Cost Effectiveness of Peer Supported Group Intervention Program Among HIV Treated Patients in Outpatient Clinics in Vietnam.

Miss Vu Thi Quynh Mai

จุฬาลงกรณ์มหาวิทยาลัย
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บทคัดย่อและแฟ้มข้อมูลฉบับเต็มของวิทยานิพนธ์ตั้งแต่ปีการศึกษา 2554 ที่ให้บริการในคลังปัญญาจุฬาฯ (CUIR)
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การวิเคราะห์ต้นทุนประสิทธิผลของโปรแกรมกลุ่มสนับสนุนท่ามกลางผู้ป่วย HIV ในคลินิคผู้ป่วยนอกในประเทศเวียดนาม

นางสาววู ธิ เหควียน ไม

จุฬาลงกรณ์มหาวิทยาลัย
Chulalongkorn University

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรมหาบัณฑิต
สาขาวิชาเศรษฐศาสตร์สาธารณสุขและการจัดการบริการสุขภาพ
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By	Miss Vu Thi Quynh Mai
Field of Study	Health Economics and Health Care Management
Thesis Advisor	Nopphol Witvorapong, Ph.D.

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วู ธิ เหควียน ไม : การวิเคราะห์ต้นทุนประสิทธิผลของโปรแกรมกลุ่มสนับสนุนท่ามกลางผู้ป่วย HIV ในคลินิคผู้ป่วยนอกในประเทศเวียดนาม (Cost Effectiveness of Peer Supported Group Intervention Program Among HIV Treated Patients in Outpatient Clinics in Vietnam.) อ.ที่ปรึกษาวิทยานิพนธ์หลัก: นพพล วิทย์วรพงศ์, 78 หน้า.

งานวิจัยนี้จัดทำขึ้นเพื่อวิเคราะห์ต้นทุนของการมีกลุ่มสนับสนุนผู้ป่วยจากมุมมองทางสังคม เพื่อวัดระดับประสิทธิผลของการมีกลุ่มสนับสนุนนี้ในกลุ่มผู้ใหญ่และเด็กที่ติดเชื้อ HIV ในประเทศเวียดนาม และใช้การวิเคราะห์ต้นทุนประสิทธิผลเพื่อวัดผลกระทบทางเศรษฐกิจของการมีกลุ่มสนับสนุนผู้ป่วยดังกล่าว

งานวิจัยนี้พิจารณาผู้ป่วย 2 กลุ่มหลัก ได้แก่ กลุ่มผู้ใหญ่และกลุ่มเด็ก ในกลุ่มผู้ใหญ่ การมีกลุ่มสนับสนุนผู้ป่วยเน้นการไปตรวจเยี่ยมที่บ้าน โดยเก็บข้อมูลพื้นฐานและติดตามต่อไป 24 เดือนหลังเริ่มโครงการ ผลลัพธ์ทางสุขภาพที่ต้องการศึกษา ได้แก่ อัตราการรับประทานยาตามที่แพทย์สั่ง ร้อยละของกรณีล้มเหลวที่ไม่มีส่วนของไวรัส และความสูญเสียปีสุขภาวะจากความผิดปกติ ในกลุ่มเด็ก การมีกลุ่มสนับสนุนผู้ป่วยเน้นการโทรศัพท์ไปที่บ้าน โดยเก็บข้อมูลพื้นฐานและติดตามต่อไป 16 เดือนหลังเริ่มโครงการ ผลลัพธ์ทางสุขภาพที่ต้องการศึกษา ได้แก่ อัตราการรับประทานยาตามที่แพทย์สั่ง และร้อยละของกรณีล้มเหลวที่ไม่มีส่วนของไวรัส ในการศึกษาของทั้งสองกลุ่ม ผู้ป่วยถูกแยกแบบสุ่มออกมาเป็น 2 กลุ่ม คือ กลุ่มเปรียบเทียบที่ไม่มีกลุ่มสนับสนุนผู้ป่วย และกลุ่มทดลองที่มีกลุ่มสนับสนุนผู้ป่วย

การวิเคราะห์ต้นทุนพิจารณาค่าใช้จ่ายทั้งหมด ทั้งในมุมมองของของผู้ป่วย ผู้ให้บริการ และ ผู้ซื้อบริการ อันหมายถึงผู้ให้ทุนในการบริหารจัดการการมีกลุ่มสนับสนุนผู้ป่วย ต้นทุนต่อหน่วยนั้นคำนวณโดยวิธีแบบ top down ที่มีการคิดลดต้นทุนในแต่ละปีเนื่องจากข้อมูลมาจากหลายปี นอกจากนี้ ยังมีการคำนวณต้นทุนประสิทธิผลด้วยการหารต้นทุนเฉลี่ยด้วยผลลัพธ์ทางสุขภาพที่ต้องการศึกษาแต่ละตัว

งานวิจัยนี้พบว่า ในกลุ่มเปรียบเทียบและกลุ่มทดลองของผู้ป่วยผู้ใหญ่ ต้นทุนเฉลี่ยอยู่ที่ 86.95 และ 72.64 เหรียญสหรัฐตามลำดับ ในขณะที่ต้นทุนประสิทธิผลส่วนเพิ่มของการมีกลุ่มสนับสนุนผู้ป่วย เมื่อเปรียบเทียบกับอัตราการรับประทานยาตามที่แพทย์สั่ง ความสูญเสียปีสุขภาวะจากความผิดปกติ และร้อยละของกรณีล้มเหลวที่ไม่มีส่วนของไวรัสเท่ากับ 2,947 และ 1,706 และไม่มีนัยสำคัญตามลำดับ ในกลุ่มเปรียบเทียบและกลุ่มทดลองของผู้ป่วยเด็ก ต้นทุนเฉลี่ยอยู่ที่ 185 และ 136 เหรียญสหรัฐตามลำดับ ในขณะที่ต้นทุนประสิทธิผลส่วนเพิ่มของการมีกลุ่มสนับสนุนผู้ป่วย เมื่อเปรียบเทียบกับอัตราการรับประทานยาตามที่แพทย์สั่งและร้อยละของกรณีล้มเหลวที่ไม่มีส่วนของไวรัสไม่มีนัยสำคัญ

สาขาวิชา เศรษฐศาสตร์สาธารณสุขและการจัดการบริการสุขภาพ ลายมือชื่อนิสิต .....

ลายมือชื่อ อ.ที่ปรึกษาหลัก .....

ปีการศึกษา 2557

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KEYWORDS: HIV/AIDS / PEER SUPPORT GROUP / COST OF PEER GROUP SUPPORT / กลุ่มสนับสนุน / อัตราการรับประทานยาต้านไวรัสตามที่แพทย์สั่ง / ต้นทุนของการมีกลุ่มสนับสนุนผู้ป่วย

VU THI QUYNH MAI: Cost Effectiveness of Peer Supported Group Intervention Program Among HIV Treated Patients in Outpatient Clinics in Vietnam.. ADVISOR: NOPPHOL WITVORAPONG, Ph.D., 78 pp.

This paper analyzes the cost of providing a peer-support group intervention from the society's perspective, measures the effects of the intervention among HIV infected adults and children in Vietnam, and employs the method of incremental cost effectiveness ratio to quantity the economic impact of the intervention.

This study considers two study cohorts: adult and children cohorts. In the (HIV-infected) adult cohort which was already completed, the principal peer-support group intervention was the provision of home visits. Data on the adult cohort include baseline data as well as data on the subsequent 24 months of follow-up. Health outcomes of interest are the drug adherence rate, the percentage of non-viral failure cases and disability adjusted live years (DALYs). In the (HIV-infected) children cohort, which is still ongoing, the main intervention has been the provision of phone calls. Data on the children cohort include baseline data as well as data on the subsequent 16 months of follow-up. Health outcomes of interest are the drug adherence rate and the percentage of non-viral failure cases. In each cohort, enrolled patients were randomly assigned into either the control group where the peer-support group intervention is not provided or the intervention group in which the intervention is provided.

The costing analysis involves expenditures from the patient's, the provider's and the purchaser's perspective, where the purchaser in this case refers to NGOs who provide funding for the intervention. The total unit cost is estimated using a top-down approach with discounting techniques taken into consideration as the data analyzed span over the period of one year. Cost-effectiveness analyses are also performed, with the cost effectiveness ratio being the average total cost divided by the respective health outcome.

The study finds that, for the control and the intervention groups within the adult cohort, the average unit costs are $86.95 and $72.64. The incremental cost effectiveness ratios per 1% drug adherence rate and per one DALY reduced are $2,947 and $1,706 respectively. The ratio is not significant for the percentage of non-viral failure cases. For the control and the intervention groups within the children cohort, the average unit costs are $185 and $136 respectively and the incremental cost effectiveness ratio proves to be insignificant for all health outcomes considered for the children cohort.

Field of Study: Health Economics and Health Care Management Student's Signature .....
Advisor's Signature .....
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List of Abbreviation

HIV:	Human immunodeficiency virus
AIDS:	Acquired immunodeficiency syndrome
WHO:	World Health Organization
VAAC:	Vietnam Administration of HIV/AIDS Control
UNAIDS:	Joint United Nations Program on HIV/ AIDS
ART:	Antiretroviral therapy
ARV:	Antiretroviral
PSG:	Peer supported groups
OPCs:	Out Patient Clinics
CD4:	Cluster of differentiation 4
VL:	Viral load
GC:	Control group
GI:	Intervention group
VCT:	Voluntary Counseling Testing
DALY:	Disability adjusted life year
YLL:	Year lives lost due to mortality
YLD:	Year lives lost due to disability
OIs:	Opportunistic infections
DOTARV:	Directly observation therapy of antiretroviral in adult cohort
HIVCHI:	PSG intervention in children cohort

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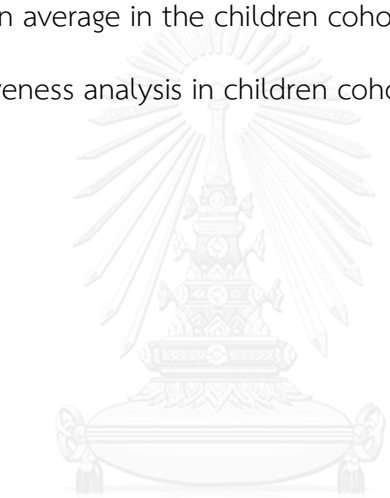

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CHAPTER 1: INTRODUCTION

1.1. Rationale

HIV/AIDS is still one of the leading diseases causing human fatality, suffering and serious medical crisis globally. In several countries, HIV/AIDS is a heavy burden to patients' families and the society. The disease affects national economy through high cost burden and consumes exorbitant a lot of national resources. According to the World Health Organization (WHO, 2014), the pandemic has taken approximately 30 million lives during the two latest decades. The number of people living with the disease reached 35 million worldwide, of which 3.5 million were children. The incidence of HIV/AIDS was at 2.1 million all around the world. Vietnam has around 250,000 people living with human immunodeficiency virus, including 5,000 children (UNAIDS, 2013). The coverage rate of antiretroviral therapy (ART) was 33% for the population general and 3,000 children received ART in particular.

There is neither a comprehensive curing medicine nor vaccine for HIV/AIDS. Currently, antiretroviral is the only therapy to control the disease. Antiretroviral therapy (ART) greatly reduced morbidity and mortality due to the HIV disease (Ledergerber et al., 1999; Palella et al., 1998). The therapy suppressed the progress of HIV ribonucleic acid (RNA) level and CD4 cells development. ART not only improves HIV infected patients' health status and quality of lives but also encourages them to be productive. However, HIV/AIDS is a chronic disease and it requires long term adherence to the treatment. Patients with strong compliance to antiretroviral drug regimen were reported to react better with ART's effects (Gulick et al., 2000). It is importance to ensure the patient compliance to maximum effects of this therapy.

In general, patient compliance to treatment of chronic illnesses remains around 50% in developed countries while in developing countries it is estimated to be much higher (WHO, 2014). Similar issue in HIV/AIDS treatment, Gavin Steel (2007) showed ARV adherence rate varied from 37% to 83%, depending on the clinical

stage. In Vietnam, a research on patient compliance to ART showed an average of 92.6% that patients sticks to the treatment Le (2008). This rate however declined gradually from 95% to 85% toward the higher antiretroviral regimen. Two studies were conducted at major pediatric hospitals in the north and the south of Vietnam namely the Vietnam National Pediatric Hospital and Vietnam Children Hospital 1. The results of the study showed the inconsistency of children complying with ARV. The adherence rate to ART in Vietnamese children ranged from 74.6% to 94.4% (Doan Thi Thuy Linh, 2011; Mai Dao Ai Nhu, 2009). Some factors may affect treatment adherence, including patient's age; connection between physicians and patients; patients' addiction to drugs or alcohol and more. Hence, it is necessity to provide more intensive care to HIV/AIDS patients to improve their compliance to the treatment.

Several meta-analyses showed the significant relationship between intensive counseling and better patient's compliance in chronic illnesses. The intensive intervention was categorized to various modes namely: the directly observed treatment (DOT), reminding via beeper or phone messages, delivering consultation directly by health professional or peer group support or health promotion. A Cochrane systematic review by Rueda et al. (2006) provided evidence of adherence outcome improvement associated with 12 weeks of patient support and education interventions. The model of trained peer supporters was applied to deliver health promotion and HIV/AIDS prevention knowledge to local community via both individual and group counseling. The intervention includes several activities such as reminder of medication adherence, sharing the experience in solving adherence difficulties and emotional, directly support via home visits, group meeting or contacting through mobile phone. For some regions, social discrimination to HIV/AIDS patients is so serious that the infected people exclude themselves from public contact. Hence, peer supported groups, who normally have strong sympathy with the HIV/AIDS issues are expected to spread awareness on the intervention to the sensitive population. Additionally, PSG also support patients at initial stage to create

the habit of taking ARV on a timely and regularly basis, thus long lasting outcomes of the model.

In Vietnam, a randomized controlled trial about the effects of peer supported group to HIV infected patients was conducted at adult population (Do Duy Cuong, 2012; Vu Van Tam, 2012). Cost effectiveness of this model has not been very popular. Evidence of intervention effects into children with HIV population is also scarce. Hence, this study proposes a cost effectiveness analysis of the counseling by peer supported groups into both adult and children to consolidate the effects of this intervention in Vietnam.

1.2. The research questions

a. Primary question

What is the cost effectiveness ratio of the counseling intervention by peer supported groups among HIV treated patients in Outpatient Clinics in Vietnam?

b. Secondary questions

Adult cohort

1. What is the cost effectiveness ratio of the counseling intervention by peer supported group per adherence rate gained among targeted patients?
2. What is the cost effectiveness ratio of the counseling intervention by peer supported group per case of non-virological failure increase, measured by CD4 cell count and viral load level among targeted patients?
3. What is the cost effectiveness ratio of the counseling intervention by peer supported group per disability adjusted life years (DALY) reduced among targeted patients?

Children cohort

1. What is the cost effectiveness ratio of the counseling intervention by peer supported group per adherence rate gained among targeted patients?

2. What is the cost effectiveness ratio of the counseling intervention by peer supported group per case of non-virological failure increase, measured by CD4 cell count and viral load level among targeted patients?

1.3. The research objectives

a. General objective

To evaluate the effectiveness and economic impact of the counseling intervention by peer supported groups among HIV treated patients in Outpatient Clinics in Vietnam.

b. Specific objectives

Adult cohort

- To analysis the total cost of doing peer supported group intervention, which observed from the society perspective or the combination of purchaser's, provider's, and patient's point of views.
- To evaluate the effectiveness and economic impact of the counseling intervention by peer supported group among targeted patients in terms of ART adherence, DALYs lost and non-viral failure, measured by CD4 cell count and viral load level.
- To assess incremental cost effectiveness among patients in difference stages of adherence and intensive counseling provided.
- To monitor the effect of PSG intervention on patient compliance via multi–method tools of measuring ART adherence via visual analog scale and subjective report.

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Children cohort

- To analysis the total cost of doing peer supported group intervention, which observed from the society perspective or the combination of purchaser's, provider's, and patient's point of views.
- To evaluate the effectiveness and economic impact of the counseling intervention by peer supported group among target patients in terms of ART adherence rate and non-viral failure result.
- To assess incremental cost effectiveness among patients in difference stages of adherence and intensive counseling provided.
- To monitor the effect of PSG intervention on patient compliance via multi–method tools of measuring ART adherence via pill count, medical refill and subjective report.

1.4. The scope of study

This cost effectiveness study uses data from two randomized controlled trials of the adult and children population. Both of trials were conducted to observe the effects of PSG intervention to first line of ART treated patients in 24 months. Adult patients were enrolled from four outpatient clinics (OPCs) in Quang Ninh province (Northern) and the children came from three OPCs of major pediatric hospitals in the north and the south in Vietnam. The trial in adult cohort was done with baseline and 24 months of follow-up from 2007 to 2009. Till now, the children cohort is still in the process with baseline and only 16 months of follow-up done with some patients. All patients were assigned randomly to two sides of the study to follow-up in 24 months, particularly:

Control group (GC): Enrolled patients were provided standard care as in national guidelines including ARV medication and routine clinical check-up. The viral load tests were also given every 6 months with CD4 and VL counts.

Intervention group (GI): Enrolled patients got the standard care, viral load test and intensive counseling by trained peer supported groups (PSG). The PSG intervention team implemented treatment through different modes of communication such as home visiting, individual counseling, peer group meeting and mobile phone counseling to the patients in this group.

1.5. Expected benefits

The study can potentially benefit to Vietnam Ministry of Health, the Vietnam Administration of HIV/AIDS Control, the national strategy of HIV/AIDS prevention program, the Infectious and Laboratory Department of study sites, the enrolled HIV infected patients and scholars related to healthcare policy, healthcare project management and health economics. The study is expected to provide the acknowledgement costing analysis for PSG intervention and its effectiveness outcomes. It also support the policy maker and healthcare planner in term of evaluate this intervention before applied widely. In particular, the main intervention focus on improve patient commitment to the treatment at both children and adult to maximize the effects of HIV/AIDS therapy. Hence, together with the cost estimation in providing control program, appropriate resources distribution would be proposed to enlarge interventions effects with acceptable cost.

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CHAPTER 2: BACKGROUND

2.1. National picture of HIV/AIDS disease

According to the report of Institution of Health Metrics and Evaluation in 2013, the burden of disease in Vietnam for HIV/AIDS has raised rapidly to the top 3 leading nation burden, following stroke and road injury in the century 21 ((IHME), 2013). Publication by the Vietnam Ministry of Health (MOH, 2006) reported that HIV/AIDS disease has spread rapidly to the whole nation since the first reported case in Ho Chi Minh City in 1990. The number of HIV infected patients increased dramatically from 3,000 reported cases in 1992 to more than 300,000 cases in 2010. The growth rate doubled every two years from 1992 to 2000, which were slower thanks to the control strategy of the Ministry of Health (Figure.1). The density of people living with HIV stayed the most at Mekong River Dental area. Figure.2 showed the estimated number of HIV patients in Vietnam by cluster in 2005, the Mekong River Dental region occupied around 23% of total HIV infected population, followed by Ho Chi Minh City with 19%. In general, the percentage of estimated of HIV infected were separated almost equally to injecting drug users, current clients of sex workers, general male and female population who transmitted by their partner and only 4% for the female sex worker population (figure.3).

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Figure 1. Estimated number of people living with HIV, Vietnam, 1992 -2010

Source: publication by the Vietnam Ministry of Health (MOH, 2006)

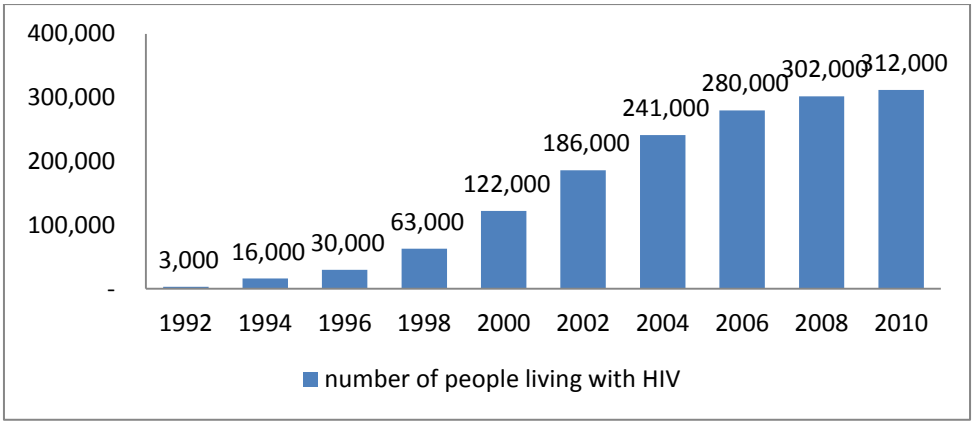


Figure 2. Estimated number of people living with HIV by provincial cluster, 2005

Source: publication by the Vietnam Ministry of Health (MOH, 2006)

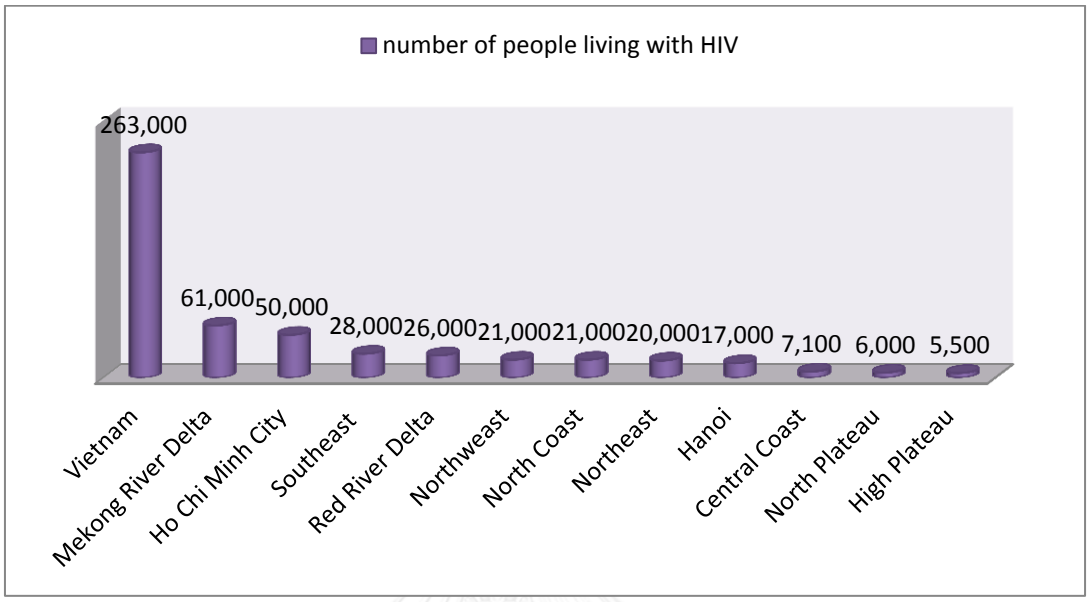
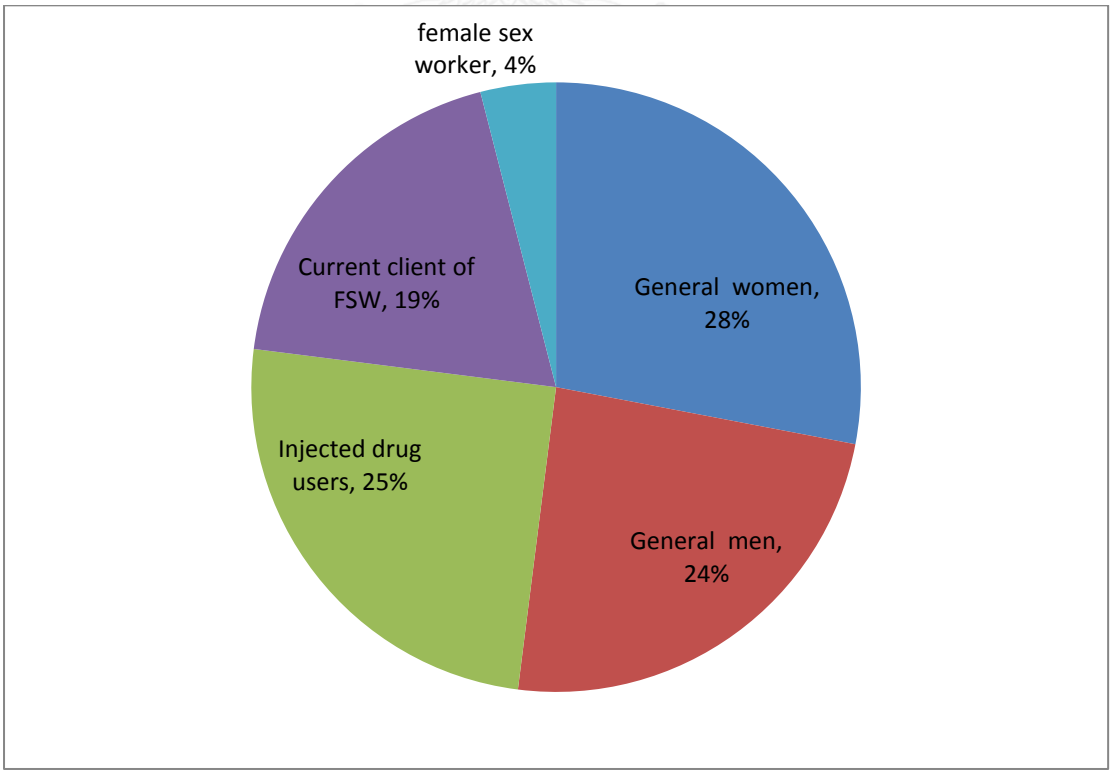


Figure 3. Distribution of estimated HIV cases by risk group, 2005

Source: publication by the Vietnam Ministry of Health (MOH, 2006)



According to the Vietnam Administration AIDS Control organization (VAAC (2005), the principle age group of HIV infected population was in the group between 20-39 years old. The incidence of children was 7 cases in 1997; 68 cases in 1998; 46 cases in 1999; 67 cases in 2000; 73 cases in 2001 and 57 cases in 2002. Hence, the disease affected a lot to the main working force and younger generation.

2.2. HIV/AIDS prevention in Vietnam

Several programs was implemented to reduce the burden of disease such as Harm reduction programs; Condom distribution campaign; Needles and Syringes programs; Methadone Maintenance Therapy; safety Blood transfusion; mother-to-child transmitted prevention and Voluntary HIV Counseling and Testing (VCT). The Ministry of Health has been working with another department to ensure the provision of services and promote needed knowledge to the society. Young people were provided more knowledge to strengthen their awareness of the disease. Media mass such as magazines, television programs, commercial film, banners and campaigns featuring HIV campaign messages have been delivered to the targeted populations. The success of these efforts is well seen through the rapid increase in the number of people who have access to HIV prevention, nation care and support services.

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Vietnam has received several funds for HIV/AIDS control from overseas, which all focus on the disease prevention and treatment component. The major donation comes from Global Fund, which is the non-profits organization created by the United Nation. They funded 12 million US dollar in 4 years to develop the comprehensive healthcare system for HIV/AIDS infected population in Vietnam. The Global Fund also provided resources to educate and up skill medical staffs and the whole community in general. Models of voluntary counseling testing; community actions and peer supported group were also created. The fund also supports the procurement of medical technologies such equipment, infrastructure and ARV medication for the healthcare system in controlling HIV/AIDS. However, this fund was decreased since Vietnam moved from the group of low-income countries to the middle-low income area. Hence, it is important to evaluate disease control program at both effectiveness

and economics aspect as Government would now have to commit partial funding from within the country. The model of peer supported group is considered as a cost effectiveness option to control the consequences of disease in the HIV patients.

2.3. Peer supported groups intervention projects

The peer supporters were generally nurses or HIV infected people working as community staffs. They were trained and educated to acquire all requirement of social ability; treatment adherence attitude, education and being an enthusiast about helping those HIV/AID patients. All supporters were trained to have general knowledge about HIV disease, opportunistic infections disease prevention, mental health, antiretroviral therapy, medication adherence support and nutrition for HIV infected people. Additionally, special skills in communication, counseling and in depth interview were provided. The training curriculum followed booklet of Family Health International in home-based care (2005) and the communication between health services and individual in the Global Observatory for e-Health series of WHO (2003).

Each supporter responded for a group of 10 – 15 patients. Supporters were required to report about their work weekly. They had to interview their group members following the provided questionnaire. Thus, information of adherence assessment was collected. PSG intervention mainly included two type of counseling. They were in particular, home visits and phone connection. The former method was conducted as home visit by the PSG twice a week in the first 2 months of follow-up, which was reduced to once/week if patient compliance improved. The latter method required at least one telephone contact with patients or caregivers per week.

2.4. Target population

This cost effectiveness study analyzes the impacts of PSG model to HIV infected patients in the first line of ART regimen. The study used information of 2 cohort that are adult and children. Adult patients came from four OPCs in Quang

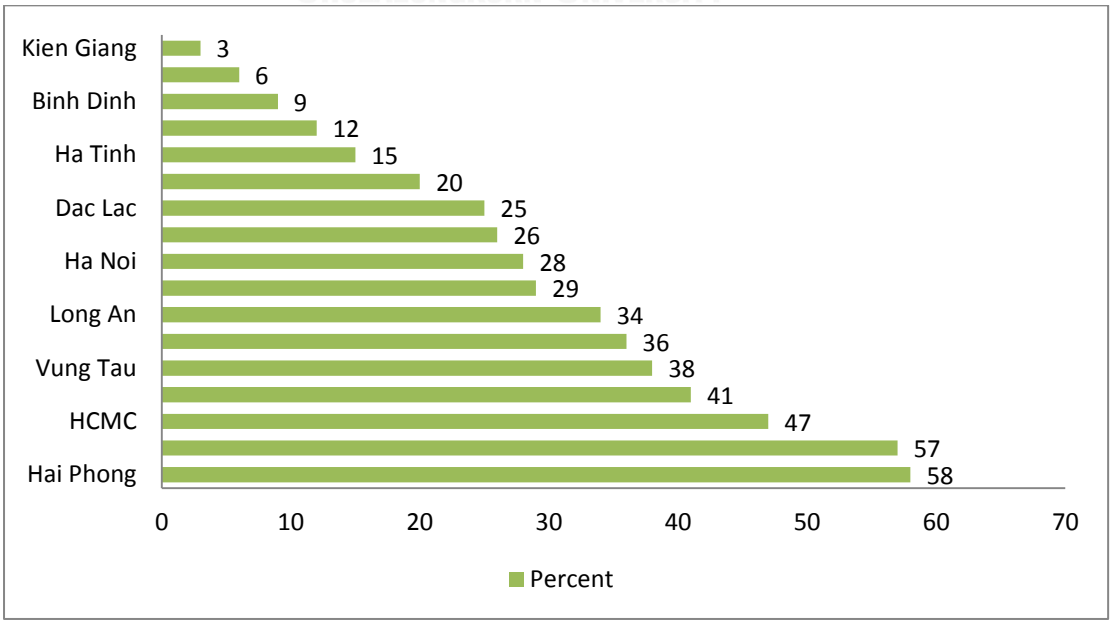
Ninh province, whilst children patients came from three OPCs of Vietnam National Pediatric Hospital in the north and Children Hospital 1 and Children Hospital 2 in the south. All of them were naïve in antiretroviral treatment.

2.5. HIV infected adult cohort

The adult cohort was conducted as institutional based in Quang Ninh province with both urban and rural settings. The province is located in the North Coast of Vietnam and also near the biggest Northern international port. The province has natural properties of coal and sea resources, thus, coal mining, fisheries, and tourism are the main industries. Quang Ninh was also one of top five regions affected by the HIV/AIDS disease (MOH, 2006). This province suffered greatly the burden of disease when it had a lot of injected drug users. In general, the population in Quang Ninh was in the very high risk group of possibly transmitting HIV/AIDS to the community. Due to the characteristic of the principle occupants or carrier of disease, who mostly lived as group and far from family, the compliance of HIV infected patient to ART was not stable. Hence, the PSG intervention brought several social benefits to this province.

Figure 4. Percentage of injected drug users testing positive for HIV, 2005

Source: Vietnam HIV/AIDS Estimates and Projection (VAAC, 2012)



Data of this cohort is borrowed from the "directly observed therapy for antiretroviral" (DOTARV) project, which was conducted from 2007 to 2009 with principally home visits intervention. This intervention program was done within 12 months of baseline and 24 months of follow-up. The control trial was assigned randomly by cluster. There were 59 enrolled clusters, which included 30 clusters in the intervention group and 29 clusters in the control one. Overall, there were total 311 patients in intervention group and 283 patients in control group.

2.5.1. Inclusion criteria:

All naïve patients were registered for long term treated at 4 commune outpatient clinics of the province. They were indicated to apply ART at first stage of treatment following the national guidance for adult with HIV. In particular, these patients used the ARVs combination of AZT; 3TC; NVP; EFV; D4T and TDF only.

2.5.2. Exclusion criteria:

To avoid the loss of follow-up, patients referred from other clinics were not invited to join the project. Patients were excluded from participating in another intervention program simultaneously; maternity care and metal related treatment to reduce the contamination.

2.5.3. Principal intervention

Beside national standard care provided by Government for HIV/AIDS patient, viral load tests were given to all enrolled patients either in intervention or control group. The additional counseling by trained peer supporters was delivered to patients in intervention group only. One supporter responded the counseling for a group of 10-15 patients. Twice a week home visits were held in the first 2 months, which was replaced by visiting monthly latter on. The supporter had to complete the adherence checklist form which included pills count, time point to take pills, doses missed and opportunistic infectious symptoms.

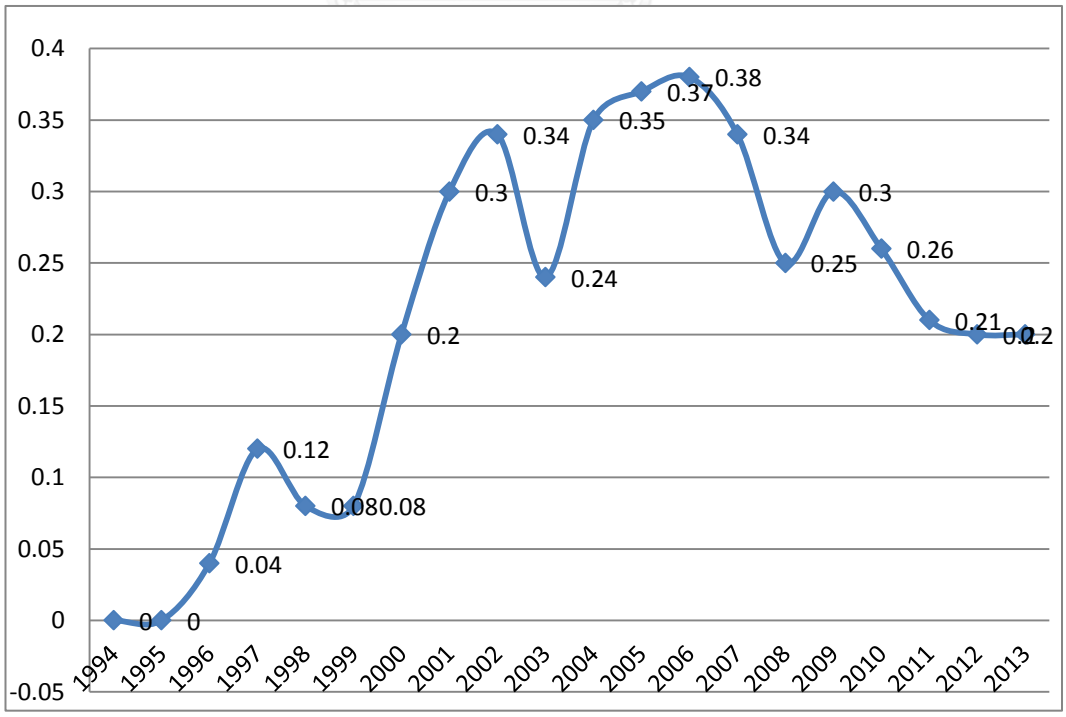
Acknowledgement of PSG intervention in this cohort was published internationally. The effects of intervention was basically shown via virological result and mortality rate in the study of Do Duy Cuong (2012); whilst the outcome of

quality of life improvement was added in the related study of Vu Van Tam (2012). This cost effectiveness study is expected to contribute in more detail about costing analysis of the intervention to consolidate the outcomes of the model.

2.6. HIV infected children cohort

According to the report of UNAIDS (2014), the accumulated of number of HIV infected pregnant women increased over the last decade in Vietnam, it however slowed down gradually. Several studies conducted in HIV pregnant women confirmed the spreading of epidemic to younger generation. The number of children living with HIV still increased gradually. Annual report of the Vietnam Administration of AIDS Control also indicated that only 57.9% of 5,000 HIV children were covered by antiretroviral therapy and treatment compliance was unstable among them. Hence, all factors show the strong requirement in doing more intervention into this part of HIV infected population.

Figure 5. HIV prevalence among pregnant women 1994-2013 (source: (VAAC, 2012).



The trial at children cohort was initiated in 2013 and is still in progress now. Enrolled children came from 3 major pediatric hospitals namely: in the north is Vietnam national pediatric hospital (NHP); in the south are Vietnam Children Hospital 1 and 2. This cohort has been done with one year of baseline and 16 months of follow-up for some patients. Majority of reported records was found to stop their series at the end of 8th and 10th month follow-up. HIV infected children came from several provinces around the country. Hence, the enrolled patients were classified based on the distance from their home to the OPC, which was summarized in table.1.

Table 1. Groups of patient by distance from their home to OPCs in children cohort

Grouping patient	Control group	Percentage	Intervention group	Percentage	Total	Percentage
Distance < 40km	83	38%	75	35%	158	36%
Distance (40km-80km)	82	38%	81	38%	163	38%
Distance > 80km	52	24%	60	27%	112	26%
Total	217	100%	216	100%	433	100%

2.6.1. Inclusion criteria:

All patients were registered for long term treated at three OPCs in mentioned hospitals. They were treated with the first regimen of ART following the national guidance for children with HIV, namely the combination of AZT; 3TC; NVP; EFV; D4T; ABC and LPV/r.

2.6.2. Exclusion criteria:

Similar to the adult cohort, all temporary patients at project sites were excluded. Children age was required to range from 0-12 years old to avoid the loss of follow-

up. To reducing the contamination, patients were excluded from participating in another intervention program simultaneously and metal related treatment. That sibling is possible to have same caregiver. To avoid the contamination of having same caregiver, children who their sibling already joined the project were excluded.

2.6.3. Principal intervention

Basically, the study design of children cohort is similar to the adult one. Standard care and viral load tests were provided to children in both groups and the additional counseling by PSG was added to intervention group only. Children were assigned randomly to either control or intervention group. All PSG activities were delivered indirectly to the children but to their caregivers. The peer supporters maintained connection with caregivers in their group principally via phone calls or phone messages. The home visit was also provided to cases where caregivers were not available by phone or cases of bad ART adherence behavior detection. The group meeting also held among project researchers, supporters; caregivers and children in the intervention group. These meetings provided knowledge in how to nourish and prevent virus resistance, experiences in educate HIV children to avoid of stigmatized or social evils were also shared.

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Evidence about effectiveness of the PSG intervention model to children has not been done well in Vietnam till now. This study is expected to briefly describe the effectiveness of PSG intervention to children population and also contributes costing analysis alike the adult cohort.

CHAPTER 3. LITERATURE REVIEW

3.1. Cost effectiveness studies

Cost effectiveness analysis (CEA) is one of principle practical tool in assessing healthcare programs and it does provide essential information for the healthcare decision makers in weighting the efficiency among interventions. In the context of scarcity resource, cost effectiveness analysis is more valuable thanks to the ability of detecting intervention that maximize effectiveness at the most competitive costs (Atherly, Culler, & Becker, 2000). Calculating the cost effectiveness ratio (CER) is primary function of a cost effectiveness analysis, which helps to compare alternative healthcare interventions regard to their resource expenditure (costs) and outcomes (effectiveness), presented as CER = C1 : E1 (: this sign indicates division or what).. In addition, the incremental cost-effectiveness ratio (ICER) is also involved to indicate additional benefits between two interventions or related to the randomized controlled trial study, it is the unit cost of an additional intervention. Particularly, the incremental cost-effectiveness ratio will be calculated by the quotient of the additional cost to the additional outcome, presented as ICER = (C1-C2) : (E1-E2). Nonetheless, the cost effectiveness analysis has some limitations in term of the uncertainty of employed data at both cost and outcomes side, which are natural sampling errors or the inappropriate measurement of inputs (cost and outcomes). Thus, sensitivity is the resolution to address the mentioned issues (Weintraub & Cohen, 2009). The simple sensitivity analysis model will vary one or multi parameter of the inputs assumption to indicate the difference and reduce the uncertainty of the ICER. The impact of each involved variable in doing CER and ICER will be illustrated partly via sensitivity analysis. In advance, a threshold analysis should be examined to identify the critical value of parameters changing the study conclusion (Briggs, Sculpher, & Buxton, 1994).

3.2 Cost analysis related to intervention in improving treatment adherence

Schackman et al. (2005) conducted a research in US in 1999 with the purpose of analyzing the direct costs of intervention programs to treatment adherence development. According to the characteristics and the frequency of each intervention, all costs were classified and assigned to different cost functional blocks namely providers, incentives, administration, home delivery, reminder tools and other indirect costs. The median direct unit cost components were defined clearly by the perspective of purchaser, provider and society, which were varied slightly amongst them. In general, the study revealed the median monthly direct costs per patient at $35 from the prospective of the purchaser, increased by $12 in societal perspective. Sensitivity and threshold analysis were mentioned and illustrated results via CEA curve graph; these studies took into consideration the variation of costs and outcomes by different perspectives, the adjustment in process of outcome measurement such as changing adherence leverage.

Before any costing calculation, all activities that might raise cost should be classified to appropriate cost categorizes to ensure that all possibility expenditure are covered and preventing the overlap (Creese, 1994). Cost can be classified by several methods such as by the difference in input, source, currency or by similar characteristic activity logs. In particular, input classification including recurrent and capital cost. The capital costs can be understood as expenditures occur only once a year and have the value greater than $100/unit. The total value of capital cost will be expense in several years by a specific depreciation method. Capital cost would include vehicle; building; equipment and non-recurrent costs. The recurrent costs mostly focus on all costs that occur regularly/monthly and have the value less than $100/unit. Recurrent cost would include human cost; maintenance and operation. Fixed cost and variable cost can be occurred at either capital or recurrent cost. The recurrent costs here are dominated the capital in term of cost component. Costs which occur for the similar function can be grouped as same activity log. In example, the training cost categorize would involve all expenditure for logistics, material

development, stipend for participants and fee for renting hall. In fact, input classification is more appropriated in analysis a completed cost database whilst the activities logs is used in estimating budget for a healthcare program.

After coding all costs, a measurement technique should be selected based on type of cost and research objective. There are three major methods in measuring cost, which are gross-costing (top-down); micro-costing (bottom-up) and the mixture of these mentioned approach (Smith, 2005). Top-down approach often applies to estimate the unit cost of homogeneous product. In this approach, total cost is combined from related cost elements at several cost categorizes, which is disaggregated to total unit of products/services. This method is appropriate in case of shortage of detail cost data, thus, the accuracy of this approach is insecure. Apart from gross-costing, the bottom-up method is more suitable for unique services/treatment. In this costing approach, every single cost is collected in detail from receipt or balance sheet. These cost elements then combine together as total unit cost or total cost of one specific group of services. Thanks to that, the quality of costing data base is ensured and all possibility costs are counted. However this process takes lot of time and resource. Furthermore, there are some costs that are very difficult to allocate to a specific unit of service such as joint cost items. Hence, to maximize the advantage of either top-down or bottom-up method, a mixture costing approach should be applied. Based on the source, the type of cost data, each cost component is assigned to apply one of two mentioned approach. Mixed approach can reduce the inaccuracy of top-down method and also control the fee of doing bottom-up approach. For the cost component that top-down or bottom-up approach is impossible to apply isolated, the mixed approach can address this problem.

3.3. The effectiveness of interventions to improve ART adherence

Several studies show the relationship between intensive counseling to HIV infected patients and their compliance to the antiretroviral therapy. Roter et al.

(1998) arranged a meta-analysis study to evaluate the effectiveness of several interventions, which was classified to three principal categories: education, behaviors and affection, from ART adherence of patients with HIV. The analysis recruited 153 related studies from 1977 to 1994 into account and also sorted their outcomes by health outcomes (opportunistic infectious diseases, compromised immune system), direct indicators (HIV RNA level, CD4 count, physical -neural development), indirect indicators (pill counting, refill record), subjective reports (patient self-report, physicians/supporter report) and utilization (clinical appointment retention). The effect side – "r" was employed as a weighted value in order to reduce the deviation due to large sample size variation. The study explored that all interventions would create certain effects to adherence indicators; however, the magnitude of them were varied amongst indicators. The direct and indirect indicators were affected by the interventions the most. Whilst the effects are quite small, it is an essential feature to improve health outcomes and utilization. There is no difference in terms of comparing the created effects amongst the interventions; the combination of the three types of intervention would result in a more significant and effective outcome if compared to any of them if isolated. In general, intensive interventions are proven to boost treatment adherence in not only antiretroviral therapy but also treatments for other chronic disease namely diabetes, hypertension.

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Researchers from the United States, Africa and Asia did find the efficacy of mobile phone counseling to HIV/AIDS infected patients. In particular, three studies from New York, Kenya and India were being reviewed to determine the effects of this type of intervention (Horvath, Azman, Kennedy, & Rutherford, 2012; Shet et al., 2014; Simoni, Pantalone, Plummer, & Huang, 2007). The target population was mainly HIV-infected adults with low socioeconomic status. All researches were created as cohort design where randomized controlled trial studies were set. Following the national guidance of each country about HIV/AIDS care, the standard was given to all subjects at control group such as routine clinical check-up, monthly medication refill and periodically internal stigma tests at some countries. The additional intervention was added into the vice versa group and generally similar in three studies. Researchers

trained physicians, health staffs or voluntary staffs in providing counseling services to HIV patient via phone. Each trained supporter had the responsibility of a group of 10 to 15 HIV patients and was communicated through various means such as phone calls, messages to their clients to educate about medication compliance and undertake health promotion. Overall, the three studies set their primary objective as the improvement in HIV/AIDS progression, defined by the raise of CD4 count and the fall of HIV RNA level. Their secondary objectives were varied at indicators but all of those measured the level of treatment adherence, the mortality and other factors of physical - neuro development. In conclusion, regardless of the improvement of both primary and secondary outcomes, they found no significant relation between their intervention to the outcomes due to the limited literature in adherence evaluation, insufficient exposure, low intensity or sample nature characteristic. Additionally, the systematic review set by Horvath et al. (2012) also proved the significance effect of weekly message to patient compliance enhancement.

3.4. Cost effectiveness analysis of intervention to improve ART adherence

There is little evidence about the cost-effectiveness of intervention into ART adherence around the world, thus, only three studies conducted in United State and Africa will be taken into account here. Firstly, Goldie et al. (2003) from the US explored the costs and effectiveness of clinical interventions (beeper, counseling, direct observed therapy) to the development of ART adherence of the HIV population in two urban health community centers at Boston. They classified the cohort population into three groups, early antiretroviral regimen, advanced antiretroviral regimen and an urban cohort. Several adherence interventions such as beeper, counseling, direct observed therapy, clinical check-up, home visit were applied additionally to the intervened group. All costs were assigned to the appropriate blocks which are annual ART regimen selection, viral test, principle adherence interventions, other interventions and monitoring costs. Together with the outcomes performed as the virologic results and the total cost to produce and increase one quality adjusted life year (QALYs) were calculated. In the early disease

cohort, the incremental ratio was indicated to reduce the risk of virological failure by 10% and increase the QALY by 3.2 months and the cost effectiveness ratio was at a low value of $50,000/QALY. The sensitivity factor here was the cost of intervention. If the cost was set at $100/month, virologic rate would be reduced by 10%, whereas, the risk would be exhausted up to 50% by adding $400 more into monthly interventions cost. The remaining cohorts were illustrated to decline only 25% of virologic failure by using $500 cost of intervention per month. Furthermore, the researcher also found that the effect of intervention to the early antiretroviral regimen is more cost effective than the other groups. The related paper of Freedberg et al. (2006) showed the cost effectiveness analysis of a specific intervention – nursing home visit. The same design and scope of study was applied with more concentration in the intensive counseling from the nurse by intervening twice weekly for the first 6 weeks. The cost effectiveness ratio was found at $14,100/ QALY gained. The viral suppression was seen to be sensitive with intervention efficacy, which would be positive with the decline of intervention's effects to target patients. All costs and outcomes were associated with the societal perspective and 3% discounting rate, and it was also weighted by other figures for more realistic such as the US wage figure.

Secondly, Zaric, Bayoumi, Brandeau, and Owens (2008) studied about the influence of high intense therapy in improving compliance to the treatment amongst third gender in United State. They estimated the cost effectiveness with 20 years simulated model. The patients were divided by 3 stages of their ART regimens that were initial regimen, the transition from 1st regimen to the 2nd regimen and the transition from HIV to AIDS; and they also located by HIV low , moderate and high prevalence regions. All of them will get the combination interventions of appropriate HIV treatment, adherence counseling and infection suppression and prevention. The authors assumed possible situation that could happen in 20 years for patient's drug resistance, HIV transmission and treatment adherence after the intervention. All costs and effectiveness outcomes were involved to this model to estimate for the future expected values. They were discounted at 3% and assumed to occur in the ideal

environment where disease transmission or population growth was stable. The odd ratio of 1.41 from literature review was employed to evaluating treatment adherence level in this 20 years simulation model. The average national wage and session time from registered nurses borrowed from outsourced literature were taken in to account for 65.7% of intervention costs. The analysis of adherence counseling was designed as the comparison of outcomes from baseline and the estimated outcomes in next 20 years among 3 cohorts classified by their adherence level. The interventions here were directly counseling from registered nurses or health professionals and in-clinical intervention via phones. Sensitivity analysis was focused on costing due to the wide range in estimation. The ICER of counseling activities was $25,500/QALYs gained in a cohort of 100,000 HIV infected individual. They also stated that cost effectiveness rate is the highest at moderate prevalence population, interpreting as the intervention impacted the most efficient at this population.

Finally, a systematic review from 24 studies at Africa was made to demonstrate the cost effectiveness of 31 interventions including voluntarily counseling and testing. Provider perspective was taken to measure the costs, categorized by treatment costs (medicine, viral testing), adherence intervention costs (home based intervention, counseling) and other not-mentioned activities. The principle outcomes were disability adjusted life years (DALYs), as the summation of year of life lost to premature mortality (YLLs) and year live lived with disability (YLDs). The incidence perspective was employed for YLDs calculation with positive tuberculosis as health event and the disability weighing for HIV patient at 0.505. The data of life expectancy and year life gained/ cured tuberculosis at both patient with and without HIV were collected. Together with 3% discounted rate, the cost effectiveness ratio voluntarily counseling and testing intervention were under $75/DALY gained, those for tuberculosis patient was only $20/DALYs gained. The home care based intervention varied from $100 to $1000 per DALYs; it confirmed the fact that this kind of intervention by specific healthcare organization was more expensive than it was conducted in community based. All the mentioned information supported the

government of Africa to address their problems of resource allocation for epidemic control in term of prevention, treatment and curing (Andrew Creese, 2002).

3.5. Lesson learn from literature review

In general, several interventions were implemented to enhance treatment adherence of HIV infected patients. From those, the direct observed therapy seems to be the most effective method; the cost of this intervention however is quite high. The cost effectiveness ratios of other interventions such as health professional and phone counseling are acceptable and feasible in the low-setting context resource. Studies in target population are various from general HIV infected patients to special cases as sex-workers, pregnancy female, patients in different ART regimens; however, most of them are in the working age. Hence, the population of children is omitted.

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CHAPTER 4: DATA & METHODOLOGY

4.1. Data recruitment

The expectation during data recruitment is to observe all enrolled patients in the timeline of 24 months, however this was quite challenging due to the destabilization of HIV/AIDS infected population. In the adult cohort, reasons such as a number of patients were sent to prison; death or some just moved to other regions. In the children cohort, there has not had death case and only 0.4% children moved out of outpatient clinic. The project is however in process, thus there are several difference in individual's total follow-up time. Hence, it is more accurate and reliable to observe the difference of two study sides within group of patients who had similar magnitude of follow-up time.

As mentioned in chapter 2, data of costs, adherence assessment; viral load test; OI infection and death are employed from two different cohorts, who are adult and children. For both cohorts, all effectiveness assessments were recorded at baseline and every 2 months for a total of 24 months of follow-up. The sub-groups are set as group of people with similar number of follow-up reports. The number of sub-groups in each cohort will be ranged from 1 to 12 representing for the magnitude of follow-up time from 2 months to 24 months.

4.2 Conceptual framework

At both cohorts, all costs are measured from the perspective of the society, which includes costs borne by purchaser, provider and patient. Effectiveness of PSG intervention is also defined and evaluated via pill counts; virological failure, DALYs lost and mortality rate. Cost effectiveness ratios and incremental cost effectiveness ratio are also calculated. From total unit cost of each year, average unit cost of the whole period is used as cost input of ICER and CER. Whilst, average effectiveness

outcome from the assessment at each sub-group is used as the remaining calculation's input. Conceptual framework is illustrated in the figure 6 and figure 7.

Figure 6. Conceptual framework for adult cohort

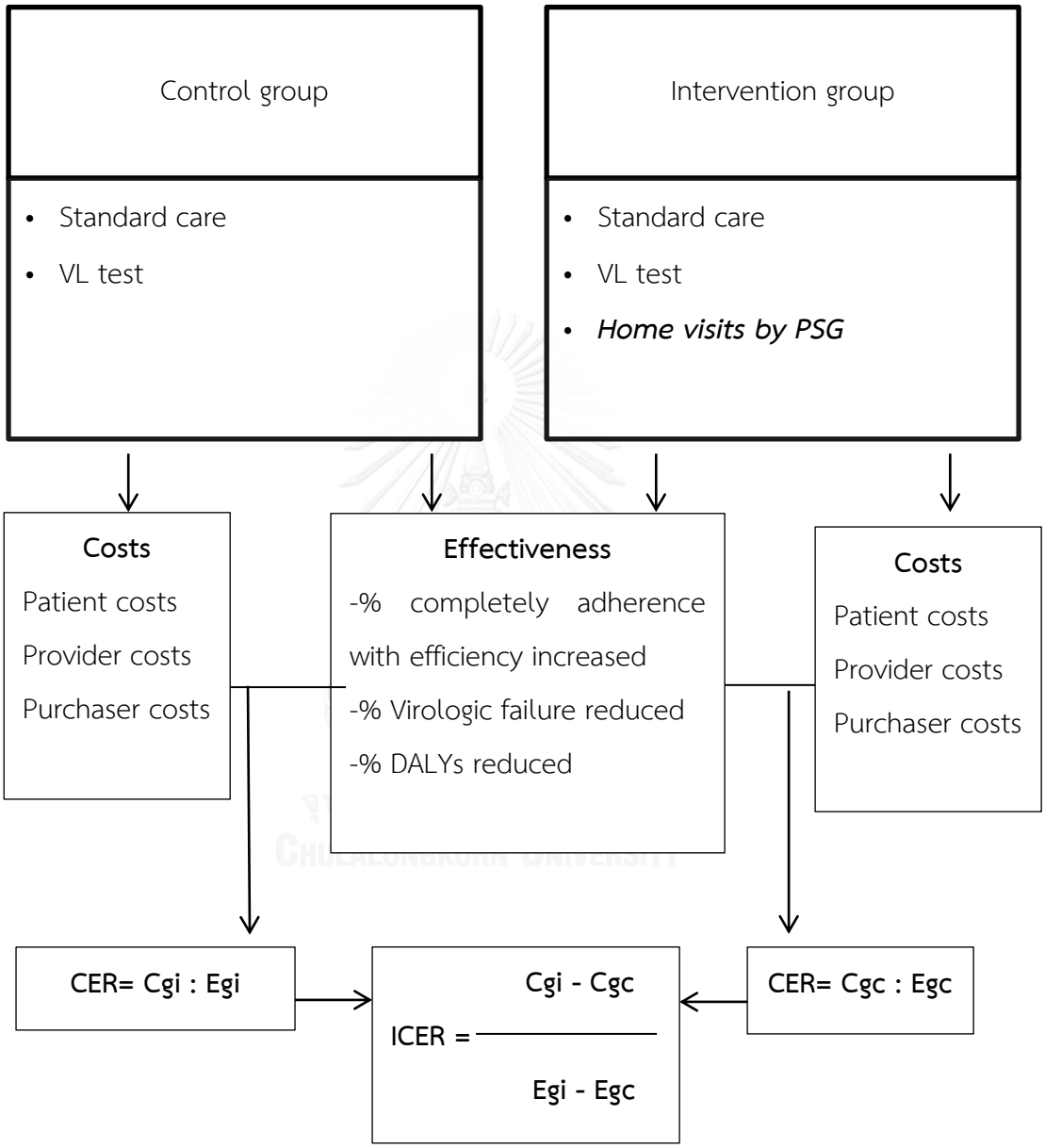
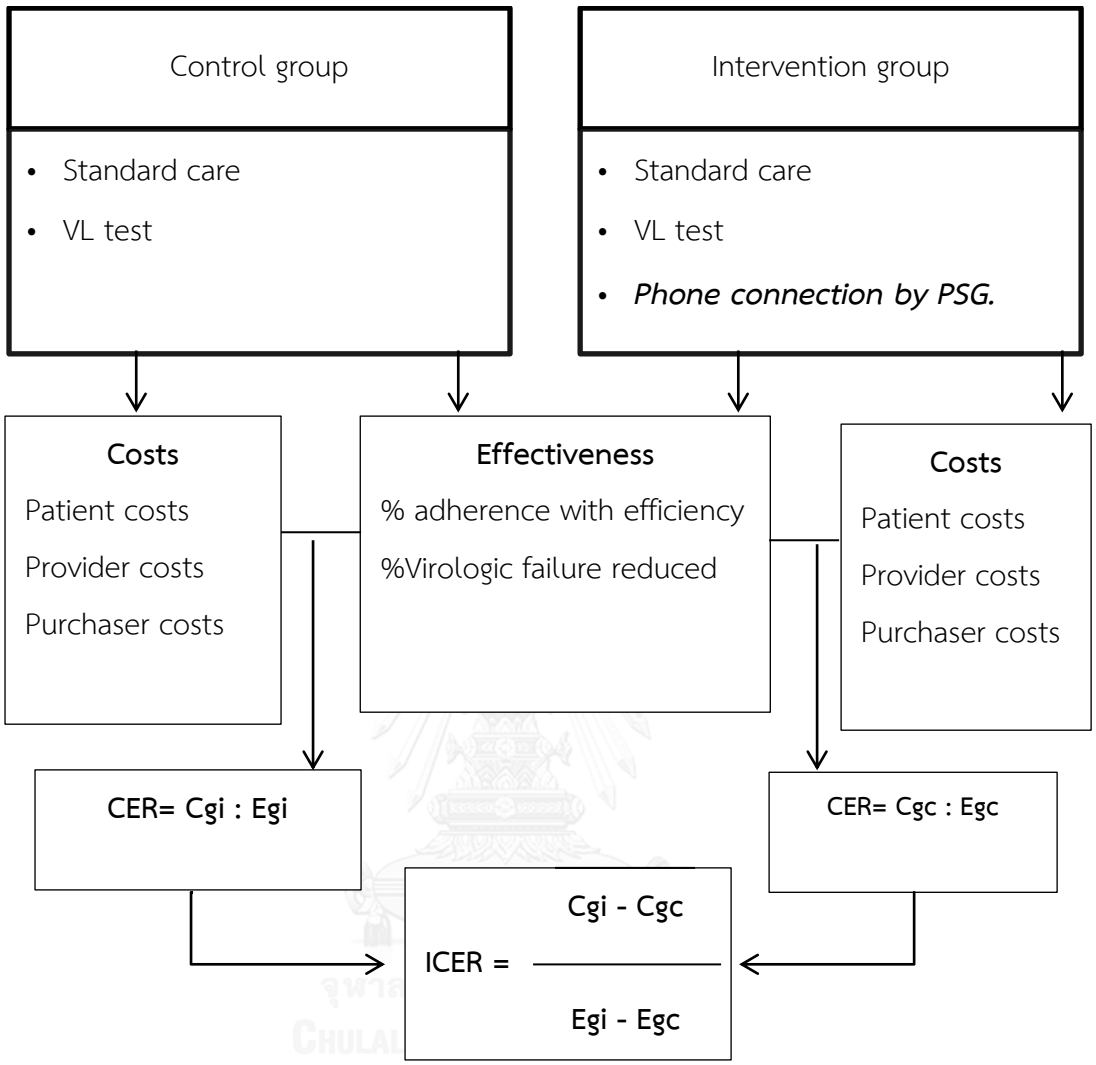


Figure 7. Conceptual framework for children cohort



4.3. Costing measurement

The cost effectiveness analysis uses secondary data and the costing is based on the societal perspective. Measurement of cost are discounted at 3% (Gold, 1996). Costs are determined and assigned to appropriate cost categorizes to cover all activities of the intervention. All costs are converted to US dollar using the exchange rate at project time, in particular the exchange rate to USD in adult cohort is $1 = dong 16,000; for the children cohort is $1= dong 20, 828.

From a societal perspective, the costs include all related cost borne by the provider; patient and purchaser. The same methodology is applied to costing analysis

at both adult and children cohort. All activities which might raise cost and their sponsor are summarized in table.2.

Table 2. Intervention Program Activities and its sponsor

No	Activities	Payer
1	Transportation cost from home to OPC	Patients
2	Non-ART treatment cost	Patients
3	ARVs medication cost	Provider
4	Salary and allowance for full time OPCs staffs	Provider
5	Salary and allowance for part time OPCs staffs	Provider
6	Medical consumable at OPCs (syringe, bandage, gauze…)	Provider
7	Stationery at OPCs (paper, ink, clipper…)	Provider
8	General cost at OPCs (electricity, water, telephone…)	Provider
9	Maintenance and repairing cost at OPCs	Provider
10	Annual Building cost of OPCs	Provider
11	Annual fixed asset cost of OPCs (equipment and furniture)	Provider
12	Salary and allowance for program staffs (coordinator, director, secretary, data manager…)	Purchaser
13	Administration fees (approval process, printing…)	Purchaser
14	Data collection (baseline & follow-up interview; data management)	Purchaser
15	Business trips	Purchaser
16	Monitoring trips	Purchaser
17	Trainings	Purchaser
18	Workshop	Purchaser

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19	Meetings	Purchaser
20	VL test cost (unit price per success test)	Purchaser
21	Renting fee for the office of the program	Purchaser
22	Stationery at programs office (paper, ink, clipper…)	Purchaser
23	General cost at program office (electricity, water, telephone…)	Purchaser
24	Maintenance and repairing cost at program offices	Purchaser
25	Annual fixed asset cost of programs (equipment and furniture)	Purchaser
26	Meetings with patients to doing health promotion	Purchaser
27	Salary and allowance for supporter	Purchaser
28	Transportation for PSG to patients house	Purchaser
29	Mobile telephone allowance for PSG to call to patients	Purchaser
30	PSG meeting to report their works	Purchaser

Following the guidance of World Health Organization in doing costing analysis in primary care, costs were classified by input to either capital or recurrent cost (Creese, 1994). The capital costs are defined as the expenditure (normally unit cost bigger than $100) which occur only once and value for more than one year. The recurrent costs mostly focus on the maintenance, which are required to expend regularly (less than 1 year). Particularly, recurrent cost included personnel, material and operation whilst capital cost included the straight line depreciation of assets. These cost categorizes are defined quite similar from the perspective of provider and purchaser. They are contributed equally to each observation at both study sides. However, the direct cost of PSG intervention is contributed to the observations in intervention group only. Hence, costs, which are related directly to PSG intervention are grouped into one cost categorize to observe in detail. Apart from the two mentioned perspective, cost borne by patient differentiated by individual. Thus, cost

classification by input is not applied to all costs borne by patients. The expenditure for activities, which borne by provider and purchaser in table2, are assigned to appropriate cost categorizes, which describes in table.3.

Table 3. Program activities assigned to each cost categorize

For Provider		
No	**Cost categorized**	**Activities**
1	**ARVs cost**	**3**
2	**Non-ARV cost**	
2.1	Personnel	4;5
2.2	Material	6 - 9
2.3	Capital	10;11

For Purchaser		
No	**Cost categorized**	**Activities**
1	Personnel	12
2	Material	13 - 24
3	Capital	25
4	PSG intervention	25 - 30

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4.3.1. Costs borne by providers/hospitals

Providers represented in the study are hospitals under the Vietnamese Ministry of Health. They bear the expenditure of standard care for HIV/AIDS. Hence, related costs of ARV medication; OPC recurrent and capital cost is involved as cost from provider perspective. Particularly, costing data in this perspective is separated by antiretroviral medicine cost and non-antiretroviral cost, including personnel; material

and capital cost. Whilst non-ARV medication cost was contributed similar to each observation, ARVs cost was recorded as individual expenditure.

4.3.1 Antiretroviral medicine cost

Recently, ARVs medication costs are borne by Vietnamese Ministry of Health. The medication is purchased from the donation received from the Global Fund Project towards the program to control HIV/AIDS in Vietnam. According to national guidance about HIV/AIDS treatment, a list of ART first line regimen and its unit cost is defined to either adult or children. Unit cost of ARV expenditure is determined by individual actual regimen using. In case of no applicable cost information from the mentioned list, data is also referred from the ARV ceiling price list by The Clinton Health Access VAAC (2012).

4.3.2. Total non ARV medicine costs

Total non ARV medicine costs are classified into three categorize as personnel; material and capital cost.

4.3.2.1. Personnel costs

Medical staff is separated by full time workers at OPC and part time specialists who work in several departments. Personnel costs include salaries, allowances, insurance fees, incentive for working with professional hazard, and effectiveness bonuses for OPCs staffs. By direct interview with staff at OPC and administration department, the average of monthly personnel cost which contributed to projecting patients are revealed.

4.3.1.2. Material costs

Material cost included medical consumable; stationary for OPCs and other operating cost. Operation cost is seen as expenditure for maintenance and general cost such as electricity, water and sanitary. By interviewing administrative staff at OPCs, the division of these costs to the projects was founded.

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4.3.1.4. Capital cost

Outpatient clinics are available in all hospitals, then, cost of infrastructure including annual building and clinic equipment are not involved as explicit costs but as the implicit one. The contribution of this cost to each observation is equally at both study sides. Annual capital cost is measured by straight line depreciation. Capital in hospital included building and equipment, which have useful life at 50 years and 10 years respectively (MOF, 2012). Total capital cost was not applicable due to the high barrier in accessing hospital actual cost. Then, according to the tariff of Vietnamese Ministry of Construction (MOC, 2013), the estimation cost to replace building and equipment in medical facility are applied in calculate capital depreciation. They are seen as annual capital cost and are contributed equally to all observations.

4.3.2. Costs borne by patients

Patients have to respond for the cost of transportation form their home to the clinics; costs for treating other diseases which are not covered by Government. The cost can be seen further as opportunity costs such as absence from work. However, these implicit costs are unsustainable due to the natural characteristic of this community. People living with HIV mostly work as freelancers, temporary or self-employed, so it is seem to be impossible to measure their income frequently. In the scope of this paper, the explicit cost borne by patients, particularly treatment and transportation cost will be focused on.

4.3.2.1. Non-ART treatment cost

At both cohort, data related to non-antiretroviral therapy and its cost is recruited from individual medical records. To prevent missing information, the questionnaires were set to interview patients or their caregivers about these additional treatments every 2 months.

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4.3.2.2. Transportation cost from home to OPCs

As mentioned that transportation cost is seen as the cost of gasoline expenditure to travel from patient home to OPC. Thus, the information of unit price for a litter of gasoline is employed from the Vietnam National Petroleum group (VNPG). The price of gasoline was unstable from 2007 to present; hence an average price is founded for particular period at 2007-2009 and 2013-now. According to the Vietnam National Petroleum group, average expenditure for a distance of 40 km is 3.7 litter of gasoline, which is applied for the most popular vehicle in Vietnam – motorbike.

In adult cohort:

The enrolled patients are from the same province (distance less than 40km), thus, unit transportation cost of each individual is similar but the total transportation cost of one is based on total time that this patient traveled to the OPC.

In children cohort:

Similar to adult cohort, transportation cost is counted as cost borne by patient at each time of visit OPCs. From the beginning, patients were classified into 3 groups of regions based on the distance from their current home to the OPCs. Thus, unit transportation cost is measured as equal as total cost for gasoline to travel from each region to the OPC.

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4.3.3. Costs borne by purchaser

The purchaser is Swedish Research Council - Vetenskapsrådet, delegating to Karolinska University and Hanoi Medical University to conduct the project. All costs related to PSG intervention and viral load tests are fully sponsored by them. Relevant activities are grouped by similar characteristic and assigned to each cost categorizes, including personnel, material, capital and PSG intervention cost.

4.3.3.1. Personnel cost

All expenditure in salary, allowance and related expenditure for human resource will be included. The personnel can be counted as project direction, coordinator, secretary, data manager, field trip supervisor and site coordinators.

4.3.3.2. Material costs

Material costs borne by purchaser included cost for supply and operating. Particularly, supply cost contained all expenditure for viral load test and stationary. The viral tests were provided every 6 months of follow-up time. Actual cost is found as equal as the fee paid for third party to do testing. Stationary cost was recorded as monthly actual expenditure.

Operation cost borne by purchaser included several activities such as data collection and management; monthly renting cost (for office place); business trips, monitoring, meeting, training, maintenance, general cost and administration fee. In particular, data were recorded at baseline and every 2 months of follow-up time. Hence, all fees to collect and manage data are involved in this cost categorize. Monitoring trips and business trips costs included stipend, accommodation, transportation and communication for staffs. Periodically scientific meetings were held to report the progression and discussing all incurred difficulties and the specific solution for each issue. Annual training for hospital nurses; physicians and laboratory associates to remind research activities to current staffs and training for new staffs about the intervention program objectives and its procedure.

4.3.3.3. Capital costs

Actual total costs of equipment were collected from annual financial reports. Annual capital cost is found by straight line depreciation. Annual cost from building is excluded from this cost categorize since this cost were collected as monthly renting cost.

4.3.3.4. Total PSG intervention costs

PSG intervention cost was allocated to patients in the intervention group only. Cost components of this categorize are all costs of recruiting supporters for the program; salary and allowance for peer supporters, including transportation fee and telephone fee; monthly meeting to report the counseling of peer supporters; every 3 months counseling meeting costs includes organizing and incentive for patient participation and annual training for peer supporters about doing HIV/AIDS

prevention, counseling to improve adherence to consolidate their knowledge and enhance the quality of intervention.

4.3.4. Total unit cost estimation

Mixture costing approach method is applied to estimated total unit cost. First step to estimate total unit cost is top-down the total annual costs of some cost categorizes or allocating these costs to the relevant observations. Cost borne by purchaser and Non ARV medication cost borne by provider are involved in this step.

Second step is bottom-up all unit cost of each cost categorizes or combining all unit costs of each cost categorize. In this step, the unit cost gained from step one are involved. ARV costs and cost borne by patients were differentiated by each sub-groups, then, their average cost for the whole period are also involved in this bottom-up step.

Final step, total unit cost at each year is discounted to the same time for being more comparable. In the adult cohort, total unit costs are discounted to the end of follow-up period at year 2009. In the children cohort, total unit costs are discounted to the starting point at year 2013.

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This process is applied similarly to both cohorts and study sides either adult - children and intervention – control.

4.4. Effectiveness measurement

4.4.1. Adherence measurement

Several researches indicated requirement rate of adherence for control chronic diseases is targeted at 95%. The obligation adherence for HIV suppression is almost comprehensive, meaning that only 100% compliance can reduce totally all opportunity of raising virus resistance. Studies also showed that 16% of mortality related to HIV/AIDS disease was caused by 10% of decline in ART compliance (Gavin Steel, 2007). Hence, measuring the level of patient compliance is essential to alarm

HIV/AIDS status and to detect appropriated antiretroviral therapy regimen. Nevertheless, due to the instability in treatment regimen, ART adherence evaluation is always a huge challenge. In low resource setting context where intensive counseling is not strong enough, treatment adherence is different among population in terms of disease acknowledgement, socioeconomic status, age or gender. There are some methods in treatment adherence assessment; in general all of them can be grouped into 2 categories that are direct and indirect method. The direct way can be obtained by directly observed treatment (DOT), therapeutic drug monitoring or medication Event Monitoring System. Whilst, the indirect method measures pharmacy record, subjective report, pills count and visual analogue scale. There is no gold standard for any single measurement tool, multi-method however provides more confidence. In scope of this study, ART adherence level will be evaluated via directly observed therapy and pill counting, self-report in follow-up interview, supporter weekly reports and medical records.

The effectiveness of PSG model will be showed by the difference in adherence assessment outcomes between intervention group and control group, which is separated by group of patient with similar time of intense care and at specific follow-up period.

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4.4.1.1. Adult cohort adherence measurement

The adult cohort information is borrowed from the “directly observed therapy for antiretroviral” (DOTARV) project, which was conducted from 2009 to 2013 and done with 24 months of follow-up after the baseline. The principal activities of PSG intervention were through home visits and counseling. The control trial was assigned randomly by cluster sampling. There were total 59 enrolled clusters with 30 clusters in the intervention group and 29 clusters in the control one. Patients were graded as completely adhering to the interventions if they never missed any doses in a month. In the other hand, the information of taking pills late was added as one of criteria to assess the efficiency of ART treatment. Patients who never missed any dose and always took pills on time were graded as completely adhering efficiently. The

percentages of observations that were completely adhering with efficiency are found as adherence assessment outcomes.

4.4.1.2. Children cohort adherence measurement

Every 2 months, questions related to pill count was made by clinic staffs to evaluate the treatment adherence of patients in both groups, whilst it was done weekly by peer supporters to the patient in intervention group. The information from these follow-up will be involved to calculate related adherence ratio, which the average are seen as adherence assessment outcomes.

$$\text{Adherence rate with efficiency} = \frac{\text{No. pills provided} - \text{No. pills remain} - \text{No. pills taken late/vomit}}{\text{No. pill prescribed}}$$

4.4.2. Non- Viral failure increased

The study of Paterson et al. (2000) showed the significant relationship between ART adherence and viral load outcome. It is believed that more compliance of patient will lead to better outcome of viral load test. Consequently, the time of virological and immunodeficiency failure will be taken into account as the secondary outcome of the intervention. The viral failure can be defined in term of viral load level and number CD4 cell. If the viral load is ≥1000 copies/ml the treating doctor will be informed. If the patient is in the intervention group individual adherence support to caretaker and child will be arranged, another viral load will be done within one month. If the second viral load is ≥1000 copies/ml the child will be reported for assessment of treatment failure according to the national treatment guidelines. According to the standard of immunodeficiency failure of Vietnam Ministry of Health, the failure is evaluated by the decline of CD4 cell in compare with patient's very first CD4 count result; the decrease by a half to the patient's highest result of CD4 cell count and the final signal is number of CD4 cell count, less than 100 copies/mm^3. In particular, the transferred cases from the first regimen to the second one, based on clinical detection, are also considered as the treatment failure.

In the scope of this study, the effectiveness of PSG intervention can be partly reflected via the percentage non-VL failure cases. These outcomes will be observed every 6 months of research period.

4.4.3. Disability adjusted life year (DALYs) reduced

DALYs can be seen as the amount burden of disease that bears by certain population in a specific time interval; hence, the intervention is expected to reduce this burden. The factor can be calculated by several different ways such as from incidence or pure prevalence perspective (Schroeder, 2012). In regular, the DALYs is the summation of years of life lost due to premature mortality (YLLs) and years of life live with disability (YLDs). The DALYs is mostly linked to both time interval and well-defined population, thus, in this study the DALYs lost will calculate for target population of adult cohort only for the specific time of 2 years intervention. The years of life lost to premature mortality (YLLs) was counted as the subtraction of total living years and life expectancy by age and gender, presented as summation of column “ex” and “x” in the life table (figure.9) in 2012 for Vietnam (WHO Observatory). The years of life live with disability (YLDs) will be calculated through incidence perspective. Here, the population of HIV infected was included, thus, to observe the years of disability experienced, some medical events should be counted. Particularly, we counted the years lost due to living with opportunity infectious diseases (OI) as part of YLDs. Year living with disease will be adjusted by disability weight for HIV disease at 0.135 standardized by (WHO (2004)).

DALYs = YLLs + YLDs

- YLLs = total life expectancy – living years

  = (age + expectancy of life at specific age) – living years

- YLDs = DW * years living with disease

  = 0.135 * total years living with disease

The outcome of disability adjusted life year reduced is seen as the mean of DALYs of either intervention or control group.

4.5. Cost effectiveness ratio and Incremental cost effectiveness ratio

The cost effectiveness ration present the total cost to produce one unit of effectiveness outcome in each study side. By looking at the total unit cost at each year, including 1 year baseline and 2 years of follow-up), the average unit cost of whole period is multiplied with number of patients in each study side for estimating total cost input. By looking at each sub-group or group of people with similar magnitude of assessment reports, the average effectiveness outcomes are counted as second input of the CER and ICER calculation.

The cost effectiveness ratio is estimated by this following formula:

$$CER = \frac{\text{Total cost}}{\text{Effectiveness outcome}}$$

The ICER showed total cost to increase 1% of effectiveness outcome by adding PSG intervention. ICER makes reference to the differences between two sides of study. Following cost effectiveness ratio calculation, similar estimation method is applied to find the total cost and effectiveness outcomes at each study sides. The incremental cost effectiveness ratio was defined by this formula:

$$\text{Incremental ratio} = \frac{Cgi - Cgc}{Egi - Egc}$$

Cgi / Cgc: total costs occurring in intervention / control group

Egi / Egc: effectiveness outcome of intervention / control group.

CHAPTER 5. RESULTS

5.1. Adult cohort

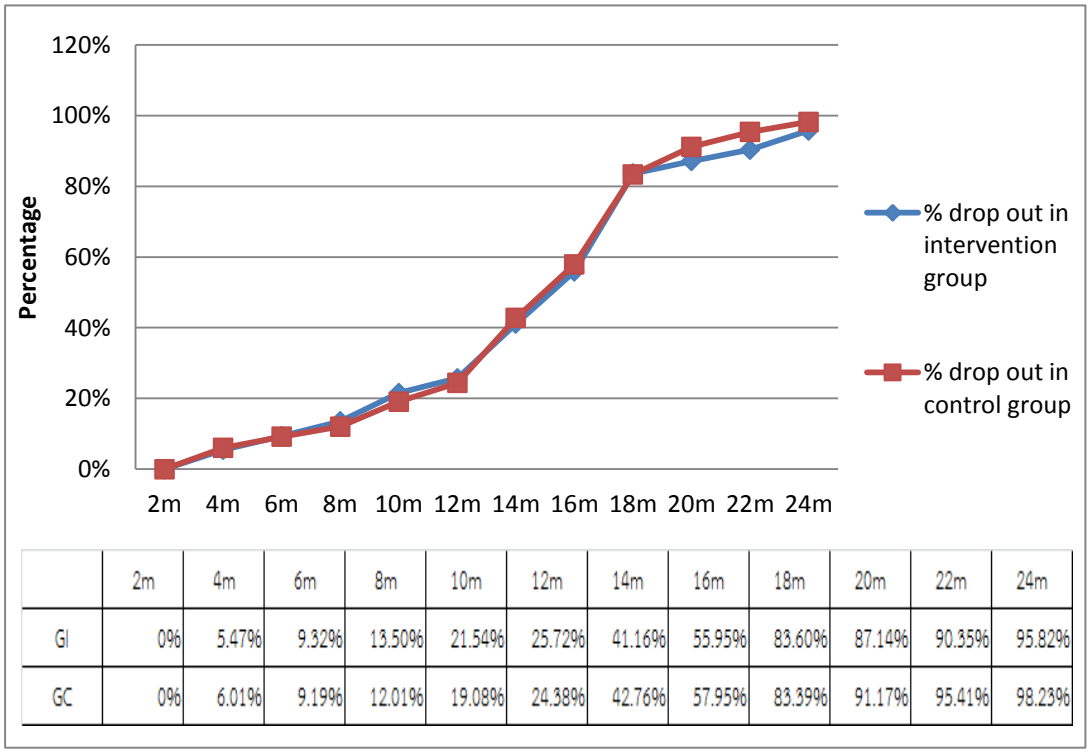
Enrolled patients in this cohort have done with baseline and 24 months of follow-up. Basically, 594 adult patients at both study sides were recorded data for 13 times including baseline in year 2007; 6 follow-up periods in year 2008 and 6 follow-up periods in year 2009. Hence, all recoded data of these 594 patients were presented as total 4,548 observations distributed 2,396 to the intervention group and 2,152 to the control group. The distribution of observation by project time period is presented in table.2. However, not all of them maintained the whole 24 months follow-up time. Several reasons would cause to the drop-out of patients. In particular, 11% (70/594) of patients were dead; 6.7% (40/594) of patients were arrested; only 5 patients transferred to other OPCs; the rest withdrew voluntarily. The number of patients who dropped out of the project increased gradually, which lead to smaller number of observations in the end of project time. Percentage of drop-out cases in adult cohort by time is present in figure.8.

Table 4. Distribution of observation in adult cohort

Follow-up period	Number of observation in intervention group	Accumulate number	Number of observation in control group	Accumulate number
2007				
Baseline	311	311	283	283
2008				
After 2 months	311	622	283	566
After 4 months	294	916	266	832
After 6 months	282	1,198	257	1,089
After 8 months	269	1,467	249	1,338
After 10 months	244	1,711	229	1,567
After 12 months	231	1,942	214	1,781
2009				

After 14 months	183	2,125	162	1,943
After 16 months	137	2,262	119	2,062
After 18 months	51	2,313	47	2,109
After 20 months	40	2,353	25	2,134
After 22 months	30	2,383	13	2,147
After 24 months	13	2,396	5	2,152

Figure 8. Percentage of drop-out cases in adult cohort



	2m	4m	6m	8m	10m	12m	14m	16m	18m	20m	22m	24m
GI	0%	5.47%	9.32%	13.50%	21.54%	25.72%	41.16%	55.95%	83.60%	87.14%	90.35%	95.82%
GC	0%	6.01%	9.19%	12.01%	19.08%	24.38%	42.76%	57.95%	83.39%	91.17%	95.41%	98.23%

Basically, patients left noticeably after first year of follow-up. In the end, almost all patients dropped out at both study sides. That raises a big suspicion about the accuracy because the information is provided as secondary data.

According to the difference in the magnitude of follow-up time of each individual, all enrolled patients were grouped based on their number of follow-up reports. There are total 12 sub-groups, represented by 12 groups of patients with follow-up period ranging from 2 months to 24 months. Overall, only 13 patients in intervention group and 5 patients in control group maintained their follow-up for

total 24 months. This means only these people had baseline and 12 follow-up reports.

5.1.1. Costing analysis

Total unit cost includes unit cost borne by provider, unit cost borne by patient and unit cost born by purchaser. As mentioned from chapter 4, the unit cost borne by purchaser and non ARV medicine cost borne by provider is applied through a top-down approach. Then a bottom-up approach combines all unit costs of each cost categorize including ARV cost, average non ART treatment cost, patient transportation cost and unit cost mentioned in step1 to comprehensive the total unit cost of each observation. Total unit cost at each year is discounted to the same time with 3% discounting rate ((MOF, 2012).

5.1.1.1. Cost borne by purchaser

Total cost borne by purchaser was recorded at baseline in year 2007 and at each follow-up year at 2008 and 2009. These costs were separated as total cost without PSG intervention and total cost of PSG intervention. The unit cost per observation in control group does not involve PSG intervention division whilst it does in the intervention group. Actual expenditure was collected from finance report of the purchaser for all cost categorizes. Annual capital cost borne by purchaser included only annual depreciation from equipment, hence, it started recording at year 2008 and 2009 when equipment were purchased. The straight line depreciation was applied to calculate annual capital cost in 2008; accumulated depreciation is founded as annual capital cost in 2009.

PSG intervention had not provided in the baseline year so the total annual cost in baseline year is smaller than it is in the follow-up years. This cost also decreased in the year 2009 due to lesser number of follow-up patients. Detail of cost component per activity in each cost categorized is shown in the appendix.

Table 5. Annual cost borne by purchaser in adult cohort (unit: USD)

Annual cost borne by Purchaser				
No	Variables	Value at year		
		2007	2008	2009
1	Annual personnel cost	$4,875	$7,594	$8,438
2	Annual material cost	$45,754	$117,826	$59,499
3	Annual capital cost	$0	$612	$1,223
4	Annual PSG intervention cost	$0	$24,268	$11,869
	Total annual purchaser cost	$50,629	$150,299	$81,028

5.1.1.2. Cost borne by provider

Data related to annual total cost borne by provider in adult cohort included ARVs medication cost; personnel cost; operating cost; material cost and capital cost. First, the information of each individual ARVs regimen was collected from medical records. Second, the information of remaining cost categorizes was collected from interview relevant OPCs staffs. In categorize of capital cost, there was uncertain information about total cost of OPC's building and its equipment. Estimation of cost needed for replace OPC's building and equipment was involved. These information based on the tariff in year 2013 of the Ministry of Construction (MOC, 2013) for general hospital. Hence, the replacement cost, which rated in 2013, is discounted back to year 2007; 2008 and 2009 to estimate the depreciation of capital cost in this cohort. The detail of each cost components in estimating total unit cost is presented in the appendix.

Table 6.Total Non ARVs cost cost borne by provider in adult cohort (unit: USD)

Annual total cost borne by provider excluding from ARVs cost				
No	Variables	Value at year		
		2007	2008	2009
1	Annual personnel cost	$0	$3,300	$1,650
2	Annual material cost	$0	$1,761	$866
4	Annual capital cost	$557	$573	$590
	Annual provider cost excluding from ARVs cost = 1+2+3+4	$557	$5,634	$3,106

As seen from the table.6, annual total cost of year 2007 was much smaller than the others. This is reasonable because of that 2007 was baseline year and there was no recurrent expenditure in this year from the perspective of provider/hospital. The annual personnel and material cost in year 2009 are smaller than it were in year 2008 due to the huge number of drop-out cases.

Even patients in the same stage of ART, they still have different ARVs regimen or different medication based on their health status and medical history. At the first stage of ART, there are 7 ARVs regimens for HIV infected adult which are recommended by the Vietnamese Ministry of Health. Enrolled patients in the adult cohort followed one of these mentioned regimens. The unit cost of each ARVs regimen was collected from financial report (year 2009) of the "***Global Health Program***", who sponsored for Vietnamese Ministry of Health to supply ARVs medication. The average ARVs cost at specific year is involved in estimating total unit cost.

5.1.1.3. Unit cost born by patient

Unit cost borne by patient includes average cost payment for non-ART treatment and transportation cost. Non ART treatment costs are not paid by Government but are borne by the patient. The information of this cost is collected from individual medical records and via direct interview with patient/ caregivers. All

adult patients are from the same region, which is not further than 40 km to the OPC. Hence, unit cost of transportation is similar to each observation. Applying the average gasoline expenditure estimated by Vietnam National Petroleum group (VNPG), the transportation cost of each individual is as equal as price of 3.7 litter gasoline. Average unit price of gasoline in period 2007-2009 is $0.97/litter. Hence, unit transportation cost for each individual in adult cohort is 3.7 litter * $0.97= $3.6. Similarly to ARVs cost, average unit cost borne by patient at specific year is applied to the total unit cost estimation.

5.1.1.4. Total unit cost for adult cohort

As mentioned, first step of estimation total unit cost is top-down total annual cost borne by purchaser and non ARVs cost borne by provider. These costs are dividing to the relevant number of observation

Table 7. First step in calculating total unit cost in adult cohort (unit: USD)

Unit non ARV cost borne by provider		**Value at year**		
No	**Variables**	**2007**	**2008**	**2009**
1	Annual provider cost excluding from ARVs cost	$557	$5,634	$3,106
2	Total observations	594	1,498	825
	Unit cost = annual cost/ total observation	$0.94	$3.76	$3.76

Unit cost borne by Purchaser		**Value at year**		
No	**Variables**	**2007**	**2008**	**2009**
1	Annual provider cost excluding from ARVs cost	$50,629	$150,299	$81,028
2	Annual PSG intervention cost	$0	$24,996	$11,869
3	Total observations in intervention group	311	1,631	454
4	Total observations in control group	283	1,498	371
	Unit cost of observation in intervention group = ([(1) - (2)]/[(3)+(4)]) + ((2)/(4))	$85	$55	$110
	Unit cost of observation in control group = [(1)-(2)]/[(3)+(4)]	$85	$40	$84

Due to the huge number of drop-out patients in year 2009, total observations in this year reduced noticeably. This leads to higher unit cost in the year 2009, regardless of the reduction in cost components.

At the second step, total unit cost is using a bottom-up costing approach. Total unit cost was combined by unit cost borne by provider, patient and purchaser. In particular, total unit cost is the combination of unit cost borne by provider excluding from ARVs cost; unit cost borne by purchaser; average cost of ARVs and cost borne by patient from 12 sub-groups. Finally, total unit cost at each year is discounted with 3% to the year 2009.

Table 8. Total unit cost in adult cohort (unit: USD)

No	Variables	Value at year					
		2007		2008		2009	
		GI	GC	GI	GC	GI	GC
1	Unit cost borne by purchaser	$85	$85	$55	$40	$110	$84
2	Unit non ARVs cost borne by provider	$0.94	$0.94	$3.76	$3.76	$3.76	$3.76
3	Average ARVs cost	1.32	1.25	1.57	1.26	2.42	1.74
4	Average non-ART cost	0	0	8.14	11.9	4.35	4.7
5	Average patient transportation cost	3.6	3.6	3.6	3.6	3.6	3.6
	Total unit cost	$91	$91	$72	$61	$124	$98
	Total unit cost discounted to 2009	$97	$97	$75	$62	$124	$98

As seen from the table.8, regardless of the higher annual cost, total unit cost in year 2008 is still lowest. This happened thank to the involvement of the economics of scale when total cost were divided to more observations. In the baseline year, total unit cost is similar because there were no difference activities between two study sides in this year.

5.1.2. Effectiveness analysis

There are three types of effectiveness outcomes in this cohort. They are adherence rate, percentage of non-viral failure and disability adjusted live years. Except DALYs lost, which will be measured as the mean at each sub-group, effectiveness outcomes are involved as percentage of people who were graded as complete adherence or percentage of non-viral failure cases.

5.1.2.1. Adherence rate

Adherence measurement had done via visual analog scale. Patients were interviewed with a list of adherence measurement questions and then were graded as complete adherence or not. Patients who were never forgot to take pills and never took pills late were graded as complete adherence to the treatment. Generally, adherence rate shows percentage of patients who were counted as complete adherence to the treatment. Hence, Pearson chi2 tests are involved to evaluate the difference of adherence rate between two study sides. For the sub-group 12 where including patients with fulfill 12 months of follow-up, adherence rate is also better at the intervention group, however this difference is not significant. Overall, patients in the intervention group had better adherence rate than those in control group and this difference is statistic significant (chi2-Pr: 7%). The average of adherence outcome from 12 sub-groups is counted in the cost effectiveness analysis.

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Table 9. Effectiveness outcomes in adult cohort (unit: %)

Group of similar number of follow-up period (sub-groups)	Adherence rate		Difference between two study sides (GI –GC)	Chi2: Pr
	Intervention group	Control group		
1 (baseline + 1 follow-up)	70.6%	61.1%	9.5%	0.56
2 (baseline + 2 follow-up)	79.2%	100%	-20.8%	0.05
3 (baseline + 3 follow-up)	79.5%	75%	4.5%	0.68
4 (baseline + 4 follow-up)	87%	81.3%	5.7%	0.29
5 (baseline + 5 follow-up)	90.8%	73.3%	17.5%	0.01

6 (baseline + 6 follow-up)	87.7%	86.5%	1.2%	0.68
7 (baseline + 7 follow-up)	82.7%	81.4%	1.3%	0.66
8 (baseline + 8 follow-up)	80.3%	76.3%	4%	0.08
9 (baseline + 9 follow-up)	85.9%	82.3%	3.6%	0.44
10 (baseline + 10 follow-up)	74%	84.2%	-10.2%	0.06
11 (baseline + 11 follow-up)	83.4%	85.2%	-1.8%	0.7
12 (baseline + 12 follow-up)	85.3%	80%	5.3%	0.35
In average	82.83%	80.63%	2.2%	0.07

5.1.2.2. Percentage of non-viral failure cases

There is a limitation about the data of VL failure rate in this cohort. Data is available as the whole project on average; it is not applicable to observe the VL failure at specific sub-group of patient who had similar number of follow-up time. In general, percentage of non-viral failure cases increased at both study sides. In comparison of the percentage of non-viral failure cases by pair of each every 6 months, the rate in intervention patients increased gradually and most growth at first 6 months of follow-up time. Adversely, the raise of percentage of non- VL failure cases in control patients was not sustainable. The difference in percentage of non-viral failure cases is not statistical significance. Average of percentage non VL failure cases is involved in cost effectiveness analysis.

Table 10. Percentage of non-viral failure cases in adult cohort

Research period	Intervention group	Control group
0	96.7%	96.5%
6	98.2%	97.1%
12	98.8%	99.7%
18	99.4%	99.4%
Average	98.3%	98.2%

5.1.2.3. Disability adjusted live year reduced

There are total 36 cases of death in intervention group and 34 cases in control group. Overall, patient in the intervention group had to live with burden of disease in average of 46.8 years and patient from control group lost an average of 50.6 healthy years due to HIV/AIDS disease. In general, patients in the intervention group had to live with burden of disease at 3.8 lesser year than the control group's and this difference is statistical significance. These average factors are involved to the cost effectiveness analysis.

Table 11. Disability Adjusted Live or Life Years in the adult cohort (unit: year)

Sub - group	GI	GC	GI -GC	Ttest -Pr
2	45.73	51.5	-5.77	0.065
4	52.1	46.4	5.7	N/A
6	47.5	53	-5.5	N/A
8	.	48.7	N/A	N/A
10	.	33.8	N/A	N/A
14	47.4	.	N/A	N/A
average	46.8	50.6	-3.8	0.07

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5.1.3. Cost effectiveness analysis and Incremental cost effectiveness analysis

There are three types of effectiveness outcomes in this cohort, which leads to three types of CER and ICER. They are CER and ICER per adherence rate, percentage of non-viral failure and disability adjusted live years. Cost effectiveness ratios are involved as total cost divide by average results of effectiveness outcomes. Total unit cost of each study side was found separately by year. The effectiveness outcomes of each individual however are needed to observe at the same follow-up records. For instance, the effectiveness reports of intervention group in the end of sixth month follow-up need to compare with the control group's reports at same follow-up period (after 6^{th} months). Due to different time of enrolling patients, effectiveness outcome with same follow-up period was not match exactly with the accounting years of costing. Hence, using average total cost divide to average outcome make

more meaning in analysis. A table of calculating total cost for adult cohort has been done.

Table 12. Total cost of adult cohort in average (unit: USD)

Intervention group			Control group			GI-GC	Ttest Pr
average unit cost	number of patients	average total cost	average unit cost	number of patients	average total cost		
$86.95	**311**	**$27,041**	**$72.64**	283	$20,557	**$6,484**	**0.00**

Applying the formula of CER and ICER in chapter 4, table of cost effectiveness analysis results for adult cohort has been done. Cost effectiveness ratio is founded by dividing average cost to average effectiveness at each study sides. The incremental cost effectiveness ratios are accessed to each sub-group by taking incremental cost divide by incremental effectiveness.

Table 13. CER and ICER in adult cohort

	Effectiveness outcomes			Average total cost			CER		ICER
	GI	GC	GI-GC	GI	GC	GI-GC	GI	GC	
%Adherence	82.83%	80.63%	2.2%	$27,041	$20,557	$6,484	$326	$255	$2,947
% non-VL failure case	98.3%	98.2%	0.1%	$27,041	$20,557	$6,484	$275	$209	$64,840
DALYs (years)	46.8y	50.6y	-3.8y	$27,041	$20,557	$6,484	$578	$406	-$1,706

In average, it costs total $326 to produce 1% of adherence rate in the intervention group and it costs $255 to produce 1% of adherence rate in the control group. Hence, providing PSG intervention is not very cost effective to improve patient attitude as complete adherence to treatment. In general, it costs $2,947 to increase 1% of adherence by adding PSG intervention. This ICER has statistical meaning at 93% confident interval (P-value: 0.07%)

Overall, it costs total $275 to produce 1% of non VL failure cases in the intervention group and it costs $209 to produce 1% of non VL failure cases in the control group. Hence, PSG intervention is not very cost effective to improve viral load results. The ICER per non VL failure case is extremely high at $64,840. This meaning that PSG intervention cost total $64,840 to increase 1% of non VL failure cases. This high rate caused by the small difference in percentage of non-viral failure cases. However, this incremental cost effectiveness ratio is not a statistical result.

Similarly, it costs total $578 to produce 1 healthy live without mortality and morbidity in the intervention group and it costs $406 to produce 1 year live without burden of disease in control group. Thus, PSG intervention is not very cost effective in term of disability adjusted live year outcome. In general, it costs $1,706 to increase 1 healthy year live without burden of disease or to reduce 1 year lost due to mortality and morbidity by adding PSG intervention. This ICER has statistical meaning at 93% confident interval (P-value: 0.07%).

PSG intervention did generate significant effects to improve patient compliance to treatment and healthy year live without burden of disease. However, the PSG intervention is quite costly at this cohort.

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5.2. Children cohort

This cohort is still on going with follow-up time. In totality, enrolled patients in this cohort have done with baseline and 16 months of follow-up for some patients. Basically, 433 children were enrolled, which contributed to 216 patients in the intervention group and 217 in the control group. Recoded data of these 433 patients were presented as total 2,002 observations distributed 967 to the intervention group and 1,035 to the control group. The distribution of observation by project time period is presented in table.14. There is no case of death reported, 8 cases left the program after given consent forms. These left cases are not included in this cost

effectiveness analysis. Number of observations who had more than 6 months of follow-up is very less due to the uncompleted data collection.

Table 14. Distribution of observation in children cohort (unit: observation)

Time	Number of observation in intervention group	Accumulated number	Number of observation in control group	Accumulate number
2013				
Baseline	216	216	217	217
2014				
After 2 months follow-up	216	432	217	434
After 4 months follow-up	200	632	211	645
After 6 months follow-up	177	809	182	827
After 8 months follow-up	80	889	89	916
After 10 months follow-up	40	929	57	973
After 12 months follow-up	18	947	27	1000
2015				
After 14 months follow-up	13	960	21	1,021
After 16 months follow-up	7	967	14	1,035

5.2.1. Costing analysis

Following the adult cohort structure, the unit cost borne by provider excluding ARV cost and purchaser is using a top-down approach. Then the bottom-up approach combines those unit costs and another unit cost such as ARV cost, actual non ART treatment cost, patient transportation cost to comprehensive the total unit cost of each observation. Total unit cost includes unit cost borne by provider, unit cost borne by patient and unit cost born by purchaser.

5.2.1.1. Cost borne by purchaser

Table 15. Unit cost borne by purchaser in children cohort (unit: USD)

No	Variables	Value at year		
		2013 (12 months)	2014 (12 months)	2015 (4 months)
1	Annual personnel cost	$14,404	$25,350	$8,450
2	Annual material cost	$41,666	$44,249	$2,721
3	Annual capital cost	$0	$266	$266
4	Annual PSG intervention cost	$0	$24,335	$4,681
	Total annual purchaser cost	$56,069	$94,199	$16,118

Only 6% of data has been done in the year 2015, thus variable cost such as data collection fee, cost for trips, training and meeting of this year is low, which leads to the smaller total annual cost. However the fixed costs in this cohort are quite high, so, total annual cost for 6% of data in year 2015 is not much smaller in compare with 82% completed data in year 2013 and 100% completed data in baseline. The detail of cost for each activity is present in the appendix.

5.2.1.2. Cost borne by provider

Table 16. Unit cost of ARVs medication for children cohort (unit: USD)

Annual total cost borne by provider excluding from ARVs cost				
No	Variables	Value at year		
		2013	2014	2015
1	Annual personnel cost	$0	$4,806	$120
2	Annual material cost	$0	$1,125	$219
4	Annual capital cost	$575	$590	$605
	Annual provider cost excluding from ARVs cost = 1+2+3+4	$575	$6,520	$944

Similar to the adult cohort, the same method of estimating annual capital cost is applied to this children cohort. From the tariff of Ministry of Construction for

replacing building and equipment in general hospital in 2013, these replacement costs are discounted to the year 2014 and 2015 with 3% discounting rate. Average ARVs cost is also estimated with same method in the adult cohort. The unit cost of each ARVs regimen for children, which recommended by Ministry of Health, is also collected from financial report year 2013 of the "Global Health Program".

5.1.2.3. Cost born by patient

Similarly to adult cohort, unit cost borne by patient includes average cost of non-ART treatment and transportation cost. The information of non-ART treatment cost is collected from individual medical records and via direct interview with patient/ caregivers.

The enrolled children come from different region around Vietnam. They are classified into three groups of regions, which are based on the distance from their home to the OPC. In general, region 1 includes children who the distance from their home to OPC is less than 40km; this distance of region 2 ranges from 40km – 80 km and finally, region 3 includes all children whose house is further than 80km to the OPC. The children cohort is applied the same method in estimating transportation cost as the adult cohort. This means transportation cost for 40km is equal as the total cost of 3.7 litter of gasoline. Average unit price of gasoline in period 2013-now is $1.16/litter. Hence, unit transportation cost for each individual in region 1 is 3.7 litter * $1.16= $4.3. The distance in region 2 and 3 is twice and three times respectively longer than it is in distance 1. Hence, the transportation cost for observation in region 2 and 3 is respectively $8.6 and $12.9. Overall, the average unit cost borne by patient is counted for total unit cost estimation.

5.1.2.4. Total unit cost for adult cohort

Similar top-down approach is applied to estimate unit cost borne by purchaser and non-ARVs unit cost borne by patient

Table 17. First step in calculating total unit cost in children cohort (unit: USD)

Unit non ARV cost borne by provider		Value at year		
No	**Variables**	2013 (12 months)	2014 (12 months)	2015 (4 months)
1	Annual provider cost excluding from ARVs cost	$575	$6,520	$944
2	Total observations	433	1,514	55
	Unit cost = annual cost/ total observation	$1.33	$4.31	$17.16

Unit cost borne by Purchaser		Value at year		
No	**Variables**	2013	2014	2015
1	Annual provider cost excluding from ARVs cost	$56,069	$94,199	$16,118
2	Annual PSG intervention cost	$0	$24,335	$4,681
3	Total observations in intervention group	216	731	20
4	Total observations in control group	217	783	35
	Unit cost of observation in intervention group = ([(1) - (2)]/[(3)+(4)]) + ((2)/(4))	$129	$96	$527
	Unit cost of observation in control group = [(1)-(2)]/[(3)+(4)]	$129	$62	$293

Regardless of the reduction in variable cost components due to lesser involved patients, unit cost in the year 2015 is extremely high due to small recorded observation.

At the second step, total unit cost is using a bottom-up costing approach. Total unit cost was combined by unit cost borne by provider, patient and purchaser. In particular, total unit cost is the combination of unit cost borne by provider excluding from ARVs cost; unit cost borne by purchaser; average cost of ARVs and cost borne by patient from reported observation. Finally, total unit cost at each year is discounted with 3% to the year 2013.

Table 18. Total unit cost in adult cohort (unit: USD)

No	Variables	Value at year					
		2013		2014		2015	
		GI	GC	GI	GC	GI	GC
1	Unit cost borne by purchaser	$129	$129	$96	$62	$527	$293
2	Unit non ARVs cost borne by provider	$1.3	$1.3	$4.3	$4.3	$17.2	$17.2
3	Average ARVs cost	$4.8	$5.0	$4.8	$5.0	$4.5	$4.9
4	Average non-ART cost	$0.8	$0.0	$0.4	$0.2	$0.2	$0.2
5	Average patient transportation cost	$8.1	$7.9	$8.1	$7.9	$6.8	$7.4
	Total unit cost	$144	$144	$113	$80	$556	$323
	Total unit cost discounted to 2013	$144	$144	$110	$77	$524	$304

Similar to the adult cohort, total unit cost is lowest at the year 2014 with highest observation even annual cost in that year is higher than the others. This happened thank to the involvement of the economics of scale again when total cost were divided to more observations. In the baseline year, total unit cost is similar because there were no difference activities between two study sides in this year.

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5.2.2. Effectiveness analysis

Apart from adult cohort, only two types of effectiveness outcomes in this cohort are possible. They are adherence rate and percentage of non-viral failure.

5.2.2.1. Adherence rate

The adherence assessment in children cohort is found by the pill counts formula, mentioned in chapter 4.4.1. Generally, adherence rate shows the level of individual adherence to the treatment. Patient is complete adherence reach the rate of 100%. They are detected if they never missed any dose and always taken pills without late or vomit over the month. The mean of adherence rate at each sub-

group or each group of patient who had similar number of follow-up periods is presented as average adherence rate outcome in cost effectiveness analysis.

Table 19. Adherence rate in children cohort

Group of similar number of follow-up period (sub-groups)	Adherence rate		Difference between two study sides (GI –GC)	ttest: Pr
	Intervention group	Control group		
1 (baseline + 1 follow-up)	98.17%	99.70%	-1.54%	0.3043
2 (baseline + 2 follow-up)	100%	99.99%	0.01%	0.1879
3 (baseline + 3 follow-up)	99.93%	99.97%	-0.04%	0.1608
4 (baseline + 4 follow-up)	99.96%	99.69%	0.27%	0.0268
5 (baseline + 5 follow-up)	99.89%	99.63%	0.26%	0.2084
6 (baseline + 6 follow-up)	99.88%	100.00%	-0.12%	0.1383
7 (baseline + 7 follow-up)	100%	99.66%	0.34%	0.1816
8 (baseline + 8 follow-up)	100%	100%	0.00%	-
In average	99.91%	99.85%	0.06%	0.2139

In general, PSG intervention did create better effects to the adherence in children, however this difference is not statistical significant.

5.2.2.2. Percentage of non-viral failure cases

Similar to the adult cohort, viral load outcome remains as percentage of non-viral failure cases detected. All outcomes are measured during 16 months of doing intervention. Percentages of non-viral load failure cases are allocated at sub-group 3 and 6, who had magnitude of follow-up time as 6 months and 12 months. Overall, non- viral failure tended to reduce or maintain as it was before.

Table 20. Percentage of non-viral failure case in the children cohort (unit: %)

sub-group	baseline test			1st test			2nd test		
	GI	GC	chi2: Pr	GI	GC	chi2: Pr	GI	GC	chi2: Pr
3	87.5	85.94	0.783	83.75	79.69	0.529	-	-	-
6	94.4	95.6	0.63	94.4	95.6	0.63	94.4	97.8	0.14

In general, PSG intervention did improve the adherence to the treatment and also viral load result in children cohort; however these differences are not statistical results. Disability adjusted live year is not applicable for this cohort yet due to the shortage of data related to morbidity. Additionally, there have not any death case reported in this cohort yet, so, the meaning of DALYs is not comprehensive at this time.

5.2.3. Cost effectiveness analysis and Incremental cost effectiveness analysis

Following the process in adult cohort, average total cost has been calculated.

Table 21. Total cost on average in the children cohort (unit: usd)

Intervention group			Control group			GI-GC	Pr
average unit cost	number of patients	average total cost	average unit cost	number of patients	average total cost		
$ 185	**216**	**$39,960**	**$136**	217	$29,512	**$10,448**	**0.0**

Cost effectiveness analysis in this cohort has been done with outcomes of adherence rate and percentage of non-viral failure cases. Applying the formula of CER and ICER in chapter 4, table of cost effectiveness analysis results for children cohort has been done.

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Table 22. Cost effectiveness analysis in children cohort

	Effectiveness outcomes			Average total cost			CER		ICER
	GI	GC	GI-GC	GI	GC	GI-GC	GI	GC	
%Adherence	99.9%	99.9%	0.06%	**$39,960**	$29,512	$10,448	$400	$296	$174,133
% non-VL failure case	89.1%	88.2%	0.93%	**$39,960**	$29,512	$10,448	$448	$335	$11,234

In average, it costs total $400 to produce a 1% of adherence rate in the intervention group and it is $296 in the control group. Hence, providing PSG intervention is not very cost effective on average. The PSG intervention costs total

$174,133 to increase 1% of adherence rate in children. However, the result of ICER is not statistical significant.

Generally, it costs $448 to produce 1% of non-viral failure cases in the intervention group whilst it costs only $335 in the control group. Thus, similar to adherence rate outcome, PSG intervention is not cost effectiveness to improve viral load result in children cohort. It costs total $11,234 to increase 1% of non-viral failure by adding PSG intervention to caregiver of children.

Overall, PSG intervention did not create any significant effects to the children cohort. The impact of PSG intervention into viral load test is greater than it does into adherence rate. Possible reason is that the intervention was given directly to children's caregiver instead of children themselves. Hence, the effects of intervention in term of improve patient compliance to treatment would not be seen clearly.

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CHAPTER 6. DISCUSSION

6.1. Study limitation

In the study of Andrew Creese (2002), he made a systematic review about cost effectiveness of several intervention to HIV/AIDS infected patients in Africa. He did cost effectiveness analysis for many type of intervention to control HIV/AIDS, including peer education for prostitutes in Cameroon in 1998. In comparison, Vietnam and Africa is similar in the context of low resource setting and currently confront with the explosion of HIV disease. The targeted population and intervention of the study in Cameroon is comparable perfectly with adult cohort in this paper. In particular, Creese found the unit cost over 805 intervened patients at $60.84 in year 2000. After discounted to the year 2009, this unit cost is around $8 lower than the unit cost per intervention patient in the adult cohort. However, the unit cost of Creese reflected only purchaser perspective and it's represented for a sample size that double adult cohort's in this paper. In the same study of Creese about providing home care visit intervention at health facility based program in Zambia, Tanzania and Zimbabwe, the unit cost per year of each intervened patients, discounted to 2009, was $439; $507 and $303 respectively. As mentioned in chapter 5, the average unit cost/ observation is $86.95, which means the cost for an adult to get PSG intervention in a year (6 observations) is around $521. The incremental unit cost per incremental DALYs (converted value to year 2009) in the Cameroon study is $5.23. This is more expensive than the ICER per DALY in the adult cohort, but the difference is not too much (Incremental unit cost to incremental DALYs = ($86.95 -$72.64)/ 3.8 year = $3.81/DALY gained). Hence, the cost to provide PSG intervention to the adult HIV patient in Vietnam is in the same range with internationality.

6.2.1. Limitation in costing analysis

Several limitations appear due to the shortage of information in dataset. Due to the time constraint and high barrier in approaching hospital costing data, numerous

assumption were created, which might lead to the uncertainty and inaccuracy. There is no applicable data for actual expenditure of transportation cost borne by patient, recurrent and capital cost borne by provider. These costs were estimated based on the information collected via interviewing relevant staffs and patients/caregivers.

6.2.2. Limitation of effectiveness measurement

There are three outcomes of effectiveness measurement, which are adherence rate, percentage of non-viral failure cases and DALY. The adherence assessment is considered as the main outcome of the PSG intervention. It shows the physically effect of PSG intervention to targeted population. It was however evaluated by indirect method via pill counts; subjective report and visual analog scale instead of direct observe therapy. Hence the accuracy of this evaluation is not ensured.

There are several factors which affect to the results of viral load test, mortality and morbidity such as individual's allergy, virus resistance level, drug/alcohol addiction, stroke, income, education, family structure and more. That only grouped patient by same ART stage is not strong enough to reject all influence of these other factors. Furthermore, a study of (McGrath, Lessells, and Newell (2015)) showed that the effects of ART is reflected in viral result over 2 year of therapy. Hence, within 24 months of PSG intervention, the effects are not really possible to observe at viral load result.

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As seen from chapter 5, the effect of PSG intervention did generate better outcomes to the intervened study side. However, adult cohort with 24 months of follow-up had more significant results than the 16 months follow-up's in children cohort. This issue might cause by the short time of follow-up in the children cohort. Plus, the intervention was given directly to children's caregiver, thus the adherence improvement depended on their caregiver characteristic more than in the children. Hence the difference between two study sides has not been shown clearly. This leads to the expensive or high cost to provide PSG intervention.

6.3.1. Solution to address the limitation

The inaccuracy issue in costing analysis is possible to solve by using actual data of expenditure in calculate cost borne by patient and cost borne by provider. Rather than estimate transportation cost by average of gasoline expenditure by distance, this cost is supposed to collect by interview each individual about their actual expenditure. Furthermore, cost borne by patient also includes depreciation of patient's vehicle (if have) and actual extra fees for food and drink at each time visit the clinic. In term of cost borne by provider, it is more critical to combine data from financial report, balance sheet, payrolls and receipts. If all mentioned cost is collected as actual expenditure, the mentioned issue will be address mostly.

The insecure of drop-out cases in adult cohort should be rechecked to consolidate the validity of cost effectiveness results. In the children cohort, the characteristic of caregivers should be analyzed to classified groups of children based on their caregiver's attitude related to treatment adherence. Both cohorts should be observe in a longer follow-up time to strengthen the difference in effectiveness outcomes.

6.2. Policy implication

It is better to spend more time to observe the difference of the effectiveness outcomes between two study sides before conclusion that peer support group is not a cost effectiveness intervention. In fact the unit cost of doing PSG intervention is reasonable within the year that had large involved patients. Hence, this intervention is possible to sustain with the economy of scale. Furthermore, the intervention should be given to group of patient with high risk of having low self-compliance. Hence the adherence evaluation should be done more carefully at baseline to detect the high risk group. By that, the incremental of effectiveness outcome can be seen stronger between study sides. This might improve the cost effectiveness of PSG intervention and support the healthcare planner to not skip an appropriate control program for HIV/AIDS.

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In conclusion, with the context of low setting resource in Vietnam, the controversy is raised about which intervention that would control the disease significantly and concurrently sustain in long time. The PSG intervention in this paper although did not show much cost effectiveness between the two study sides. But it did generate better effects to the intervened population significantly when it was provided in a longer time. Additionally, this is expected to be more cost effectiveness by involving the economics of scale and focusing the intervention into high risk group. Hence, PSG intervention is still a good offer for nation program to control the disease.

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APPENDIX

Appendix 1. Life table to calculate DALYs

x	ex	
Age	Expectancy of life at age x	
	Male	**Female**
<1 year	70.5	80.2
1-4	71.0	80.5
5-9	67.3	76.8
10-14	62.6	71.9
15-19	57.9	67.0
20-24	53.2	62.1
25-29	48.7	57.2
30-34	44.1	52.5
35-39	39.6	47.8
40-44	35.1	43.0
45-49	30.8	38.2
50-54	26.6	33.6
55-59	22.8	29.0
60-64	19.1	24.7
65-69	15.7	20.6
70-74	12.8	16.7
75-79	10.2	13.4
80-84	8.1	10.4
85-89	6.3	8.0
90-94	4.9	6.0
95-99	3.9	4.4
100+	3.1	3.3

Data source: from WHO (http://apps.who.int/gho/data/?theme=main&vid=6)

Appendix2. Cost borne by purchaser in the adult cohort

Personnel cost				
No	Variables	Value at year		
		2007	2008	2009
	Annual personnel cost = [(1*2)+(3*4)] * 12 months	**$4,875**	**$7,594**	**$8,438**
Material cost				
No	Variables	Value at year		
		2007	2008	2009
1	Data collection and management	$8,688	$37,686	$18,843
2	VL test	$25,425	$50,850	$25,425
3	Stationery (paper, ink, clipper..)	$803	$3,076	$3,076
4	Annual cost of hiring office location	$1,500	$1,500	$1,500
5	Administration fees (approval process, printing..)	$1,010	$1,120	$976
6	General cost ar program office (electricity, water, telephone...)	$389	$412	$389
7	Maintenance and repairing cost at program offices	$52	$212	$211
8	Business trips	$3,333	$4,000	$3,523
9	Monitoring trips	$0	$5,525	$0
10	Trainings	$1,979	$2,979	$2,979
11	Workshop	$0	$7,890	$0
12	Meetings	$2,576	$2,576	$2,576
	Annual material cost = sum(1:12)	**$45,754**	**$117,826**	**$59,499**
Capital cost				
No	Variables	Value at year		
		2007	2008	2009
1	Cost of purchasing equipment	$0	$6,115	$6,115
2	Total life of the equipment	10	10	10
	Annual capitals cost= cost/ useful life	$0	$612	$612
PSG intervention cost				
No	Variables	**Value at year**		

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		2007	2008	2009
1	Salary and allowance for supporter	$0	$10,500	$5,250
2	Transportation for PSG to patients house	$0	$7,500	$3,750
3	Mobile telephone allowance for PSG to call to patients	$0	$1,500	$750
4	PSG meeting to report their works	$0	$3,179	$1,589
5	Meetings with patients to doing health promotion	$0	$1,589	$530
	Annual PSG intervention cost	$0	$24,268	$11,869

Appendix3: Non ARVs cost borne by provider in adult cohort

Personnel cost				
No	Variables	Value at year		
		2007	2008	2009
1	Average monthly salary for full time staffs	$0.00	$12.50	$12.50
2	Number of full time staffs	16	16	8
3	Average monthly salary for part time staffs	$0	$6.25	$6.25
4	Number of part time staffs	12	12	6
	Annual personnel cost = [(1*2)+(3*4)] * 12 months	**$0**	**$3,300**	**$1,650**
Material cost				
No	Variables	Value at year		
		2007	2008	2009
1	Non-ARVs medication	$0	$30	$0
2	Medical consumable at OPCs (syringe, bandage, gauze..)	$0	$584	$292
3	Stationery at OPCs (paper, ink, clipper..)	$0	$416	$208
4	General cost at OPCs (electricity, water, telephone...)	$0	$550	$275
5	Maintenance and repairing cost at OPCs	$0	$181	$91
	Annual material cost	**$0**	**$1,761**	**$866**

Capital cost				
No	Variables	Value at year		
		2007	2008	2009
1	Estimated cost to replace building at OPCs with 3% discounting from the year 2013	$17,666	$18,196	$18,742
2	Total life of the building	50	50	50
3	Estimated cost to replace equipment at OPCs with 3% discounting from the year 2013	$2,033	$2,094	$2,156
4	Total life of the equipment	10	10	10
5	**Annual capitals cost = (1 : 2) + (3 : 4)**	$557	$573	$590

Appendix4: Antiretroviral cost by sub-group in adult cohort

Year	Unit cost borne by patient		Difference ARVs cost (GI –GC)	ttest: Pr
	intervention group	control group		
1 (baseline + 1 follow-up)	0.3	2.5	-2.23	0.0007
2 (baseline + 2 follow-up)	0.92	0.65	0.27	0.22
3 (baseline + 3 follow-up)	0.36	1.98	-1.62	0.0001
4 (baseline + 4 follow-up)	3.82	4.59	-0.77	0.08
5 (baseline + 5 follow-up)	1.63	0.89	0.74	0.03
6 (baseline + 6 follow-up)	2.35	1.06	1.29	0.00
7 (baseline + 7 follow-up)	1.18	0.88	0.30	0.02
8 (baseline + 8 follow-up)	1.39	1.52	-0.13	0.17
9 (baseline + 9 follow-up)	1.36	1.22	0.14	0.31
10 (baseline + 10 follow-up)	2.08	0.57	1.50	0.00
11 (baseline + 11 follow-up)	0.59	0.92	-0.33	0.04
12 (baseline + 12 follow-up)	3.69	0.96	2.73	0.00
In average	**1.7**	**1.3**	**0.36**	**0.00**

Appendix5: Unit cost borne by patient in adult cohort (unit: USD)

Group of similar number of	Unit cost borne by patient	Difference in	ttest: Pr

follow-up period (sub-groups)	intervention group	control group	unit cost (GI –GC)	
1 (baseline + 1 follow-up)	19.5	62.0	-42.5	0.1783
2 (baseline + 2 follow-up)	4.7	16.2	-11.6	0.0105
3 (baseline + 3 follow-up)	7.5	7.6	-0.2	0.4579
4 (baseline + 4 follow-up)	6.9	6.6	0.3	0.4165
5 (baseline + 5 follow-up)	10.0	10.8	-0.8	0.3831
6 (baseline + 6 follow-up)	7.2	7.2	0.0	0.4887
7 (baseline + 7 follow-up)	6.7	9.8	-3.2	0.1219
8 (baseline + 8 follow-up)	11.3	14.5	-3.1	0.2179
9 (baseline + 9 follow-up)	18.7	10.0	8.7	0.0257
10 (baseline + 10 follow-up)	12.8	20.6	-7.8	0.0546
11 (baseline + 11 follow-up)	15.1	13.8	1.3	0.3006
12 (baseline + 12 follow-up)	5.1	17.4	-12.3	0.0001
In average	10.0	12.7	-2.7	0.0437

Appendix6: Cost effectiveness ration per adherence rate in adult cohort

sub-group	Intervention group					Control group				
	Adherence rate	Unit cost	total obs	total cost	CER	Adherence rate	Unit cost	total obs	total cost	CER
1	70.6%	$86.1	34	$2,929	$34	61.1%	$123.4	36	$4,441	$73
2	79.2%	$64.1	36	$2,306	$36	100%	$65.4	24	$1,569	$16
3	79.5%	$62.4	52	$3,244	$52	75%	$52.9	32	$1,694	$23
4	87%	$62.9	125	$7,867	$125	81.3%	$51.4	100	$5,140	$63
5	90.8%	$62.3	78	$4,856	$78	73.3%	$49.8	90	$4,484	$61
6	87.7%	$59.0	322	$18,999	$322	86.5%	$44.9	364	$16,339	$189
7	82.7%	$71.6	384	$27,513	$384	81.4%	$56.5	344	$19,437	$239
8	80.3%	$87.4	772	$67,487	$772	76.3%	$68.9	649	$44,684	$586
9	85.9%	$103.9	110	$11,424	$110	82.3%	$69.9	220	$15,371	$187
10	74%	$105.9	110	$11,653	$110	84.2%	$84.4	132	$11,140	$132

11	83.4%	$112.8	204	$23,010	$204	85.2%	$81.9	96	$7,860	$92
12	85.3%	$111.1	169	$18,772	$169	80%	$88.8	65	$5,774	$72

Appendix7: Incremental cost effectiveness ratio per adherence rate in adult cohort

sub-group	Effectiveness				Total cost				ICER
	Adherence rate of GI	Adherence of GC	**GI - GC**	chi2: Pr	total cost of GI	total cost of GC	GI - GC	ttest: Pr	mean base
1	70.6%	61.1%	9.5%	0.56	$2,929	$4,441	-$1,512	0.204	-$159
2	79.2%	100%	-20.8%	0.05	$2,306	$1,569	$737	0.429	-$35
3	79.5%	75%	4.5%	0.68	$3,244	$1,694	$1,550	0.032	$344
4	87%	81.3%	5.7%	0.29	$7,867	$5,140	$2,728	0.000	$479
5	90.8%	73.3%	17.5%	0.01	$4,856	$4,484	$371	0.001	$21
6	87.7%	86.5%	1.2%	0.68	$18,999	$16,339	$2,660	0.000	$2,217
7	82.7%	81.4%	1.3%	0.66	$27,513	$19,437	$8,075	0.000	$6,212
8	80.3%	76.3%	4%	0.08	$67,487	$44,684	$22,803	0.000	$5,701
9	85.9%	82.3%	3.6%	0.44	$11,424	$15,371	-$3,946	0.000	-$1,096
10	74%	84.2%	-10.2%	0.06	$11,653	$11,140	$513	0.002	-$50
11	83.4%	85.2%	-1.8%	0.7	$23,010	$7,860	$15,151	0.000	-$8,417
12	85.3%	80%	5.3%	0.35	$18,772	$5,774	$12,998	0.004	$2,452

Appendix8: Unit cost borne by purchaser in children cohort

Personnel cost				
No	Variables	Value at year		
		2013 (12 months)	2014 (12 months)	2015 (4 months)
	Annual personnel cost	**$14,404**	**$25,350**	**$8,450**

Material cost				
No	Variables	Value at year		
		2013 (12 months)	2014 (12	2015 (4 months)

			months)	
1	Data collection and management	$999	$6,203	$262
2	VL test cost	$16,234	$19,318	$0
3	Stationery (paper, ink, clipper..)	$5,545	$3,327	$111
1	Annual cost of hiring office location	$1,728	$1,728	$1,728
2	Administration fees (approval process, printing..)	$1,248	$1,248	$25
3	General cost at program office (electricity, water, telephone...)	$432	$679	$185
4	Business trips	$9,897	$5,889	$198
5	Monitoring trips	$0	$1,388	$47
6	Trainings	$2,830	$2,830	$0
7	Meetings	$2,753	$1,638	$165.16
	Total annual operating cost	**$41,666**	**$44,249**	**$2,721**

Capital cost				
No	Variables	Value at year		
		2013 (12 months)	2014 (12 months)	2015 (4 months)
1	Cost of purchasing equipment	$0	$2,657	$0
2	Total life of the equipment	10	10	10
	Annual capitals cost= cost/ useful life	$0	$266	$266

PSG intervention cost		
No	Variables	Value at year

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		2013 (12 months)	2014 (12 months)	2015 (4 months)
1	Salary and allowance for supporter	$0	$8,815	$2,938
2	Transportation for PSG to patients house	$0	$2,938	$979
3	Mobile telephone allowance for PSG to call to patients	$0	$1,959	$653
4	PSG meeting to report their works	$0	$900	$91
5	Meetings with patients to doing health promotion	$0	$9,722	$19
	Annual PSG intervention cost	$0	$24,335	$4,681

Appendix9: Non ARVs cost borne by provider in adult cohort

Personnel cost				
No	Variables	Value at year		
		2013 (12 months)	2014 (12 months)	2015 (4 months)
1	Average monthly salary for full time staffs	$0.00	$17.16	$17.16
2	Number of full time staffs	15	12	1
3	Average monthly salary for part time staffs	$0	$7.60	$7.60
4	Number of part time staffs	32	26	2
	Annual personnel cost = [(1*2)+(3*4)] * working months	**$0**	**$4,806**	**$120**

Material cost				
No	Variables	Value at year		
		2013 (12 months)	2014 (12 months)	2015 (4 months)
1	Non-ARVs medication	$0	$25	$0
2	Medical consumable at OPCs (syringe, bandage, gauze...)	$0	$205	$10
3	Stationery at OPCs (paper, ink, clipper...)	$0	$288	$7

4	General cost at OPCs (electricity, water, telephone…)	$0	$456	$152
5	Maintenance and repairing cost at OPCs	$0	$150	$50
	Total annual material cost	**$0**	**$1,125**	**$219**
Capital cost				
No	Variables	Value at year		
		2013 (12 months)	2014 (12 months)	2015 (4 months)
1	Estimated cost to replace building at OPCs discounted to 2013	$12,963	$13,223	$13,487
2	Total life of the building	50	50	50
3	Estimated cost to replace equipment at OPCs (in 2015 rate)	$3,159	$3,254	$3,351
4	Total life of the equipment	10	10	10
5	**Annual capitals cost without discounting = (1 : 2) + (3 : 4)**	$575	$590	$605

Appendix10: ARVs cost born by provider in children cohort (unit: USD)

Year	Unit cost borne by patient		Difference ARVs cost (GI –GC)	ttest: Pr
	intervention group	control group		
1 (baseline + 1 follow-up)	$5.5	$5.2	$0.3	0.0007
2 (baseline + 2 follow-up)	$4.2	$4.3	-$0.1	0.2644
3 (baseline + 3 follow-up)	$5.0	$5.4	-$0.4	0.0019
4 (baseline + 4 follow-up)	$4.6	$4.3	$0.2	0.0432
5 (baseline + 5 follow-up)	$4.6	$5.0	-$0.5	0.0116
6 (baseline + 6 follow-up)	$3.5	$4.4	-$0.8	0.0001
7 (baseline + 7 follow-up)	$4.4	$5.0	-$0.6	0.0018
8 (baseline + 8 follow-up)	$4.9	$5.0	-$0.1	0.2759
In average	**$4.7**	**$5.0**	**-$0.3**	**0.0006**

Appendix11: Unit cost borne by patient in children cohort (unit: USD)

Group of similar number of follow-up period (sub-group)	Unit cost borne by patient		GI –GC	ttest: Pr
	intervention group	control group		
1 (baseline + 1 follow-up)	7.77	7.05	0.723	0.275
2 (baseline + 2 follow-up)	10.23	9.04	1.192	0.028
3 (baseline + 3 follow-up)	8.61	7.91	0.703	0.018
4 (baseline + 4 follow-up)	9.51	9.27	0.237	0.248
5 (baseline + 5 follow-up)	8.31	7.68	0.634	0.044
6 (baseline + 6 follow-up)	6.77	6.61	0.164	0.402
7 (baseline + 7 follow-up)	4.3	7.54	-3.243	0.000
8 (baseline + 8 follow-up)	4.63	7.15	-2.528	0.000
In average	8.304383	7.999456	0.305	0.042

Appendix12. Cost effectiveness ratio per adherence rate in children cohort

sub-group	Intervention group					Control group				
	Adherence rate	Unit cost	total obs	total cost	CER	Adherence rate	Unit cost	total obs	total cost	CER
1	0.981	**$140**	32	$4,480	$4,567	0.997	**$119**	12	$1,428	$1,432
2	1	**$140**	69	$9,660	$9,660	1	**$110**	87	$9,570	$9,570
3	0.998	**$142**	388	$55,096	$55,206	0.999	**$108**	372	$40,176	$40,216
4	1	**$134**	200	$26,800	$26,800	0.997	**$100**	160	$16,000	$16,048
5	0.999	**$131**	**132**	$17,292	$17,309	0.996	**$94**	180	$16,920	$16,988
6	0.999	**$128**	35	$4,480	$4,484	1	**$89**	42	$3,738	$3,738
7	0.999	**$126**	48	$6,048	$6,054	0.997	**$89**	56	$4,984	$4,999
8	1	**$127**	63	$8,001	$8,001	1	**$88**	126	$11,088	$11,088

Appendix13: Incremental cost effectiveness ration in adult cohort

sub-group	Effectiveness measurement				Costing measurement				ICER
	Adherence rate in GI	Adherence rate in GC	**GI - GC**	ttest: Pr	Unit cost in GI	Unit cost in GC	**GI - GC**	ttest: Pr	
1	0.9808	0.9970	**-0.01619**	0.29	$140	$119	$21.18	0.004	-$1,308
2	**1.0000**	**0.9996**	**0.00042**	**0.06**	$140	$110	$30.77	**0.000**	**$74,019**
3	0.9981	0.9986	**-0.00046**	0.25	$142	$108	$33.92	0.000	-$73,998
4	**0.9995**	**0.9969**	**0.00268**	**0.03**	$134	$100	$34.74	**0.000**	**$12,982**
5	0.9987	0.9961	**0.00260**	0.21	$131	$94	$37.49	0.000	$14,391
6	0.9988	1.0000	**-0.00119**	0.14	$128	$89	$39.69	0.000	-$33,336
7	0.9991	0.9966	**0.00253**	0.25	$126	$89	$36.70	0.000	$14,502
8	1.0000	1.0000	**0.00000**	N/A	$127	$88	$39.16	0.000	N/A

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