THE POTENTIAL OF PROVIDER-INITIATED VOLUNTARY HIV COUNSELING AND TESTING AT HEALTH CARE SETTINGS IN THAILAND

Final Report

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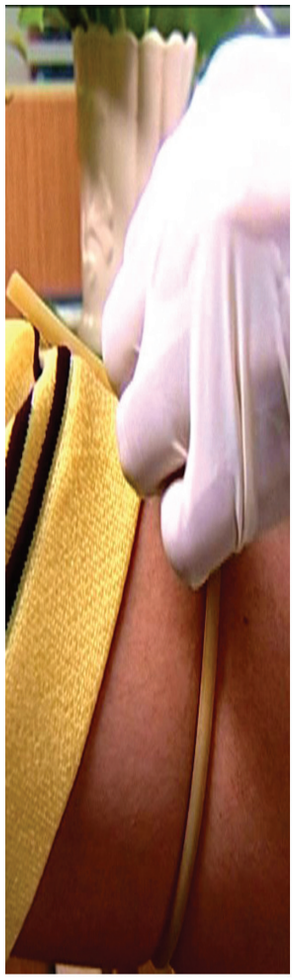

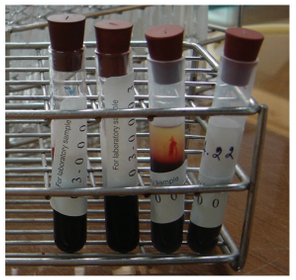

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HEALTH INTERVENTION AND TECHNOLOGY ASSESSMENT PROGRAM
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DEPARTMENT OF DISEASE CONTROL, MINISTRY OF PUBLIC HEALTH

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ABSTRACT

WHO and UNAIDS advocated healthcare providers to consider provider-initiated HIV counseling and testing for clients attending healthcare facilities. However, there is a lack of evidence, concerning the effectiveness of such interventions in Thailand and other settings with large outbreaks of the HIV epidemic, needed to support policy decisions. A cluster-randomization trial with pre-post test design was conducted to assess the effectiveness of provider-initiated voluntary HIV counseling and testing compared with the current practice in which HIV testing is provided upon the client's request. Sixteen district hospitals (clusters) with high- and low-HIV prevalence were randomly assigned to either receiving the new intervention or the current practice with a 1:1 allocation ratio. Patients aged between 13-64 years, receiving ambulatory care in the participating hospitals, were eligible. The main outcome measures were the acceptance rate of HIV testing and the HIV detection rate.

During the first 8-week baseline period, there was no significant difference between the control and experimental clusters on the acceptance rate and HIV detection. However, after the 8-week intervention period, the acceptance rate and HIV detection rate in the experimental clusters was significantly higher than those of the control clusters. The results from the generalised estimating equations and multilevel modeling also confirmed the findings. Economic appraisal alongside this study suggested that the intervention is very cost-effective under the Thai health care setting.

Classification codes: C93 (Field Experiments) and I18 (Government Policy; Regulation; Public Health)

Keywords: HIV/AIDS, HIV counseling and testing, provider-initiated HIV counseling and testing, cluster-randomised trial, Thailand

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TABLE OF CONTENTS

TABLE OF TABLES

TABLE OF FIGURES

INTRODUCTION

HIV/AIDS is a leading cause of deaths and socioeconomic devastation in many low- and middle-income countries. During the 25 years of the pandemic's known existence, the disease has claimed over 20 million lives around the world. By the end of 2007, approximately 33.2 million people were living with the virus. An estimated 2.5 million people were newly infected, and 2.1 million died from AIDS in 2007 (UNAIDS 2007). About two thirds of all people with HIV live in sub-Saharan Africa. Although effective interventions for the prevention of disease transmission are available and widely implemented, the number of people living with HIV/AIDS (PHA) has continued to rise. According to UNAIDS (2007), every day, more than 68,000 people become infected with HIV and more than 5,700 people die from AIDS, mostly because of inadequate access to HIV prevention and treatment services.

Strategies to control and mitigate the impact of HIV/AIDS comprise prevention, treatment, care and support, all of which should be introduced as a comprehensive, continuum package (WHO/UNAIDS 2000). These include voluntary counseling and testing (VCT) for HIV infection, home and community based care, diagnosis and treatment of HIV-related diseases, antiretroviral treatment (ART), prophylaxis of HIV-related diseases, diagnosis and treatment of sexually-transmitted infections, interventions to reduce mother-to-child transmission, the promotion of safe sex and condom use, and the avoidance of stigma and discriminating attitudes. VCT is a critical entry point to all essential services for PHA. The primary goal of this health-sector intervention is to inform people about their HIV status, which then contributes to the prevention of further transmission of the disease and early uptake of appropriate services such as medical care, family planning, emotional care and social support among the positive cases including their family (UNAIDS 2001). However, VCT is not adequately provided in HIV-prevalent countries, and surveys in these settings show that the knowledge of HIV status is limited (WHO, UNAIDS et al. 2007). The poor access to VCT services is associated with people's socioeconomic status including wealth, education and residential areas.

As the limited coverage for VCT may hamper the expansion of HIV prevention and access to treatment and care in a timely manner, WHO and UNAIDS recognize the need for scaling up this intervention. In May 2007, the two agencies recommended an opt-out approach to provider-initiated HIV testing and counseling in health facilities (WHO/UNAIDS 2007). With regard to introducing this approach in generalized epidemics, an HIV test is recommended for all adults, adolescents and children visiting healthcare settings of all types, irrespective of their clinical symptoms or other reasons for which they seek care. However, individuals have to be ensured that they are not being forced to take the test, i.e. they have the right to decline if they do not want to obtain the service. On the provider side, such an approach

should be accompanied by a package of appropriate treatment, care and support services, while the test results must be kept confidential. Post-test counseling has to be performed in order to maximize the positive benefits and minimize the potential negative consequences for patients. Following this guidance, the decision to implement provider-initiated VCT should be informed by the assessment of the situation in particular countries, for example HIV epidemiology, health delivery infrastructure, availability of workforces and financial resources, and the existing legal frameworks for protection against HIV-related discrimination.

The provider-initiated VCT approach was suggested in the USA in 2006 – one year before the WHO/UNAIDS' guidance was issued. According to the Centres for Disease Control and Prevention, HIV screening should be offered to all patients aged between 13 and 64 years who visit healthcare institutions, at any levels, in both the public and private sectors (Branson, Handsfield et al. 2006). The test will be performed unless the patient declines. The benefits of this service provision include that when HIV is diagnosed early, appropriate and timely interventions, especially highly active antiretroviral therapy, can lead to improved health outcomes, including slower clinical progression and reduced mortality. Furthermore, evidence suggests that PHA reduced high-risk behaviour substantially when they became aware of their infection.

The literature suggests that provider-initiated VCT was first adopted as a national policy, in Botswana in 2003, after a pilot study indicating that this service would be well-accepted among pregnant women (Steen, Seipone et al. 2007). The major goals of the 'routine HIV testing, RHT' were to make people aware of their HIV status and subsequently increase the uptake of treatments such as ART and prevention of vertical HIV transmission at the most appropriate stage, and also to reduce the stigma associated with HIV/AIDS. Meanwhile, no patient would be tested against his/her wish. This means that all of the patients are well-informed that they have a right to refuse. The information on this initiative was disseminated by the Health Ministry through public media networks and group education. According to Steen et al (2007), during the first two and a half years of implementation, the RHT was widely accepted by the population, without reported adverse implications. In addition, the early detection of HIV cases and subsequent early recruitment of PHA to the ART programme as a benefit of this VCT approach was reflected in this study. In a similar vein, Weiser et al (2006) maintains that the RHT policy in Botswana was well supported by the public, as people had good attitudes towards the routine testing.

In some areas, this approach is introduced for particular groups of people. For instance, VCT for HIV has been offered to pregnant women at antenatal clinics in urban Zimbabwe since 2005, with the aim of preventing mother-to-child HIV transmission. An assessment by Chanisarewa et al (2007) suggests that

routine offers of the service were feasible and acceptable. This in turn led to a significant increase in HIV testing rates. Furthermore, the exit survey indicates that most of the clients were well-informed by counsellors, and that they had been adequately prepared for the results, and were also satisfied with the service quality.

The low rate of knowing HIV status, late diagnosis of the infection and the need for strengthened HIV testing are not critical only in developing countries but these issues should also be taken into account in the developed world (The Lancet Editorial 2006). In France, although 50% of the population has had at least one HIV test, it is believed that routine testing should be expanded, since many people are diagnosed when the infection is in the advanced stage (Delpierre, Cuzin et al. 2007). Experts in the UK have called for a similar policy: the wide-spread use of HIV testing in a variety of clinical settings. Hamill et al (2007) maintain that an opt-out approach to testing, as a standard component of medical care, and which makes no judgment about individuals' risk, will be an effective strategy to increase knowledge of HIV infection status.

Meanwhile, scholars have expressed different opinions. Among others, Asante (2007) points out that although routine HIV testing may contribute significantly to HIV/AIDS prevention and treatment, this approach is not feasible for sub-Saharan Africa. This is because Africans, especially the poor, do not seek care at health delivery facilities unless they are severely sick or there is a specific need. The concepts of health promotion and disease prevention are largely foreign to the general public. The author also suggests that AIDS-related stigma and discrimination remain severe problems in the region, and that a routine HIV testing approach cannot normalise this intervention or help it to become widely accepted. In fact, such a policy may generate a paradoxical effect: driving people away from health facilities.

Concerns about negative consequences, including human rights violations and the ineffectiveness of the provider-initiated VCT are at the center of discussion, even in Western societies (Csete and Elliott 2006). These include, for instance, the cautions associated with existing state legal frameworks on informed consent, counseling and HIV-testing policies in the USA (Lifson and Rybicki 2007). Moreover, it has been suggested that high-risk populations, such as the uninsured, the poor and drug addicts, usually have limited access to health services; thus, the VCT service should be offered through community-based and other outreach programs. Another caveat is that as this initiative, which targets low-literacy and under-privileged people, is integrated in busy clinical settings, it may be difficult to provide comprehensive information to patients and make them realize that they have a right to decline the test offered by health providers. As Csete and Elliott (2006) put it, without three underpinning principles of VCT, namely confidentiality, counseling and consent, a routine testing policy would violate human rights. They went

on to stress that alongside the increase in the number of people tested, the emphasis should be put on the potential negative effects of this approach including depression, suicide, abandonment, and other forms of violence. In addition, the authors argue that there is no evidence suggesting reduced stigma and discrimination as a consequence of routine testing.

Apart from the undesirable effects and other outcomes of a routine, provider-initiated HIV testing policy, economic consequences, in terms of program efficiency, is among the concerns. According to Hamill et al (2007), cost-effectiveness of opt-out testing depends on several factors such as HIV prevalence among the population to be screened, and cost-effectiveness analysis is required for any decision to be made in relation to the expansion to HIV testing in the UK. A study in the USA suggests that when rapid tests were carried out in the areas where HIV prevalence of 0.1% and annual incidence of 0.12%, the incremental cost-effectiveness ratios would be 30,800 USD per QALY gained (one-time screening), 32,300 USD (screening every 5 years) and 55,500 USD per QALY gained (screening every 3 years) (Paltiel, Walensky et al. 2006). This study confirms the preventive benefit of HIV screening for uninfected persons exceeds the medical benefits to infected cases, and also argues that routine, rapid HIV testing for all adults in the USA should not be implemented in those areas where the prevalence of undiagnosed HIV infection is above 0.2%. Meanwhile, some argue that economic evaluation models for infectious diseases, including HIV/AIDS, often underestimate the benefits to society of particular interventions. This indicates the need for methodological improvement in the assessment of the cost-effectiveness of provider-initiated HIV testing scheme (Branson 2006).

In Thailand, the HIV/AIDS epidemic began in the late 1980s. The disease was spread from limited high-risk groups, such as male homosexuals, intravenous drug users and commercial sex workers, to the general population through heterosexual relationships (Thanprasertsuk, Lertpiriyasuwat et al. 2004). The number of PHA peaked in the mid 1990s and has continually declined thereafter owing to effective prevention programs, especially 100% condom use with intensive education and information campaigns (UNDP-Thailand 2004). Despite this, an estimated one million Thai people became infected with HIV, and the accumulated AIDS deaths amounted to 600,000 in 2007 (Thai Working Group on HIV/AIDS Projections 2001). Recent surveys of sexual behavior and risk of HIV infection indicate a lack of knowledge about HIV prevention and an increasing trend of unsafe-sex practices among secondary-school and vocational students.

To counter the epidemic and its consequences, Thailand has adopted comprehensive, continuum of care for HIV/AIDS as its principal policy. ART and prophylaxis, along with treatment for opportunistic infections can be accessed through publicly-financed health benefit schemes. The VCT service was first

provided in Thailand in 1991, and then expanded to health care settings, mostly in the public sector, around the country. Counselling and HIV testing is available in 1,000 hospitals and clinics. The service has been delivered free-of-charge under the universal health coverage plan if prescribed by a doctor, while those seeking the service by themselves had to pay out-of-pocket. During the period from October 2007 to March 2008, the number of VCT clients under the National AIDS Program accounted for 80,118 among which 11.6% were found positive. A survey in 2006 suggested that 30% of the general population had at some stage been tested for HIV, and that if publicly-financed VCT was available, 29% of these low-risk respondents would take the test (IHPP 2006). A provider-initiated approach has been introduced in all pregnant women at ANC and patients with tuberculosis. In 2006, the coverage for hospital-based VCT among pregnant women had reportedly mounted to 99.6% while the infection rate stood at 0.85% (National AIDS Prevention and Alleviation Committee 2008).

Constraints due to the shortage of human resources, inadequate training of staff and the lack of referral for psychological support were identified as major impediments in VCT provision in Thailand (WHO SEARO 2005). Most of the practitioners counted VCT as a diagnostic test rather than an opportunity to promote prevention. According to external reviewers of the national HIV program in 2005, VCT should be scaled up to cover vulnerable populations including IDUs, MSM, mobile populations, children and adolescents. During 2007, the Thai government actively campaigned to create knowledge and raise awareness about VCT in all groups of people, especially youth and people in reproductive age. As the National AIDS Prevention and Alleviation Committee (2008) suggested, the quality of VCT should be improved.

It is expected that provider-initiated VCT will increase the rates of HIV detection, which subsequently contributes to the success of the disease control effort. However, the move to make HIV screening routinely available in middle-income and low-HIV prevalence settings like Thailand requires a thorough understanding of the feasibility and efficiency of the policy, and its ethical and human rights consequences.

MDG being addressed and importance of the intervention and link to MDGs

This study addresses MDG number 6: combat HIV/AIDS, malaria and other diseases. VCT is an important component of the comprehensive, continuum care for PHA. The service is expected to facilitate earlier uptake of appropriate treatment, prevention, care and support among infected people. Awareness of HIV infection status can help to reduce unsafe-sex and other risk behavior in afflicted people. A provider-initiated, opt-out approach is an effort to expand VCT to a wider population.

Objectives of the study

This study aims to assess the value, feasibility and acceptability of providing provider-initiated HIV counselling, testing and referral in district hospitals in Thailand. The specific objectives include the following:

(1) to assess the efficacy of provider-initiated VCT in terms of the acceptance rates of HIV testing and the numbers of new HIV infections detected;
(2) to explore the factors, at both cluster and individual levels, associated with the acceptance rates and the detection of HIV infections;
(3) to examine the costs and consequences of provider-initiated VCT, in comparison to current practice where VCT is performed only upon a request by patients or physicians;
(4) to develop a decision-based analytic model for the assessment of the clinical and economic impact of provider-initiated VCT, compared to current practice;
(5) to investigate the perceptions of key stakeholders concerning the introduction of provider-initiated VCT in district hospitals.

INTERVENTION DESCRIPTIONS

This study aims to assess the efficacy of provider-initiated VCT compared to the VCT which is the current practice in Thailand. **Table I** shows key features of the provider-initiated VCT and the current practice. A brief explanation of the intervention under investigation is that the hospital reception is a starting point where invitation cards are presented to each of the patients aged between 13-64 years visiting the out patient department (OPD). The invitation card reveals that “the hospital is now conducting a study that offers free counseling and HIV testing and this card can be used as a coupon for getting a free HIV test. Detailed information can be found from a presentation on the television or from staff presented at the OPD”.

Table I A comparison of key characteristics between the client-initiated counseling and testing, and provider-initiated counseling and testing

	The current practice	Intervention of interest
Name	Voluntary counseling and HIV testing (VCT)	Provider-initiated counseling and testing (PICT)
Features	- It is client-initiated counseling and testing; the clients need to ask health care provider if they want to take the test. - Pre- and post-test counseling are often offered individually (face-to-face) in a private counseling room. - Most of the cases without signs and symptoms suggestive of underlying HIV infection need to pay themselves for the cost of the test which ranges between $5 and $10.	- It is designed to integrate routine offering of HIV counselling and testing into OPD. - It is an 'opt-in' service meaning that each client must specifically consent to a HIV test. - It is offered as a free package including VDO pretest counseling to all individuals visited OPD plus anonymous HIV test and individual post-test counseling.
Advantages	- Clients seeking the test are likely at risk, so the test is more likely to be cost-effective compared to the provider-initiated test. - Clients seeking the test may be most ready for behavior change, so it is the best opportunity for HIV prevention.	- Because it is offered to all patients, it is likely to increases access to and acceptance of HIV testing among populations. - It is more likely to detect unrecognised or unsuspected HIV infection, so it may help to prevent further transmission of HIV in the community.
Disadvantages	- Not all people at risk of HIV infection willing to take the test - Time and resources consumed for both clients and health care providers	- It is expected that HIV prevalence among clients who take the test is lower than the current practice, so it may not be cost-effective. - A group/brief pretest-counseling may be less effective in terms of providing necessary information required for pretest of HIV infection than individual counseling.

According to this protocol, a 7-minute TV program was presented at the OPD for patients waiting to see the doctor. This TV program is specially designed by researchers to represent 'pre-test HIV counselling' so that it includes important information about the following issues.

- Basic information about 'HIV/AIDS' and its routes of transmission
- The clinical and prevention benefits of testing and the potential risks, such as discrimination, abandonment or violence
- Interpretation of the test results including information about the window period
- The services available in the case of an HIV-positive test result, including antiretroviral treatment
- The fact that the test result will be treated confidentially and will not be shared with anyone other than heath care providers directly involved in providing services to the patient
- The fact that the patient has the right to decline the test without affecting the patient's access to services that do not depend upon knowledge of HIV status
- An opportunity to ask the health care provider questions

The TV program also reveals information about the study and invites patients to take the test voluntarily. The TV program is also available with an English subtitle at www.hitap.net. In addition, there was one nurse in each hospital, who was specially trained for the project, helping patients to clarify issues related to HIV/AIDS, HIV testing and the study project.

After seeing the doctor, those patients who wished to get tested for HIV could present the invitation card to the officer at the laboratory room in order to get a free HIV test. At this point, an information sheet that provides details information about the study project and the inform consent will be given to each patient. If the consent was obtained, the patient was then asked to complete a self-administrative questionnaire that contains individual information, i.e. age, sex, education, occupation, and HIV risk behaviours. Please note that the questionnaire does not include any identification that could be used to identify the patient. After taking a blood sample, the patient was asked to return for individual post-test counseling within 2 weeks. The patients who received a positive test result were then referred to HIV clinics, where routine investigation and prophylaxis and treatment medications were provided for free to all PHA in Thailand.

According to the recommendations provided by UNAIDS and WHO (UNAIDS & WHO 2007), monitoring and evaluation are essential components of the programme. The effectiveness and impact of provider-initiated VCT should be evaluated in terms of:

- increasing access to HIV testing, counseling, and test results;

- increasing access to and uptake of HIV-related prevention, treatment, care and support services;
- decreased morbidity and mortality;
- increased HIV awareness and treatment literacy;
- social impact on rates of disclosure, stigma and discrimination, and adverse outcomes.

However, some of the proposed outcome measures are long-term effects e.g. morbidity and mortality, so they are difficult to assess within a limited time. A primary aim of this study is, therefore, to assess the efficacy of provider-initiated VCT in Thailand, using both process and outcome indicators i.e. acceptance rates of HIV testing (the number of patients taking the test divided by those being offered) and number of new HIV infections detected.

EMPIRICAL STRATEGY

Selection of treatment and control groups

The intervention to be evaluated was conceived as a whole community approach by providing free counseling and HIV testing for the catchment population who visited the OPD in the district hospital. Thus, a cluster-randomisation trial was the design of choice from the outset. In addition, only a small number of clusters are possible for this study, and allocation of the intervention to one of a matched pair is, therefore, appropriate to ensure that there were good matches for the primary outcomes at the baseline and on variables strongly associated with their change.

In this study, 16 community or district hospitals from four regions throughout the country with a mixture of high- and low-HIV prevalence were randomly assigned either to the experimental group or control group with a 1:1 allocation ratio. The participants consisted of patients attending outpatient departments at the participating community hospitals, who met the eligibility criteria, as specified in **table II**.

Table II Eligibility criteria at the patients' level

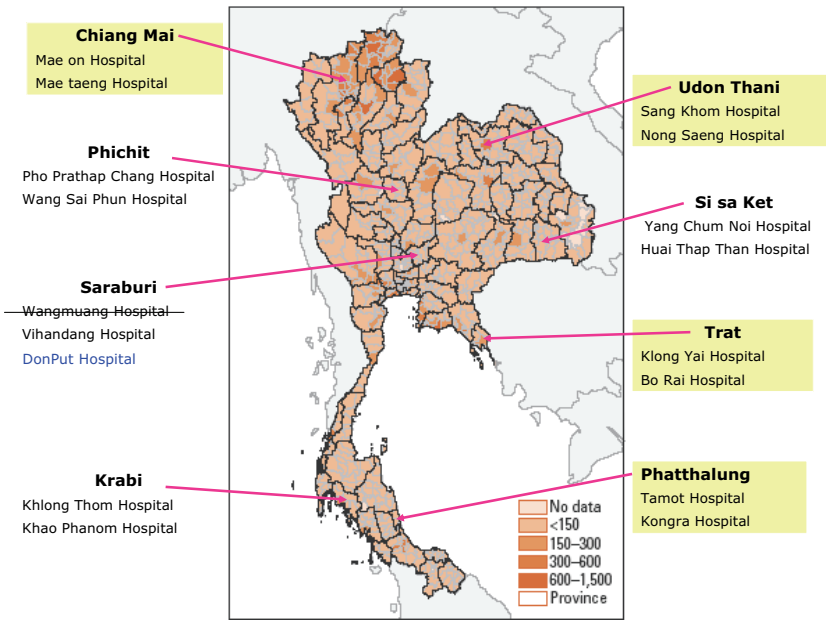
Inclusion criteria	Exclusion criteria
• Patient receiving care at out-patient department in the participating community hospitals during official working days/hours • Ages between 13 and 64 years old	• Patient receiving care at the special outpatient clinic • Patients with cognitive disability • Patients who have previous recorded HIV positive result • Pregnant women • Patients who did not live in the service area of the participated hospitals

The procedure for the selection and randomisation of the community hospitals was specified as follows;

1) Community hospitals in Thailand were stratified into eight stratums, based on prevalence of HIV infection according to the national database of HIV infection among pregnant women in 2005 (low if HIV prevalence <0.1% and high if HIV prevalence ≥ 2%) and geographical locations, i.e. northern, northeastern, southern, and central regions. Due to the current violent situation in the four southernmost provinces, namely Yala, Pattanee, Narathiwas, and Satoon, they were initially excluded from the study.
2) For each stratum, we randomly selected one hospital.
3) Another hospital was selected from a previously matched hospital based on the location (the same province), hospital size and local economy. If more than one matched hospital was identified, a hospital was randomly selected from the candidates. Any refusals to participate were recorded and the random selection was performed until the samples were satisfied.
4) The randomisation within each matched-pair was carried out by the research team after the first eight weeks of the pre-intervention period (see details in the section below). A random allocation sequence was generated, using simple randomisation method with a 1:1 allocation ratio. Based on the nature of the intervention, blinding was not performed.

Figure 1 shows 16 clusters in four regions selected from the randomisation process. It was noted that only one hospital, namely Wangmuang hospital, refused to take part in the study. The research team randomly selected Donput hospital to be the replacement.

Figure 1 Map of Thailand showing locations of 16 sample hospitals



Note: Sample hospitals situated in high HIV prevalence areas were highlighted in yellow

Procedures

The study was carried out between August 6th and November 23rd, 2007. Over the 16 weeks of the study period, the first eight weeks was assigned as a 'pre-intervention period' when no intervention was introduced. All 16 hospitals collected information on the numbers of patients undergoing HIV counselling and testing and the number of new HIV infections detected. Well-trained local research coordinators also randomly selected patients (one in every ten), who visited OPD clinics in all 16 hospitals, to complete the self-administrative individual questionnaire. The same questionnaire was also used by all patients that undertook the HIV test.

For the last eight weeks, which was an 'intervention period', an intervention was introduced to the hospitals assigned to the experimental group. Similarly, all patients who undertook the HIV test in hospitals, in both the experimental and the control groups, were requested to complete the self-

administrative individual questionnaire. One out of every ten patients not taking the test was also selected randomly to complete the same questionnaire.

The study was reviewed and approved by the Institutional Review Board of the Faculty of Medicine, Chulalongkorn University (No.195/50).

Sample size

The study samples were calculated to ensure precision estimates for measures of effect for a primary outcome--the acceptance rate of the HIV test. To allow for a pair-matched cluster randomisation design, the number of clusters required was determined using the formula developed by Hayes RJ & Bennett S (Hayes and Bennett 1999) as follows.

$$C = 2 + \left(Z_{\alpha/2} + Z_{\beta}\right)^2 \left[\frac{\pi_0\left(1-\pi_0\right)}{n} + \frac{\pi_1\left(1-\pi_1\right)}{n} + K^2\left(\pi_0^2 + \pi_1^2\right)\right] / \left(\pi_0 - \pi_1\right)^2$$

where

$$K = \hat{\sigma}_c^2 / p \text{ and } \hat{\sigma}_c^2 = S^2 - p(1-p)Av(1/n_j)$$

when

α	=	level of significance
1-β	=	power of the test
$Z_{\alpha/2}$	=	standard normal distribution value corresponding to upper tail probabilities of α/2
Z_{β}	=	standard normal distribution value corresponding to upper tail probabilities of β
n	=	number of individual sampled in each cluster
C	=	the number of clusters required
π_0	=	the true (population) proportion in the absence of the intervention
π_1	=	the true (population) proportion in the presence of the intervention
K	=	the coefficient of variation of true proportions between clusters within each group
S^2	=	the empirical variance of cluster proportion
P	=	the overall proportion computed from all clusters combined
n_j	=	the sample size within each cluster

A $v(1/n_j)$ = average of $(1/n_j)$

Before the study undertaken, we estimated an increase in the acceptance rate of HIV testing from 1% (π_0) to 30% in the experimental clusters (π_1) and the variance of cluster proportion, S^2, equals to 0.000144 (International Health Policy Program 2006). Therefore, the sample size calculation based on a two-sided 5% significance level and 80% power. For a two-sided test with α= 0.05 the critical value is 1.96 for $Z_{\alpha/2}$ and 0.84 for Z_{β}. This leads to 13 pair-matched clusters required (average 1,300 eligible OPD visits per biweekly per cluster; n_j).

Due to the budget constraints, only 8 pair-matched clusters were available. Fortunately, a post-hoc sample size calculation was performed just after the completed data collection indicated that with the increased acceptance rate from 0.39% (π_0) to 5% (π_1) (the variance of cluster proportion, S^2, equals to 0.000004) only 3 pair-matched clusters were required to detect a significant change between the clusters and the study periods of the experimental clusters.

Outcomes being evaluated and the proposed methods used for statistical measures

The primary outcome of the study is the HIV test acceptance rate measured every 2 weeks (bi-weekly). A justification for measuring the outcome variable on several different occasions is that the effect of the intervention on the outcome is unlikely to be consistent over time. For example, the HIV test acceptance rate may lessen later on because many clients will have already taken the test.

The effect of the intervention—provider-initiated VCT, on the acceptance rate in this study can be measured at the cluster level using the Generalised Estimating Equation (GEE) (Zeger and Liang 1986). The GEE is often used to model correlated data from longitudinal repeated measures studies or clustered studies. It allows for the specification of a within-group correlation structure for the panels, which are also known as population-averaged panel-data models. In this case, the GEE can provide the effect of the intervention on the average acceptance rate taking into account the variations of the various cluster variables, e.g. location, HIV prevalence, and the study period.

Although this study is a pair-matched cluster randomised design, it has been suggested by Martin et al. (Martin, Diehr et al. 1993) and Diehr et al. (Diehr, Martin et al. 1995) that a small number of pairs in matching design (10 or less) would lead to the loss of a degree of freedom. The unpaired analysis of data from such a matched design may be more powerful than a paired analysis. Hence, this study adopted unpaired analysis.

In the GEE method, the marginal distribution of the response variable is assumed to follow a generalized linear model (GLM) in which the variance is the function of the mean (Zeger and Liang 1986). The model parameters are estimated by the method of quasi-likelihood estimation. It relaxes the assumption on the exact distribution of the response variable, whereas normal distribution is required in the standard maximum likelihood method. Therefore, GEE is useful for modelling the effects of covariates on continuous or discrete outcome variables looking at the differences in population-averages. The relationship between the marginal mean of the response, $\mathrm{E}(Y_{ij}) = \mu_{ij}$, and explanatory variables, x_{ij}, is described by a known link function, g, in which $g(\mu_{ij}) = x'_{ij}\beta$. For example, link functions for the normal, binary, and Poisson response variables are defined as:

Identity link: $g(\mu_{ij}) = \mu_{ij}$ for normal measured responses

Logit link: $g(\mu_{ij}) = log(\frac{\mu_{ij}}{1-\mu_{ij}})$ for binary responses

Log link: $g(\mu_{ij}) = log(\mu_{ij})$ for Poisson counts

The correlation between repeated observations on each hospital is accounted for through the use of marginal models. In GEE, there are several structures available for working with correlation such as independent, unstructured, exchangeable, or autoregressive (Horton and Lipsitz 1999). The GEE method is not sensitive to the type of the correlation structure chosen. Therefore, the method is robust against misspecification of the working correlation matrix.

We constructed the GEE model for the number of HIV testing at each biweekly in each cluster (hospital). The response outcomes are count data and its distribution is assumed to be a Poisson. This model was constructed to take into account the likelihood that cluster level factors correlated within cluster members. The model can be specified as follows:

$$\log(\mu_{ijt}) = \log(n_{ijt}) + \beta_0 + \beta_1(study\ group_{ijt}) + \beta_2(prevalence_{ij}) + \beta_3(region_{ij}) + \beta_4(biweekly_t) + \beta_5(study\ group_{ijt} \times prevalence_{ij}) + \beta_6(study\ group_{ijt} \times region_{ij})$$

The offset, $\log(n_{ijt})$, is included because it represents "the population at risk" in the (*ij)th* cluster (hospital) at biweekly *t*.

or

$$\log(\mu_{ijt} / n_{ijt}) = \beta_0 + \beta_1(study\ group_{ijt}) + \beta_2(prevalence_{ij}) + \beta_3(region_{ij}) + \beta_4(biweekly_t) + \beta_5(study\ group_{ijt} \times prevalence_{ij}) + \beta_6(study\ group_{ijt} \times region_{ij})$$

where i = 1, 2, …, 8 paired - clusters, j = 1, 2 (1= control hospital, 2 = experimental hospital), and t = 1, 2, …, 8 bi-weekly;

$\mu_{ijt} = E(Y_{ijt})$ is defined as the number of HIV testing at the (*ij)th* cluster (hospital) at biweekly t. The acceptance rate of HIV test is given by μ_{ijt} / n_{ijt}, where n_{ijt} is the number of eligible patients for the (*ij)th* cluster (hospital) at biweekly t.

study groups were assigned for the (*ij)th* cluster (hospital) at biweekly t. There are four different groups as follows; 1) control group at pre-intervention period of biweekly 1-4 (reference), 2) control group at intervention period of biweekly 5-8, 3) experimental group at pre-intervention period of biweekly 1-4, and 4) experimental group at intervention period of biweekly 5-8.

prevalence was defined as a dummy variable for high prevalence and low prevalence (see detail in page 12). The high prevalence was treated as a reference.

regions are represented for four parts of Thailand: 1) Central (reference), 2) Northern, 3) North-eastern, and 4) Southern.

β_0 is the log of expected acceptance rate at baseline (all covariates = 0).

β_1, β_2, and β_3 are the regression coefficients of the main effects, i.e., each β describes for the change in the log expected acceptance rate when its corresponding covariate has a specific value after being adjusted other relevant covariates in the model (when compared to the reference).

β_4 represents for the change in the log expected rate per unit increase in biweekly after being adjusted other covariates.

β_5 is the regression coefficient of the interaction effect of study group × prevalence. It represents the change in the log expected rate of each study group that depends on the HIV prevalence.

β_6 is the regression coefficient of the interaction effect of study group × region. It represents the change in the log expected rate of each study group that depends on the region.

The secondary outcome is the detection rate of new HIV infections (new HIV infections detected divided by the number of eligible patients) which is measured as aggregate data within each cluster for each bi-weekly result. As a result, it is proposed that the GEE be used to assess the intervention effect concerning the differences in the cluster level factors, namely location, HIV prevalence, and the study period.

$$\log(m_{ijt}) = \log(n_{ijt}) + \beta_0 + \beta_1(study\ group_{ijt}) + \beta_2(prevalence_{ij}) + \beta_3(region_{ij}) + \beta_4(biweekly_t) + \beta_5(study\ group_{ijt} \times prevalence_{ij})$$

or

$$\log(m_{ijt} / n_{ijt}) = \beta_0 + \beta_1(study\ group_{ijt}) + \beta_2(prevalence_{ij}) + \beta_3(region_{ij}) + \beta_4(biweekly_t) + \beta_5(study\ group_{ijt} \times prevalence_{ij})$$

where i = 1, 2, …, 8 paired – clusters, j = 1, 2 (1= control hospital, 2 = experimental hospital), and t = 1, 2, …,8 bi-weekly;

$m_{ijt} = E(Y_{ijt})$ is defined as the number of new HIV infections detected in the (*ij)th* cluster (hospital) at biweekly *t*. The HIV detection rate is given by μ_{ijt} / n_{ijt}, where n_{ijt} is the number of eligible samples for the (*ij)th* cluster (hospital) at biweekly *t*.

β_0 is the log of detection rate of HIV infections when all covariates = 0.

β_1, β_2, β_3 and β_4 are the regression coefficients, i.e., each β represents the change in the log expected rate when its corresponding covariate has a specific value after being adjusted for other covariates in the model.

β_5 is the regression coefficient of an interaction effect. It represents the change in the log expected rate of each study group that depends on the HIV prevalence.

In addition, because this study collected individual level information from both those exposed to and those not exposed to the intervention, it is possible that the evaluation estimates the effect of the intervention on the individual acceptances of the HIV test (willingness to take the HIV test by each individual) concerning both cluster and individual factors, e.g. sex, age, education, occupation, HIV risk behaviours. This can be done using multilevel modeling (Leyland and Groenewegen 2003). In this study, we have two levels of clustered data where patients are nested within hospital units. A logistic regression model that incorporates cluster and hospital specific random effects is considered to fit the data by assuming that the random effects are distributed randomly as normal distribution. The model formulation is denoted as:

$$\log\left(\frac{p_{ijr}}{1-p_{ijr}}\right) = (\beta_{0(ij)} + \beta_1 T_{(ij)} + \sum_{l=1}^{16} \beta_{1l} x1\ell_{(ijr)}) + (\sum_{m=1}^{3} \gamma_{2m} x2m_{(ij)}) + (u_{0(ij)} + e_{ijr})$$

where $r = 1, 2, \ldots, n_{ij}$; $\sum_{i,j} n_{ij} = 7{,}665$ patients;

Please note that we used only 'no intervention' group and 'intervention' group. Because an analysis of GEE shows no significant difference between 'experimental cluster/pre-intervention period', 'control cluster/pre-intervention period' and 'control cluster/intervention period', these three groups were named as 'no intervention' group. Also, 'experimental cluster/intervention period' was renamed as 'intervention group'.

i = 1, 2, …, 8 paired-match cluster

j = 1, 2 (1 = control hospital, 2 = experimental hospital)

l = 1, 2, …, 16 (covariates id at level 1)

m = 1, 2, 3 (covariate id at level 2)

p_{ijr} is the probability of undertaking HIV test for the *rth* subject in the *(ij)th* cluster , i.e p_{ijr} = P[y = 1|x].

$\beta_{0(ij)}$ is the fixed quantity applying to all the subjects in the study.

$u_{0(ij)}$ is the random quantity applying to all subjects in the *(ij)th* cluster (level- 2 error), and $\mu_{0(ij)} \sim N(0, \sigma^2_{u0})$.

e_{ijr} is another random quantity applying to the *rth* subject in the *(ij)th* cluster (level-1 error), and $e_{ijr} \sim N(0, \sigma^2_e)$.

$x1\ell_{ijr}$ are the predictors at subject level (level 1).

$x2m_{(ij)}$ are the predictors at hospital level (level 2), including intervention, prevalence, and region.

$T_{(ij)}$ is the intervention status for the *(ij)th* cluster.

$\beta_1, \beta_{1l},$ and γ_{2m} are the regression coefficients, i.e., each coefficient is the change in log odds (in acceptance HIV test) when its corresponding covariate has a specific value after being adjusted for other covariates in the model.

$u_{0(ij)}$ and e_{ijr} are assumed to be uncorrelated.

The proportion for the *(ij)th* cluster (random intercept) is now given by $\beta_{0(ij)} + u_{0(ij)}$

σ^2_{u0}: represents the variation between clusters, and σ^2_e represents the variation among subjects within clusters.

The estimate of the ICC (intra-cluster correlation) or $\hat{\rho} = \dfrac{\hat{\sigma}^2_{u0}}{\hat{\sigma}^2_{u0} + \hat{\sigma}^2_e}$

In this study, both data from different hospitals and data from different subjects under each cluster are independent. The heterogeneity outcomes for both cluster level (hospitals) and within-cluster (subject measurements) level were accounted for by assuming a simple (variance component: VC) covariance structure for model fitting.

Covariance Structure for Variance Component (VC) type is denoted as

$$\begin{bmatrix} \sigma_A^2 & 0 & 0 & 0 \\ 0 & \sigma_B^2 & 0 & 0 \\ 0 & 0 & \sigma_C^2 & 0 \\ 0 & 0 & 0 & \sigma_D^2 \end{bmatrix}$$

Variations among clusters are estimated 0.6473 ($\hat{\sigma}_{u0}^2$).

Variations among subjects under each cluster are estimated 0.9283 (σ_e^2).

Intra-cluster correlation (ICC) = $\hat{\rho} = \frac{\hat{\sigma}_{u0}^2}{\hat{\sigma}_{u0}^2 + \hat{\sigma}_e^2} = \frac{0.6473}{0.6473 + 0.9283} = 0.4108$

Because the cross-contamination of the experimental and control clusters can lead to an underestimate of the overall effect of the intervention, all analyses undertaken in this study were based on "the intention to treat" basis. This means that the analyses included only individual residents within the clusters at the baseline. Those individuals who had begun the trial as residents of one cluster and then moved or visited hospitals within another cluster were, therefore, excluded from the analyses.

For the analysis of quasi-experiment approach we assumed that there was no the control clusters and, thus, the analyses were mainly based on the pre- and post-test design. For example, the analysis of the primary outcome on acceptance rate using GEE can be specified as follows:

$$\log(\mu_{it} / n_{it}) = \beta_0 + \beta_1(study\ period_t) + \beta_2(prevalence_i) + \beta_3(region_i) + \beta_4(biweekly_t) + \beta_5(study\ period_t \times prevalence_i)$$

where i = 1, 2, …, 8 clusters (hospitals); t = 1, 2, …, 8 bi-weekly.

Study period at biweekly j (pre-intervention period is between biweekly 1-4, intervention period is between biweekly 5-8)

$\mu_{it} = E(Y_{it})$ is defined as the number of HIV testing in the *ith* cluster (hospital) at biweekly *t*. The acceptance rate of HIV test is given by μ_{it} / n_{it}, where n_{it} is the number of eligible patients for the *ith* hospital at biweekly *t*.

β_0 is the log of expected rate of acceptance rate when all covariates = 0.

β_1, β_2, β_3 are the regression coefficients, i.e., each β represents for the change in the log expected rate when its corresponding covariate has a specific value after adjusted for other covariates in the model (when compared to the reference group).

β_4 represents for the change in the log expected rate per unit increase in biweekly after adjusted for other covariates in the model.

β_5 is the regression coefficients of interaction effects. It describes the difference between the change in the log expected acceptance rate when its corresponding interaction effects of covariates have a specific value after adjusted for other covariates in the model (when compared to the reference group).

Similarly, the model for the secondary outcome on HIV detected rate using GEE can be formulated as follows:

$$\log(\mu_{it} / n_{it}) = \beta_0 + \beta_1(study\ period_t) + \beta_2(prevalence_i) + \beta_3(region_i) + \beta_4(biweekly_t)$$

where i = 1, 2, …, 8 clusters (hospitals); t = 1, 2, …, 8 bi-weekly.

Study period at biweekly *j* (pre-intervention period is between biweekly 1- 4, intervention period is between biweekly 5-8)

$\mu_{it} = E(Y_{it})$ is defined as the number of HIV testing in the *ith* cluster (hospital) at biweekly *t*. The HIV detected rate is given by μ_{it} / n_{it}, where n_{it} is the number of eligible patients for the *ith* hospital at biweekly *t*.

β_0 is the log of expected rate of detected rate when all covariates = 0.

β_1, β_2, β_3 are the regression coefficients, i.e., each β represents for the change in the log expected rate when its corresponding covariate has a specific value after adjusted for other covariates in the model (when compared to the reference group).

β_4 represents for the change in the log expected rate per unit increase in biweekly after adjusted for other covariates in the model.

Evaluating value for money of the intervention

Using the government's perspective costs and consequences of the provider-initiated VCT were assessed in comparison to the current practice, VCT. The intervention costs included capital, labour and materials of offering the service, pre- and post-test counselling, and HIV testing. The costs of antiretroviral treatment were not included in the economic assessment since the majority of cases detected were asymptomatic. On the other hand, because there is need to standardise the intervention provided in this study, a number of activities, for example a questionnaire survey amongst those refused to take the HIV test and field supervision by researchers, that would have not been performed under normal practice were required. This created so call "protocol-induced costs". There is no common agreement whether to include or exclude the protocol-induced costs in economic evaluation studies. Hence, this study presents the intervention costs both with and without the protocol-induced costs. The costs were presented in international US dollar (PPP USD) in 2007 using Purchasing Power Parity exchange rate of the International Monetary Fund (16.36 Baht = 1 PPP USD) (International Monetary Fund 2008).

The consequences were presented in terms of new HIV infections detected as well as HIV infections avoided. The first outcome was directly measured from this experimental study while the latter was estimated using the disease model namely the Bernoulli-process model of the sexual transmission of HIV (Pinkerton, Holtgrave et al. 1998). Briefly, the model predicted the cumulative probability that an uninfected individual with known sexual behaviour profiles, i.e. number of unsafe sex and number of partners given certain rate of HIV prevalence amongst the partners, would become infected during a specific time period. This is so called primary infection (P). Furthermore, the model also calculated the cumulative probability that an infected individual with a given behaviour profile would infected his/her partners during the specific time period. The latter is so called secondary infection (S).

where:

$P = 1-\{(1 - \pi) + \pi(1 - \alpha n)n(1 - \alpha k)k\}m$

S = $m(1 - \pi)\{1 - (1 - \alpha n)n(1 - \alpha k)k\}$

π = the probability that the partner is infected

α_n = the infectivity of an unprotected intercourse

α_k = the infectivity of a condom-protected intercourse

n = the number of unprotected sex acts

k = the number of protected sex acts

m = the number of sex partners in one year

Let P_1 and P_2 denote the mean risks for uninfected samples in the control and experimental clusters. The difference, $\triangle P = P_1 - P_2$, is an estimate of the average number of primary HIV infections averted per uninfected samples.

Let S_1 and S_2 denote the mean values for the expected number of secondary infections arising from risk sexual behavior of infected samples in the control and experimental clusters, respectively. The difference, $\triangle S = S_1 - S_2$ is the average reduction in the expected number of secondary infections.

The average number of all HIV infections averted (including both primary and secondary prevention) can be estimated as follows:

$$\Delta T = (1 - \pi')\Delta P + \pi'\Delta S$$

π' = M/N is the proportion of samples who were infected at baseline

ΔP = the estimate of the average number of primary HIV infections averted

ΔS = the average reduction of the secondary HIV infections

Table III reveals transitional probabilities used in the model. The HIV prevalence among partners of non-HIV infected population was assigned at 1% which is equal to the current prevalence rate of HIV infection among pregnant women in Thailand. Because there was no data available, we assumed the prevalence rate of HIV infection among partners of HIV infected population at 2%. We reviewed literature and found that the transmission risk of HIV (the per-act probability of HIV transmission) from HIV infected male to uninfected female was 0.002 (Mastro and de Vincenzi 1996) and from infected female to uninfected male was 0.0015 (WB Thailand). A modelling study estimated the efficacy of condom in prevention of HIV transmission at 95% (Pinkerton and Abramson 1997). The numbers of unsafe sex activities in one year and the numbers of sex partners for those never obtained VCT were

derived from the 2006 National Sex Behaviour Survey which is a national representative survey conducted by the Institute for Population and Social Research (Chamratrithirong, Kittisuksathit et al. 2007). For those never obtained VCT and no HIV infection, the numbers of unsafe sex activities and the numbers of sex partners were assumed to be equivalent to the general population. For those HIV infected who never obtained VCT, the numbers of unsafe sex activities and the numbers of sex partners were supposed to be equal to the high-risk population. The numbers of unsafe sex activities and the numbers of sex partners in one year among those obtained VCT with HIV infection were gathered from 1,289 AIDS patients following up at HIV clinics in 16 sample hospitals. We assigned the numbers of unsafe sex activities in one year among those with no HIV infection using empirical evidence from sub-Saharan Africa which suggested 35% and 39% of reduction of unsafe sex behaviour among males and females who obtained VCT (The voluntary HIV-1 counselling and testing efficacy study group 2000). The numbers of sex partners of those obtained VCT with no HIV infection were assumed to be similar to the general population.

Table III Input parameters used in decision analytic model

Groups	The probability that the partner is infected (π)	The infectivity of an unprotected intercourse (α_n)	The infectivity of a condom-protected intercourse (α_k)	The number of unprotected sex acts within one year (n)	The number of protected sex acts within one year (k)	The number of sex partners in one year (m)
Males who never been obtained VCT						
Uninfected men (P1)	0.01	0.0015	0.000075	49.34	10.90	1.32
Infected men (S1)	0.02	.002	0.0001	55.59	12.29	1.32
Males who obtained VCT						
Uninfected men (P2)	0.01	0.0015	0.000075	28.25	31.99	1.32
Infected men (S2)	0.02	.002	0.0001	18.25	49.63	0.59
Females who never been obtained VCT						
Uninfected women (P1)	0.01	.002	0.0001	37.95	2.72	0.86
Infected women (P2)	0.02	0.0015	0.000075	30.52	2.19	0.86
Females who obtained VCT						
Uninfected women (P1)	0.01	.002	0.0001	22.08	18.59	0.86
Infected women (P2)	0.02	0.0015	0.000075	10.23	22.48	0.65

Since the sub-Saharan Africa study suggested that VCT significantly reduced unprotected sex among individuals and sex-partner couples during the follow-up period of 13.9 months (The voluntary HIV-1 counselling and testing efficacy study group 2000). It was assumed in this study that the efficacy of VCT in reducing unprotected sex among clients will last within one year (i.e. a time horizon used in this study). Thus, all costs and outcome were not discounted.

DATA AND DESCRIPTIVE STATISTICS

The trial profile is shown in **figure 2**. Between August 6th and November 23rd, 2007, there were 45,817 and 37,565 eligible OPD visits in experimental and control clusters respectively. The numbers of the visits were higher during the pre-intervention period compared to the intervention period in all groups except for those control clusters with high baseline HIV prevalence.

Figure 2 Trial profile

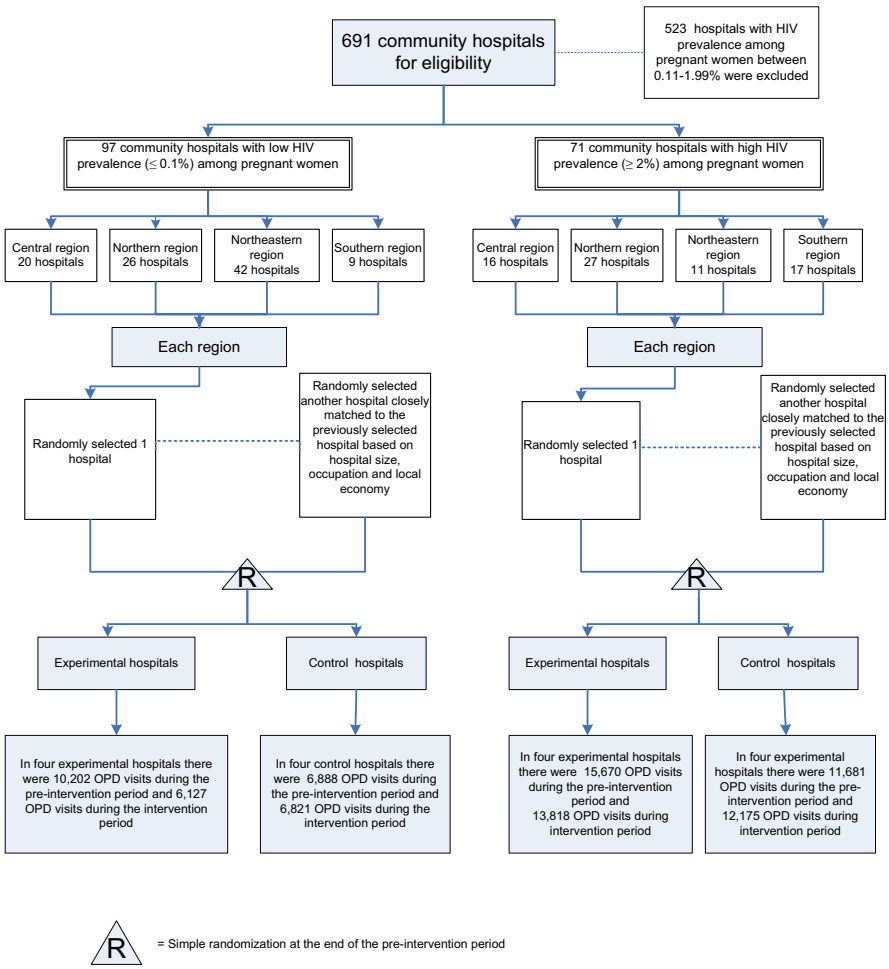


Table IV summarizes findings at the cluster level from the trial. There was no significant difference in the acceptance rates for HIV testing between the control and experimental clusters during the pre-intervention period, or between the pre-intervention and intervention periods of the control clusters. However, a significantly higher difference rate of acceptance can be observed when looking at the control and experimental clusters during the intervention period, and between the pre-intervention and intervention periods of the experimental clusters both in the areas with low and high HIV prevalence. The numbers of new HIV infections detected were higher for both the control and experimental clusters with high baseline HIV prevalence and also for the experimental clusters during the intervention period than other groups.

Table IV Acceptance rate of HIV test and number of HIV infection detected between experimental and control clusters classified by HIV prevalence levels (95% Confidential Interval)

Hospitals	Time (period)	Eligible patients	Number of HIV test performed	% acceptance rate for HIV test	Number of new HIV infection detected
Low HIV prevalence					
Control	Pre-intervention	6,888	23	0.28 (0.19,0.39)	1
	Intervention	6,821	32	0.42 (0.27,0.56)	1
Experiment	Pre-intervention	10,202	39	0.38 (0.26,0.50)	3
	Intervention	6,127	544	8.88 (8.16,9.59)	9
High HIV prevalence					
Control	Pre-intervention	11,681	54	0.47 (0.34,0.59)	8
	Intervention	12,175	33	0.27 (0.18,0.36)	8
Experiment	Pre-intervention	15,670	48	0.3 (0.21,0.38)	8
	Intervention	13,818	486	3.52 (3.21,3.82)	12

Table V presents descriptive statistics of the individual-level parameters of those undertaking an HIV test, those not undertaking an HIV test, and those newly diagnosed with HIV. The data was classified by randomization arm and study period. For those undertaking HIV testing at study hospitals there was no significant difference of individual characteristics between control and experimental clusters in both the low and high HIV prevalence areas during the pre-intervention period. The significant differences in acceptance rate were only observed when compared between the control and experimental clusters during the intervention period. These included percentages of farmers taking the test (low HIV prevalence), percentages of having extra-marital sex (high HIV prevalence, percentages of not using condoms when having extra-marital sex (low HIV prevalence area).

For those not taking an HIV test, some characteristics differed significantly between the control and experimental clusters during the pre-intervention period. These included percentages of low or equal to primary school education among those not taking an HIV test (high HIV prevalence area), percentages of blue collar workers (low and high HIV prevalence areas), percentages of farmers (low HIV prevalence area), percentages of drinking alcohol during the past month (low HIV prevalence area), percentages of having extra-marital sex (low HIV prevalence area), percentages of not using condoms when having extra-marital sex (low HIV prevalence area), and percentages of those that perceived that his/her spouse was at risk (high HIV prevalence area).

Table V Characteristics of selected individual-level variables by different randomisation arm (95% Confidential Interval)

	Low HIV prevalence				High HIV prevalence			
	Control clusters		Experimental clusters		Control clusters		Experimental clusters	
	Pre-intervention	Intervention	Pre-intervention	Intervention	Pre-intervention	Intervention	Pre-intervention	Intervention
HIV test clients								
number of samples	23	32	39	544	54	33	48	486
average age	31 (25,36)	34 (29,39)	33 (29,37)	36 (35,37)	35 (32,38)	38 (34,42)	38 (36,41)	40 (39,41)
% male gender	48 (29,96)	50 (33,66)	54 (39,70)	45 (41,49)	57 (45,69)	30 (16,46)	50 (36,64)	42 (37,46)
% single marital status	35 (18,54)	25 (12,41)	33 (20,48)	18 (15,21)	22 (12,34)	18 (7,32)	11 (4,20)	13 (10,16)
% lower or equal to primary school education	56 (37,75)	44 (27,62)	62 (46,76)	56 (52,60)	61 (48,75)	63 (50,79)	67 (53,79)	67 (63,72)
% white-collar workers	9 (1,23)	19 (8,33)	2 (0,8)	13 (10,16)	13 (5,23)	12 (3,24)	19 (9,29)	14 (11,18)
% blue-collar workers	22 (8,40)	12 (4,26)	59 (43,74)	47 (43,51)	41 (28,55)	27 (14,43)	48 (34,62)	43 (38,47)

	Low HIV prevalence				High HIV prevalence			
	Control clusters		Experimental clusters		Control clusters		Experimental clusters	
	Pre-intervention	Intervention	Pre-intervention	Intervention	Pre-intervention	Intervention	Pre-intervention	Intervention
% farmers	48 (29,68)	47 (29,63)	23 (11,36)	21 (18,25)	30 (19,42)	27 (13,43)	19 (8,30)	24 (20,28)
% alcohol drinking during the past month	35 (18,55)	19 (8,34)	46 (31,62)	36 (32,40)	41 (28,55)	33 (19,50)	44 (29,58)	48 (43,52)
% ever taken illegal drug	75 (0,16)	6 (0,15)	3 (0,9)	11 (8,13)	13 (5,23)	3 (0,11)	15 (6,26)	11 (8,13)
% having extra-marital sex	43 (24,62)	35 (16,48)	31 (21,51)	30 (26,34)	33 (20,47)	15 (5,30)	40 (26,53)	38 (34,43)
% not using condom when having extra-marital sex	90 (66,99)	0 (0,0)	93 (76,99)	78 (72,84)	83 (64,96)	80 (38,99)	73 (52,90)	72 (65,78)
% perceived that his/her spouse was at risk	33 (14,58)	16 (5,34)	30 (14,50)	31 (27,35)	51 (36,65)	59 (39,76)	56 (43,69)	44 (40,49)
Those not taking HIV test								

	Low HIV prevalence				High HIV prevalence			
	Control clusters		Experimental clusters		Control clusters		Experimental clusters	
	Pre-intervention	Intervention	Pre-intervention	Intervention	Pre-intervention	Intervention	Pre-intervention	Intervention
number of samples	495	596	727	482	883	604	1337	1282
average age	37 (37,39)	34 (33,35)	39 (39,40)	39 (38,41)	38 (37,39)	37 (36,38)	40 (39,41)	39 (38,40)
% male gender	34 (30,38)	30 (26,33)	37 (34,41)	36 (32,41)	37 (34,40)	39 (36,43)	32 (30,35)	34 (32,37)
% single marital status	16 (13,20)	19 (16,22)	15 (13,18)	13 (10,16)	13 (11,16)	19 (17,23)	13 (12,15)	13 (12,16)
% lower or equal to primary school education	59 (55,64)	46 (43,51)	61 (58,65)	61 (57,66)	62 (59,66)	56 (53,61)	71 (69,74)	70 (68,73)
% white-collar workers	13 (11,17)	12 (10,16)	12 (10,15)	14 (11,17)	13 (11,15)	13 (10,16)	13 (11,15)	11 (10,13)
% blue-collar workers	24 (20,27)	18 (15,22)	43 (39,46)	33 (29,37)	32 (29,35)	32 (29,36)	41 (38,44)	40 (38,43)
% farmers	42 (38,47)	53 (49,57)	22 (20,26)	27 (24,32)	30 (27,34)	32 (29,37)	29 (27,32)	30 (28,33)

	Low HIV prevalence				High HIV prevalence			
	Control clusters		Experimental clusters		Control clusters		Experimental clusters	
	Pre-intervention	Intervention	Pre-intervention	Intervention	Pre-intervention	Intervention	Pre-intervention	Intervention
% alcohol drinking during the past month	17 (15,21)	18 (16,22)	29 (26,32)	24 (21,29)	23 (21,26)	30 (27,34)	22 (20,25)	26 (24,29)
% ever taken illegal drug	1 (0,2)	1 (0,2)	3 (2,4)	11 (9,14)	3 (2,4)	2 (1,4)	3 (2,4)	3 (2,4)
% having extra-marital sex	3 (2,5)	3 (2,5)	10 (8,13)	6 (5,9)	7 (6,9)	11 (9,14)	8 (7,10)	8 (7,10)
% not using condom when having extra-marital sex	55 (33,79)	57 (36,78)	13 (6,21)	48 (31,66)	31 (20,42)	17 (9,27)	44 (35,54)	40 (31,49)
% perceived that his/her spouse was at risk	11 (8,14)	6 (4,8)	16 (14,19)	14 (11,17)	21 (18,23)	23 (19,27)	11 (9,13)	15 (13,17)
New HIV infection detected								

	Low HIV prevalence				High HIV prevalence			
	Control clusters		Experimental clusters		Control clusters		Experimental clusters	
	Pre-intervention	Intervention	Pre-intervention	Intervention	Pre-intervention	Intervention	Pre-intervention	Intervention
number of samples	1	1	3	9	8	8	8	12
average age	40	31	29 (23,35)	35 (26,43)	36 (30,41)	38 (32,44)	41 (37,56)	36 (32,46)
% male gender	0 (0,0)	100 (100,100)	100 (100,100)	66 (33,97)	63 (32,89)	25 (4,58)	75 (41,97)	66 (39,88)
% single marital status	0 (0,0)	0 (0,0)	33 (0,84)	22 (3,53)	13 (0,39)	12 (0,41)	0 (0,0)	17 (2,42)
% lower or equal to primary school education	0 (0,0)	100 (100,100)	66 (16,99)	55 (23,88)	74 (42,95)	87 (59,99)	88 (60,99)	83 (57,98)
% white-collar workers	100 (100,100)	0 (0,0)	0 (0,0)	0 (0,0)	12 (0,40)	12 (0,41)	0 (0,0)	17 (2,42)
% blue-collar workers	0 (0,0)	100 (100,100)	66 (14,99)	56 (25,84)	25 (4,57)	51 (18,82)	63 (29,91)	50 (25,77)
% farmers	0 (0,0)	0 (0,0)	34 (2,85)	22 (3,50)	63 (29,89)	12 (0,42)	25 (3,58)	8 (0,27)

	Low HIV prevalence				High HIV prevalence			
	Control clusters		Experimental clusters		Control clusters		Experimental clusters	
	Pre-intervention	Intervention	Pre-intervention	Intervention	Pre-intervention	Intervention	Pre-intervention	Intervention
% alcohol drinking during the past month	0 (0,0)	0 (0,0)	100 (100,100)	33 (10,67)	50 (19,83)	25 (4,59)	25 (3,56)	50 (22,74)
% ever taken illegal drug	0 (0,0)	0 (0,0)	33 (1,84)	22 (4,51)	44 (17,83)	0 (0,0)	12 (0,41)	25 (5,51)
% having extra-marital sex	0 (0,0)	100 (100,100)	100 (100,100)	55 (26,82)	62 (26,90)	25 (3,57)	51 (20,81)	58 (30,83)
% not using condom when having extra-marital sex	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)	80 (42,99)	50 (2,97)	75 (29,99)	0 (0,0)
% perceived that his/her spouse was at risk	100 (100,100)	0 (0,0)	100 (100,100)	72 (38,96)	100 (100,100)	85 (83,99)	63 (30,91)	40 (13,71)

Noted that for each 'cell' that N < 100, we applied Bayesian statistics (assigning Beta-distribution) and Monte-Carlo simulation to compute mean and 95% confidential interval

In conclusion, the above descriptive data reveals a degree of sameness between the control and experimental clusters in both low and high HIV prevalence areas.

IMPACT RESULTS

The intervention's effect on the acceptance rate of HIV testing at the cluster level

Table VI shows that the acceptance rate of HIV testing for the experimental clusters during the intervention period was significantly higher than the other three arms (IRR = 49.69 95%CI = 20.17, 122.43). There was also significant difference of acceptance rate between low and high HIV prevalence areas but not for location (regions). The higher HIV prevalence the greater acceptance rate observed. The rate was significantly lower in both the control and experimental clusters during the intervention period in high HIV prevalence areas and the experimental clusters during the pre-intervention period in high HIV prevalence area. In addition, the rate was significantly lower in the control and experiment clusters of the northern region during the intervention period and in the experimental cluster of the northern region during the pre-intervention period. The detection rate did not change significantly over time (bi-weekly variable) during the study period in either the control cluster or the experimental cluster.

Table VI Results of Generalised Estimating Equations on the acceptance rate of HIV test in a 16-cluster randomised trial

Variables	Sub-categories	Coefficient	Standard Error	Z	P-value	Incidence rate ratio (IRR)	95% CI of IRR	
							lower	upper
Intercept		-5.283	0.392	-13.49	<0.0001*			
Study groups	Control/pre-intervention period	0.000	.	.	.	1.00	.	.
	Control/intervention period	0.385	0.406	0.95	0.343	1.47	0.66	3.26
	Experiment/pre-intervention period	0.365	0.374	0.97	0.329	1.44	0.69	3.00
	Experiment/Intervention period	3.906	0.460	8.49	<0.0001*	49.69	20.17	122.43
HIV prevalence	Low	0.000	.	.	.	1.00	.	.
	High	0.459	0.191	2.41	0.016*	1.58	1.09	2.30
Regions	Central	0.000	.	.	.	1.00	.	.
	Northern	-0.468	0.339	-1.38	0.168	0.63	0.32	1.22
	North-eastern	0.234	0.285	0.84	0.400	1.27	0.73	2.22
	Southern	-0.436	0.280	-1.56	0.119	0.65	0.37	1.12
Study groups×HIV prevalence	Experiment /Intervention period×High prevalence	-1.254	0.348	-3.60	0.0003*	0.29	0.14	0.56
	Experiment/Pre-intervention period×High prevalence	-0.716	0.280	-2.56	0.0104*	0.49	0.28	0.85
	Control/intervention period×High prevalence	-0.888	0.250	-3.56	0.0004*	0.41	0.25	0.67
Study groups×Regions	Experiment/intervention period×Northern	0.244	0.490	0.5	0.619	1.28	0.49	3.34

Variables	Sub-categories	Coefficient	Standard Error	Z	P-value	Incidence rate ratio (IRR)	95% CI of IRR	
							lower	upper
	Experiment/pre-intervention period × Northern	0.481	0.414	1.16	0.245	1.62	0.72	3.64
	Control/intervention period × Northern	0.514	0.294	1.75	0.081	1.67	0.94	2.98
	Experiment/intervention period × North-eastern	-0.906	0.439	-2.06	0.039*	0.40	0.17	0.96
	Experiment/pre-intervention period × North-eastern	-1.194	0.330	-3.62	0.0003*	0.30	0.16	0.58
	Control/intervention period × North-eastern	0.748	0.346	2.16	0.0305*	2.11	1.07	4.16
	Experiment/intervention period × Southern	-0.335	0.349	-0.96	0.337	0.72	0.36	1.42
	Experiment/pre-intervention period × Southern	-0.608	0.359	-1.69	0.090	0.54	0.27	1.10
	Control/intervention period × Southern	0.423	0.317	1.33	0.182	1.53	0.82	2.84
Bi-weekly		-0.124	0.082	-1.52	0.1292	0.88	0.75	1.04

NOTE: * P < 0.05

The intervention's effect on the detection rate of HIV infection

The detection rate was significantly higher among the experimental clusters than other study groups during the intervention period (IRR = 12.94 95%CI = 1.44, 116.08) (see **table VII**). The detection rate was also significantly higher in high HIV prevalence areas but lower in northern and southern regions. The detection rate did not change significantly over time during the study period in either the control cluster or the experimental cluster.

Table VII Results of Generalised Estimating Equations on the number of new HIV infections detected in a 16-cluster randomised trial

Variables	Sub-categories	Coefficient	Standard Error	Z	P-value	Incidence rate ratio (IRR)	95%CI of IRR	
							lower	upper
Intercept		-7.780	0.798	-9.74	<0.0001*			
Study groups	Control/pre-intervention period	0.000	.	.	.	1.00	.	.
	Control/intervention period	0.559	0.699	0.80	0.424	1.75	0.44	6.89
	Experiment/pre-intervention period	0.624	0.822	0.76	0.448	1.87	0.37	9.35
	Experiment/intervention period	2.560	1.119	2.29	0.022*	12.94	1.44	116.08
HIV prevalence	Low	0.000	.	.	.	1.00	.	.
	High	1.620	0.788	2.06	0.039*	5.05	1.08	23.66
Regions	Central	0.000	.	.	.	1.00	.	.
	Northern	-0.981	0.276	-3.56	0.0004*	0.38	0.22	0.64
	North-eastern	-0.508	0.623	-0.82	0.415	0.60	0.18	2.04
	Southern	-1.282	0.476	-2.69	0.0071*	0.28	0.11	0.71
Study groups× HIV prevalence	Experiment/Intervention	-1.715	0.971	-1.77	0.077	0.18	0.03	1.21
	Experiment/Pre-intervention	-0.904	0.924	-0.98	0.328	0.40	0.07	2.47
	Control/intervention period×High	-0.007	0.207	-0.04	0.972	0.99	0.66	1.49
Bi-weekly		-0.138	0.167	-0.83	0.408	0.87	0.63	1.21

Note: * $p < 0.05$

The intervention's effect on the willingness of each individual to take the HIV test

Table VIII demonstrates that providing provider-initiated VCT significantly increased the likelihood of the individuals to take the HIV test by 23.7 times (95%CI = 13.09, 41.36). It also shows that those: aged 20-40 years, who were blue collar workers, that perceived that his/her spouse was at risk, drinking alcohol during the past month, having extra-marital sex, not using condoms every time while having extra-marital sex, and married in the intervention group (Intervention*Married) were of a significantly increased likelihood to accept the HIV test than those in other groups. Meanwhile, those married or ever having been diagnosed with a sexual transmitted disease, those allocated to an intervention group in high HIV prevalence areas (Intervention*High prevalence) and those allocated to an intervention group in northern, northeastern and southern parts were less likely to accept the test.

Table VIII Results of Multilevel model on the acceptance of HIV test in 16-cluster randomised trial

Variables	Sub-categories	Coefficient	Standard Error	t Value	Pr > |t|	Odds Ratio (OR)	95% CI of OR	
							Lower	Upper
Intercept		-4.05	0.56	-7.22	<.0001*			
Cluster-level variables								
Study groups	No intervention	0.00	.	.	.	1.00		
	Intervention	3.15	0.29	10.73	<.0001*	23.27	13.09	41.36
Prevalence	Low	0.00	.	.	.	1.00		
	High	-0.20	0.44	-0.46	0.652	0.82	0.32	2.11
Regions	Central	0.00	.	.	.	1.00		
	Northern	1.03	0.62	1.65	0.124	2.79	0.72	10.72
	North-eastern	0.99	0.64	1.55	0.144	2.69	0.68	10.59
	Southern	0.62	0.62	1.01	0.333	1.87	0.49	7.17
Individual-level variables								
Age groups	> 40 years	0.00	.	.	.	1.00		
	20-40 years	0.24	0.09	2.63	0.009*	1.27	1.06	1.51
	< 20 years	0.27	0.19	1.45	0.148	1.31	0.91	1.89
Gender	Male	0.00	.	.	.	1.00		
	female	0.09	0.09	0.99	0.322	1.10	0.91	1.31
Marital status	Single	0.00	.	.	.	1.00		
	Married	-0.37	0.19	-2.00	0.046*	0.69	0.48	0.99

Variables	Sub-categories	Coefficient	Standard Error	t Value	Pr > |t|	Odds Ratio (OR)	95% CI of OR	
							Lower	Upper
Education	Bachelor degree or higher	0.00	.	.	.	1.00		
	High-school or vocational school	-0.28	0.20	-1.38	0.169	0.76	0.51	1.12
	Primary school or lower	-0.29	0.21	-1.41	0.159	0.75	0.50	1.12
Occupation	Others	0.00	.	.	.	1.00		
	White collar workers	0.12	0.14	0.82	0.414	1.12	0.85	1.49
	Farmer	0.13	0.13	0.98	0.326	1.14	0.88	1.47
	Nightlife workers	1.05	0.59	1.78	0.074	2.86	0.90	9.09
	Blue collar workers	0.26	0.12	2.27	0.023*	1.30	1.04	1.63
Perceived that his/her spouse was at risk	No	0.00	.	.	.	1.00		
	Yes	2.81	0.17	16.83	<.0001*	16.69	12.02	23.16
Alcohol drinking during the past month	No	0.00	.	.	.	1.00		
	Yes	0.31	0.09	3.50	0.0005*	1.37	1.15	1.63
Ever had HIV test	No	0.00	.	.	.	1.00		
	Yes	-0.13	0.10	-1.37	0.171	0.88	0.73	1.06
Ever been diagnosed with sexual transmitted diseases	No	0.00	.	.	.	1.00		
	Yes	-0.34	0.13	-2.66	0.008*	0.71	0.55	0.91
Ever taken illegal drug	No	0.00	.	.	.	1.00		
	Yes	0.13	0.16	0.83	0.408	1.14	0.84	1.55

Variables	Sub-categories	Coefficient	Standard Error	t Value	Pr > |t|	Odds Ratio (OR)	95% CI of OR	
							Lower	Upper
Ever used intravenous drug	No	0.00	.	.	.	1.00		
	Yes	0.57	0.49	1.18	0.240	1.77	0.68	4.62
Having extra-marital sex	No	0.00	.	.	.	1.00		
	Yes	1.28	0.17	7.69	<.0001*	3.58	2.59	4.95
Not using condom every time while having extramarital sex	No	0.00	.	.	.	1.00		
	Yes	0.93	0.18	5.20	<.0001*	2.53	1.78	3.59
Study groups×HIV prevalence	Intervention×High	-0.74	0.26	-2.87	0.004*	0.48	0.29	0.79
Study groups×Marital status	Intervention×Married	0.89	0.22	4.12	<.0001*	2.44	1.59	3.72
Study groups×Regions	Intervention×Northern	-0.85	0.31	-2.76	0.006*	0.43	0.23	0.78
	Intervention×North-eastern	-1.26	0.46	-2.76	0.006*	0.28	0.12	0.70
	Intervention×Southern	-0.92	0.36	-2.57	0.010*	0.40	0.20	0.81

Note: * $p < 0.05$

COMPARING EXPERIMENTAL AND QUASI-EXPERIMENTAL ANALYSES

The intervention's effect on the acceptance rates of HIV testing at the cluster level

Using the quasi approach, **table IX** illustrates that the effect of the intervention on the acceptance rate of HIV testing was quite similar to those using the analysis of experiment approach, though the 95% confident interval of estimated odd was relatively smaller (IRR = 39.52 95%CI = 18.56, 84.19). In contrast to the analysis of experiment, there was no significant difference of the acceptance rate between low and high HIV prevalence areas. The model also indicates that the acceptance rate was significantly lower in the north-eastern and southern parts of the country compared to the central region. The rate was also lower in high HIV prevalence in the intervention group.

Table IX Results of Generalised Estimating Equations on the acceptance of HIV test among 8 clusters using a quasi-experimental approach

Variables	Sub-categories	Coefficient	Standard Error	Z	P-value	Incidence rate ratio (IRR)	95% Conf. IRR	
							lower	upper
Intercept		-5.071	0.238	-21.34	<.0001*	1.00		
Study period	Intervention	3.677	0.386	9.53	<.0001*	39.52	18.56	84.19
	Pre- intervention	0.000	0.000	.	.	1.00		
HIV prevalence	High	-0.042	0.275	-0.15	0.878	0.96	0.56	1.64
	Low	0.000	0.000	.	.	1.00		
Regions	Northern	-0.268	0.318	-0.84	0.399	0.76	0.41	1.43
	North-eastern	-0.681	0.316	-2.16	0.031*	0.51	0.27	0.94
	Southern	-0.797	0.193	-4.13	<.0001*	0.45	0.31	0.66
	Central	0.000	0.000	.	.	1.00		
Study period × HIV prevalence	Intervention ×High	-0.698	0.231	-3.03	0.003*	0.50	0.32	0.78
	Pre-intervention × High	0.000	0.000	.	.			
	Intervention ×Low	0.000	0.000	.	.			
	Pre-intervention × low	0.000	0.000	.	.			
Bi-weekly		-0.125	0.092	-1.36	0.174	0.88	0.74	1.06

Note: * $p < 0.05$

The intervention's effect on the detection rate of HIV infection

No evidence indicates that the intervention increased the rate of new HIV infection detected (IRR = 1.62 95%CI = 0.29, 9.23) (see table X). There was no significant difference in the detection rate of HIV infections within different HIV prevalence areas or over time (bi-weekly) but the detection rate was significantly lower in the northern and southern regions.

Table X Results of Generalised Estimating Equations on the number of new HIV infections detected among 8 clusters using a quasi-experimental approach

Variables	Sub-categories	Coefficient	Standard Error	Z	P-value	Incidence rate ratio (IRR)	95% Conf. IRR	
							lower	upper
Intercept		-7.332	0.330	-22.19	<.0001*			
Study period	Intervention	0.486	0.886	0.55	0.584	1.62	0.29	9.23
	Pre- intervention	0.000	0.000	.	.	1.00		
HIV prevalence	High	0.304	0.201	1.51	0.130	1.35	0.91	2.01
	Low	0.000	0.000	.	.	1.00		
Regions	Northern	-1.121	0.195	-5.74	<.0001*	0.33	0.22	0.48
	North-eastern	-2.319	1.216	-1.91	0.057	0.10	0.01	1.07
	Southern	-0.753	0.181	-4.16	<.0001*	0.47	0.33	0.67
	Central	0.000	0.000	.	.	1.00		
Bi-weekly		0.088	0.162	0.55	0.585	1.09	0.80	1.50

Note: * $p < 0.05$

The intervention's effect on the willingness of the individual to take the HIV test

Table XI shows that the intervention significantly increased the likelihood of the subjects to take the HIV test (Odds ratio = 28.92 95%CI = 14.50, 57.69). Similar to the results from the analysis of the experiment, those subjects: aged 20-40 years, who were blue collar workers, who perceived that his/her spouse was at risk, and those that drank alcohol during the past month were more likely to accept the HIV test and those subjects who had previously been diagnosed with sexual transmitted diseases were less likely to take the test. In contrast, the analysis of the quasi-experiment found that the subjects who worked at night-time are more likely to accept the HIV test.

Table XI Results of Multilevel model on the acceptance of HIV test among 8 clusters using a quasi-experimental approach

Variables	Sub-categories	Coefficient	Standard Error	t Value	Pr > |t|	Odds Ratio (OR)	95% Conf. OR	
							Lower	Upper
Intercept		-4.24	0.90	-4.69	0.01*			
Cluster-level variables								
Intervention	No	0.00	.	.	.	1.00		
	Yes	3.36	0.35	9.55	<.0001*	28.92	14.5	57.69
HIV prevalence	Low	0.00	.	.	.	1.00		
	High	-0.25	0.76	-0.33	0.76	0.78	0.09	7.05
Regions	Central	0.00	.	.	.	1.00		
	Northern	1.67	1.05	1.58	0.20	5.29	0.22	125.96
	North-eastern	0.57	1.13	0.51	0.64	1.77	0.09	36.57
	Southern	0.23	1.08	0.22	0.84	1.26	0.06	28.3
Individual-level variables								
Age groups	> 40 years	0.00	.	.	.	1.00		
	20-40 years	0.20	0.10	2.06	0.04	1.23	1.01	1.49
	< 20 years	0.15	0.21	0.70	0.48	1.16	0.77	1.76
Gender	Male	0.00	.	.	.	1.00		
	Female	0.17	0.10	1.64	0.10	1.18	0.97	1.44
Marital status	Single	0.00	.	.	.	1.00		
	Married	-0.22	0.30	-0.74	0.46	0.8	0.45	1.44

Variables	Sub-categories	Coefficient	Standard Error	t Value	Pr > |t|	Odds Ratio (OR)	95% Conf. OR	
							Lower	Upper
Education	Bachelor degree or higher	0.00	.	.	.	1.00		
	High-school or vocational school	-0.36	0.24	-1.51	0.13	0.7	0.44	1.11
	Primary school or lower	-0.42	0.24	-1.72	0.09	0.66	0.41	1.06
Occupation	Others	0.00	.	.	.	1.00		
	Blue collar workers	0.31	0.13	2.47	0.01*	1.37	1.07	1.76
	White collar workers	0.15	0.16	0.95	0.34	1.16	0.85	1.59
	farmer	0.24	0.15	1.59	0.11	1.27	0.95	1.69
	Night-life workers	1.97	0.78	2.51	0.01*	7.16	1.54	33.24
Perceived that his/her spouse was at risk	No/unknown	0.00	.	.	.	1.00		
	Yes	3.02	0.21	14.16	<.0001*	20.5	13.5	31.15
Alcohol drinking during the past month	No	0.00	.	.	.	1.00		
	Yes	0.39	0.10	3.99	<.0001*	1.48	1.22	1.79
Ever had HIV test	No	0.00	.	.	.	1.00		
	Yes	-0.14	0.11	-1.32	0.19	0.87	0.71	1.07
Ever been diagnosed with sexual transmitted diseases	No	0.00	.	.	.	1.00		
	Yes	-0.40	0.14	-2.79	0.01*	0.67	0.51	0.89
Ever taken illegal drug	No	0.00	.	.	.	1.00		
	Yes	0.02	0.17	0.15	0.88	1.03	0.74	1.42

Variables	Sub-categories	Coefficient	Standard Error	t Value	Pr > |t|	Odds Ratio (OR)	95% Conf. OR	
							Lower	Upper
Ever used intravenous drug	No	0.00	.	.	.	1.00		
	Yes	1.24	0.59	2.09	0.04*	3.46	1.08	11.12
Having extra-marital sex	No	0.00	.	.	.	1.00		
	Yes	1.36	0.18	7.49	<.0001*	3.88	2.72	5.54
Not using condom every time while having extramarital sex	No	0.00	.	.	.	1.00		
	Yes	0.89	0.20	4.53	<.0001*	2.44	1.66	3.59
Intervention ×HIV prevalence	Intervention × High	-0.71	0.27	-2.63	0.01*	0.49	0.29	0.83
Intervention ×Marital status	Intervention × Married	0.71	0.32	2.23	0.03*	2.03	1.09	3.78
Intervention ×Regions	Intervention ×Northern	-0.95	0.32	-2.98	0.00*	0.39	0.21	0.72
	Intervention ×North-eastern	-1.18	0.52	-2.28	0.02*	0.31	0.11	0.85
	Intervention ×Southern	-0.83	0.39	-2.14	0.03*	0.44	0.2	0.93

Note: * $p < 0.05$

To sum up, we found similar results using the analyses of the experiment and the quasi-experiment in this study. Both methods of analyses suggest that the intervention significantly increased the outcomes. However, the analysis using the quasi-experiment approach (without using information from the control clusters) undervalued the estimated IRRs (the acceptance rate of 39.52 vs. 46.69 and the HIV detection rate of 1.62 vs. 12.94 for analysis of the quasi-experiment and the experiment respectively). Furthermore, the analysis of the experiment gave a lower intervention effect on the individual's likelihood to accept the HIV test than the analysis of the quasi-experiment (23.27 vs. 28.92).

COST-EFFECTIVENESS RESULTS

Table XII summarises all costs and outcomes, in terms of both HIV cases detected and HIV infections averted, obtained from the experimental and control groups. The intervention costs with and without including protocol-induced costs, were nearly three times higher in the experimental clusters compared to the control. Meanwhile, there were additional twelve HIV infections detected or 1.74 HIV infections averted from offering provider-initiated VCT. Incremental cost per HIV cases detected from offering provider-initiated VCT instead of VCT alone were 5,364 PPP USD, if the protocol-induced costs were included, and 4,141 PPP USD, if the protocol-induced costs were excluded. In other words, incremental costs per HIV infection averted of provider-initiated VCT were 36,979 PPP USD, if the protocol-induced costs were included, and 28,551 PPP USD, if the protocol-induced costs were excluded.

Table XII Results of economic evaluation

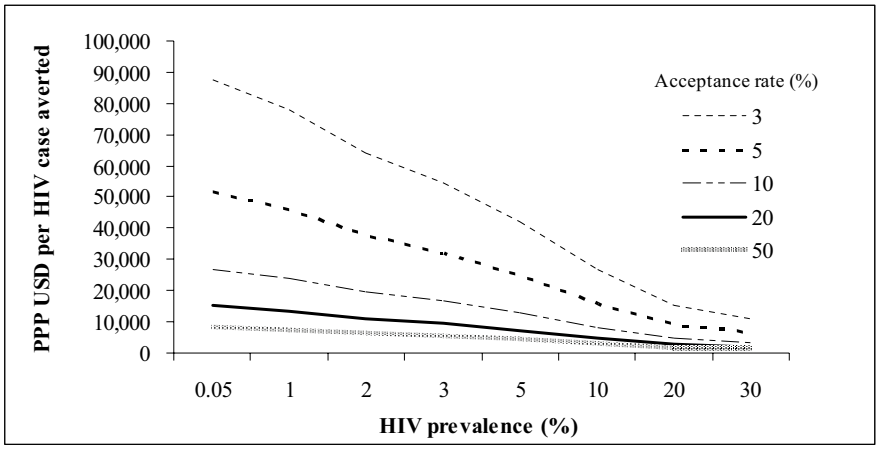
		Including protocol inducted costs	**Excluding protocol inducted costs**
Costs	Experimental clusters	104,158	69,928
	Control clusters	39,795	20,235
HIV cases detected	Experimental clusters	21	
	Control clusters	9	
HIV infections averted	Experimental clusters	1.86	
	Control clusters	0.12	
Incremental cost		64,363	49,693
Incremental outcomes	HIV cases detected	12	
	HIV infections averted	1.74	
ICER (PPP USD per HIV case detected)		5,364	4,141
ICER (PPP USD per HIV infection averted)		36,979	28,551

PPP USD = international US dollar

ICER = Incremental cost-effectiveness ratio

Figure 3 illustrates results of the sensitivity analysis of two key parameters, i.e. acceptance rate of HIV test and HIV prevalence. It shows that the higher acceptance rate the more cost-effective of provider-initiated VCT especially at the acceptance rate lower than 10%. If the acceptance rate higher than 10%, the increased acceptance of HIV test had less effect on the cost-effectiveness ratio. Similarly, the higher HIV prevalence the more cost-effective of the intervention. However, if the acceptance rate greater than 10%, HIV prevalence had less influence on the cost-effectiveness ratio.

Figure 3 Results of sensitivity analysis



THE PERCEPTION OF KEY STAKEHOLDERS CONCERNING THE IMPLEMENTATION OF THE INTERVENTION AT A NATIONAL LEVEL

One of the specific objectives of this study is to assess the positions and perceptions of stakeholders towards the introduction of the provider-initiated VCT in hospitals in Thailand. The elements of analyses involve policy actors' anticipation on the potential benefits, impediments, undesirable consequences and other implementation issues if such an intervention is extended from research-based program to a larger-scale including national initiative. According to the study proposal, key informants to be included in the interviews and discussions comprise policymakers at national level, hospital administrators, healthcare workers, service recipients at OPD and civil society organizations.

A workshop was convened on January 22nd, 2008 where the researchers presented preliminary findings of the study to 16 research teams, consisting of 33 directors and practitioners from district hospitals, both experiment and control groups. Led by a health policy analyst, a two-hour session was allocated to discussion on the feasibility of scaling-up the provider-initiated VCT. The deliberations covered a wide range of issues and were actively participated. To most discussants, the provision of provider-initiated VCT would be effective in controlling HIV/AIDS, since it not only provided people with the opportunity to get easy access to the service and let them know their HIV status, but also might encourage those who received the information distributed in the OPD to be aware of the disease and employ prevention strategies. In view of health providers, early detection and awareness of HIV/AIDS in

community would be helpful in reducing the disease burden including associated treatment and care they had to shoulder in the future.

The major concerns expressed in this forum were the anticipated little benefits of providing this service in the areas with low HIV prevalence, and related cost-ineffectiveness. Also, these health workers argued that there were many challenges in integrating the study intervention into routine delivery practices. For instance, it would significantly incur workloads of OPD nurses, counselors and laboratory scientists. In addition, space and necessary facilities for service provision with confidentiality were limited in some hospitals. As many pointed out, policymakers should consider beyond finding out HIV/AIDS cases, i.e. the subsequent demands for comprehensive, continuum of care for PHA and their family, such as the prevention of opportunistic diseases, antiretroviral therapy and social care and support. At the same time, the directors and practitioners suggested the needs for implementation flexibility in different aspects if the provider-initiated VCT became a national policy. They maintained that dealing with HIV/AIDS problems was context-specific so that a 'one-size fits all' initiative would not always work in different settings.

The assessment of policymakers' perspective about getting the provider-initiated VCT into practice nationwide is omitted in this project, as the decisions in relation to this innovation were made by two organizations while the study was still conducted. First, the Bangkok Metropolitan Administration (BMA)'s Health Department, in collaboration with the Thai Red Cross Society's AIDS Program, adopted this policy in August 2008. Although the features of the BMA initiative and the service under study were different in details, both shared the core principle: promoting early diagnosis of HIV infection through the VCT proactively offered by healthcare providers to patients regardless of the causes of care seeking. While the said initiative would cover hospitals and health centers in Bangkok Metropolitan area that served 12 million populations, the other program was devised by the National Health Security Board's Subcommittee for Benefits and Services Development, and planned to implement as a component of the universal health coverage scheme throughout the country.

The researchers of this study were involved in the above initiatives, by providing the information and comments drawn on the research experience to policymakers. According to our observation, the policymakers and their health professional and technical staff recognized the public health consequences of expanding the provider-initiated VCT and were aware of the differences in the research-based intervention and practical policy development

DISCUSSION AND CONCLUSIONS

This study provides strong evidence to support the fact that provider-initiated VCT can improve the acceptance rate of HIV testing among patients visiting OPDs at district hospitals in Thailand. The intervention tends to be more attractive to those with higher HIV risk behaviors, e.g. having extramarital sex, not using condoms when having extra-marital sex or perceiving that his/her spouse was at risk. In addition, the intervention leads to a significant improvement of the HIV detection rate. However, this was not the primary objective of this study, and so no power calculation was performed before the analysis. If awareness of HIV infection status can encourage good practice to reduce risk behaviors in both infected and uninfected people, and also facilitate earlier an uptake of an appropriate prevention, treatment, care and support among HIV infected persons; then these findings suggest that provider-initiated counseling and HIV testing has the potential to reduce the burden of HIV/AIDS. It can be used to speed up the progress towards the MDG on combating the infection, which has faltered in many settings in Asia and sub-Saharan Africa.

Economic appraisal alongside this experimental study suggests that an incremental cost-effectiveness ratio of the provider-initiated VCT compared to the VCT ranges between 36,979 and 28,551 PPP USD per HIV infection averted. If one HIV infection averted offers approximately 19 Disability Adjusted Life Years or DALYs[1] as found in South Africa (Sweat, Gregorich et al. 2000), this means that the provider-initiated VCT yields between 1,946 and 1,503 PPP USD per DALY gained. Given that the Thai government recommends a ceiling threshold of 7,900 PPP USD (which is equal to Gross Domestic Product per capita) per or DALY gained as a threshold for a public health intervention, the provider-initiated VCT is likely to represent good value for money under the Thai health care system.

At this stage in Thailand the provider-initiated VCT is very attractive by decision makers. The health authority of Bangkok city already adopted this initiative as a routine practice in all hospitals and health centers in Bangkok Metropolitan area, covering more than ten millions of population. Meanwhile, the National Health Security Board's Subcommittee for Benefits and Services Development is under consideration to implement nation-wide the provider-initiated VCT for the entire population of Thailand. Findings from this study were used as significant

[1] Disability Adjusted Life Years (DALY) is a measure of disease burden initially developed by health economists from the World Bank and the World Health Organization. It is designed to quantify the impact of premature death (years of life lost) and disability (years lived with disability) on a population by combining them into a single, comparable unit.

inputs for health care planners of both BMA and the National Health Security Board's Subcommittee for Benefits and Services Development.

Furthermore, this study shows promising results regarding the use of the quasi-experiment approach in assessing the intervention's effectiveness when the data was carefully collected (during the pre- and post-intervention periods) and in those cases when the intervention was also blinded to those recipients during the pre-intervention period (in this case the randomisation was only performed after completing the pre-intervention period). As a result, it is possible that when the research resources are severely limited, the use of pre- and post-design of quasi-experiment can be used to assess the effectiveness of similar interventions in other settings.

This study had several strengths. First, the prospective pair-matched cluster randomized design is less susceptible to bias, especially when the control and experimental clusters are well matched. The descriptive analysis of this study indicates that the control and experimental clusters are comparable in most aspects. Second, the study collected data at both cluster and individual levels; thus, it is possible to explore the intervention's effectiveness concerning the acceptance rate of HIV testing at the cluster level, i.e. the overall acceptance rate, and at the individual level, namely the individual's likelihood to take the test. This information would be very useful for policy decision makers if they want to target the offer to only those likely to accept the test. Third, the intervention—the provider-initiated VCT used in this study, is well set and standardised. The study protocol was clearly described and strictly implemented across the experimental clusters which lead to internal validity of the study. In addition, the study samples were randomly selected and the intervention was applied to all patients with minimum inclusion and exclusion criteria. This also reflects its external validity.

However, this study has some limitations. Importantly, the prediction of the remote impact of the intervention in terms of prevention of further HIV infections was made through the disease modeling in which a number of assumptions were made. The onward transmission from HIV-positive clients and the change of risk behavior after knowing HIV status could not be investigated with the current study design. This study measured only the immediate effects in terms of the acceptance to HIV testing and the testing results. We suggest that the longer-term impact of provider-initiated VCT mentioned above need to be taken into account and they do merit further investigation. For example, a prospective observational study or risk behaviour surveillance should be conducted to monitor the long-term outcomes of the provider-initiated VCT. In addition, the better health outcomes, for example longer survival,

better quality of life due to fewer opportunistic infections which often occur in the late stages of the infection, for the early detection of HIV infections were not taken into account in the economic assessment. If included, it is likely that the intervention yields better results of cost-effectiveness analysis.

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