Promoting early detection of HIV and anal dysplasia in Thai men who have sex with men
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CHAPTER 1

General introduction
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Men who have sex with men (MSM) are at high risk for human immunodeficiency virus (HIV) and anal human papillomavirus (HPV) infections. HIV and HPV infections both have strong influence on health outcomes of MSM at an individual level and at community level.

MSM and HIV

Globally and in Asia, MSM have become one of the key affected populations with sustained high rates of HIV prevalence and incidence (Figure 1). The high probability of HIV transmission per act through receptive anal intercourse is believed to be the key factor explaining the epidemics among MSM.1

Figure 1. Global HIV prevalence in MSM, from studies published 2007-2011. Data are prevalence (95% confidence interval).1

The prevalence of HIV infection among general population in Thailand was estimated to be around 1.2%, with CRF01_AE being the predominant subtype across all risk groups. The 2005-2025 Asian Epidemic Model (AEM) projections showed a shift of the dominant mode of HIV transmission from sex work to sex between MSM (Figure 2). Clustering of HIV infections in MSM networks has been demonstrated which supports rapid transmission of HIV among the MSM population.1

Figure 2. Changes in contribution of risk groups to the total number of new HIV infections over time in Thailand.5
In the last decade, HIV prevalence among MSM in Bangkok, Thailand, ranged from 17% to 31%. Structural factors commonly contribute to low HIV testing rate among MSM and low linkage to HIV treatment and care once diagnosed with HIV infection. HIV testing is the key entry point to HIV prevention. Knowing one's HIV-positive status as early as possible in the course of HIV disease could reduce the period of unintentional spread of HIV to others in the community.

**MSM and HPV**

Anal infection with HPV is very common in MSM. HIV-positive MSM have an approximately 1.5 times higher prevalence of anal HPV infection than HIV-negative MSM, and are more likely to have infection with multiple HPV types. Persistent anal HPV infection, particularly with high-risk HPV types, is an important risk factor for the development of anal cancers. Recent studies demonstrated that the incidence of anal cancer among HIV-positive MSM has continued to increase in the era of highly active antiretroviral therapy (HAART), ranging from 75 to 137 per 100,000 person-years. This risk for anal cancer in HIV-positive MSM is 5 times higher than that in HIV-negative MSM.

The majority of HPV-related dysplastic lesions in the anal canal are found in the transformation zone, and the spectrum of dysplasia can be graded histologically into low-grade anal intraepithelial neoplasia and high-grade intraepithelial neoplasia (HGAIN) (Figure 3). HGAIN is the putative precursor of anal cancer. HGAIN screening programs for MSM are increasingly being implemented in many settings, based on the evidence that the incidence of cervical cancer has markedly declined through aggressive screening programs. Anal cancer and cervical cancer share many similar biologic characteristics, although the progression of HGAIN to anal cancer as a consequence of high-risk HPV infection has been estimated to be lower than that of cervical intraepithelial neoplasia and cervical cancer.

![Figure 3. Schematic representation of morphologic continuum of anal dysplasia. Source: Prof. Dr. Joel M. Palefsky.](image-url)
Anal cytology is generally used as a screening tool in these settings and MSM with abnormal anal cytology are referred to receive high-resolution anoscopy (HRA) to identify abnormal anal tissue which needs to be biopsied. MSM with HGAIN diagnosed histologically are referred for treatment, usually by infrared coagulation. Although data are limited, previous reports have shown a 9-15% progression rate from HGAIN to anal cancer during a median follow-up of 3-5 years.\(^{19-21}\) Consistent with the lack of benefit of HAART on the incidence of anal cancer, despite the widespread use of HAART, HGAIN remains common among HIV-positive MSM.\(^{23-26}\) It has been postulated that the increased incidence of anal cancer in the HAART era is due mainly to the prolonged survival after HAART, the continued high prevalence of HGAIN, and the lack of routine screening for HGAIN allowing for the progression to anal cancer.\(^{27}\)

Countries with a high prevalence of HIV infection among MSM, like Thailand urgently need to evaluate the burden of anal HPV infections and HGAIN among HIV-positive and HIV-negative MSM. In addition, countries should begin to consider the implementation of HGAIN screening programs that incorporate tests with well-balanced sensitivity and specificity. Tests associated with HPV infection or HPV-mediated cell transformation, such as high-risk HPV DNA, E6/E7 mRNA, and p16 immunocytochemistry, have the potential to be used in HGAIN screening program. These tests will be needed to identify MSM at high risk for HGAIN who need referral to HRA where services are generally limited.

**The Thai Red Cross AIDS Anonymous Clinic in Bangkok and outline of the thesis**

Based on the initiative to normalize HIV testing in Thailand, the Thai Red Cross Anonymous Clinic (Figure 4) serves as the most popular HIV voluntary counseling and testing (VCT) center used by the majority of MSM in Bangkok.\(^{28}\) The Clinic is located in the city center and provides sexual health services, including HGAIN screening and sexually transmitted diseases treatment, which effectively attract MSM into HIV testing. The Clinic also has an integrated CD4 count service which aims to facilitate linkage to HIV treatment and care programs among MSM who test HIV-positive. During 2008-2012, approximately 12,000 clients from a total of 25,000 clients each year came for HIV testing at the Clinic. Around one third of the clients were MSM.

This thesis includes 2 parts. Part 1 contains 3 chapters on the early detection of HIV infection in Thai MSM at the Thai Red Cross Anonymous Clinic. Chapter 2 describes how active VCT with an integrated CD4 count service can enhance early HIV testing and early CD4 count measurement. Chapter 3 evaluates HIV molecular epidemiology among high-risk clients, including MSM, attending the Thai Red Cross Anonymous Clinic. Chapter 4 studies the incidence and characterization of acute

Figure 4. Thai Red Cross Anonymous Clinic, a major HIV testing center for MSM, located in the center of Bangkok, Thailand.
HIV infection in clients of the Thai Red Cross Anonymous Clinic, using pooled nucleic acid testing and sequential anti-HIV antibody testing.

Part 2 contains 4 chapters on early detection of anal intraepithelial neoplasia in Thai MSM at the Thai Red Cross Anonymous Clinic. In chapter 5, the burden of anal intraepithelial neoplasia among HIV-positive and HIV-negative Thai MSM is evaluated by anal cytology screening. Chapter 6 then compares the performance of conventional and liquid-based cytology in diagnosing anal intraepithelial neoplasia in these MSM. In chapter 7, the prevalence and incidence of HGAIN among these MSM is investigated by using HRA and biopsy. Chapter 8 describes prevalence, incidence, and persistence of anal HPV infection in this population. Finally, chapter 9 studies the use of various biomarkers, including HPV DNA, E6/E7 oncogenic mRNA, and p16 immunocytochemistry to detect and predict HGAIN among HIV-positive and HIV-negative MSM.

Findings from these studies can be used to plan for strategies to promote early detection of HIV and anal intraepithelial neoplasia among Thai MSM. Early HIV testing and immediate linkage to care after HIV diagnosis are key steps to control HIV epidemic among MSM. HGAIN data from Thai MSM would also greatly benefit the development of country's recommendations on how to screen and treat HGAIN in this population.

References


