行政院國家科學委員會專題研究計畫 成果報告

女性愛滋感染者與非感染者於子宮頸抹片篩檢利用率及子宮頸癌發生率之比較（GM03）
研究成果報告(完整版)

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計 畫 編 號 ：NSC 100-2629-B-006-002-
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計 畫 主 持 人：柯乃熒
共 同 主 持 人：柯文謙、李欣純、李中一、徐淑婷
計畫參與人員：碩士級-專任助理人員：陳嬿今

報 告 附 件 ：出席國際會議研究心得報告及發表論文

公 開 資 訊 ：本計畫涉及專利或其他智慧財產權，2 年後可公開查詢

中 華 民 國 101 年 10 月 29 日

中文摘要： 背景：1993年子宮頸癌被指定為愛滋病相關診斷症候羣，亦是女性愛滋感染者常見之惡性腫瘤。而國內尚無針對女性愛滋感染者子宮頸抹片篩檢利用率的調查，女性感染者在接受抗愛滋病毒藥物治療之後，其子宮頸癌的發生率目前尚無相關實證研究。

研究目的：探討2000~2008年台灣女性愛滋感染者子宮頸抹片篩檢利用率趨勢，並比較女性愛滋感染者與非感染者於子抹篩檢利用率及每年子宮頸癌發生率之差異。

研究方法：本研究採用世代研究法，女性愛滋感染者資料來自2000~2008年全民健康保險學術資料庫內之特殊需求檔，並以2000年為世代之系統抽樣百萬歸人檔資料，扣除愛滋感染者後之非感染女性做對照比較。透過SAS 9.1與SPSS17版套裝軟體以分析，調整年齡（以10年間距計算）、年度及性別標準化抹片篩檢率，探討女性愛滋感染者與非感染者之間子抹篩檢利用率之差異。針對子宮頸癌發生率的分析，採取標準化發生比率，女性愛滋感染者相對於一般非感染婦女發生子宮頸癌的相對危險比。

結果：2000-2008年間總共有 344 位女性感染者(25.4%)曾接受過子宮頸抹片檢查，顯著高於一般婦女HIV(19.54%) (OR= 1.40, 95% CI= 1.23-1.59, p<0.0001). 其中13位位女性感染者(0.96%) 在診斷HIV之後確認罹患子宮頸癌。大於18歲的女性感染者其子宮頸癌發生率顯著高於與一般婦女約5.24倍 (95% CI 2.55- 10.76)。以Cox 風險模式分析發現子宮頸癌發生率與接受抗愛滋病毒藥物時間(HR, 0.88； 95% CI, 0.78-0.98)、接受子宮頸抹片頻率(HR, 1.27； 95% CI, 1.1-1.48)及診斷後出現伺機性感染(HR, 2.9； 95% CI, 1.27－6.66)有顯著相關。

結論: 本研究發現女性感染者其子宮頸癌發生率為一般婦女的5.24倍。健康專業人員須提醒女性感染者定期接受子宮頸抹片篩檢，並且提醒尚未開始服用抗愛滋病毒藥物及出現伺機性感染的愛滋感染婦女定期接受子宮頸抹片篩檢以及早診斷及早治療子宮頸相關癌症。

中文關鍵詞： 女性愛滋感染者、子宮頸抹片篩檢、子宮頸癌、全民健保資料庫

英文摘要： Background: Cervical cancer was defined as an AIDS-related malignancy in 1993 and was the most common malignancy among women with human immunodeficiency virus (HIV). HIV became a chronic illness after initiation of antiretroviral therapy； however, there

was no evidence-based study on the incidence of cervical cancer in Taiwan.
Objectives: This study investigated the frequency of pap smears during 2000-2008 among women with HIV, and to compare the screening rate and incidence of cervical cancer between women with HIV and uninfected women.
Methods: A population-based cohort study was conducted, and the National Health Insurance Research Database (NHIRD) from 2000-2008 was used to estimate the Pap smear screening rate for 1,500 HIV-infected women aged 18 years and over. Multiple logistic regression analysis was used to identify factors associated with HIV-infected women who had received Pap smears.
Results: Overall, 344 HIV infected women (25.4%) had received one or more Pap smears which is significantly higher than control group (19.54%), during the period 2000-2008 (OR= 1.40, 95% CI= 1.23-1.59, p<0.0001). A total of 13/1537 (0.96%) patients with HIV were identified to have cervical cancer after the diagnosis of HIV. The adjusted hazard ratio (AHR) for cervical cancer was 5.24 (95% CI 2.55 to 10.76) for patients with HIV of all ages older than 18 years. A multivariate analysis using the Cox proportional risk model showed that the risk associated with malignant neoplasm of the cervical was lower among women who had longer exposure years to antiretroviral theory (HR, 0.88； 95% CI, 0.78-0.98), higher among women who frequently received Pap screening tests after HIV diagnosed (HR, 1.27； 95% CI, 1.1-1.48) and among those who had opportunity infections (HR, 2.9； 95% CI, 1.27－6.66).
Conclusions: The findings indicate that the incidence of cervical cancer among women with HIV is five times higher than women without HIV infection. HIV care providers should ensure a Pap smear at the first visit to the HIV clinic and remind HIV-infected women who had opportunity infections and haven’t initiated with antiretroviral therapy to receive Pap screening annually.

英文關鍵詞： HIV-infected women, Pap smear screening, National Health Insurance Research Database (NHIRD)

行政院國家科學委員會補助專題研究計畫

■ 成 果 報 告
□期中進度報告

女性愛滋感染者與非感染者於子宮頸抹片篩檢利用率及子宮頸癌發生率之比較 (GM03)

計畫類別：■個別型計畫　□整合型計畫

計畫編號：NSC 100 - 2629 - B - 006 - 002

執行期間： 100 年 8 月 1 日至 101 年 7 月 31 日

執行機構及系所：國立成功大學護理學系

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徐淑婷　財團法人長庚紀念醫院

計畫參與人員：陳嬿今

成果報告類型(依經費核定清單規定繳交)：■精簡版

本計畫除繳交成果報告外，另須繳交以下出國心得報告：

■出席國際學術會議心得報告

處理方式：除列管計畫及下列情形者外，得立即公開查詢

■涉及專利或其他智慧財產權，□一年■二年後可公開查詢

中　華　民　國　101　年 10　月　27　日

摘要

背景：1993 年子宮頸癌被指定為愛滋病相關診斷症候羣，亦是女性愛滋感染者常見之惡性腫瘤。而國內尚無針對女性愛滋感染者子宮頸抹片篩檢利用率的調查，女性感染者在接受抗愛滋病毒藥物治療之後，其子宮頸癌的發生率目前尚無相關實證研究。

研究目的：探討 2000~2008 年台灣女性愛滋感染者子宮頸抹片篩檢利用率趨勢，並比較女性愛滋感染者與非感染者於子抹篩檢利用率及每年子宮頸癌發生率之差異。

研究方法：本研究採用世代研究法，女性愛滋感染者資料來自 2000~2008 年全民健康保險學術資料庫內之特殊需求檔，並以 2000 年為世代之系統抽樣百萬歸人檔資料，扣除愛滋感染者後之非感染女性做對照比較。透過 SAS 9.1 與 SPSS17 版套裝軟體以分析，調整年齡（以 10 年間距計算）、年度及性別標準化抹片篩檢率，探討女性愛滋感染者與非感染者之間子抹篩檢利用率之差異。針對子宮頸癌發生率的分析，採取標準化發生比率，女性愛滋感染者相對於一般非感染婦女發生子宮頸癌的相對危險比。

結果：2000-2008 年間總共有 344 位女性感染者(25.4%)曾接受過子宮頸抹片檢查，顯著高於一般婦女 HIV(19.54%) (OR= 1.40, 95% CI= 1.23-1.59, p<0.0001). 其中 13 位位女性感染者(0.96%) 在診斷 HIV 之後確認罹患子宮頸癌。大於 18 歲的女性感染者其子宮頸癌發生率顯著高於與一般婦女約 5.24 倍 (95% CI 2.55-

10.76)。以 Cox 風險模式分析發現子宮頸癌發生率與接受抗愛滋病毒藥物時間(HR, 0.88; 95% CI, 0.78-0.98)、接受子宮頸抹片頻率(HR, 1.27; 95% CI, 1.1-1.48)及診斷後出現伺機性感染(HR, 2.9; 95% CI, 1.27–6.66)有顯著相關。

結論: 本研究發現女性感染者其子宮頸癌發生率為一般婦女的 5.24 倍。健康專業人員須提醒女性感染者定期接受子宮頸抹片篩檢，並且提醒尚未開始服用抗愛滋病毒藥物及出現伺機性感染的愛滋感染婦女定期接受子宮頸抹片篩檢以及早診斷及早治療子宮頸相關癌症。

關鍵詞：女性愛滋感染者、子宮頸抹片篩檢、子宮頸癌、全民健保資料庫

ABSTRACT

Background: Cervical cancer was defined as an AIDS-related malignancy in 1993 and was the most common malignancy among women with human immunodeficiency virus (HIV). HIV became a chronic illness after initiation of antiretroviral therapy; however, there was no evidence-based study on the incidence of cervical cancer in Taiwan.

Objectives: This study investigated the frequency of pap smears during 2000-2008 among women with HIV, and to compare the screening rate and incidence of cervical cancer between women with HIV and uninfected women.

Methods: A population-based cohort study was conducted, and the National Health Insurance Research Database (NHIRD) from 2000-2008 was used to estimate the Pap smear screening rate for 1,500 HIV-infected women aged 18 years and over. Multiple logistic regression analysis was used to identify factors associated with HIV-infected women who had received Pap smears.

Results: Overall, 344 HIV infected women (25.4%) had received one or more Pap smears which is significantly higher than control group (19.54%), during the period 2000-2008 (OR= 1.40, 95% CI= 1.23-1.59, $p<0.0001$). A total of 13/1537 (0.96%) patients with HIV were identified to have cervical cancer after the diagnosis of HIV. The adjusted hazard ratio (AHR) for cervical cancer was 5.24 (95% CI 2.55 to 10.76)

for patients with HIV of all ages older than 18 years. A multivariate analysis using the Cox proportional risk model showed that the risk associated with malignant neoplasm of the cervical was lower among women who had longer exposure years to antiretroviral theory (HR, 0.88; 95% CI, 0.78-0.98), higher among women who frequently received Pap screening tests after HIV diagnosed (HR, 1.27; 95% CI, 1.1-1.48) and among those who had opportunity infections (HR, 2.9; 95% CI, 1.27–6.66).

Conclusions: The findings indicate that the incidence of cervical cancer among women with HIV is five times higher than women without HIV infection. HIV care providers should ensure a Pap smear at the first visit to the HIV clinic and remind HIV-infected women who had opportunity infections and haven't initiated with antiretroviral therapy to receive Pap screening annually.

Key words: HIV-infected women, Pap smear screening, National Health Insurance Research Database (NHIRD)

Introduction

There are an estimated 33.3 million people living with human immunodeficiency virus (HIV) in the world, and 15.7 million (47%) of these are women. [1] An estimated 1.68 million women are living with HIV/AIDS in Asia. [2] Yet, according to the Taiwan Center for Disease Control (Taiwan CDC), HIV and AIDS diagnoses have been reported for relatively few women and female adolescents in Taiwan, and the male-female ratio was 20:1 until 2003. Taiwan has experienced an outbreak of HIV infection among injected drug users (IDUs) since 2003. [3] In 2005, IDUs accounted for about two-thirds (71%) of all reported HIV/AIDS cases in Taiwan, and the male-female ratio reached a peak of 7:1. Then, the ratio fell to 17:1 by 2010 after the implementation of a national harm reduction program in 2006 to combat the HIV outbreak among IDUs. [3, 4] At the end of 2010, 1,573 (7.84%) of 20,057 people living with HIV were women, with 70% of them at the childbearing age of 18-30 years. [4]

Invasive cervical cancer was defined as an AIDS-related malignancy in 1993 and was the most common malignancy among women with HIV. [5, 6] Due to immunosuppression, women with HIV were not only 5 times more likely to develop cervical dysplasia, [7] but also had a 2-12-fold increased risk of cervical cancer, compared to HIV-negative women. [8-11] In addition, HIV-infected women with invasive cervical cancer were more likely to present with advanced clinical disease, [12]

have persistent or recurrent disease at follow-up, a shorter time to recurrence, and a shorter survival time after diagnosis, and die of cervical cancer. [11] Nearly 1 in 4 women did not receive an annual Pap test in the United States. [13] Little information is available as to how well HIV primary care clinics perform cervical cancer screening for women with HIV.

Cervical cancer is preventable through Papanicolaou (Pap) smear screening if detected at an early stage. In Taiwan, the national Pap smear screening program has targeted women aged 30 or over since 1995, with coverage of only 50-60% of the general population, [14, 15] Pap smear screening has demonstrated high specificity and sensitivity in detecting cervical cytologic abnormalities in both uninfected and HIV-infected women. [16] Following the guidelines of the United States, the Taiwan CDC in 2010 recommended that all HIV-infected women receive two Pap smears in the first year of HIV-diagnosis, with annual screening thereafter for women with normal results on both tests. [17, 18] Despite these recommendations, limited information is available on Pap smear rates and factors associated with recipients of Pap smears among HIV-infected women in Taiwan.

Despite the significance of regular Pap smear screening, no studies to date have evaluated the rate at which HIV-infected women receive Pap smear screening during their first year after HIV diagnosis in Taiwan. Furthermore, longitudinal studies with

involvement of national survey data are scarce in Taiwan. This study investigated the frequency of pap smears during 2000-2008 among women with HIV, and to compare the screening rate and incidence of cervical cancer between women with HIV and uninfected women.

Methods

Data sources

This was a retrospective population-based cohort study using outpatient clinic files retrieved from the NHIRD for the years 2000-2008 in Taiwan. The Bureau of National Health Insurance (BNHI), Taiwan Department of Health, consolidated all of the health insurance systems into a universal NHIRD in 1995. As of 2007, the NHIRD covered approximately 99% of the 23 million people living in Taiwan and contracted with 99% of the hospitals and clinics on the island.[19] The large sample size and high quality of Pap smear utilization claims data have ensured that this dataset provides a valuable opportunity to estimate the utilization of Pap smear services among patients with disabilities [20] and nurses.[21] Claims data of ambulatory care facilities were used for analysis in this study, and included the records of all outpatient departments of hospitals or clinics, and various bits of information, including personal identification number (PIN), date of birth, sex, insurance area, insurance monthly salary, date of medical visit, preventive health service utilization, and a maximum of three leading outpatient

diagnoses of patients. Individually identifiable health information was encrypted by the BNHI. This study was exempt from full review by the Institutional Review Board of National Cheng Kung University Hospital since the dataset used consisted of de-identified secondary data released to the public for research purposes.

Cohort of women with HIV

In this study, the cohort of women with HIV (n= 1,382) is confined to those age≧18 years, then excluded cervical cancer history (ICD9: 2331, 180) prior HIV diagnosed (n= 15) and no health insurance (n= 10) between 2000 to 2008 who were approved for the Taiwan CDC as a result of their HIV. Finally, the study group contained 1,357 HIV-infected women. To get a diagnosed with HIV, the patient's attending physician is required to provide relevant clinical and laboratory information (eg, western blot test) as part of the application for review. Tests of goodness of fit by age between study group and CDC reported data during 2000-2008 showed no difference (χ^2= 7.51, p= 0.18).

Control group - women without HIV

The comparison group of women without HIV (n= 301,027) also limited the selected subjects to those ages 18 and over (n= 51,796), also excluding who were diagnosed with cervical cancer before observed of starting time (n= 1,193) and infected with HIV (n= 80), then were randomly extracted 13,570 observed of year-, age- and geographic

region- matched subjects (ten for every HIV-infected women) from the 2000 Registry of Medical Personnel of the Longitudinal Health Insurance Database 2000 (LHID2000).

Study endpoints and potential confounders

Information of the primary dependent variables (i.e., receipt of Pap smears and diagnosed with cervical cancer) were retrieved examination codes (00, 31, 33, 35) and diagnosis codes (2331, 180) during the 9-year study period, 2000-2008. Under the NHI program, physicians and hospitals apply for reimbursement after providing cervical cancer, so retrieved cervical cancer codes can be reliable identified from the medical claims data. Information of the potential confounding factors was also retrieved from the claim data, including age, urbanization level, premium-based monthly salary, occupation, anti-retroviral therapy (ART) use, number of ob/gyn ambulatory care visits, prenatal examination, drug dependence, alcohol abuse, and history of STD.

Statistical analysis

Summary statistics were expressed as frequency or percentage for categorical data and mean ± standardized distribution (SD) to approximate normally distributed continuous variables. Prevalence of Pap smear screening was calculated using the number of patients that had received a Pap smear as the numerator (deletion of duplicate cases) and the annual number of diagnosed HIV-infected women as the

denominator. Multivariate logistic regression analysis was used to determine the likelihood that HIV-infected women had received Pap tests from 2000–2009.

We first described the participant characteristics differences between HIV and control group, and then calculated incidence of cervical cancer (cases per 1000 person-years) in patients with HIV and those without categories by age during 2000 to 2008. To examine whether patients with HIV had a higher risk of cervical cancer comparison the control group matched for observed of year-, age- and geographic region, then computed the age-specific hazard rates and 95% CIs for HIV and control group. We also calculated hazard rates by the periods that were data-tracked to determine if the probability of a cervical cancer diagnosis appearing in the claims data was affected by the length of period observed. All analyses were performed with 17.0 SPSS and the 9.2 SAS statistical package.

Results

A total of 14,927 subjects (1357 study group and 13570 control group) aged≧18 years between 2000 and 2008. Two-thirds of the women (79.8%, n=1,083) were diagnosed with HIV after 2004. The mean follow-up time was 3 years. The mean age at the first time visit HIV care was 34.8 years (range: 18-89 years). Patients enrolled in this study were generally of low socioeconomic status; 83.8% were blue-collar workers, 72.9% had lower incomes, a lower number of ob/gyn ambulatory care visits, more

likely received prenatal examination, a higher number of diagnosed with drug dependence, alcohol abuse and STDs than control group (all p <0.001) (Table 1).

Prevalence of Pap smear screening

Overall, 344 HIV women (25.4%) had received one or more Pap smears during the period 2000-2008 (annually of Pap smear rate between 9-15%), comparison control group that Pap smear rates were 2652 (19.54%) (annually of Pap smear rate between 5-12%), screening rates were highest among HIV-infected women when compared to the control group(OR= 1.40, 95% CI= 1.23-1.59, p<0.0001) (Figure 1).

Of the 460 women who received cervical Pap smear screening, 149 (32.4%) had abnormal results: 140 (30.4%) had cervical dysplasia, 1 (0.2%) had carcinoma in situ, and 8 (1.7%) were diagnosed with cervical cancer. With the exception of a 6% decrease, from 14.26% in 2005 to 8.09% in 2006, the proportion of Pap smear screening during the defined time periods remained constant: 9.9% in 2000, 15.25-14.26% between 2001 and 2005, 8.09-10.57% between 2006 and 2007, and 14.20-14.13% between 2008 and 2009 (Figure 1). The sharp decrease in the screening rate from 2005 to 2006 was negatively associated with the percentage of drug dependence among women with HIV (r = -.403, p< .001).

Factors associated with receipt of a Pap smear

Univariate analysis showed that receipt of a Pap smear was significantly associated

with age at first visit to the HIV clinic, monthly income, occupation, history of prenatal examination, history of cervical and sexually transmitted disease, and a diagnosis of opportunistic infection. Multivariate logistic regression revealed that receipt of a Pap smear was significantly associated with increasing age (adjusted odds ratios [AOR] per 10 years = 1.49, 95% CI = 1.32, 1.68), monthly income ≥ NT$43,900 (AOR = 5.9, 95% CI = 2.78, 12.47) and a history of cervical disease (AOR = 2.54, 95% CI = 1.85, 3.49) (Table 2).

Incidence of cervical cancer

A total of 13/1537 (0.96%) patients with HIV were identified to have cervical cancer after the diagnosis of HIV during the observation period of 3978.01 person years. The incidence of cervical cancer among patients with HIV increased with age, and HIV group had higher incidence than control group. The adjusted hazard ratio (AHR) for cervical cancer was 5.24 (95% CI 2.55 to 10.76) for patients of all ages with HIV (≧18 years), 7.14 (95% CI 1.31 to 38.84) for patients aged 30-39 years, 6.92 (95% CI 2.01 to 23.81) for patients aged 40-49 years, 14.64 (95% CI 2.80 to 76.63) for patients aged 50-59 years. Specially, comparison control group that age between 30-59 years significantly increased the rates of malignant neoplasm of the cervical with HIV (Table 3). A multivariate analysis using the Cox proportional risk model showed that the risk associated with malignant neoplasm of the cervical was lower among women who had

longer exposure years to antiretroviral theory (HR, 0.88; 95% CI, 0.78-0.98), higher among women who Frequently received Pap screening tests after HIV diagnosed (HR, 1.27; 95% CI, 1.1-1.48) and among those who had opportunity infections (HR, 2.9; 95% CI, 1.27–6.66) (Table 4).

Discussion

To our knowledge, this study is the first to use population-based claims data to report longitudinal trends of Pap smear screening rates among HIV-infected women in Asia. Our study found that 30% of women living with HIV received one or more Pap smears from 2000 to 2009, which is much lower than the 77% in the United States from 2002 to 2004, [13] and the 77.9% in California from 2002 to 2006. [22] Furthermore, our study showed that only 12% of HIV-infected women received a Pap test during the first year after HIV diagnosis, which is much lower than the 83% in Florida from 2000 to 2006, [23] and 76.2% in United Kingdom.[24] The low Pap smear screening rate was consistent with a previous report that Asian women were less likely than white women to receive Pap smear screening.[25] The reason for the low Pap smear screening rate of HIV-infected women in Taiwan may be socio-cultural barriers (e.g., rejection of male doctors, embarrassment about having a pelvic examination), resulting in the non-use of Pap smear screening services.[26] Cervical cancer poses a significant but preventable risk to HIV-infected women. Our findings suggest healthcare professionals should

comply with the guideline to conduct Pap smear screening for HIV-infected women to allow early detection of cervical intraepithelial neoplasia. More studies are needed to further examine the reasons for the failure of healthcare professionals to meet these evidence-based guidelines, and for the barriers preventing HIV-infected women from receiving the recommended two Pap smear screenings during the first year after diagnosis.

The proportion of Pap smear screening remained constant, around 8-15%, during the period 2000-2009, except the decrease to 6% from 2005 to 2006. One potential explanation for the decreased Pap smear rate in 2006 was the outbreak of HIV infection among IDUs in Taiwan beginning in 2003. [3] Our finding is consistent with previous studies [27, 28] that reported current IDUs or women with substance abuse were associated with a decreased rate of adherence to both gynecological appointments and primary care visits. Female IDUs who sell or trade sex for drugs are at risk of sexually transmitted diseases, and most of these women are from economically disadvantaged backgrounds. Thus, the finding that the majority of HIV-infected women with substance dependence did not receive Pap smear screening suggests local health departments should be an important source of preventive care targeting HIV-infected women, especially those women with substance abuse.

Three main factors were significantly associated with having at least one Pap smear

after HIV diagnosis during the period 2000-2009. The first of these was increasing age (per 10 years). This finding is in contrast with previous reports from Western countries. [13, 27] The difference may be related to the national Pap smear screening program in Taiwan, which targets women aged 30 and over, and ethno-cultural differences (e.g., Taiwanese women usually have more gynecological ailments, and are also more likely to have a Pap test). [29] However, HIV-infected women are not only younger (average age, 20-39 years), but also at higher risk of HPV infection [30], and both advanced and early cervical pathology. [11] Therefore, Pap smear screening of HIV-infected women should be a high priority. The second factor associated with receiving a Pap smear was higher income, which is consistent with previous reports on the general population in Taiwan.[31] For low-income HIV-infected women who are not likely receive a Pap smear, ensuring the recommended Pap smear screening requires additional rewards (e.g., coupons or bonuses) to increase the rate of women from low-income households that receive screening. The last factor associated with receiving a Pap smear was previous cervical dysplasia, which is also consistent with previous studies, [13, 27] and indicates that HIV-infected women usually had an HIV-related syndrome that would arouse the attention of health providers. Based on that, Pap smear screening should be recommended at their first HIV care visit and continued annually.

Limitations

Some limitations of this study merit attention. First, the study reports only those patients who received a Pap smear in outpatient settings. However, the study stands out for being able to draw on an extensive nationwide population-based database, leaving little room for selection and non-response bias. Second, the study was limited by the nature of a retrospective design, which relies on existing data sources. Certain clinical factors, such as CD4, viral load, socioeconomic status and social stigma might lead some patients to decline healthcare. The NHIRD lacks detailed clinical information and other lifestyle-related potentially confounding factors in analysis that might compromise our findings.

Conclusion

The findings indicate that the incidence of cervical cancer among women with HIV is five times higher than women without HIV infection. HIV care providers should ensure a Pap smear at the first visit to the HIV clinic and remind HIV-infected women who had opportunity infections and haven't initiated with antiretroviral therapy to receive Pap screening annually.

Conflict of interest statement

None.

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Pap

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Table 1. Characteristics of study population in Taiwan, 2000-2008 (N= 14,927)

Variable	HIV group	Control group	p value
	n= 1,357	n= 13,570	
Follow-up time〔 mean, SD (range) 〕	2.93, 2.38 (0-9)	3.08, 2.20 (0-9)	
Age at the first visit HIV care (year)			1
18-19	11 (0.80)	110 (0.80)	
20-29	525 (38.70)	5250 (38.60)	
30-39	454 (33.50)	4540 (33.70)	
40-49	212 (15.60)	2120 (15.70)	
50-59	101 (7.40)	1010 (7.40)	
≧60	54 (4.00)	540 (4.00)	
Urbanization level			1
1 (most urbanized)	351 (25.90)	3510 (25.90)	
2	565 (41.60)	5650 (41.60)	
3 (least urbanized)	441 (32.50)	4410 (32.50)	
Premium-based monthly salary (NT $)			<0.001
<=17280	989 (72.90)	6335 (46.68)	
17281-26400	236 (17.40)	3985 (29.37)	
26401-43900	85 (6.30)	2470 (18.20)	
>43901	47 (3.50)	780 (5.75)	
Occupation			<0.001
Blue collar	1137 (83.79)	7226 (53.54)	
White collar	220 (16.21)	6304 (46.46)	
ART use	668 (49.23)	NA	NA
Number of ob/gyn ambulatory care visits[¥]			<0.001
0	221 (16.30)	6810 (50.18)	
1-10	541 (39.90)	2731 (20.13)	
11-20	259 (19.1)	1243 (9.16)	
21-30	155 (11.40)	917 (6.76)	
>30	181 (13.30)	1869 (13.77)	
Prenatal examination	200 (14.70)	1454 (10.71)	
Any drug dependence (ICD9: 304)	218 (16.10)	11 (0.08)	<0.001
Any alcohol abuse (ICD9: 303、3050)	55 (4.10)	57 (0.42)	<0.001
History of STDs (ICD9: 0541、0781、0788、091-099、131)	217 (15.99)	788 (5.81)	<0.001

[¥]Excluding visits for Pap smear tests

Table 2. Associations between Selected Factors and Receipt of a Pap Smear, 2000 -2009

Variables	All subjects (N=1,500)	With Pap tests[a] (n=460)		Unadjusted OR (95% CI)	Adjusted OR (95% CI)
	No. (%)	No.	%[b]		
Age (yrs)					1.49 (1.32, 1.68)*[c]
18-29	576 (38.4)	67	11.6	Referent	
30-39	508 (33.9)	207	40.7	5.23 (3.83, 7.12)*	
40-49	237 (15.8)	113	47.7	6.92 (4.83, 9.93)*	
50 or over	179 (11.9)	73	40.8	5.23 (3.54, 7.74)*	
Drug dependence					
No	1218 (81.2)	386	31.7	Referent	Referent
Yes	282 (18.8)	74	26.2	0.77 (0.57, 1.03)	0.94 (0.69, 1.33)
Monthly income (NTD)					
≦17280	1098 (73.2)	278	25.3	Referent	Referent
17281-26400	264 (17.6)	109	41.3	2.07 (1.57, 2.75)*	1.74 (1.26, 2.40)*
26401-43899	91 (6.1)	44	48.4	2.76 (1.79, 4.26)*	2.21 (1.25, 3.91)*
≧43900	47 (3.1)	29	61.7	4.75 (2.60, 8.70)*	5.90 (2.78, 12.47)*
Urbanization status					
Rural	490 (32.7)	138	28.2	Referent	Referent
Urban	1010 (67.3)	322	31.9	1.19 (0.94, 1.51)	1.02 (0.77, 1.36)
Occupation					
Blue collar	1259 (83.9)	365	29.0	Referent	Referent
White collar	241 (16.1)	95	39.4	1.59 (1.20, 2.12)*	1.05 (0.69, 1.60)
ART use					
Never	745 (49.7)	236	31.7	Referent	Referent
Ever	755 (50.3)	224	29.7	0.91 (0.73, 1.13)	1.08 (0.83, 1.40)
Prenatal examination					
No	1267 (84.5)	406	32.0	Referent	Referent
Yes	233 (15.5)	54	23.2	0.64 (0.46, 0.89)	0.87 (0.59, 1.28)
HIV screening					
No	1497 (99.8)	458	30.6	Referent	Referent
Yes	3 (0.2)	2	66.7	4.54 (0.41, 50.16)	1.49 (0.04, 52.69)
Previous cervical dysplasia (ICD-9)					

No	1236 (82.4)	311	25.2	Referent	Referent
Yes	264 (17.6)	149	56.4	3.85 (2.93, 5.07)*	2.54 (1.85, 3.49)*
Cervical dysplasia (V762)	247 (16.5)	140	30.4		
Carcinoma in situ of cervix uteri (2331)	4 (0.3)	1	0.2		
Malignant neoplasm of cervix uteri (180)	13 (0.8)	8	1.7		
History of STD (ICD-9)					
No	1252 (83.5)	352	28.1	Referent	Referent
Yes	248 (16.5)	108	43.5	1.97 (1.49, 2.61)*	1.33 (0.96, 1.85)
Viral warts (0781)	70 (4.7)	26	5.7		
Syphilis (091-097)	60 (4.0)	32	7.0		
Venereal disease (099)	54 (3.6)	20	4.3		
Trichomoniasis (131)	51 (3.4)	24	5.2		
Others (Genital herpes, Clamydia, Gonorrhea, Pediculosis)	13 (0.8)	6	1.3		
History of OI (ICD-9)					
No	1087 (72.5)	300	27.6	Referent	Referent
Yes	413 (27.5)	160	38.7	1.66 (1.31, 2.11)*	1.12 (0.85, 1.50)
Candidiasis (112)	226 (15.1)	90	19.6		
Varicella-zoster virus infection (0539)	70 (4.7)	27	5.9		
Herpes simplex virus infection (054)	42 (2.8)	17	3.7		
Tuberculosis (010-018)	40 (2.7)	18	3.9		

Others (Bacterial pneumonia, Cryptococcal meningitis, Cryptosporidiosis, Isosporidiasis, MAC infection, Penicilliosis, PCP, Salmonellosis)	35 (2.2)	8	1.7

[a]Results from those who had received Pap smears.

[b] % may not equal 100% due to all subjects as the numerator.

[c] Per 10-year increase in age.

[*]Significant at $p<0.05$

OR, odds ratio; STD, sexually transmitted disease; OI, opportunistic Infection; MAC, mycobacterium avium complex; PCP, pneumocystis pneumonia.

Table 3. Age-specific hazard rates of malignant neoplasm of the cervical (ICD-9: 2331, 188) in associated with HIV group

Variable	HIV Group			Control Group			Crude HR (95% CI) in Associated With HIV	Adjusted HR (95% CI) in Associated With HIV§	P value
Age	No. of HIV	No. of Events	Incidence (per 1000-PYs)	No. of Control	No. of Events	Incidence (per 1000-PYs)			
18-29 years	536	1	0.70	5360	2	0.13	5.43 (0.49-58.90)	3.0 (0.20-44.32)	0.42
30-39 years	454	2	1.54	4540	5	0.37	4.31 (0.84-22.22)	7.14* (1.31-38.84)	**0.02**
40-49 years	212	5	7.35	2120	6	0.82	8.82*** (2.70-28.91)	6.92** (2.01-23.81)	**0.002**
50-59 years	101	3	8.43	1010	3	0.81	10.79* (2.18-53.51)	14.64*** (2.80-76.63)	**0.001**
≧60 years	54	2	8.74	540	6	2.70	3.26 (0.66-16.13)	2.47 (0.48-12.77)	0.28
All (>=18 years)	1357	13	3.27	13570	22	0.53	6.33*** (3.19-12.56)	5.24*** (2.55-10.76)	**<0.001**

§Adjusted for Premium-based monthly salary, occupation, number of ob/gyn ambulatory care visits, prenatal examination, drug dependence, alcohol abuse and history of STD

Table 4. **Hazard rates of malignant neoplasm of the cervical (ICD-9: 2331, 188) in Associated With HIV-infected women**

Variable	Crude HR (95% CI) in Associated With HIV	P value	§Adjusted HR (95% CI) in Associated With HIV	P value
HAART exposure time (yr)	0.94 (0.84-1.06)	0.3	0.88 (0.78-0.98)	0.03
Frequency of Pap test after HIV diagnosed	1.27 (1.10-1.45)	0.001	1.27 (1.1-1.48)	0.002
OI occured after dignosis with HIV	2.94 (1.33-6.53)	0.008	2.9 (1.27-6.66)	0.01

§Adjusted for Age in HIV diagnosed, Premium-based monthly salary, Urbanization level, Occupation, Number of of prenatal care visit, Drug dependence, Alcohol abuse and History of STDs

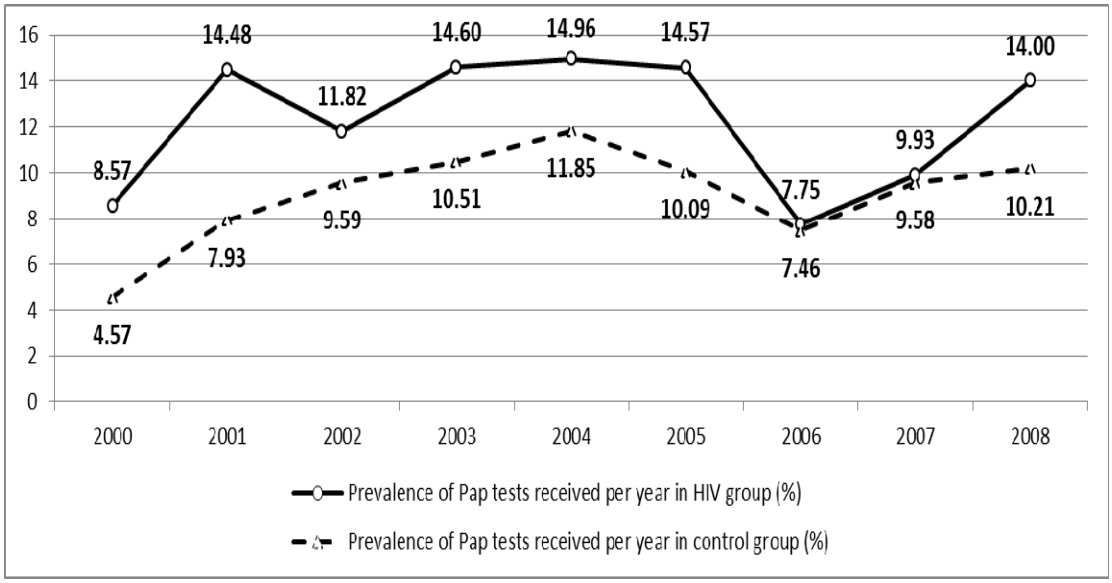

Figure 1. Comparison prevalence of Pap smear screening among HIV-infected women and whose without during the past year, 2000-2008.

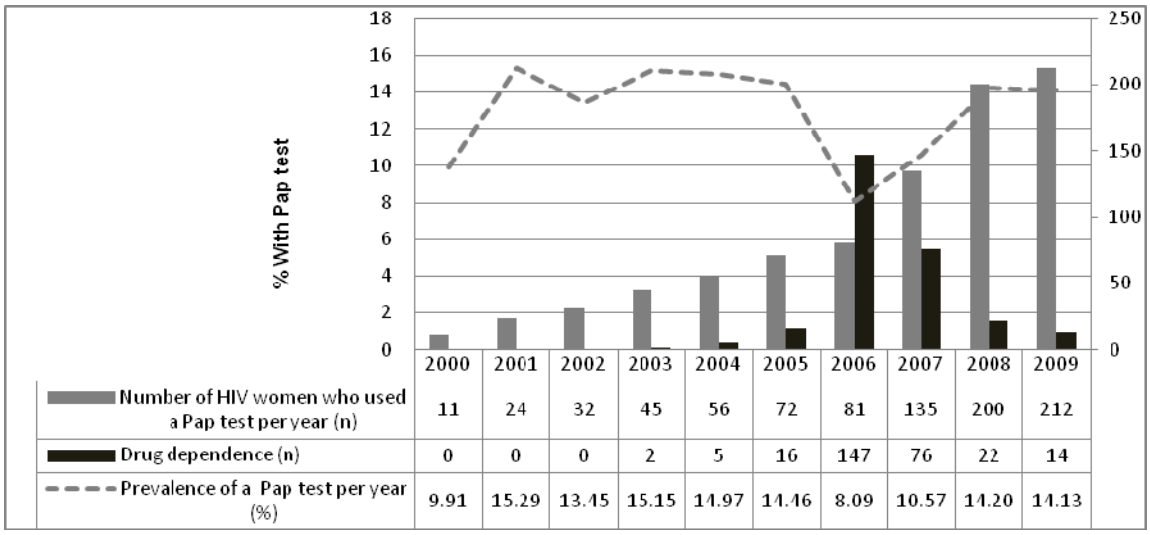

Figure 1. Prevalence of HIV-infected women who had received a Pap test during the past year and had a negative association with drug dependence, 20

行政院及所屬各機關出國報告

（出國類別：出席國際學術會議）

參加 2012 年 19 屆世界愛滋病會議

The 19th International AIDS Conference (AIDS 2012)

服務機關：國立成功大學

姓名職稱：陳嬿今 專案工作人員

派赴國家：Washington DC, USA

出國期間：2012 年 7 月 22 日至 7 月 27 日

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摘　　要

2012 年第 19 屆世界愛滋病會議 (The 19th International AIDS Conference, AIDS2012)的主題是：Turning The Tie Together，強調全球抗愛滋病行動及防治需要集結各個領域的愛滋病專家、政策制定者、愛滋病患團體及弱勢族群的力量，共同來終止全球愛滋病流行的情勢。在大會中本人以海報型式發表論文「Low Pap Smear Screening Rate among HIV-Infected Women in Taiwan, 2000-2009: A Nationwide Population-Based Study」，在會議期間亦透過參與不同的議程討論獲得目前在全球在愛滋病治療及預防的趨勢(尤其本人更專注於女性愛滋感染者在全球愛滋病治療及預防的部分)，其中所獲得的相關資訊也能提供無法出國之健康照顧專業同仁及專家學者做為從事臨床照顧、實務教學或學術研究之參考。

壹、目的

世界愛滋病會議為全球每二年一次的國際性愛滋病會議，今年為第 19 屆，每年超過二萬名來自全球各國的學者專家及民間團體等參與此次會議，同時也辦理學術論文發表會，對全球愛滋病患醫療照顧及國際政策的實踐、教育、研究和社會經濟福利等具有國際影響力。

而此次 2012 年第 19 屆世界愛滋病會議 (The 19th International AIDS Conference, AIDS 2012)的主題是：Turning The Tie Together，強調愛滋病的防治需全面努力、團結，扭轉劣勢。而此次會議的主軸更是強調治療即是預防(Treatment as Prevention)，期以透過早期愛滋病篩檢全面治療，並聯至醫療系統降低傳染。而目前全球更全力朝向尋找愛滋解藥(Toward an HIV Cure)，讓下一代免於愛滋感染的恐懼 (Next generational free from HIV)。

貳、過程

本人在大會發表海報論文「Low Pap Smear Screening Rate among HIV-Infected Women in Taiwan, 2000-2009: A Nationwide Population-Based Study」(附件一)，並透過展示海報與各個來自國內外學者討論目前針對女性感染者在子抹篩檢政策的異同，普遍說來在

歐美自 1993 年即有相關的實證顯示子宮頸癌是愛滋病相關疾病診斷症候群之一，故自 1995 年起即建議感染者應於診斷後一年內施行兩次子抹篩檢，也因為國情的不同，在歐美對於子抹篩檢的接受度相當高，目前幾乎均有近 80-90%以上的婦女有做過子抹篩檢，如以已開發國家相較，我國年度子抹篩檢率僅 8-15%是很低的，其中有可能的因素是在國內的女性感染者近 70-80% 均為靜脈藥癮患者，而其就醫特性屬不規律也較少接受相關預防性篩檢，而我國針對女性感染者的子抹篩檢政策屬較晚期，截至 2010 年才大力呼籲，故會有此差異。

本人在會議期間亦積極參與不同的小組討論，其中大部分以「care of women living with HIV」為主軸，瞭解到目前全球對於女性感染者的治療及預防，在治療面向，目前大多提倡於早期診斷應即早藥物治療，才會終止其感染力；而預防面向，大多係以母子垂直感染的預防、早期執行子抹篩檢及鼓勵男性割包皮等。而大會中有一堂議程讓我印象非常深刻，背景是以一位非洲美裔女性從 22 歲診斷HIV到 55 歲，從注射藥物感染HIV、面臨懷孕、產後憂鬱再度注射藥物感染C肝，到年老的醫療及生涯面臨的問題，一一整合醫療、健康、社會與人生的討論，讓醫療人員有身歷其境的感染，且議程中主持的專家學者會透過電子互動式系統，與與會者共同討論如何解決其醫療問題。可為日後臨床服務、教學與研究收集了不少可貴的教材與資訊。

參、心得與建議

此次參與議程的討論中有幾點重大的獲得：

1.在早期研究中發現免疫力指數的高低，會影響子宮頸上皮細胞惡化的速度，而如以抗病毒藥物治療會提升其免疫力，有可能會延緩子宮頸上皮細胞惡化的速度，而近期對於子宮頸癌的研究中亦進一步指出感染者如使用抗病毒藥物治療其子宮頸上皮細胞回覆率(regression)相較於沒有使用藥物治療者多達 2 倍，亦可降低約 45%的子宮頸癌發生率。而這個部份，是很耐人尋味的，而我國的健保資料庫也可以進一步去應證這個結果。

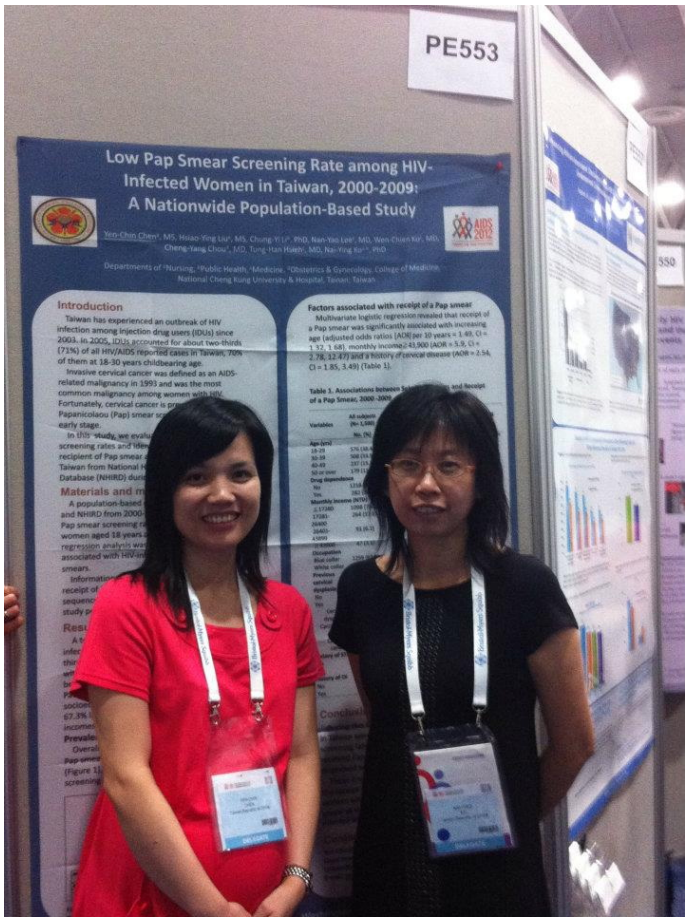
2.目前全球的愛滋病防治趨勢為『提早發現提早治療』，而男女在性別及構造本有就有所不同，在未來似乎可以利用資料庫去進一步確認男女於早發性的疾病(伺機性感染)之不同，其以進一步早期發現早期治療疾病。

3. EFV 不再被視為懷孕婦女的禁忌，研究指出致畸胎的機率微乎其微，但臨床醫師仍擔心法律的爭議，而另一方面即早 HCV 治療對感染者是非常重要的議題。

期待國科會或其他教育行政機構，應建立更積極的制度，未來能補助國內學者每年多次參與國際會議並發表論文，鼓勵學者多走向國際，以台灣學者的身份發表論文，透過發表與學者間互相提問的互動

中，讓不同國家學者認識台灣愛滋病護理及臨床照顧經驗。

附件一 大會發表海報論文，並與指導老師（柯乃熒副教授）共同展示海報



AIDS 2012 | XIX INTERNATIONAL AIDS CONFERENCE JULY 22 - 27 WASHINGTON DC USA
TURNING THE TIDE TOGETHER

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Letter of Invitation
XIX International AIDS Conference
22 - 27 July 2012, Washington DC, USA

Dear Yen-chin Chen,

The International AIDS Society (IAS) is pleased to invite you to attend the XIX International AIDS Conference (AIDS 2012) to be held at the Walter E. Washington Convention Center in Washington DC, USA, 22 - 27 July 2012.

As a result of your recent registration for AIDS 2012, this letter is provided as an official invitation to facilitate the process of obtaining a visa or other travel documents needed to enable you to attend the conference. This Letter of Invitation does not commit the conference, the IAS, or the AIDS 2012 Registration Department to any kind of financial support or hosting arrangements, nor does it guarantee an entry visa to the United States of America. Please note that you should apply for your visa as early as possible and, if possible, no later than 90 days before your intended travel to the conference to ensure the authorities have enough time to process your application.

The biennial International AIDS Conference is the premier gathering for those working in the field of HIV, as well as policymakers, people of living with HIV and others commited to ending the epidemic. It will be a tremendous opportunity for researchers from around the world to share the latest scientific advances in the field, learn from one another's expertise, and develop strategies for advancing all facets of our collective efforts to treat and prevent HIV.

Due to the large number of international delegates expected, every Letter of Invitation is signed using authorized, electronically scanned signatures. We kindly ask the embassies and consulates to accept the signatures on this letter and consider this Letter of Invitation as a valid document originating from the AIDS 2012 conference.

Any inquiries relating to this Letter of Invitation should be directed to the AIDS 2012 Registration Department at letterofinvitation@aids2012.org or +41 61 560 75 35.

We look forward to welcoming you to Washington DC!

Sincerely,

Elly Katabira
International Chair
XIX International AIDS Conference
President, International AIDS Society
Professor of Medicine,
Makerere University, Kampala, Uganda

Diane Havlir
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Low Pap Smear Screening Rate among HIV-Infected Women in Taiwan, 2000-2009: A Nationwide Population-Based Study

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Running title: Pap smear screening rate among HIV-infected women

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Abstract

OBJECTIVE: To estimate the trends in Pap smear screening rates and associated factors among women with HIV in Taiwan.

METHODS: A population-based cohort study was conducted, and the National Health Insurance Research Database (NHIRD) from 2000-2009 was used to estimate the Pap smear screening rate for 1,500 HIV-infected women aged 18 years and over. Multiple logistic regression analysis was used to identify factors associated with HIV-infected women who had received Pap smears.

RESULTS: During a 10-year study period, 460 (30%) women received at least one Pap test. Only 12.0% of the HIV-infected women received Pap smears within one year after being diagnosed with HIV. Logistic regression analysis showed that the factors associated with receiving at least one Pap smear after HIV diagnosis during the period 2000-2009 were: increasing age (per 10-year intervals) (adjusted odds ratio [AOR] = 1.49, 95% CI = 1.32, 1.68), high monthly income (AOR = 5.9, 95% CI = 2.78, 12.47) and a previous history of cervical disease (AOR = 2.54, 95% CI = 1.85, 3.49).

CONCLUSIONS: These findings provide evidence of disparities in the receipt of Pap smear screening services among women with HIV. HIV care providers should ensure a Pap smear at the first visit to the HIV clinic and remind HIV-infected women to receive Pap screening annually.

Key words: HIV-infected women, Pap smear screening, National Health Insurance Research Database (NHIRD)

Introduction

There are an estimated 33.3 million people living with human immunodeficiency virus (HIV) in the world, and 15.7 million (47%) of these are women. [1] An estimated 1.68 million women are living with HIV/AIDS in Asia. [2] Yet, according to the Taiwan Center for Disease Control (Taiwan CDC), HIV and AIDS diagnoses have been reported for relatively few women and female adolescents in Taiwan, and the male-female ratio was 20:1 until 2003. Taiwan has experienced an outbreak of HIV infection among injected drug users (IDUs) since 2003. [3] In 2005, IDUs accounted for about two-thirds (71%) of all reported HIV/AIDS cases in Taiwan, and the male-female ratio reached a peak of 7:1. Then, the ratio fell to 17:1 by 2010 after the implementation of a national harm reduction program in 2006 to combat the HIV outbreak among IDUs. [3, 4] At the end of 2010, 1,573 (7.84%) of 20,057 people living with HIV were women, with 70% of them at the childbearing age of 18-30 years. [4]

Invasive cervical cancer was defined as an AIDS-related malignancy in 1993 and was the most common malignancy among women with HIV. [5, 6] Due to immunosuppression, women with HIV were not only 5 times more likely to develop cervical dysplasia, [7] but also had a 2-12-fold increased risk of cervical cancer, compared to HIV-negative women. [8-11] In addition, HIV-infected women with invasive cervical cancer were more likely to present with advanced clinical disease, [12] have persistent or recurrent disease at follow-up, a shorter time to recurrence, and a shorter survival time after diagnosis, and die of cervical cancer. [11]

Nearly 1 in 4 women did not receive an annual Pap test in the United States. [13] Little information is available as to how well HIV primary care clinics perform cervical cancer screening for women with HIV.

Cervical cancer is preventable through Papanicolaou (Pap) smear screening if detected at an early stage. In Taiwan, the national Pap smear screening program has targeted women aged 30 or over since 1995, with coverage of only 50-60% of the general population, [14, 15] Pap smear screening has demonstrated high specificity and sensitivity in detecting cervical cytologic abnormalities in both uninfected and HIV-infected women. [16] Following the guidelines of the United States, the Taiwan CDC in 2010 recommended that all HIV-infected women receive two Pap smears in the first year of HIV-diagnosis, with annual screening thereafter for women with normal results on both tests. [17, 18] Despite these recommendations, limited information is available on Pap smear rates and factors associated with recipients of Pap smears among HIV-infected women in Taiwan.

Despite the significance of regular Pap smear screening, no studies to date have evaluated the rate at which HIV-infected women receive Pap smear screening during their first year after HIV diagnosis in Taiwan. Furthermore, longitudinal studies with involvement of national survey data are scarce in Taiwan. In this study, we evaluated the trends in Pap smear screening rates and identified factors associated with recipients of Pap smears among HIV-infected women in Taiwan, using the National Health Insurance Research Database

(NHIRD) for 2000-2009.

Methods

Data sources

This was a retrospective population-based cohort study using outpatient clinic files retrieved from the NHIRD for the years 2000-2009 in Taiwan. The Bureau of National Health Insurance (BNHI), Taiwan Department of Health, consolidated all of the health insurance systems into a universal NHIRD in 1995. As of 2007, the NHIRD covered approximately 99% of the 23 million people living in Taiwan and contracted with 99% of the hospitals and clinics on the island.[19] The large sample size and high quality of Pap smear utilization claims data have ensured that this dataset provides a valuable opportunity to estimate the utilization of Pap smear services among patients with disabilities [20] and nurses.[21] Claims data of ambulatory care facilities were used for analysis in this study, and included the records of all outpatient departments of hospitals or clinics, and various bits of information, including personal identification number (PIN), date of birth, sex, insurance area, insurance monthly salary, date of medical visit, preventive health service utilization, and a maximum of three leading outpatient diagnoses of patients. Individually identifiable health information was encrypted by the BNHI. This study was exempt from full review by the Institutional Review Board of National Cheng Kung University Hospital since the dataset used consisted of de-identified secondary data released to the public for research purposes.

58 Cohort of patients with HIV

59 Patients (*n*=22,037) who visited ambulatory care facilities (outpatient clinics) with
60 principal and secondary diagnoses of HIV infection (ICD-9-CM codes 042 or V08) were
61 selected. Since the 1990s, HIV-related treatment costs have been paid by the Taiwan CDC,
62 and 16,433 patients were categorized using the code 91 for reimbursement. We excluded 45
63 patients (0.27%) who were younger than 18 years, 14,839 (90.30%) who were male, and 49
64 (0.29%) whose records had incomplete information on gender. The final sample included
65 1,500 women who were diagnosed with HIV between 2000 and 2009.

66 Study endpoints and potential confounders

67 Information on the primary dependent variable (i.e., receipt of Pap smears) was retrieved
68 using a code (card sequence numbers: 31, 33, 35) during the 10-year study period from
69 2000-2009. Only Pap smears performed after the time of HIV diagnosis were counted.
70 Information on potential confounding factors was also retrieved from the claim data,
71 including age at first visit to a HIV clinic, monthly income, level of urbanization, occupation,
72 drug dependence (ICD-9: 304), anti-retroviral therapy (ART) use (cure item number: 53),
73 prenatal examination (card sequence number: IC41-60), HIV screening (card sequence
74 number: IC10), history of previous cervical dysplasia (ICD-9: 180, 2331, V762), history of
75 sexually transmitted disease (STD) (ICD-9: 0541, 0781, 0788, 091-097, 098, 099, 131, 132),
76 and diagnosis of opportunistic infection (OI) (ICD-9: 4829, 112, 3210, 0074, 0785, 054, 1369,

0088, 0312, 1179, 1363, 130, 010-018, 0030, 0539).

Statistical analysis

Summary statistics were expressed as frequency or percentage for categorical data and mean ± standardized distribution (SD) to approximate normally distributed continuous variables. Prevalence of Pap smear screening was calculated using the number of patients that had received a Pap smear as the numerator (deletion of duplicate cases) and the annual number of diagnosed HIV-infected women as the denominator. Multivariate logistic regression analysis was used to determine the likelihood that HIV-infected women had received Pap tests from 2000–2009. All analyses were performed with 17.0 SPSS and the 9.2 SAS statistical package.

Results

A total of 1500 women older than 18 years and with HIV infection were identified for the period 2000-2009. Two-thirds of the women (80.2%, n=1,203) were diagnosed with HIV after 2004. Of them, 72.3% first sought HIV care between the ages of 18-39 years (mean ±SD, 35.13±1.28). Patients enrolled in this study were generally of low socioeconomic status; 83.9% were blue-collar workers, 67.3% lived in highly urbanized areas, and 73.2% had lower incomes (Table 1).

Prevalence of Pap smear screening

Overall, 460 women (30%) had received one or more Pap smears during the period

2000-2009 (range, 8-15%) (Figure 1), and only 12% of them received Pap smear screening in their first year after diagnosis of HIV. Of the 460 women who received cervical Pap smear screening, 149 (32.4%) had abnormal results: 140 (30.4%) had cervical dysplasia, 1 (0.2%) had carcinoma in situ, and 8 (1.7%) were diagnosed with cervical cancer. With the exception of a 6% decrease, from 14.26% in 2005 to 8.09% in 2006, the proportion of Pap smear screening during the defined time periods remained constant: 9.9% in 2000, 15.25-14.26% between 2001 and 2005, 8.09-10.57% between 2006 and 2007, and 14.20-14.13% between 2008 and 2009 (Figure 1). The sharp decrease in the screening rate from 2005 to 2006 was negatively associated with the percentage of drug dependence among women with HIV ($r = -.403$, $p < .001$).

Factors associated with receipt of a Pap smear

Univariate analysis showed that receipt of a Pap smear was significantly associated with age at first visit to the HIV clinic, monthly income, occupation, history of prenatal examination, history of cervical and sexually transmitted disease, and a diagnosis of opportunistic infection. Multivariate logistic regression revealed that receipt of a Pap smear was significantly associated with increasing age (adjusted odds ratios [AOR] per 10 years = 1.49, 95% CI = 1.32, 1.68), monthly income ≥ NT$43,900 (AOR = 5.9, 95% CI = 2.78, 12.47) and a history of cervical disease (AOR = 2.54, 95% CI = 1.85, 3.49) (Table 1).

Discussion

To our knowledge, this study is the first to use population-based claims data to report longitudinal trends of Pap smear screening rates among HIV-infected women in Asia. Our study found that 30% of women living with HIV received one or more Pap smears from 2000 to 2009, which is much lower than the 77% in the United States from 2002 to 2004, [13] and the 77.9% in California from 2002 to 2006. [22] Furthermore, our study showed that only 12% of HIV-infected women received a Pap test during the first year after HIV diagnosis, which is much lower than the 83% in Florida from 2000 to 2006, [23] and 76.2% in United Kingdom.[24] The low Pap smear screening rate was consistent with a previous report that Asian women were less likely than white women to receive Pap smear screening.[25] The reason for the low Pap smear screening rate of HIV-infected women in Taiwan may be socio-cultural barriers (e.g., rejection of male doctors, embarrassment about having a pelvic examination), resulting in the non-use of Pap smear screening services.[26] Cervical cancer poses a significant but preventable risk to HIV-infected women. Our findings suggest healthcare professionals should comply with the guideline to conduct Pap smear screening for HIV-infected women to allow early detection of cervical intraepithelial neoplasia. More studies are needed to further examine the reasons for the failure of healthcare professionals to meet these evidence-based guidelines, and for the barriers preventing HIV-infected women from receiving the recommended two Pap smear screenings during the first year after

diagnosis.

The proportion of Pap smear screening remained constant, around 8-15%, during the period 2000-2009, except the decrease to 6% from 2005 to 2006. One potential explanation for the decreased Pap smear rate in 2006 was the outbreak of HIV infection among IDUs in Taiwan beginning in 2003. [3] Our finding is consistent with previous studies [27, 28] that reported current IDUs or women with substance abuse were associated with a decreased rate of adherence to both gynecological appointments and primary care visits. Female IDUs who sell or trade sex for drugs are at risk of sexually transmitted diseases, and most of these women are from economically disadvantaged backgrounds. Thus, the finding that the majority of HIV-infected women with substance dependence did not receive Pap smear screening suggests local health departments should be an important source of preventive care targeting HIV-infected women, especially those women with substance abuse.

Three main factors were significantly associated with having at least one Pap smear after HIV diagnosis during the period 2000-2009. The first of these was increasing age (per 10 years). This finding is in contrast with previous reports from Western countries. [13, 27] The difference may be related to the national Pap smear screening program in Taiwan, which targets women aged 30 and over, and ethno-cultural differences (e.g., Taiwanese women usually have more gynecological ailments, and are also more likely to have a Pap test). [29] However, HIV-infected women are not only younger (average age, 20-39 years), but also at

higher risk of HPV infection [30], and both advanced and early cervical pathology. [11] Therefore, Pap smear screening of HIV-infected women should be a high priority. The second factor associated with receiving a Pap smear was higher income, which is consistent with previous reports on the general population in Taiwan.[31] For low-income HIV-infected women who are not likely receive a Pap smear, ensuring the recommended Pap smear screening requires additional rewards (e.g., coupons or bonuses) to increase the rate of women from low-income households that receive screening. The last factor associated with receiving a Pap smear was previous cervical dysplasia, which is also consistent with previous studies, [13, 27] and indicates that HIV-infected women usually had an HIV-related syndrome that would arouse the attention of health providers. Based on that, Pap smear screening should be recommended at their first HIV care visit and continued annually.

Limitations

Some limitations of this study merit attention. First, the study reports only those patients who received a Pap smear in outpatient settings. However, the study stands out for being able to draw on an extensive nationwide population-based database, leaving little room for selection and non-response bias. Second, the study was limited by the nature of a retrospective design, which relies on existing data sources. Certain clinical factors, such as CD4, viral load, socioeconomic status and social stigma might lead some patients to decline healthcare. The NHIRD lacks detailed clinical information and other lifestyle-related

potentially confounding factors in analysis that might compromise our findings.

Conclusion

During this 10-year study period, HIV-infected women in Taiwan were observed to have low Pap smear screening rates. Only 12.0% of the HIV-infected women received Pap smears within one year after being diagnosed with HIV. Our findings suggests that HIV care providers should ensure a Pap smear at the first visit to the HIV clinic and remind HIV-infected women to receive Pap screening annually, and be particularly alert to ensuring Pap smears for women of younger age, low income, and without previous cervical dysplasia.

Conflict of interest statement

None.

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276 Table 1. Associations between Selected Factors and Receipt of a Pap Smear, 2000 -2009

Variables	All subjects (N=1,500)	With Pap tests[a] (n=460)		Unadjusted OR (95% CI)	Adjusted OR (95% CI)
	No. (%)	No.	%[b]		
Age (yrs)					1.49 (1.32, 1.68)*[c]
18-29	576 (38.4)	67	11.6	Referent	
30-39	508 (33.9)	207	40.7	5.23 (3.83, 7.12)*	
40-49	237 (15.8)	113	47.7	6.92 (4.83, 9.93)*	
50 or over	179 (11.9)	73	40.8	5.23 (3.54, 7.74)*	
Drug dependence					
No	1218 (81.2)	386	31.7	Referent	Referent
Yes	282 (18.8)	74	26.2	0.77 (0.57, 1.03)	0.94 (0.69, 1.33)
Monthly income (NTD)					
≦17280	1098 (73.2)	278	25.3	Referent	Referent
17281-26400	264 (17.6)	109	41.3	2.07 (1.57, 2.75)*	1.74 (1.26, 2.40)*
26401-43899	91 (6.1)	44	48.4	2.76 (1.79, 4.26)*	2.21 (1.25, 3.91)*
≧43900	47 (3.1)	29	61.7	4.75 (2.60, 8.70)*	5.90 (2.78, 12.47)*
Urbanization status					
Rural	490 (32.7)	138	28.2	Referent	Referent
Urban	1010 (67.3)	322	31.9	1.19 (0.94, 1.51)	1.02 (0.77, 1.36)
Occupation					
Blue collar	1259 (83.9)	365	29.0	Referent	Referent
White collar	241 (16.1)	95	39.4	1.59 (1.20, 2.12)*	1.05 (0.69, 1.60)
ART use					
Never	745 (49.7)	236	31.7	Referent	Referent
Ever	755 (50.3)	224	29.7	0.91 (0.73, 1.13)	1.08 (0.83, 1.40)
Prenatal examination					
No	1267 (84.5)	406	32.0	Referent	Referent
Yes	233 (15.5)	54	23.2	0.64 (0.46, 0.89)	0.87 (0.59, 1.28)
HIV screening					
No	1497 (99.8)	458	30.6	Referent	Referent
Yes	3 (0.2)	2	66.7	4.54 (0.41, 50.16)	1.49 (0.04, 52.69)
Previous cervical dysplasia (ICD-9)					

No	1236 (82.4)	311	25.2	Referent	Referent
Yes	264 (17.6)	149	56.4	3.85 (2.93, 5.07)*	2.54 (1.85, 3.49)*
Cervical dysplasia (V762)	247 (16.5)	140	30.4		
Carcinoma in situ of cervix uteri (2331)	4 (0.3)	1	0.2		
Malignant neoplasm of cervix uteri (180)	13 (0.8)	8	1.7		
History of STD (ICD-9)					
No	1252 (83.5)	352	28.1	Referent	Referent
Yes	248 (16.5)	108	43.5	1.97 (1.49, 2.61)*	1.33 (0.96, 1.85)
Viral warts (0781)	70 (4.7)	26	5.7		
Syphilis (091-097)	60 (4.0)	32	7.0		
Venereal disease (099)	54 (3.6)	20	4.3		
Trichomoniasis (131)	51 (3.4)	24	5.2		
Others (Genital herpes, Clamydia, Gonorrhea, Pediculosis)	13 (0.8)	6	1.3		
History of OI (ICD-9)					
No	1087 (72.5)	300	27.6	Referent	Referent
Yes	413 (27.5)	160	38.7	1.66 (1.31, 2.11)*	1.12 (0.85, 1.50)
Candidiasis (112)	226 (15.1)	90	19.6		
Varicella-zoster virus infection (0539)	70 (4.7)	27	5.9		
Herpes simplex virus infection (054)	42 (2.8)	17	3.7		
Tuberculosis (010-018)	40 (2.7)	18	3.9		

Others (Bacterial pneumonia, Cryptococcal meningitis, Cryptosporidiosis, Isosporidiasis, MAC infection, Penicilliosis, PCP, Salmonellosis)	35 (2.2)	8	1.7

[a]Results from those who had received Pap smears.

[b] % may not equal 100% due to all subjects as the numerator.

[c] Per 10-year increase in age.

[*]Significant at $p<0.05$

OR, odds ratio; STD, sexually transmitted disease; OI, opportunistic Infection; MAC, mycobacterium avium complex; PCP, pneumocystis pneumonia.

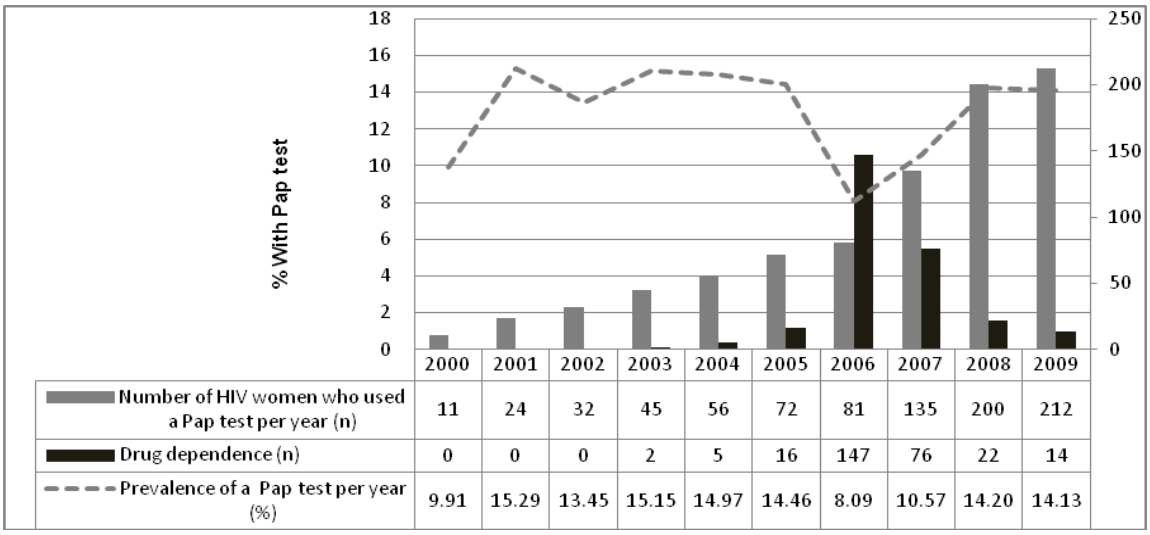

Figure 1. Prevalence of HIV-infected women who had received a Pap test during the past year and had a negative association with drug dependence, 2000-2009.

國科會補助計畫衍生研發成果推廣資料表

日期:2012/10/27

國科會補助計畫	計畫名稱: 女性愛滋感染者與非感染者於子宮頸抹片篩檢利用率及子宮頸癌發生率之比較（GM03）
	計畫主持人: 柯乃熒
	計畫編號: 100-2629-B-006-002- 學門領域: 性別主流科技計畫

無研發成果推廣資料

100 年度專題研究計畫研究成果彙整表

計畫主持人：柯乃熒	計畫編號：100-2629-B-006-002-
計畫名稱：女性愛滋感染者與非感染者於子宮頸抹片篩檢利用率及子宮頸癌發生率之比較（GM03）	

成果項目			量化			單位	備註（質化說明：如數個計畫共同成果、成果列為該期刊之封面故事...等）
			實際已達成數（被接受或已發表）	預期總達成數(含實際已達成數)	本計畫實際貢獻百分比		
國內	論文著作	期刊論文	1	1	100%	篇	90. Chen YC& Ko NY* (2011). Management for abnormal Pap smear among HIV-infected women. Journal of AIDS Care. 75, 27-42.
		研究報告/技術報告	0	0	100%		
		研討會論文	0	0	100%		
		專書	0	0	100%		
	專利	申請中件數	0	0	100%	件	
		已獲得件數	0	0	100%		
	技術移轉	件數	0	0	100%	件	
		權利金	0	0	100%	千元	
	參與計畫人力（本國籍）	碩士生	0	0	100%	人次	
		博士生	0	0	100%		
		博士後研究員	0	0	100%		
		專任助理	0	0	100%		
國外	論文著作	期刊論文	0	1	100%	篇	2. Chen YC, Liu HY, Li CY, Lee NY, Ko WC, Chou CY, & Ko NY* (2012). Low Pap smear screening rate among HIV-infected women in Taiwan, 2000-2009: A nationwide

							Environmental and Occupational Health 10/140；Medicine, General and Internal category, 18/151) in review
		研究報告/技術報告	0	0	100%		
		研討會論文	1	1	100%		12. Chen YC & Ko NY* (2012). Low utilization of cervical cancer screening among HIV-infected women in Taiwan: A nationwide population-based study. Poster presentation at the XIX International AIDS Conference (AIDS 2012) Washington D.C., 22-27 July 2012.
		專書	0	0	100%	章/本	
	專利	申請中件數	0	0	100%	件	
		已獲得件數	0	0	100%		
	技術移轉	件數	0	0	100%	件	
		權利金	0	0	100%	千元	
	參與計畫人力（外國籍）	碩士生	0	0	100%	人次	
		博士生	0	0	100%		
		博士後研究員	0	0	100%		
		專任助理	0	0	100%		
其他成果 (無法以量化表達之成果如辦理學術活動、獲得獎項、重要國際合作、研究成果國際影響力及其他協助產業技術發展之具體效益事項等，請以文字敘述填列。)		無					

成果項目	量化	名稱或內容性質簡述

科教處計畫加填項目	測驗工具(含質性與量性)	0	
	課程/模組	0	
	電腦及網路系統或工具	0	
	教材	0	
	舉辦之活動/競賽	0	
	研討會/工作坊	0	
	電子報、網站	0	
	計畫成果推廣之參與（閱聽）人數	0	

國科會補助專題研究計畫成果報告自評表

請就研究內容與原計畫相符程度、達成預期目標情況、研究成果之學術或應用價值（簡要敘述成果所代表之意義、價值、影響或進一步發展之可能性）、是否適合在學術期刊發表或申請專利、主要發現或其他有關價值等，作一綜合評估。

1. 請就研究內容與原計畫相符程度、達成預期目標情況作一綜合評估

■達成目標

□未達成目標（請說明，以 100 字為限）

□實驗失敗

□因故實驗中斷

□其他原因

說明：

2. 研究成果在學術期刊發表或申請專利等情形：

論文：□已發表 □未發表之文稿 ■撰寫中 □無

專利：□已獲得 □申請中 ■無

技轉：□已技轉 □洽談中 ■無

其他：(以 100 字為限)

3. 請依學術成就、技術創新、社會影響等方面，評估研究成果之學術或應用價值（簡要敘述成果所代表之意義、價值、影響或進一步發展之可能性）(以 500 字為限)

本實證研究結果可提供目前對於台灣女性感染者子抹篩檢次數建議的參考，並期未來作為政府修訂、推廣及擬訂愛滋感染婦女相關健康照護政策之參考依據。