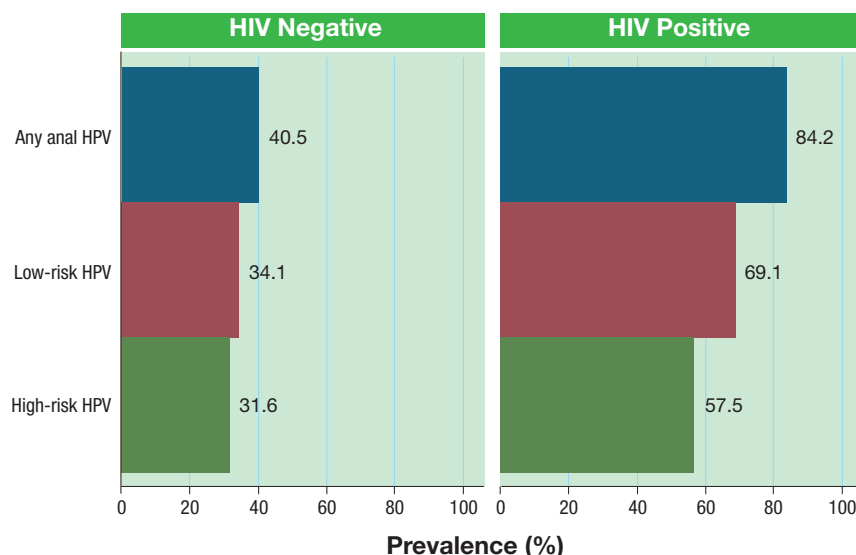
**Table 2: Prevalence of abnormal anal lesions identified by HRA and AIN prevalence among HIV-negative and HIV-positive MSM in the TRC-AC cohort**

	HIV+ (n=123)	HIV- (n=79)	Total (n=202)	P-value
Abnormal HRA	69%	37%	56%	<0.001
AIN I	6.5%	2.5%	5%	0.32
AIN II-III	18%	10%	15%	0.13

## Anal HPV infection results

- HIV-positive MSM had a higher prevalence of anal HPV infection (84% vs 41%,  $p < 0.001$ ) and HR-HPV infection (58% vs 32%,  $p < 0.001$ ) than HIV-negative MSM (Figure 1).

**Figure 1: Prevalence of anal HPV infection among MSM in the TRC-AC cohort**

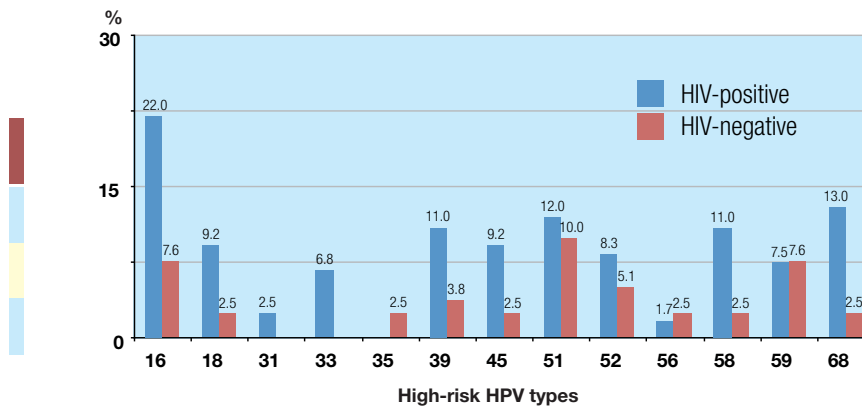


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- The most common HR-HPV type identified was HPV16 (16.1%), followed by HPV51 (11.1%), 68 (9.0%), 39 (8.0%), 58 and 59 (7.5%).
- HPV16 (22% vs. 7.6%,  $p=0.01$ ), 58 (11% vs. 2.5%,  $p=0.03$ ) and 68 (13% vs. 2.5%,  $p=0.01$ ) were significantly more prevalent among HIV-positive than HIV-negative MSM (Figure 2).
- HPV16 and 18 were found from anal samples in 21.9% of HGAIN cases while other HR-HPV types were found in 43.8%.

**Figure 2: Prevalence of anal HR-HPV infection among MSM in the TRC-AC cohort**



## CONCLUSIONS

- HIV-positive Thai MSM had 18% HGAIN prevalence while HIV-negative Thai MSM had 10% HGAIN prevalence. The prevalence is quite alarming given their younger age as compared to other cohorts.
- HIV-positive MSM had a higher prevalence of any anal HPV infection and HR-HPV infection than HIV-negative MSM.
- HR-HPV types, other than those included in the current HPV vaccines, were commonly identified in the anal samples from Thai MSM. To evaluate impact of HPV vaccination on HGAIN/anal cancer prevention in the region, HR-HPV types in HGAIN/anal cancer tissues need to be studied.



**ABSTRACT**

**Background:** The highest prevalence and incidence of HIV, genital and anal HPV, and anal intraepithelial neoplasia (AIN) or anal squamous cell carcinoma (ASCC) are found in men who have sex with men (MSM). Data from Asia are limited to guide appropriate AN surveillance and management for at-risk men in the region.

**Methods:** HIV-positive and HIV-negative Thai MSM, aged 18 years and older were enrolled from Dec 2008–Jun 2010. Demographic and sexual behavior data were collected. HIV RNA was measured using a sensitive, high-resolution assay (HRA) for HIV-1 and anal sample collection in LiquiPrep<sup>®</sup> for anal cytology and HPV typing.

**Results:** Among 202 MSM enrolled, 123 were HIV-positive (60.9%) and 79 were HIV-negative MSM (39.1%). Median age was 28 (IQR 23–33) years. Median age at first sex was 18 (IQR 16–20) years and 85% had >5 lifetime sexual partners. Among HIV-positive men, median CD4 count was 343 (IQR 248–455) cells/mm<sup>3</sup>; median plasma HIV RNA was 5.42 (IQR 3.82 to 4.94) log<sub>10</sub> copies/mL, and 11% were taking antiretroviral treatment.

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 HPV DNA amplification was done using AMPLICOR HPV DNA kit. HPV typing was done using the LINEAR ARRAY HPV Genotyping Test (LA HPV GT; Roche Molecular Systems, Inc.) which can identify 37 anal genital HPV DNA genotypes including 13 high-risk genotypes which are 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 59, 59 and 68.

**Conclusions:** The prevalence of HGAIN is quite alarming given the younger age of our Thai HIV-positive MSM. The prevalence of any anal HPV infection (95% vs 32%, p<0.001) and HR-HPV infection (59% vs 32%, p<0.001) in HIV-positive and HIV-negative MSM. With the exception of HPV type 16, none of the common HR-HPV types identified in the MSM are included in the current HPV vaccine.

**INTRODUCTION**  
 Incidence of anal cancer in MSM has risen sharply in the past decade. Risk in HIV-positive MSM is twice that in HIV-negative MSM. High grade anal intraepithelial neoplasia (HGAIN), is a putative precancerous lesion for anal cancer with increased prevalence and incidence in HIV-positive MSM in the HAART era.

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# High-grade anal intraepithelial neoplasia and high-risk HPV infection among HIV-positive and HIV-negative Thai men who have sex with men

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**METHODS**

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**RESULTS**

We enrolled 202 MSM, 123 were HIV-positive (60.9%) and 79 were HIV-negative MSM (39.1%). Median age was 28 (IQR 23–33) years. Median age at first sex was 18 (IQR 16–20) years and 85% had >5 lifetime sexual partners. Among HIV-positive men, median CD4 count was 343 (IQR 248–455) cells/mm<sup>3</sup>; median plasma HIV RNA was 5.42 (IQR 3.82 to 4.94) log<sub>10</sub> copies/mL, and 11% were taking antiretroviral treatment.

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Transgender	0 (0)	0 (0)	0 (0)
The ethnicity, n (%)			
Thai	79 (100)	123 (100)	202 (100)
Marital status, n (%)			
Single	72 (91)	113 (92)	185 (92)
Widowed	3 (4)	6 (5)	9 (4)
Living together/married	4 (5)	2 (2)	6 (3)
Education, n (%)			
Never	1 (1)	1 (1)	2 (1)
Primary	26 (33)	41 (33)	67 (33)
High school/less	45 (57)	68 (55)	113 (56)
Bachelor Degree	4 (5)	6 (5)	10 (5)
Don't want to answer	5 (6)	4 (3)	9 (4)
Occupation, n (%)			
Student	7 (9)	15 (11)	22 (11)
Office or factory worker	54 (68)	88 (72)	142 (70)
Don't want to answer	5 (6)	7 (6)	12 (6)
Monthly income, n (%)			
<10,000 Baht	27 (34)	32 (26)	59 (29)
10,000 – 20,000 Baht	37 (47)	41 (33)	78 (39)
20,000 – 50,000 Baht	15 (19)	22 (18)	37 (18)
>50,000 Baht	5 (6)	5 (4)	10 (5)
Don't want to answer	7 (9)	23 (19)	30 (15)
STI diagnosed in previous year, n (%)			
None	16 (20)	32 (26)	48 (24)

**Anal cytology results**

Abnormal anal cytology from ASC-US and above was found in 7.3% of all MSM.

HIV-positive MSM had a higher prevalence of abnormal anal cytology (10.3% vs. 2.6%, p=0.05).

**HRA and histology results (Table 2)**

Higher proportion of HIV-positive MSM had abnormal HRA (69% vs. 37%, p<0.001).  
 Histology identified AIN I in 5% (6.5% in HIV-positive vs. 2.5% in HIV-negative MSM, p=0.32).  
 HGAIN (AIN I and II) were identified in 6.4% and 8.4%, respectively. The prevalence of AIN I–III was 19% in HIV-positive and 10% in HIV-negative MSM (p=0.13). Abnormal anal cytology was found in 9.7% of HGAIN cases.

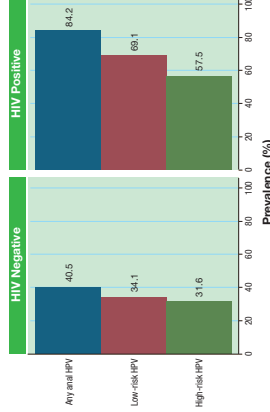
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AIN I	18%	5%	10%	0.32
AIN I+II+III	18%	10%	15%	0.13

**Anal HPV infection results**

HIV-positive MSM had a higher prevalence of anal HPV infection (84% vs 41%, p<0.001) and HR-HPV infection (59% vs 32%, p<0.001) than HIV-negative MSM (Figure 1).

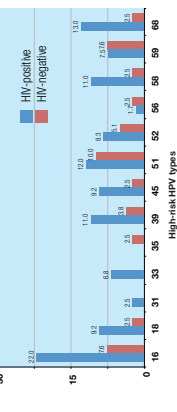
**Figure 1. Prevalence of anal HPV infection among MSM in the TRC-AC cohort**



The most common HR-HPV type identified was HPV16 (16.1%), followed by HPV51 (11.1%), 68 (8.0%), 39 (8.0%), 58 and 59 (7.5%).  
 HPV16 (22% vs. 7.6%, p<0.01), 58 (11% vs. 2.5%, p=0.03) and 68 (13% vs. 2.5%, p<0.01) were significantly more prevalent among HIV-positive than HIV-negative MSM (Figure 2).

HPV16 and 18 were found from anal samples in 21.9% of HGAIN cases while other HR-HPV types were found in 43.8%.

**Figure 2. Prevalence of anal HR-HPV infection among MSM in the TRC-AC cohort**



**CONCLUSIONS**

- HIV-positive Thai MSM had 18% HGAIN prevalence while HIV-negative Thai MSM had 10% HGAIN prevalence. The prevalence is quite alarming given their younger age as compared to other cohorts.
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This study was funded by the US NIH, through a grant to amAR for the International Epidemiologic Database to Evaluate AIDS (I-DEA); NIAID/NCI, UO1AI09097.