Improving The Efficiency of HIV Care:

Exploring The Role of Global Donor Strategies on Access to Prevention, Testing And Treatment

PhD thesis

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Declaration

I, Sung Wook Kim, confirm that the work in this thesis is my own. The work contained is original, and when other source of information was used, appropriate references were provided. Also, this thesis has never been submitted for any other degree.

Glossary

ART: Anti retroviral Therapy

CEA: Cost Effectiveness Analysis

CER: Cost Effectiveness Ratio

CHAI: Clinton Health Access Initiative

CI: Concentration Index

DHS: Demographic and Health Survey

DID: Difference In Difference

GFATM: The Global Fund to Fight AIDS, Tuberculosis and Malaris

GPRM: Global Price Purchasing Mechanism

HI: Horizontal inequity

HIV: Human Immunodeficiency Virus

ICER: Incremental Cost-Effectiveness Ratio

IDU: Injection Drug Users

MSF: Medecines Sans Frontiers

NSP: Needle and Syringe Programme

NNRTI: non-nucleoside reverse transcriptase inhibitor

NRTI: Nucleoside Reverse Transcriptase Inhibitor

OST: Opioid Substitution Therapy

PI: Protease Inhibitor

PPP: Purchasing Power Parity

PSA: Probability Sensitivity Analysis

QALYs: Quality-adjusted life year

TRIPS: Trade-Related Aspects of Intellectual Property Rights

UNDP: United Nations Development Programme

UNICEF: the United Nations Children's Fund

PEPFAR: US Presidents' Emergency Plan for AIDS Relief

VCT: Voluntary Counselling and Testing

WHO: World Health Organisation

Abstract

As the growth of donor funding for HIV/AIDS begins to slow and the increasing burden of non-communicable diseases forces funders and policy makers to reassess health systems priorities – it is important to understand the most efficient way to allocate scarce health resources. The aim of this PhD thesis is to investigate whether the activities of global donors improved the efficiency of HIV programmes from a global perspective. This thesis will use a case study approach to focus on three key activities of global donors in the HIV treatment process: harm reduction, HIV testing and drug procurement.

This thesis will provide empirical evidence on the cost effectiveness of harm reductive in the Ukraine, the equity of HIV testing in Malawi, and the efficiency of centralising procurement of HIV drugs at the international level. Each theme is explored using a single country case study. Research methods exploit widely available datasets not yet used to answer these questions. Each chapter describes the methods used for the analyses i.e., Markov Monte-Carlo simulation, a decomposed concentration index and difference-in-difference analysis.

The findings of these analyses are as follows; Chapter 2 concludes that the harm reduction programme in the Ukraine is cost effective in terms of QALYs gained and infections averted. Chapter 3 demonstrates that existing inequity in HIV testing has been reduced and highlights how socio economic factors such as income, education and gender influence inequity in HIV testing in Malawi. Chapter 4 shows that voluntary pooled procurement can effectively reduce the procurement price of an HIV drug.

Given these findings, this thesis suggests that strategies adopted by global donors have improved the efficiency of HIV care in these contexts.

Dissemination of the thesis

- Chapter 2: ‘CEA of harm reduction interventions in the Ukraine’ was published in *Cost effectiveness and resource allocation*: Kim et al. (2014), Comparing the cost effectiveness of harm reduction strategies: a case study of the Ukraine, *Cost Effectiveness and Resource Allocation* 2014 12:25.

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- Chapter 4: “Can Voluntary Pooled Procurement Reduce the Price of Antiretroviral Drugs?: A case study of Efavirenz” was accepted in *Health Policy and Planning* as of 13th Nov 2016.

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1.1 Introduction

The *Human Immunodeficiency Virus (HIV) and* Acquired Immunodeficiency Syndrome (AIDS) have been a major priority for global donors for over a decade. The emergence of the Global Fund to Fight AIDS, Tuberculosis, and Malaria (GFATM) in 2002, and the US President's Emergency Plan for AIDS Relief (PEPFAR) in 2003, have supported the global response to HIV/AIDS (1).

The main source of financial support for HIV prevention and treatment, particularly in resource limited countries, include multilateral institutions, bilateral agencies, non-government organisations and public private partnerships (2). Multilateral institutions include the World Bank and UN agencies such as UNICEF and WHO. Bilateral agencies are linked to national governments and include the U.S Agency for International Development (USAID) and U.K Department for International Development (DFID) (2). Public private partnerships in this context are commonly also known as global health initiatives (GHIs). In addition to conventional global donors, global health initiatives (GHIs) have emerged since 2000 (3). Global health initiatives (GHIs) can be defined as 'a blueprint for financing, resourcing, coordinating and/or implementing disease control across at least several countries in more than one region of the world' (4). This term generally includes four major global donors; the World Bank, the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM), the US President's Emergency Plan For AIDS Relief (PEPFAR) and the Global Alliance for Vaccines and Immunization (GAVI) (3) although other organisations may be included.

This variety of donors has increased global health funding and particularly, resources for the global HIV response (5). The GFATM scaled up funding for HIV programmes globally from 1% of total support for health in 2002, to 8.3% of total support in 2007 (6). The budgeted totals of GFATM HIV spending were US$ 16 million for Round 1 in 2002, but increased to US$ 135 million for Round 10 in 2010 (7). Similarly, PEPFAR invested US$ 81 million and US$ 89 million for HIV

programmes in Zambia and South Africa, respectively, in 2004 and that funding was increased to US$ 266 million and US$ 546 million in 2009, respectively (8). Between 1999 and 2009, GAVI received approximately US$ 3.8 billion for vaccine programmes including HIV but it was merely US$ 2 million in 2000 only (9). Since 2000 the Multi-Country HIV/AIDS programme (MAP), which is implemented by the World Bank for Africa, raised up to US$1.2 billion compared with the first phase of $ 500 million between 1987 to 1997 (10). These examples are good evidence that GHIs have successfully raised large amounts of funding to support the global HIV response – with positive implications for HIV care.

The significant expansion of HIV financing enabled a great number of people to receive antiretroviral therapy (ART) in 2015. Since 2000, the World Bank delivered ART to approximately 2 million adults and children living with HIV (11). As of September 2011, the 'US Presidents' Emergency Plan for AIDS Relief (PEPFAR)' directly supported ART for 3.9 million patients worldwide (12). In 2014 approximately 40 % of people living with HIV can receive ARV whereas less than 1 % of people could have access to HIV treatment in 2000 (13). Approximately nine millions of people living with HIV are being supported ART through programmes by GFATM in 2016 while the number of people on ART was less than 1 million in 2004 (14). Clearly, the number of people accessing ART has increased with the funding of the GHIs.

Despite progress in improving access, achieving universal access to HIV treatment remains a major concern in terms of global health. In 2015, the rate of coverage for ART was less than 50 % of 35 million HIV infected, and 1.1 million people are newly infected with HIV globally (15). This means that more than 18 million of HIV infected people are living without access to ART treatment. Approximately 23% of pregnant women living with HIV are exposed to a risk of HIV transmission to their babies due to the absence of ART (15).

Furthermore, in the current financial climate, and with a growing burden of disease attributable to non-communicable diseases, HIV funding is not likely to increase at the same rate as previously observed. In fact, the growth rate of donor funding for HIV/AIDS has already slowed significantly (16,17). Since the financial recession in 2008, funding has stagnated and the growth rate of development assistance by UN agencies slowed from 6 percent to 2 percent (17). This is critical because current HIV programmes are not sustainable with the reduced rate of HIV funding (18). Given this situation, 'How to do more with less' is a priority for global donors aiming to improve access to HIV treatment (19). In brief, it is necessary to consider improving the efficiency of HIV programmes within currently available, or even contracting, budgets for HIV care.

In conclusion, the emergence of multi-country global donors has historically resulted in a significant increase in the number of people benefiting from HIV programmes. However, in the current funding climate, sustained or expanded access will likely only be achieved by increasing efficiency. Current HIV funding would not be sufficient to cover the majority of people living with HIV if current trends continue. The goals of improving efficiency for global donors and their concomitant activities to achieve the goals will be discussed in the next section.

1.2 The goals of global donors for improving efficiency

Pursuing efficiency with scarce resources is a common concern for decision makers. In general, three concepts of efficiency are used in health economics: technical, productive and allocation efficiency (20,21), each of which is described in more detail below. This thesis will present one case study for each of these forms of efficiency, as described in Section 1.3.

1.2.1 Technical efficiency

Technical efficiency refers to the production of health output on the production possibilities frontier. This means that a given level of output should be achieved using a minimum level of inputs (20). Technical efficiency thus refers to the optimal combination of resources for the delivery of health services (22). For example, if treatment A needs 10 tablets to generate 1 Quality adjusted life years (QALYs) but treatment B needs 20 tablets, treatment A is technically more efficient (21). Technical efficiency can be improved by reducing the unit cost (23,24). The majority of cost-effectiveness papers have informed questions regarding technical efficiency (22). [1]

In terms of improving technical efficiency, harm reduction intervention programme is useful because it is a more cost effective intervention than ART (anti-retroviral therapy). The unit cost of the intervention is much lower than the cost of ART. Once infected with HIV, ARV costs are much higher to gain the same level of health outcome than the costs of prevention interventions because HIV patients should take medicine during their life (25,26). If harm reduction intervention is properly used, HIV transmission can be prevented at much lower costs (25). Technical efficiency is assessed based on the unit cost of a service (23). Overall, harm reduction interventions are useful to improve technical efficiency.

1.2.2 Allocative efficiency

In the context of health economics, allocative efficiency means maximising the population health of the community by appropriately allocating scarce resources (21). When allocative efficiency is achieved, it is not possible to increase outputs by reallocating resources between programmes or social groups (27). In other

[1] Opinions differ as to which efficiency cost effectiveness analysis is linked with. Palmer et al. (21) mention that productive efficiency is to compare alternatives. However, a number of health economic studies link the concept of technical efficiency with cost effectiveness analysis (18,22,27). This thesis follows the views of the majority.

words, someone cannot be made better off without making others worse off in this situation. Allocative efficiency is related to welfare economics and a societal perspective (21).

Reaching high burden population groups to supply HIV testing is likely to improve allocative efficiency. Greatest global burden of disease (GBD) frequently exists in these communities as marginal communities often suffer from multiple co-morbidities and vulnerabilities (25). As such, targeting these groups will tend to have a high(er) impact on DALY reduction (28). Moreover, use of needles by injection drug users (IDU) is a significant route of HIV transmission as it accounts for 5-10% transmission of HIV globally (29). Men who have sex with men (MSM) groups in Africa have been reported to have a higher HIV prevalence rate, ranging from 8.8% to 20% (30). In particular, migrants in Malawi have been observed to be more exposed to HIV infection (31). Once these high burden groups get infected, they can jeopardize the whole society in a number of ways. To start with, people infected through interaction with high risk groups will more than likely transmit HIV to their spouses (31). Subsequently, HIV can then be transmitted to other parts of the country through transport routes by lorry drivers or by fishermen on the shores in Africa (32). In South Africa, IDU which only make up 1.2% of total population, account for 6% of total HIV prevalence (25).[2]

The main problem is that once people get infected the treatment costs skyrockets compared to prevention costs such as HIV testing and counseling (33). For example, the cost of HIV testing per patient is US$ 11 (95% CI: US$ 10.81-12.86) (34), but the cost per patient year initiated on ARV soars to US$ 208 in Malawi (35). As another example, in Kenya, the cost of mobile HIV testing reaching people in rural areas was $8 - $20 (36), while the cost per patient on ART was $206 (37). As a consequence, resources will be inevitably concentrated on HIV infected people with high treatment

[2] As an extreme example, in USA, MSM groups account for 61% of HIV infection among adults (245).

costs; thus, maximising the population health of the community becomes impossible. The investments in these communities will yield a greater number of cases averted than similar investments in communities already at lower risk of infection. Clearly, considering that HIV is a communicable disease and the at-risk groups such as IDU, MSM and commercial sex workers are more likely to transmit HIV than the general population (25), it would be more beneficial to reach these deprived groups in a targeted approach thus improving allocative efficiency.

Measuring equity is one way to assess service access for vulnerable groups. Equity of access to health services is considered a way to address health inequity (38). The concentration index will be negative if marginalised groups use health services less than the whole population does (39). Inequity in HIV testing in low- and middle-income countries, such as those in sub-Saharan Africa, is generally higher since inequity is strongly affected by socioeconomic factors such as gender or marital status (3,40,41). In short, service access for vulnerable groups can be assessed by measuring equity.

As such, improved equity could be viewed as a proxy for improved allocative efficiency in the context of HIV testing in developing countries. In this connection, Mcpake et al. (42) argue that equity may be viewed as a proxy for allocative efficiency in an imperfect competitive market.

1.2.3 Productive efficiency

The conventional concept of the productive efficiency is maximising outputs within a given level of inputs (18,20,21). In the context of HIV, this efficiency is generally interpreted as maximising the number of uptake of HIV treatment (18).

In the majority of resource limited countries, health systems will encounter financial challenges as donor funding declines and goals ambitiously encourage 90:90:90 (43). Considering a reduction in donor HIV spending from US$ 7.7 billion in 2009 to US$ 6.9 billion in 2010 (44), it is important to maximise outputs with currently available funding. This example shows that pursuing productive efficiency is an important task for global donors.

Extensive efforts have been made to improve the productive efficiency when global donors supply HIV drugs(18). To do so, global donors focus on the strategy such as voluntary pooled procurement to buy more HIV drugs with given quantities of budgets (45). This is attributed to the fact that ARV price is a main component of HIV treatment. For example, mean treatment costs per person are approximately US$ 880 per patient, of which US$ 514 were for drugs costs in the PEPFAR funded HIV programme (18). To sum up, global donors began to concentrate on producing maximum quantity of outputs in order to supply more HIV drugs and pursue productive efficiency of HIV programmes.

1.3 The activities of the global donors for local problems

This section will briefly describe the three case studies used to explore efficiency improvements in HIV programming in this thesis. As previously mentioned, improvements in technical efficiency will be explored through the case of harm reduction in the Ukraine, allocative efficiency will be explored using the case of

equity in treatment access in Malawi and productive efficiency will be explored using the case of voluntary pooled procurement to reduce the price of an HIV drug.

Within each section below, a brief description of the ‘intervention’ or ‘case’ is provided before a brief review of the literature, describing what is already known about harm reduction, equity in HIV treatment access and voluntary pooled procurement and where knowledge gaps remain.

1.3.1 Improving harm reduction to promote technical efficiency

Harm reduction is a public health intervention designed to reduce the multiple harmful outcomes of injecting drug use, including increased risk of HIV transmission (46,47). Needle and syringe programmes (NSPs) and opioid substitution therapy (OST) are typical harm reduction interventions for injecting drug users (IDUs), typically combined with ART, condom distribution and health education programmes. In addition to preventing HIV, these efforts can be understood as an attempt to overcome equity concerns and reach marginalised groups(48). From 2004 to 2008, the GFATM supported approximately US$ 180 million in harm reduction programmes in 42 countries. The GFATM is thus a major funder of harm reduction interventions in developing countries (49).

Given the fact that the global donors consistently support harm reduction interventions in low- and middle-income countries such as Ukraine, the evidence on the cost-effectiveness of the interventions is essential to evaluate their activities. Injecting drug use in Eastern Europe accounts for up to 80% of HIV infections (25) whereas the injecting drug use in Africa was negligible (50). Most IDUs need harm reduction interventions, but existing harm reduction services in Eastern Europe do not cover most IDUs, accounting for merely 10% of IDUs in the region (25). Based on the fact that GFATM supports harm reduction as its commitment to fund evidence-based, cost-effective interventions (7), it is required to have the evidence

on cost-effectiveness to secure the funding for harm reduction interventions and call funders' attention on this intervention.

In addition, harm reduction interventions are effective to improve technical efficiency. This point was already mentioned in Section 1.2.1. This intervention can save ARV costs if it is appropriately implemented. Also, this intervention can increase QALYs by preventing HIV infection. In sum, harm reduction intervention can improve technical efficiency.

Chapter 2 will explain that the cost effectiveness of a single intervention is known from available evidence. However, the CEA of harm reduction has only been partially established. A literature review was performed to summarise existing evidence on the cost-effectiveness of the most common harm reduction strategies; NSPs, OST, and combined NSP and OST. The literature review found an evidence gap about the cost-effectiveness of combined intervention of NSPs and OST. The detailed literature review on harm reduction intervention is incorporated in Section 2.2, Chapter 2.

Thus, harm reduction interventions conducted by GFATM appear to be an appropriate case study to offer evidence on cost-effectiveness in order to assess interventions of global health initiatives (GHI) given the fact that GFATM is one of the major funder for harm reduction interventions (7). As it is possible that global donors and health system apply for different levels of thresholds, WHO CHOICE threshold can be used for this empirical study (51). This thesis is expected to better inform our understanding of the cost-effectiveness of harm reduction in this context. The second chapter of this thesis will conduct a cost-effectiveness analysis of combined harm reduction intervention in Ukraine. Two types of harm reduction interventions will be combined: NSPs and OST.

The main method that will be used in this chapter is a Markov model. This model was chosen for the following reasons. First, primary data for harm reduction interventions carried out in Ukraine were not available. Therefore, it was not available to conduct a cost-effectiveness analysis using a randomised controlled trial (RCT) data. Alternatively, cost-effectiveness analysis based on modelling can be employed (52). Second, the Markov model is useful to estimate cost-effectiveness of a chronic disease such as HIV or asthma (53). This is because it assumes current patient state is independent from previous state (52). Consequently, in this study, the model would be appropriate to estimate costs and outcomes in terms of QALYs and HIV infection for the three strategies of harm reduction intervention. The model also attempts to estimate uncertainty with probability distributions. Monte Carlo simulation will be used based on these distributions, due to uncertainty in the results of the model.

The main data for cost is grant data obtained from the GFATM website. This offers costs spent on the harm reduction interventions implemented by the GFATM. The value of QALYs and HIV infection averted will be obtained from existing researches. Costs per cycle will be presented to use the Markov model.

In the context of global HIV finance, there are grant givers and grant receivers. Then, should whose willingness to pay (WTP) be applied when we carry out a cost effectiveness analysis? Given the fact that there are multiple donors in a global HIV setting, this is a relevant question since the answer for this question can change the conclusions of a cost effectiveness analysis. Also, this question is related with technical efficiency since the level of appropriate resource allocation is decided by WTP and cost-effectiveness (CE) threshold. This point will be discussed in the next section.

1.3.1.1 Cost-effectiveness threshold and willingness to pay (WTP): Whose WTP counts?

Cost-effectiveness analysis (CEA) starts from the notion that there is a limited budget that can be used for improving population health. To maximise the population health with given budgets, cost-effectiveness (CE) threshold is used for CEA. Although WHO CHOICE threshold is widely used at the moment, it is not without critics. This section explores the relationship between willingness to pay and the threshold, whose willingness to pay (WTP) counts, and recent debate around the appropriate value of threshold in a global health setting.

In principle, the appropriate threshold needs to be decided based on how much a health system should be willing to pay for improving population health (54). As various global funders emerge, however, it is not straightforward to decide which cost-effectiveness threshold needs consideration when the role of donors and health systems are ambiguous.

The threshold of cost-effectiveness analysis informs whether a new treatment is cost-effective under the current budget constraints. Due to the limited budget of health care provider, the appropriate threshold is the opportunity cost replaced by a new treatment (55). For example, the threshold ranges from 20,000 to 30,000 per QALYs in the UK despite criticism (56). That is to say, incremental cost-effectiveness ratio (ICER) should not exceed this threshold to be accepted as a cost-effective treatment.

As a classical way of presenting WTP, threshold can be presented as a single number. In that case, the threshold may reflect the view of health care system (57), a medical programme (58) or institutions such as NICE (59) on WTP. These thresholds can be labelled ‘local thresholds’. As aforementioned, UK use threshold of GBP 20,000–30,000 since 2004 (56,60). Amongst the low- and middle-income

countries, Thailand use their own threshold value of 100,000 Baht in 2008 values (51). However, the problem here is that there exist two parallel thresholds simultaneously. With respect to the Thailand case, some cost-effectiveness studies use local threshold value as a threshold while other studies use WHO CHOICE threshold (51). As a result, it is difficult to make a decision on which intervention is regarded as cost-effective depending on what thresholds have been applied.

In some studies, the WTP of individual patients rather than donors or health systems is the matter of interest. The WTP of individual measures how much individuals are willing to pay when they use a certain health service (61). Sachs (62) argues that critical diseases such as HIV/AIDS that incur high burden of treatment to patients can go well beyond income losses. If so, threshold based on WTP of individuals will increase the risk of death as the threshold does not appropriately measure the cost of the disease (63). This approach is based on the notion that each individual is entitled to spend GDP per capita as a fair share of a country's wealth (64,65). However, it is unrealistic to assume a country is willing to allocate its whole GDP to health care (65). This example shows the WTP of individual patients can be a major concern for health economic studies.

Similarly, cost-effectiveness threshold estimated on the willingness to pay (WTP) may reflect the WTP of the citizen living in the country. Willingness to pay approach is to define social value by preference approach rather than based on opportunity costs (54,66). Shiroiwa et al. (67) explored WTP per QALY in 6 countries: US, UK, Japan, Korea, Taiwan, and Australia. Randomly sampled respondents answered questionnaires asking how much of money you are willing to pay for increasing QALYs. The estimated WTP values were WTP values were Japan: JPY 5 million, Korea: KWN 68 million, Taiwan: NT$ 2.1 million, UK: £23 000, Australia: AU$ 64 000, and US: US$ 62 000.

However, as the authors acknowledged, if respondents do not think about budget, the WTP of respondents can increase expenditure on health care as they wish to pay more. In other words, the public's view on the WTP can be different from the view of politicians or decision makers, and may not properly reflect the allocation of health care budgets (68).

Only a few disease-specific WTP studies exist and estimated values of WTP that may vary significantly depending on the methodology such as a sample selection (63). If each country's cost-effectiveness threshold simply reflects the WTP of its own citizens, these values may be different appropriately across countries (69). Therefore, there is no clear guideline regarding which WTP based threshold needs to be applied for countries where WTP was not estimated. In other words, it is needed to consider another type of threshold for cost-effectiveness studies at global level.

In the context of the global health funding, there exists two players in the healthcare market: a donor and a recipient country. In general, donors implement interventions in low- and middle-income countries while a recipient country acts merely as a grant receiver. Usually, donors not only provide interventions but also support finance. As an example, UNICEF and UNAIDS directly carry out prevention of mother-to-child transmission (PMTCT) interventions in resource limited countries (70). In this case, the donors work as a both funder and health service provider.

GFATM relies on the different type of funding mechanism. It only disburses the grants to the recipient countries (45,71,72). Then countries merely play roles as healthcare providers. For example, in a number of countries, ARV intervention was carried out with the financing from GFATM. But the role of GFATM is restricted to the disbursement of grants, which is what differs from other international organisations such as UNAIDS. Local intervention is carried out in the country

where GFATM grants were given (46). This makes it of no use to distinguish a payer and a provider since the payer and the provider are separated under the GFATM system.

For this case, a threshold based on the human capital approach such as WHO threshold will be useful (51). It is because that it may be possible that donors and health system can apply for different levels of thresholds. In other words, the donors and the governments of the recipient countries may have different budget constraints (51). WHO Commission on Macroeconomics and Health (73) reported the WHO CHOICE threshold of three times GDP per capita at a given country was deemed ‘cost-effective’ and one times GDP per capita deemed ‘very cost-effective’ for averting DALYs. When one times GDP or three times GDP is used as a threshold for cost-effectiveness analysis, it assumes that a country is willing to pay that much to increase DALYs (66). However, local decision makers would not think that people living with HIV should pay for the treatments when GFATM support grants. As such, it is unclear what donors or countries have payer roles.

1.3.1.2 Criticism of WHO CHOICE threshold

There also exists criticism about whether the WHO CHOICE threshold is practically useful. The problem of adopting a generalised GDP-based threshold to all over the world is that the threshold cannot reflect opportunity costs varying across countries (54,74).

In addition, some have argued that there is no empirical basis of this estimation on WHO CHOICE threshold (75). Recent studies argue that the current threshold based on WHO CHOICE (three times GDP per capita) is so high that the new treatment can easily fall within the threshold although it is not sure whether the new treatment is more cost-effective than the conventional treatment (54). For instance, in Kenya, a new clean water intervention was cost-effective at I$ 614 per

DALY averted. Even if the effectiveness is reduced by half, I$ 1228 per DALY averted is still far lower than three times GDP per capita in Kenya (66). As such, in that case, it is difficult to insist that the new intervention cannot be accepted under the current threshold.

Another criticism of the WHO CHOICE threshold is that using entire GDP per capita to obtain QALYs requires substantial sacrifice from both individuals and society. If a certain intervention is cost-effective at the threshold of one times GDP per capita in a certain country, the entire GDP per capital should be spent every year per person (66,76). In terms of WHO CHOICE guideline, this is deemed cost-effective, but in most cases the healthcare budget is limited. In line with this, some have argued it is not possible to offer health care for much of the population without increasing tax or government debt when threshold is above GDP per capita (64). This approach is unrealistic as it assumes a country is willing to spend its whole GDP to health care (65). In addition, this approach is based on average cost-effectiveness ratio rather than the ICER, so it is doubtful whether it can serve as an appropriate value for the threshold using ICER (77). In brief, recent debate on the WHO CHOICE threshold acknowledges that the current value of the threshold is high without empirical evidence. Bearing this in mind, a few researches work on econometric analysis to estimate appropriate level of threshold for countries. Woods et al. (54) argued that threshold value should range from 1% to 51% of low income countries rather than 3 times or 1 times GDP, assuming different income elasticity across countries.

Nevertheless, the recent studies regarding an appropriate level of the threshold still does not emphasise the issue of ‘who is payer’ in the global donor market. When GFATM is involved, this issue becomes more complicated because it mainly works as a funder, not a provider. In current circumstances, where external funding from international donors is a main resource of HIV intervention in low- and middle-income countries, consideration on the issue of ‘payer’ is also

necessary as the discrepancy of budget constraints between donor and health system can result in a different decision on the CEA of the identical intervention.

1.3.2 HIV testing to improve allocative efficiency

Global donors mainly support sub-Saharan countries for HIV testing services. For instance, the United States Agency for International Development (USAID) promotes counselling with HIV test to reduce risky behaviour causing HIV/AIDS in African countries, allocating funds for at least 11 new HIV testing centres in 2001(78).

Malawi was one of the first two countries receiving the support from GFATM. With the support from GFATM, the Malawi Ministry of Health planned to increase the number of HIV testing services including VCT facilities (79). By late 2004 and early 2005, testing began to be available in rural areas, first at district hospitals and then at clinics (80). The number of VCT centres increased significantly: by the end of 2005, Malawi had 249 VCT centres (81). In 2004, although there were many HIV test sites such as private hospitals, three major Malawi AIDS Counselling and Resource Organization (MACRO) sites were located at only big cities: Mzuzu, Lilongwe, and Blantyre. In 2008, a national programme offering HIV testing to pregnant women was implemented at more than 500 sites in Malawi (82). Consequently, mobile and door-to-door testing have been widely supplied (82). These examples show the efforts of global donors to supply HIV testing in Malawi.

The literature review presented in Chapter 3 will explain that HIV testing in low- and middle-income countries such as sub-Saharan Africa is more strongly associated with socioeconomic factors such as gender or marital status from available evidence. Also, it will be addressed that the efforts of global donors to improve access to HIV testing appear successful so far in Malawi. However,

equity of HIV test access has not been explored in the Malawian context. The full literature review can be found in section 3.2, Chapter 3.

In addition, achieving equity in HIV testing is an effective way of improving allocative efficiency in HIV treatment for the whole society. Compared to ARV therapy, HIV testing is relatively cheap and highly cost-effective in terms of DALYs (83). This means that the uptake of HIV testing would be less affected by affordability for individuals. MSM groups are known to have 19.3 times higher odds of HIV infection than the general population (84). Particularly, gender inequity in HIV testing can have critical effects not only on individual health but also on health systems. Firstly, it can raise the possibility of transmitting HIV from mother to children, as the mother is not aware of her HIV infection (85). Secondly, the failure to detect HIV in its early stages will diminish the benefits of ARV (85). As a result, if inequity in HIV testing is increased, scarce resources will not be used in a Pareto optimal way, significantly increasing the HIV treatment costs. In brief, this case study is appropriate to understand allocative efficiency.

As such, this case study in Chapter 3 explores a recent change in inequity for the HIV test uptake. In other words, this is to see whether supports of global donors for increasing the uptake of HIV testing have reduced inequity in it. Chapter 3 in this thesis will carry out an analysis on the socioeconomic inequity of HIV test uptake in Malawi. Using need and non-need variables, decomposed concentration index will be estimated. The need variables include symptoms of sexually transmitted infections (STIs), while non-need variables include wealth, education, literacy, and marriage status.

Concentration index is a standard tool to measure equity in the use of health service (39). A main method used in this study is a decomposed concentration index introduced by Van de Poel et al. (86). This concentration index is different from a standard concentration index in that the highest income group is used as a

reference to show hidden inequity. This is mainly because higher prevalence of HIV among the highest income group is expected to put a new complexion on horizontal inequity. In general, a disease is more common for the poor group, so needs are concentrated in the poor group (87). However, conversely, HIV is more common for the highest-income group in Malawi (88,89). This can change the degree of horizontal inequity, and the decomposed concentration index by Van de Poel et al. is expected to perform better.

The main data used in this study is from the DHS. DHS data, funded and collected by the United States Agency for International Development (USAID), reflects the activity done by USAID (78), so the data is appropriate to assess whether equity was enhanced by global donors' support on grant recipients countries. Voluntary HIV testing has been implemented in 29 sub-Saharan countries since 2001, and information on this has been collected by 47 DHS surveys (90). DHS survey was designed to offer health and demographic indicators at both country and regional levels. DHS 2010 and DHS 2004 collected detailed HIV-related data including whether respondents received an HIV test and symptoms of STIs. The age of the respondents ranges from 15 to 49 for women and from 15 to 54 for men (88). This survey includes following districts: Mulanje, Thyolo, Kasungu, Salima, Machinga, Zomba, Mangochi, Mzimba, Blantyre, and Lilongwe. GPS information was also collected by field staff. Men and women in the age between 14 and 59 year after providing consent were interviewed with questionnaires. Asset index and the variable of whether they received HIV test were included. In sum, this data is appropriate for this study as the data contains information about needs, socioeconomic status of interviewees and receipt of HIV test.

This study explores the effect of all types of HIV testing included in the data rather than merely focusing on the HIV testing facilities. Despite intensive literature search, very few literatures were found mentioning the information about the location of HIV testing facilities in Malawi. Literature search using the keywords

HIV testing facilities, Malawi, and *policy* identified 17 works of literature (#1–3 in Appendix 2-1). Likewise, a literature search using the keywords *HIV testing, location,* and *Malawi* identified 11 works of literature (#4 #5 #6 in Appendix 2-1). Combining the search strategies of#1–3 and #4–6 identified 27 papers. Excluding duplicates, 24 literatures were included. Google Scholar was also used for the additional literature review. However, none of these articles informed the detailed location of HIV testing facilities in Malawi. As a result, it is not possible to explore the role of policy decision making in the location of testing facilities and the consequent equity with current information.

In brief, this empirical study attempts to explore whether how the support of global donors, expressed as increasing supply of HIV testing, is associated with equity in HIV test uptake. A decomposed concentration index will address this research question in Chapter 3.

1.3.3 Drug procurement to improve productive efficiency

Currently, global donors dominate the procurement of ARV markets. Major donors such as GFATM and the US President's Emergency Plan for AIDS Relief (PEPFAR) currently purchase large volume of ARVs to supply national treatment programmes (91). For instance, PEPFAR captures 40% of the total market for the first fixed-dose combination (FDC) version of 3TC/NVP/d4T30 in 2008 (92). By 2008, PEPFAR accounts for 27–34% of market volume for first line ARVs such as EFV, 3TC, NVP, d4T and ZDV while GFATM captures 47–57% (92). Given this fact, it is no exaggeration to say that global donors play a major role in the procurement of ARV.

This domination is mainly caused by the large volume of purchasing ARV.[3] What happens by purchasing large quantities is to allow global donors for the power of monopsony. As they purchase in large quantities, the global donors can play a dominant role in global ARV markets. Global donors are able to control ARV prices as they use competitive tendering (69). They buy HIV drugs in large quantities, deciding which manufacturers will supply ARVs among the bidders.

One of the tools that help global donors to dominate the procurement markets is pooled procurement. Pooled purchasing can simplify the process of procurement for both manufacturers and buyers, but risks distorting the market with monopsony (93). In the end, pooled procurement will reduce the number of purchasers and thus could result in restructuring of the current global ARV market (94). Pooled procurement is also called group purchasing and involves bulk purchasing (95). In the process of implementing pooled procurement, purchasing is done by one procurement body on behalf of a group of countries. The main advantage of the pooled procurement process is to reduce drug costs through economies of scale.

GFATM initiated voluntary pooled procurement (VPP) in 2010 to reduce the prices of HIV test kits, ARVs, long-lasting insecticide-treated nets (LLINs) and artemisinin-based combination therapies (ACTs). Between 2009 and 2011, 47 countries joined and VPP purchased 5 core health products: ARVs for HIV, artemisinin-based combination therapy (ACTs) for malaria, long-lasting insecticidal bed nets (LLINs), rapid diagnostic tests (RDTs) for *tuberculosis (*TB), and condoms. Between 2009 and 2011, approximately 23% of above products that

[3] In addition, global donors were able to negotiate the prices of ARVs with holding the position of monopsony. This is referred to as 'third-party negotiation' (94). For example, the Clinton Health Access Initiative (CHAI) negotiated to reduce the price of the first-line treatment tenofovir + emtricitabine + efavirenz (TDF + FTC+ EFV) from the 2007 price of US$487 to US$349 in 2008 (92,189). This negotiation power gives global donors an advantage in procurement markets. This is encouraging in terms of expanding access of HIV patients, especially in low-income setting since it was possible for global donors to supply HIV drugs at reduced prices.

GFATM financed were procured through the VPP programme, and GFATM estimates that the VPP saved $58 million between 2010 and 2011 (96). Under the VPP system, each principal recipient (PR) country volunteered to join the procurement programme. Overall, 307 million daily doses of antiretroviral drugs were procured and approximately 336,000 people received ARV therapy through this programme (97).

The literature review presented in Chapter 4 reveals that pooled procurement lowered costs for condoms and other HIV commodities. However, evidence for the effectiveness of VPP in reducing drug prices is incomplete. The full literature review can be found in Section 4.2, Chapter 4.

In addition, for the goal of improving productive efficiency in HIV intervention programmes, drug procurement is an important process to maximise outputs (98). Productive efficiency needs that all companies (or global donors) run using best practice processes. It was known that improved efficiency in ARV procurement can lower the cost of treatment for HIV (12). For example, Improved procurement system reduced PEPFAR's treatment costs per patient to US$ 335 in 2012 from US$ 1100 in 2005 (12). Inefficient procurement and supply systems, and high ARV costs remain to be the main obstacles to expanding access to essential HIV drugs in resource limited countries (98). Pharmaceutical markets in resource limited countries are constrained by insufficient procurement systems for HIV drugs (99). Given this fact, global donors used strategies to improve productive efficiency of the supply of HIV drugs and other commodities transported by logistic systems (3). Likewise, the purpose of VPP is to improve productive efficiency. If the strategy of VPP is effective, global donors or health systems can purchase more ARV drugs with the same amount of budget, reducing the procurement prices. In conclusion, this case study is appropriately linked with productive efficiency.

As such, chapter 4 in this thesis aims to estimate the impact of VPP on the procurement prices of ARV drugs using econometric methods. The purpose of Chapter 4 in this thesis is to assess whether the new strategy of procurement of global donors, voluntary pooled procurement, can be maintained in a near future and reduce procurement prices of drugs for people living with HIV to antiretroviral therapy.

The main method used in this chapter is difference-in-difference (DID) analysis. DID is an appropriate method to use when comparing the effect of a policy change. This method has a few advantages. First, DID is less subject to biases caused by policies implemented at different time points across countries (100). Considering that voluntary pooled procurement was implemented in different years by countries, this is an appropriate method to estimate the policy effect. Second, DID controls confounding factors by using fixed effects model (101). DID wipes away time invariant factors (101) ; so, this is a preferred analysis to 'before and after' analysis. When it compares over time within a country, DID eliminates the country fixed effect.

The main source of data used in this study is provided by the purchase price report of the Global Price Reporting Mechanism (GPRM). These are panel data consisting of price data, mainly from low and middle-income countries. The data set shows transaction volume, procurement price, destination country and procurement date for the period 1999–2014. The data is freely available on the WHO website, and a researcher can choose according to his/her interest, the type of drug (generic or brand), name, strength of drug, and manufacturers. These data are mainly obtained from international organisations such as the GFATM, the Clinton Foundation, Crown Agent, the Global Drug Facility (GDF), the International Dispensary Association (IDA), Mission Pharma, Management Sciences for Health (MSH), the Partnership for Supply Chain Management (PFSCMS), the United Nations Development Programme (UNDP), the United Nations Children's Fund (UNICEF), and the WHO/Contracting and Procurement Service (WHO/CPS).

In conclusion, an examination is needed of the effect of this programme on price reduction of antiretroviral drugs. Given the amount of commodities related to HIV treatment procured through this programme, the dominance of global donors on procurement market using the VPP will be boosted up in the near future. Depending on the result, this case study can be used as evidence encouraging more countries to join VPP, justifying global donors' dominance of ARV procurement markets.

1.4 Conclusion

The emergence of global health initiatives have boosted health care financing and improved both access and coverage of HIV treatment for people living with HIV in low and middle income countries. However, although global donors grow rapidly, some aspects of them have been overlooked.

This introductory chapter demonstrated a paucity of evidence of their performance related with the efficiency of HIV programmes. Thus, this thesis attempts to fill this gap by dealing with several neglected issues of both intervention on people living with HIV and the procurement of HIV commodities of global donors, which the existing literature has omitted. This thesis attempts to evaluate the effect of global donors' activities on deprived groups in the context of HIV treatment such as injection drug users and low-income countries such as Malawi. Also, this thesis will assess the policy impact of the programme implemented by the global donors. To sum up, this thesis aims to not only evaluate the results of interventions such as harm reduction interventions but also provide implications for a policy on the procurement process of HIV drugs conducted by the global donors.

In the context of contracting funding and expanding demand for spending on HIV programs to achieve 90:90:90 goals, this thesis will explore whether global donors and their beneficiary countries can maximise the effectiveness of every dollar spent. Three case studies will be used to explore the potential for improving efficiency; in Chapter 4, voluntary pooled procurement is used as a case to explore the potential for improving productive efficiency; in Chapter 2, cost-effectiveness of harm reduction interventions as an example of the potential for improving technical efficiency; and in Chapter 3, equity in HIV testing is used as a proxy for improvements in allocative efficiency. In brief, this thesis is to explore the role of Global Donors in improving the efficiency of HIV prevention and treatment.

2 Economic evaluation on harm reduction intervention[4]

[4] This chapter was published in Dec 2014 in 'Cost effectiveness and resource allocation' : Kim et al. (2014), Comparing the cost effectiveness of harm reduction strategies: a case study of the Ukraine, Cost Effectiveness and Resource Allocation 2014 12:25. This paper was attached in appendix.

2.1 Introduction

There are an estimated 15.9 million injecting drug users (IDUs) worldwide, 80% of whom live in developing and transitional countries (25). The concurrent epidemics of HIV and injecting drug use have rapidly increased HIV prevalence (49), with 10% of HIV/Acquired Immunodeficiency Syndrome (AIDS) cases worldwide attributed to IDUs (29,102).

HIV prevalence in Eastern Europe and Central Asia has almost tripled since 2000 (25), to an estimated 1.4 million people in 2011 (103). The region is also home to 3.7 million IDUs (25). Ukraine's HIV prevalence is the highest in Europe and a 2010 study found that 50% of IDUs in Ukraine were HIV positive (104). The Global Fund to Fight AIDS, Tuberculosis, and Malaria (GFATM) has spent approximately $20m on harm reduction in the Ukraine (105).

Harm reduction interventions aim to reduce the harmful results of drug use. Although there is no agreed definition, a small number of interventions are commonly described in the literature as "harm reduction" including; condom provision, community based outreach, peer-led interventions, needle and syringe programmes (NSP) and opioid substitution therapy (OST) (106). Needle and syringe programmes offer a clean needle and syringe to injecting drug users (IDUs), while opioid substitution therapy (OST) replaces heroin with a less addictive drug such as methadone or buprenorphine under medical supervision. As IDUs undergoing OST may continue drug use outside of the programme (107), combining NSP with OST may be more effective in reducing HIV transmission than a single intervention (108). This paper will focus only on three harm reduction strategies; NSP, OST, and combined therapy (NSP and OST).

This study's purpose is to improve our understanding of the relative cost effectiveness of harm reduction strategies. A literature review on the cost-

effectiveness of harm reduction describes what is known, and what is not. A cost-effectiveness analysis of harm-reduction is then conducted using data from GFATM for the Ukraine. The analysis compares NSP, OST and a combined intervention. To the best of our knowledge, this is the first study comparing a combined intervention with NSP or OST alone, in any setting.

2.2 Literature Review

The literature on harm reduction cost-effectiveness was reviewed to summarise current evidence. Web of Science, Econlit and Pubmed were the primary databases searched. A supplementary search was conducted using Google Scholar. Reference lists of identified papers were hand-searched for further appropriate papers. The search terms were: cost-effectiveness, HIV, NSP, OST, harm reduction, needle and syringe, and methadone. Only papers published in English, in peer-reviewed journals were considered.

The initial search identified 18 papers. After reviewing titles and abstracts, 3 were excluded. After reading the full papers, 3 further papers were excluded and 3 were added following a hand search of the reference lists. The final review includes 15 papers listed in Table 1, two of which are literature reviews themselves.

This literature review summarizes the systematic review papers(109,110) and then lists the papers published since their publication(108,111–120). One exceptional case is the research by Van den berg et al. (121). This study was added to bolster the evidence around the combined intervention because the majority of the papers since the systematic reviews focus on a single therapy. Only one retrieved study by Degenhardt et al. (108) focused on the effectiveness of combined intervention of NSP and OST.

The first two papers in Table 1 are reviews of harm reduction strategies by Connock et al. (109) and Jones et al. (110). Connock et al. (109) conducted a

systematic review and cost effectiveness analysis of OST. They conclude that methadone dominates buprenorphine, both of which are licensed for use as opioid substitutes. Jones et al. (110) conducted a systematic review of NSP. Jones et al. (110) conclude from their review that in terms of reducing HIV incidence and prevalence among IDUs, NSPs are cost-effective.

While the review papers aimed to explore the cost effectiveness of a single intervention, a number of studies conducted since the reviews, have attempted to compare these single interventions with an alternative. For example, Van den berg et al. (121), (cited in the review by Jones et al.) compared a combined intervention with incomplete harm reduction. They concluded that combined intervention is more cost effective than incomplete harm reduction. Van den berg et al. (13) compared full harm reduction(NSP +OST) vs incomplete harm reduction (NSP +OST). However, they assumed incomplete harm reduction always offers OST, just changing 'the dose of OST'. Therefore, patients who get incomplete harm reduction always get OST as a base case. Likewise, Degenhardt et al. (108) compared combined intervention (OST+NSP) with ART and found that combined intervention of OST and NSP and ART gained more effectiveness than either OST+NSP or ART .

All NSP studies that reported NSP as a primary intervention used 'no NSP and no intervention' as a comparator. However, studies of OST show more varied comparators; 'no OST' (113–115) , combined ART intervention (108,118), and buprenorphine(109).

TABLE 1 : SUMMARY OF SYSTEMATIC REVIEW RESULT

Study	Comparator	Intervention Evaluated	Form of economic analyses	Perspective taken	Model used	Time horizon	Outcome measure
Jones et al. (110)†			Cost utility(N=12) Cost benefit(N=1)		Behavioural models using simplified Bernoulli process(N=4) Simulated the transmission(N=2) The theory of needle circulation originally developed by Kaplan and O'Keefe (N=4)		HIV incidence(N=11) HCV incidence(N=1) HIV and HCV incidence(N=1)
Connock et al. (109)†			cost–utility(N=5)	Societal perspective(N=5) Healthcare system(N=6)	Markov(N=3) Dynamic(N=3) Monte Carlo(N=1)		QALY(N=6)
Belani and Muennig (111)	no NSP	NSP	Cost utility	Societal	Decision model	1 year	Infection averted & QALYs
Wammes et al. (112)	OST	OST (coverage 5% to 40%)	Cost effectiveness/cost analysis	Societal	Mathematical transmission model	20 year	Infection averted
Guinness et al. (113)	non intervention	OST	Cost utility	Provider	Mathematical model	3 year	Infection averted & DALYs
Tran, Mills, et al. (115)	non OST	OST	Cost utility	Health service provider	Real cohort data	9 month	QALYs
Tran, Nguyen, et al. (114)	non OST	OST	Cost utility	Vietnam health care system	Decision analytical model	1 year	Infection averted & QALYs
Tran, Ohinmaa, et al. (122)	OST&ART	OST	Cost utility	Vietnam health care system	Decision tree monte carlo simulation	1 year	Infection averted & QALYs
Connock et al. (109)**	Buprenorphine	OST(methadone vs buprenorphine)	Cost utility	NHS	Markov monte carlo simulation	1 year	QALYs
Degenhardt et	ART,	Combined(NSP&OST)	Cost		Transmission model	5 years	Infection

al. (108)	NSP&OST&ART		effectiveness				aveted
Alistar, Owens, and Brandeau (117)	OST&ART ART alone	OST	Cost utility	Provider	dynamic compartmental model	20 year	Infection averted & QALYs
Li et al. (118)	ART, VCT	Combined(NSP&OST)	Cost utility		Mathematical	30 year	Infection averted & QALYs
Van den berg et al.*(121)	Methadone dose or NEP use alone	Combined(NSP& OST)		Not stated	Cohort study	20 years	Incidence rate ratio
Kwon et al. (119)	no NSP	NSP	Cost utility	Health sector	Mathematical model	lifetime	Infection averted & QALYs
Zhang et al. (120)	no NSP	NSP	Cost utility	Societal	Mathematical model	7 years	Infection averted & DALYs

†: Systematic review

*: included in Jones et al. (110)

**:Connock et al. (109) carried out a systematic review and a cost effectiveness analysis in one paper.

Of the papers listed in Table 1, ten used either QALYs gained or DALYs averted as a measure of outcome. All of the papers estimated both cost per infection averted and cost per either QALY or DALY.

This review highlights a gap in the evidence regarding the cost effectiveness of harm reduction, it is necessary to compare which mono-therapy (OST or NSP) is more cost effective, and whether mono-therapy is more cost effective than combined intervention – whether or not ART is offered. This is not because the provision of ART is unimportant, but because the literature has moved on to evaluate the cost effectiveness of the provision of ART with harm reduction – without first considering what is the most cost effective harm reduction package. As described above, there are studies arguing for the relative cost effective of NSP (111), of OST (112) and of combined intervention (108,118,121). However, no study that we could find compared the cost effectiveness of these three harm reduction alternatives. To fill this evidence gap, we conduct a CEA of harm reduction comparing NSP, OST, and combined intervention, using each intervention as a comparator.

2.3 Section 2: Case study of the Ukraine

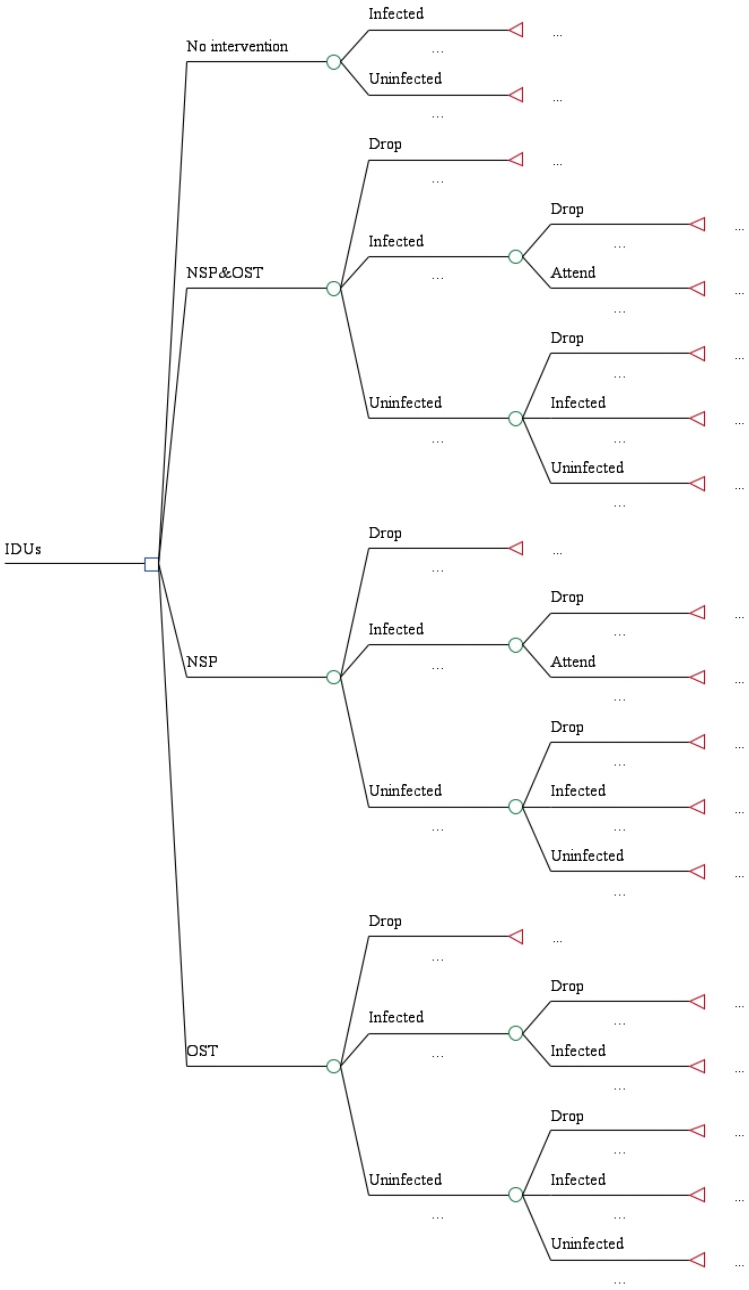
The largest IDU populations in Eurasia are in the Russian Federation (1.8 million) and the Ukraine (296,000) (25). Nearly half of IDUs in the Ukraine live with HIV(25), the highest prevalence rate in Europe(104). GFATM has spent approximately $ 20m on harm reduction in the Ukraine since 2004(105). Considering that GFATM disbursed US$ 361 million through 120 grants in 55 countries between 2002 and 2009 (7), the amount spent in the Ukraine is significant for a single country. That said, while GFATM provides significant international support for harm-reduction programs (7,49), these investments have seldom been evaluated.

2.4 Methods

Consistent with previous research in this area (109,123), this study uses a Markov model, assuming three states of 'infected', 'uninfected (well)', and 'dropped'. The model is designed to estimate costs and outcomes in terms of QALYs and HIV infections averted over 60 months, for the three strategies. The model estimates uncertainty using probability distributions. Monte Carlo simulation was then carried out using these distributions to account for uncertainty in the results of the model.

Figure 1 illustrates one cycle of the Markov decision model in this study. 'Infected' status occurs when patients are confirmed as HIV positive while 'uninfected' occurs when patients are HIV negative. 'Dropped' means that IDUs quit any harm reduction interventions they were attending. It is assumed that there is no mortality within the 5 year harm reduction period. This is consistent with the approach used by Vickerman et al. (124). As the objective of this study is to compare the cost effectiveness of harm reduction strategies irrespective of ART provision, ART is not offered in any intervention including 'no intervention'.

FIGURE 1: DECISION MODEL



A Markov Monte Carlo simulation with 10,000 iterations was conducted. It is known that at least 440 iterations should be run to be 95% sure that the estimate of the mean of the output is accurate(125). Consequently, it can be said that 10,000 iterations are sufficient to get a 95% confidence interval. This figure of 10,000 iterations is consistent with other research on HIV(126,127) and is recommended for medical decision making generally (128). The main outcomes are expressed as cost effectiveness ratios (CE) and incremental cost-effectiveness ratios (ICERs).

Treeage software was used to construct the model. Sensitivity analysis was carried out to account for uncertainty in the cost data. Affordability of the three strategies was assessed using probability sensitivity analysis (PSA) with the GDP of the Ukraine as a threshold. Based on WHO recommendations, an intervention may be considered cost effective if the cost per QALY is less than the country's GDP per capita(129)

2.4.1 Interventions compared

$$\text{ICER}=\frac{c1-c0}{E1-E0}=\frac{c1}{E1}$$

C1 is the cost of the new intervention, and E1 is the effect of the new intervention, whereas C0 and E0 are the cost and effect of the base case or comparator. Six cases were considered in this study: NSP vs OST, NSP vs NSP&OST, NSP vs no intervention, OST vs NSP&OST, OST vs no intervention, NSP&OST vs no intervention. The result is shown as a form of PSA in Figures 2 and 3. The base case is a no intervention, in which IDUs do not get any harm reduction intervention.

TABLE 2: MODEL PARAMETERS

Simulation parameters				
HIV incidence	Base case value	Duration	Distribution	Source
Number of injections	400.00	1 year		Degenhardt et al. (10), Aceijas et al. (29)
reduction in frequency of drug injections per day (α)	0.85	1 year		Alistar, Owens, and Brandeau(117)
Pr of transmission (β)	0.01	1 year		Gouws et al. (130)
Using sterile injection equipment or condom or methadone (γ)	0.90	1 year		Calculated using formula (32)
number of days follow up (n)	60 cycle (5 years)	60 month (Treatment)		Global Fund
HIV prevalence among IDUs (NSP) (P)	0.43	1 year		Calculated using Vickerman et al. (124)
HIV prevalence among IDUs (OST) (P)	0.28	1 year		Calculated using Vickerman et al. (124); Alistar, Owens, and Brandeau(117)
HIV prevalence among IDUs (NSP&OST) (P)	0.18	1 year		Calculated using Degenhardt et al. (108)
Decrease in HIV incidence (NSP)	0.22	1 year		Vickerman et al. (124)
Decrease in HIV incidence (OST)	0.53	1 year		Alistar, Owens, and Brandeau (117)
Decrease in HIV incidence (NSP&OST)	0.66	1 year		Degenhardt et al. (108)
Probability				

Pr(attend to intervention)	0.0750	1 cycle	Beta	Assumed
Pr(mortality) if no intervention	0.03	1 cycle	Beta	Vickerman et al. (124)
Pr(infected) if no intervention	0.0446	1 cycle	Beta	Vickerman et al. (124)
Pr(well) if no intervention	0.0388	1 cycle	Beta	calculated
Pr(drop) from NSP&OST	0.0083	1 cycle	Beta	Calculated Pr(attend to intervention)
Pr(infected) from NSP&OST	0.0003	1 cycle	Beta	Degenhardt et al. (108)
Pr(well) from NSP&OST	0.9914	1 cycle	Beta	Calculated
Pr(drop) from NSP	0.0083	1 cycle	Beta	Calculated Pr(attend to intervention)
Pr(infected) from NSP	0.0005	1 cycle	Beta	Vickerman et al. (124)
Pr(well) from NSP	0.9912	1 cycle	Beta	Calculated
Pr(drop) from OST	0.0083	1 cycle	Beta	Calculated Pr(attend to intervention)
Pr(infected) from OST	0.0004	1 cycle	Beta	Alistar, Owens, and Brandeau(117)
Pr(well) from OST	0.9913	1 cycle	Beta	Calculated
Pr(infected) if dropped from intervention	0.0446	1 cycle	Beta	Vickerman et al. (124)
Pr(well) if dropped from intervention	0.9554	1 cycle	Beta	Calculated
Pr(drop) if infected from NSP&OST	0.0102	1 cycle	Beta	Yin et al. (131) ; Jones et al. (110)
Pr(attend) if infected from NSP&OST	0.9898	1 cycle	Beta	Calculated

Pr(drop) if infected from NSP	0.0196	1 cycle	Beta	Jones et al. (110)
Pr(attend) if infected from NSP	0.9804	1 cycle	Beta	Calculated
Pr(drop) if infected from OST	0.0433	1 cycle	Beta	Yin et al. (131)
Pr(well) if infected from OST	0.9567	1 cycle	Beta	calculated
QOL				
NSP	0.85		Normal	Vickerman et al. (124)
OST	0.74(average value for 54 week)		Normal	Connock et al. (109)
NSP & OST	0.95		Normal	Vickerman et al. (124)
Infected(dropped)	0.63		Normal	Connock et al. (109)
Cost				
NSP				
unit cost per patient	151.14	1 year	gamma	Global Fund (105)
Fixed	1197008.80	1 year	gamma	Estimated from GFATM grant proposal
OST				
unit cost per patient	1752.00	1 year	gamma	WHO medical database
Fixed	700050.60	1 year	gamma	Estimated from GFATM grant proposal
NSP&OST				
unit cost per patient(per year)	1903.14	1 year	gamma	Global Fund (105), WHO medical database

Fixed	168286.96	1 year	gamma	Assumed from GFATM grant proposal
Other parameters				
Consumer price index(CPI)	1.5680			World Bank (132)
Time horizon	5 years			WHO (129)
Discount rate for cost	0.03		Uniform	WHO (129)
Discount rate for outcome	0.03		Uniform	WHO (129)
Population(NSP)	11000.00			Global Fund (105)
Population(OST)	5000.00			Global Fund (105)
Population(NSP & OST)	6000.00			Global Fund (105)
Initial HIV prevalence among IDUs	0.53	1 year		Vickerman et al. (124)
IDU mortality rate per 1000 person-years	0.4	1 year		Vickerman et al. (124)

HIV incidence was obtained from previous literature. Given the initial HIV prevalence(124), the effectiveness of each intervention was estimated. HIV incidence and infections averted, were calculated with the following formula (115,130):

$$HIV\ incidence = S[1 - p(1 - \beta)^{\alpha(1-\gamma)} + (1 - p)^{n}]$$

Where S = total no of susceptible individuals (IDUs)

α=reduction in frequency of drug injections per day from the cohort data

β = Pr of transmission

γ =reported using sterile injection equipment or condom or methadone

n= number of days follow up

p= HIV prevalence among IDUs

It was assumed that IDUs inject needles and syringes 400 times per year (133) and that they inject constantly for the entire program period. The HIV prevalence rate of IDUs for each intervention was calculated with parameters assuming that they are on each intervention. The values of alpha and gamma are shown as a proportion, and corresponding parameter values are presented in Table 2.

2.4.2 Distribution of parameters

To implement Monte Carlo simulation, the costs of each intervention were estimated based on gamma distribution, which is nonnegative and allows the maximum likelihood estimate of the population mean to be the sample mean[Table 2] (134). The probability distribution of each intervention was estimated with beta distribution, the value of which is between 0 and 1. Normal distribution was used for

utilities of outcome for interventions. For the discount rate, a uniform distribution between 0 and 1 was used.

2.4.3 Probability

In this study, transition probabilities for the 'infected', 'uninfected (well)', and 'dropped' state are shown in Table 2. QALYs for each state were obtained from existing research(109,124).

Cycle times of 1 month or 1 year are generally used in Markov model for chronic diseases (53). Although 1 year can be used for HIV(61), IDUs can drop out of the interventions sooner. Therefore, a cycle length of 1 month is more appropriate for this model. Since each cycle in the model is 1 month, these transition probabilities were adjusted for a monthly base.

The prevalence rates of each intervention were obtained from previous research that calculated the rates considering needle sharing between IDUs, condom use and sexual behaviours(124).The dropout rates at each cycle, for each intervention, were obtained from existing research(110,131) [table 2].

2.4.4 Costs

Cost data were collected from GFATM website (www.theglobalfund.org). GFATM's intervention in the Ukraine includes various harm-reduction packages (7). In addition, other interventions were carried out simultaneously including public health education campaigns around harm reduction for IDUs, and other complementary activities. As a result, the exact proportion allocated to the combined intervention is not clear. For the purposes of this analysis then, it was conservatively assumed that all budgets for Round 6 (2006-2010) were used for the combined intervention, although OST alone

and the combined intervention was simultaneously implemented. This limitation in the cost data will be tested with sensitivity analysis.

The summarized grant data for the Ukraine is presented in Table 3-a. Costs per cycle were estimated based on the summarized data in Table 3-b, which describe how the harm reduction interventions of NSP and OST were conducted for 5 years. The variable cost of NSP for each cycle in the Ukraine comprises disposable syringes, needles, disinfectant solutions, and alcohol wipes(105). The variable cost of OST is from the WHO medical database, using the price from Pharmascience.inc (105).

Costs were incurred in United States dollars (USD) and adjusted for inflation to 2011 values using the consumer price index (CPI) for the Ukraine from the World Bank [ref]. All costs other than the variable costs of NSP and OST were classified as start-up costs (Table 3-b), which are generated at each Markov cycle of 1 month irrespective of the number of patients. The information regarding the total number of patients to calculate a cost per patient was obtained from GFATM website(135) and is presented in Table 2.

It was conservatively assumed that the variable cost of the combined strategy is simply the sum of the variable costs for NSP and OST.

Staff costs and other delivery costs were included in start-up costs for each cycle. The variable costs of each intervention were annualised. Indirect costs, such as productivity loss, were not taken into account in this study and noted as a limitation of this analysis.

TABLE 3: COST DATA

a) Grant data Summary

	Intervention	Year 1	Year 2	Year 3	Year 4	Year 5	Total
Ukraine	Harm reduction_syringe	522,600	1,372,411	1,901,061	1,900,411	1,951,061	7,647,544
	Substitution therapy	1,127,125	1,443,544	3,099,845	3,194,531	3,395,208	12,260,253

*USD

b) Cost per cycle

Cost per 1 cycle	NSP	OST	Combined
Starting up cost	99750.73	58337.55	14023.91
Cost per patient	2.52	29.20	31.72
Total cost per 1 cycle			
Cost per patient	11.59	40.87	34.06

2.4.5 Discounting, Perspective and Time horizon

The intervention's benefits were evaluated over the duration of the grant period i.e. from the start of 2002 to the end of 2006. Annualized costs were used for each year. As the World Health Organisation (WHO) recommended, an identical discount rate of 3% was applied to both costs and effectiveness. A provider perspective was applied.

2.4.6 Population

Using data from the literature, it was assumed that half of IDUs attending the interventions were infected at the outset (25,124) [Table 2] and the average age was assumed to be 39 (136).

2.5 Results

The results of the Markov Monte Carlo simulation are given with 95% confidence intervals in Table 4. The result of costs and effectiveness of deterministic analysis is located within the confidence interval of probabilistic analysis, showing the robustness of the result regarding the parameters for this model.

Combined therapy of NSP and OST averted the most infections (1848 HIV infections averted). After this, OST alone averted the most infections (1053 HIV infections averted). Combined therapy averted more infections than the sum of OST alone and NSP alone (1848 HIV infection averted vs 1559 HIV infection averted). Considering QALY gains, combined therapy still gained most (4183.5 QALYs). After this, NSP alone gained slightly more QALYs than OST alone (2970 QALYs vs 2599 QALYs).

Although combined therapy strictly dominated in terms of benefits, NSP alone was most cost effective at $487.4/infection averted and $83.3/QALY gained compared with combined therapy of NSP and OST together at $851.6/infection averted and $373.7/QALYs (table 4). OST alone had the highest cost effectiveness ratios at $1145.9/infection averted and $459.9/QALYs.

TABLE 4 : 10,000 TIMES MONTE CARLO SIMULATION RESULTS AND A DETERMINISTIC RESULT OF COST AND EFFECTIVENESS

Infection averted		Monte Carlo Simulation			Deterministic		
		Combined	NSP	OST	combined	NSP	OST
Cost		1,574,559.00	247,108.68	1,206,760.80	1,565,967.17	247,148.20	1,199,134.00
	Std	580,415.89	67,045.82	419,480.75			
	Upper CI(95%)	1,585,935.20	248,422.78	1,214,982.60			
	Lower CI(95%)	1,563,182.90	245,794.58	1,198,539.00			
Effect		1,848.76	506.98	1,053.10	1,848.74	506.98	1,053.03
	Std	6.78	5.33	5.39			
	Upper CI(95%)	1,848.89	507.08	1,053.21			
	Lower CI(95%)	1,848.63	506.88	1,052.99			
CE		851.68	487.41	1,145.91	847.05	487.49	1,138.75
	Std	95.06	54.01	128.57			
	Upper CI(95%)	853.55	488.47	1,148.43			
	Lower CI(95%)	849.82	486.35	1,143.39			
QALY							

		Combined	NSP	OST	combined	NSP	OST
Cost		1,563,571.10	247,577.10	1,195,319.80	1,565,967.17	247,148.20	1,199,134.00
	Std	579,705.31	66,864.85	418,960.03			
	Upper CI(95%)	1,574,933.30	248,887.65	1,203,531.40			
	Lower CI(95%)	1,552,208.90	246,266.55	1,187,108.10			
Effect		4,183.51	2,970.21	2,599.08	4,183.51	2,970.21	2,599.04
	Std	7.47	5.69	5.71			
	Upper CI(95%)	4,183.66	2,970.32	2,599.19			
	Lower CI(95%)	4,183.36	2,970.10	2,598.97			
CE		373.75	83.35	459.90	374.32	83.21	461.38
	Std	95.06	54.01	128.57			
	Upper CI(95%)	374.57	83.55	460.93			
	Lower CI(95%)	372.92	83.15	458.87			

2.5.1 Sensitivity analysis

The costs of combined NSP and OST are uncertain due to the limitations of the cost data, which do not explicitly state the total costs of the combined intervention. Consequently, one-way sensitivity analysis was conducted to relax this limitation. The uncertainty of both effectiveness and costs was examined using PSA.The three strategies were compared with a single therapy in Table 5.

Irrespective of the variation in the starting costs of combined intervention, the results are consistent at both outcome measures. It was found that the variation in the start up costs of combined intervention did not affect the rank of strategies in terms of ICER. Although the ICER of combined intervention varies between $428 and $461/infection averted, the rank of ICER for each intervention did not change. Similarly, when presented in QALYs, the ICER of each intervention did not change regardless of the variation in starting up costs.

On the other hand, it was found that the variable cost of OST can affect the relative rank of strategies. At the lower end of OST, OST was most cost effective strategy at both QALYs and infection averted. The ICER of combined intervention [$428-$461/infection averted] was slightly lower than the ICER of NSP [$487/infection averted] although NSP alone is more cost effective. This results from the fact that OST has 'extended dominance' in terms of HIV infections averted and so combined intervention was compared with OST instead of NSP.

In brief, this result relaxes the uncertainty in the start up cost of combined intervention, and offers supporting evidence that the combined intervention and NSP alone are preferred strategies to OST alone. Also, the high variable cost of OST makes OST alone,a less cost effective strategy.

TABLE 5: SENSITIVITY ANALYSIS

Averted		Lower end	ICER	CI(95%)	Higher End	ICER	CI(95%)	Comparator
Variable_NSP	No intervention	0.00	0.00		2.52	0.00		
Variable_NSP	NSP	0.00	296.71	293.40:298.60	2.52	487.49	484.89:490.09	vs no intervention
Variable_NSP	OST	0.00	1920.53	1911.68:1929.38	2.52	1743.40	1734.55:1752.25	vs NSP
Variable_NSP	NSP and OST	0.00	461.01	452.98:469.04	2.52	461.01	452.98:469.04	vs OST
Variable_OST	No intervention	0.00	0.00		29.20	0.00		
Variable_OST	OST	0.00	83.17	82.73:83.61	29.20	1743.40	1734.55:1752.25	vs NSP
Variable_OST	NSP	0.00	-292.22	(-294.6): (-289.4)	29.20	487.49	484.89:490.09	vs no intervention
Variable_OST	NSP and OST	0.00	1857.95		29.20	461.01	452.98:469.04	vs OST
startingcost_NSP	No intervention	0.00	0.00		99750.75	0.00		
startingcost_NSP	NSP	0.00	190.78	187.4:192.6	99750.75	487.49	484.89:490.09	vs no intervention
startingcost_NSP	OST	0.00	2018.89	2009.95:2027.65	99750.75	1743.40	1734.55:1752.25	vs NSP
startingcost_NSP	NSP and OST	0.00	461.01	452.98:469.04	99750.75	461.01	452.98:469.04	vs OST
startingcost_combined	No intervention	0.00	0.00		14023.92	0.00		

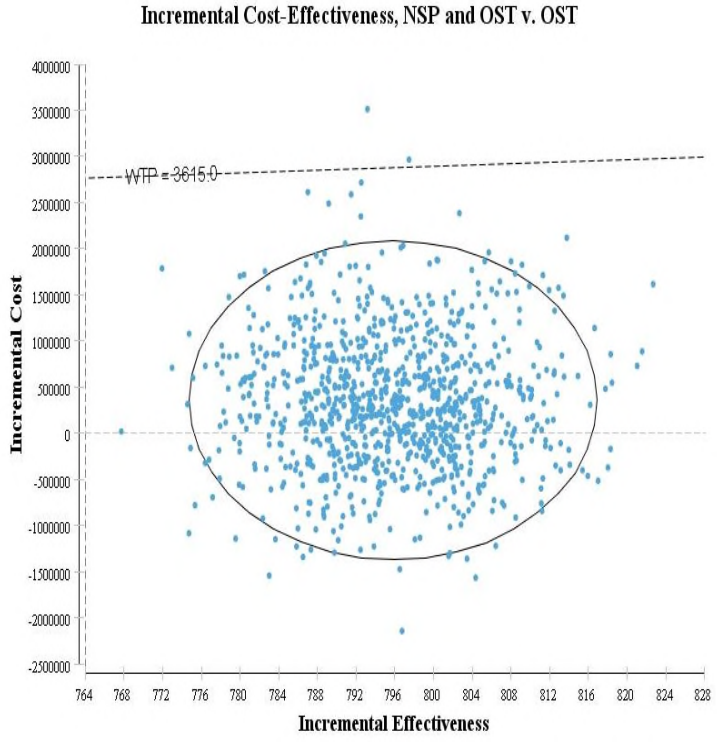
startingcost_combined	NSP	0.00	487.49	484.89:490.09	14023.92	487.49	484.89:490.09	vs no intervention
startingcost_combined	OST	0.00	1743.40	1734.55:1752.25	14023.92	1743.40	1734.55:1752.25	vs NSP
startingcost_combined	NSP and OST	0.00	428.49	419.96:436.03	14023.92	461.01	452.98:469.04	vs OST
startingcost_OST	No intervention	0.00	0.00		58337.53	0.00		
startingcost_OST	NSP	0.00	487.49	484.89:490.09	58337.53	487.49	484.89:490.09	vs no intervention
startingcost_OST	OST	0.00	1583.01	1574.15:1591.85	58337.53	1743.40	1734.55:1752.25	vs NSP
startingcost_OST	NSP and OST	0.00	571.08	562.97:579.03	58337.53	461.01	452.98:469.04	vs OST
QALYs								
Variable_NSP	No intervention	0.00	0.00		2.52	0.00		
Variable_NSP	NSP	0.00	50.65	50.2:51.08	2.52	83.21	82.76:83.65	vs no intervention
Variable_NSP	OST	0.00	-2825.37	(-2836.71):(-2793.29)	2.52	-2564.79	(-2585.71):(-2542.29)	vs NSP
Variable_NSP	NSP and OST	0.00	1166.69	1150.94:1181.07	2.52	1086.97	1077.76:1096.24	vs NSP
Variable_OST	No intervention	0.00	0.00		29.20	0.00		
Variable_OST	OST	0.00	33.70	30.63:36.75	29.20	83.21	79.94:86.06	vs no intervention
Variable_OST	NSP	0.00	429.90	419.96:436.03	29.20	-2564.79	(-2585.71):(-2542.29)	vs OST

Variable_OST	NSP and OST	0.00	1086.97	1077.76:1096.24	29.20	1086.97	1077.76:1096.24	vs NSP
startingcost_combined	No intervention	0.00	0.00		14023.92	0.00		
startingcost_combined	NSP	0.00	83.21	82.76:83.65	14023.92	83.21	82.76:83.65	vs no intervention
startingcost_combined	OST	0.00	-2564.79	(-2585.71):(-2542.29)	14023.92	-2564.79	(-2585.71):(-2542.29)	vs NSP
startingcost_combined	NSP and OST	0.00	1065.64	1049.93:1080.07	14023.92	1086.97	1077.76:1096.24	vs NSP
startingcost_NSP	No intervention	0.00	0.00		99750.75	0.00		
startingcost_NSP	NSP	0.00	32.56	29.49:35.62	99750.75	83.21	82.76:83.65	vs no intervention
startingcost_NSP	OST	0.00	-2970.06	(-2991.71):(-2948.29)	99750.75	-2564.79	(-2585.71):(-2542.29)	vs NSP
startingcost_NSP	NSP and OST	0.00	1210.95	1194.93:1225.06	99750.75	1086.97	1077.76:1096.24	vs NSP
startingcost_OST	No intervention	0.00	0.00		58337.53	0.00		
startingcost_OST	NSP	0.00	83.21	82.76:83.65	58337.53	83.21	82.76:83.65	vs no intervention
startingcost_OST	OST	0.00	-2328.83	(-2350.54):(-2307.12)	58337.53	-2564.79	(-2585.71):(-2542.29)	vs NSP
startingcost_OST	NSP and OST	0.00	1086.97	1077.76:1096.24	58337.53	1086.97	1077.76:1096.24	vs NSP

2.5.2 Probability sensitivity analysis

Figure 2 and 3 shows the results of probabilistic sensitivity analysis with 95% confidence interval using Monte-Carlo simulation.

FIGURE 2: THE RESULT OF PROBABILISTIC SENSITIVITY ANALYSIS(HIV INFECTION AVERTED, WTP=GDP PER CAPITA OF THE UKRAINE)



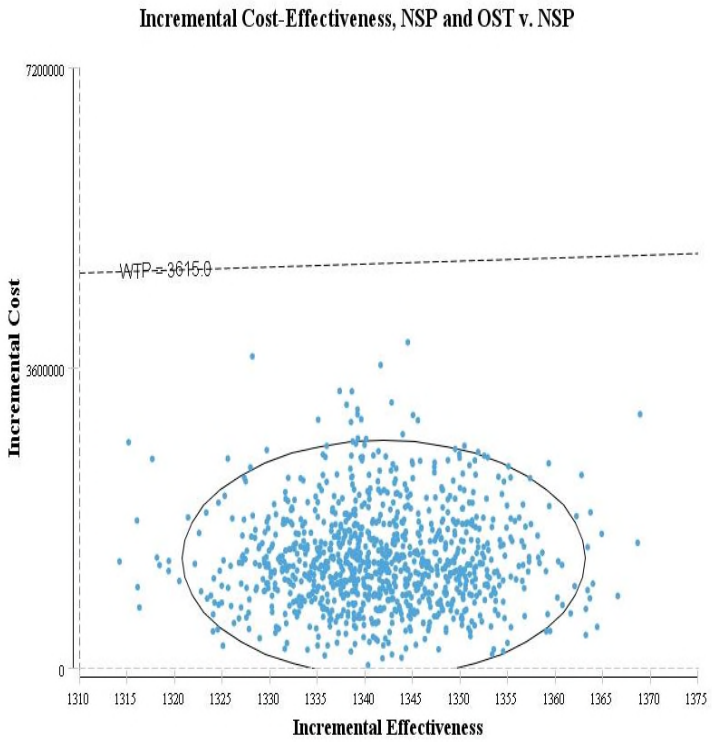
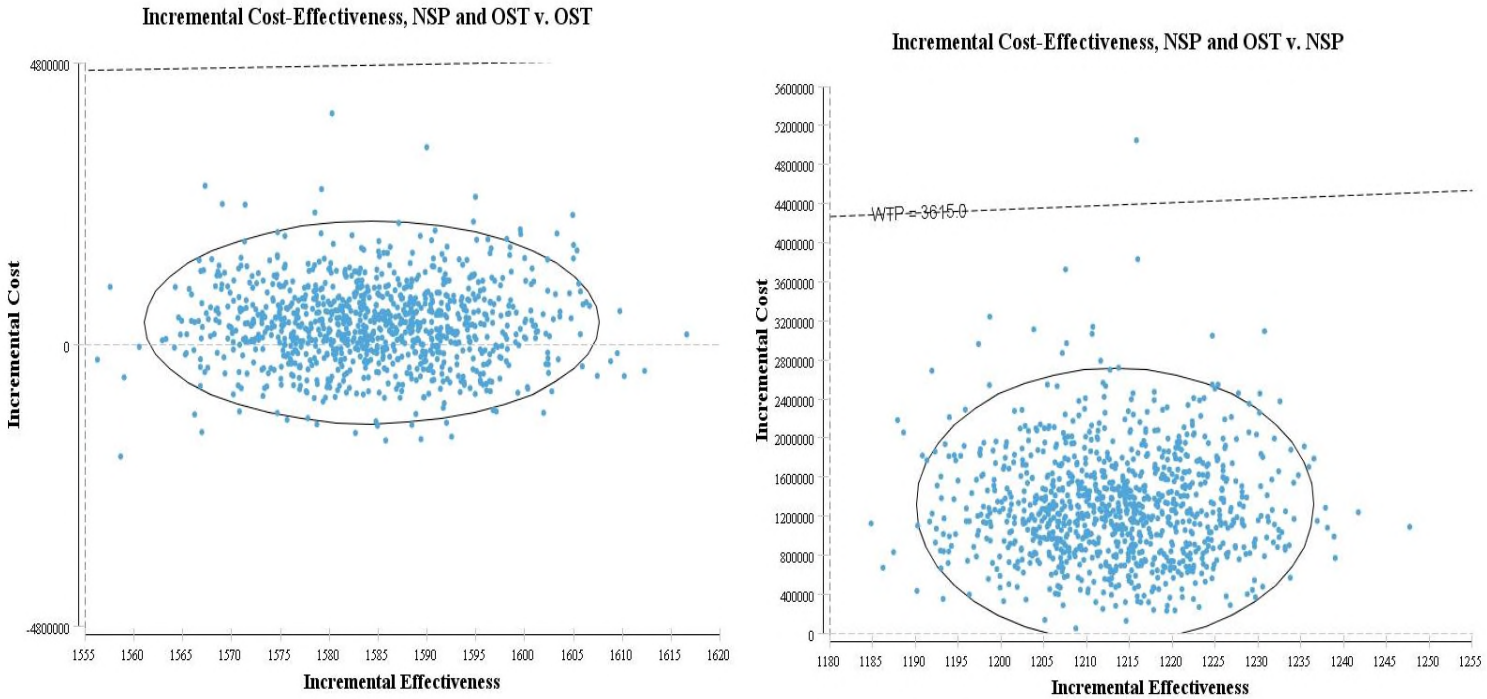


FIGURE 3: THE RESULT OF PROBABILISTIC SENSITIVITY ANALYSIS (QALYS, WTP=GDP OF THE UKRAINE)



The result of combined intervention vs NSP alone is located in the first quadrant, suggesting that the combined intervention is incrementally cost effective compared with NSP alone. However, the results indicate that the combined intervention may in fact cost less than OST as a single therapy and therefore be the dominant strategy when compared with OST: 31% of results are in the fourth (south east) quadrant. This means that the probability that the combined intervention is more effective at higher cost, in terms of infection averted, than OST alone is 69 % (first quadrant).

Irrespective of the outcome measures, the combined intervention is located below the line of willingness to pay (WTP) for the Ukraine.

2.6 Discussion

In this paper, an updated systematic review of the cost-effectiveness of harm reduction highlighted a gap in existing evidence: the lack of an incremental approach to comparing the cost effectiveness of combined versus mono-therapy. To fill the evidence gap, this study has attempted to determine the cost-effectiveness of harm reduction by GFATM in the Ukraine. A Markov Monte Carlo Model was used to conduct n incremental economic analysis comparing 3 harm-reduction interventions with one another and with no intervention; i.e. NSP alone, OST alone and combined OST and NSP.

The analysis found that all interventions were cost effective in terms of QALYs gained and HIV infections averted. NSP alone was the most cost effective and OST alone was the least cost effective option. While combined therapy did not have the lowest cost effectiveness ratio, it was significantly more effective in both outcome measures than any alternative. The relatively high variable cost of OST ($31.72 per patient per cycle) explains, to a large extent, why the combined strategy is not as cost effective as NSP alone.

The result that NSP is most cost-effective, is consistent with previous research on harm-reduction (117,124). NSP alone [$83.35/QALY in Table 4] is shown to be more cost-effective in the Ukraine than in Australia [$416–8,750/QALY] (119) or Kazakhstan [$132–147/QALY] (137). However, the cost effectiveness ratio of NSP alone in this study, at $487.41 per HIV infection averted, is significantly higher than that from another study in the Ukraine study [$97–162 per HIV infection averted] (124). OST, at $459.90 per QALY, was slightly more cost-effective than other analyses for the Ukraine suggest [$530/QALY] (117). Regardless, OST was a dominated strategy for both outcome measures and this is attributed to the high variable cost of OST. The results of the sensitivity analysis support this conclusion.

From the result of PSA, the samples are located below the slope of willingness to pay (WTP). Considering that the GDP of the Ukraine was $3,615 in 2011(132), all three interventions were found to be located below the cost effectiveness threshold suggested by the WHO (129). As a result, and given the significant dominance of combined therapy in terms of benefits, this is may be the preferred strategy in the Ukraine context. That said, a discussion about affordability and the ethics of selecting a less effective strategy may be warranted in this context.

Some caveats exist in this study and the generalizability of the findings, which should be noted. Firstly, the start-up costs of combined intervention are uncertain. This makes it more important to measure uncertainty and sensitivity in costs. Likewise, probability of transmission used in this study assumes normal IDUs. However, depending on the IDUs status such as sex workers or men sex with men (MSM), the probability will be varied. Another caution is that the effectiveness parameters, such as drop-out rates, will vary depending on how an intervention is implemented in practice. Therefore, the ‘dominance’ of each strategy over comparators should be carefully interpreted.

More detail on the number of IDUs reached by Global Fund NSP and OST programs would further improve the accuracy of estimates. With more evidence

regarding the effectiveness of harm reduction programs, including those supported by GFATM, greater support for effective – and cost effective - harm reduction can be fostered.

3 Socioeconomic equity in HIV testing in Malawi[5]

[5] This chapter was published in *Global Health Action* on Oct 2016. The published article is attached in the Appendix. Due to the request from the journal, the structure of this chapter is slightly different from the published paper.

3.1 Introduction

Malawi has a generalised, high-level HIV epidemic. An estimated 1,100,000 people were living with HIV in 2012, approximately 11% of the total population (103). Malawi's HIV prevalence is representative of other countries in the southern and eastern regions of sub-Saharan Africa including Botswana and South Africa (41).

In 2013, UNAIDS set the '90:90:90 goals' to mobilise the global response to HIV. According to these goals, by 2020; ninety percent of people living with HIV should be aware of their HIV status, ninety percent of those known to be HIV positive should be on treatment and ninety percent of people on treatment should be virally suppressed (138). Malawi is one of five countries in which less than one in 10 HIV-exposed children obtained early infant diagnostic services along with Angola, Chad, the Democratic Republic of Congo and Nigeria among 21 priority countries (138). In 2014, only 40% of men in Malawi aged 15-49 had received an HIV test in the previous 12 months despite the generalized nature of the epidemic (139). A better understanding of testing and diagnosis in the Malawian context is thus critical to the achievement of the 90:90:90 goals. Without access to testing, diagnosis and treatment cannot follow.

Receipt of an HIV test in Malawi is likely to be determined by both need and non-need factors. Gravelle et al. (140) discuss the definition of health equity as "Equal Treatment for Equal Need", according to which, *need variables* should affect use of health service and *non-need variables* should not. Need variables thus reflect heath status, while non- need variables tend to reflect socioeconomic status such as wealth or education. Key findings of the Demographic and Health Survey (DHS) 2010 show that HIV prevalence in Malawi is three times higher for men in the highest income group than men in the lowest income group (88). HIV prevalence among urban residents is also greater than in rural areas. For example, urban men are almost twice as likely to be infected as rural men. A similar pattern is observed among women; 11.2% of women living in urban areas are HIV positive, compared to 3.7% in rural areas (88). This suggests that the need for HIV testing may not be

equally distributed across the population in Malawi. These figures should however, be interpreted with caution; firstly, because the calculation of prevalence rates may be affected by the intensity of testing for HIV; and secondly, although rural prevalence may be lower, the absolute number of people living with HIV may be greater in rural areas where the majority of the Malawian population reside.

While a number of studies demonstrate that HIV test uptake varies by socio-demographic and economic characteristics (41,80,141–143), there is a lack of evidence about whether there is equal access for equal need in Malawi. In general, equal treatment for equal need is referred to as horizontal equity (144). 'Equal access for equal need' means that patients who have an equal need for a health service, make equal use of care without being disproportionately affected by non-need factors such as socioeconomic status (144).Furthermore, there is little evidence regarding rural-urban differences in HIV testing in Malawi, despite the fact that urbanity is one of the major socioeconomic factors widely employed in inequity studies (86,145,146).

Most studies of access to HIV testing have taken either an urban or rural focus, and have tended to focus on single or clustered districts (78,147). These study designs preclude urban-rural comparisons and analyses of geographic variation at the national level. For example, Yoder et al. (78) carried out qualitative research on access to HIV testing in Malawi using data from four study sites in Blantyre, Chiradzulu, Lilongwe and Dowa districts. They explored the reasons why people in those sites sought an HIV test and found that most women receiving an HIV test were worried about HIV infection from their partners. Helleringer et al. (147) studied the uptake of home-based testing in rural areas including 6 villages of Likoma Island and found that uptake was highest among the poorest groups.

Currently, there is lack of information regarding equity in HIV testing at a national scale in Malawi. As such, our understanding of the likely barriers to achieving global goals in Malawi remains incomplete. No study of HIV testing uptake that we could

identify was carried out on a national sample, none studied inequity using standard tools such as the concentration index, and no study has yet explored the determinants of inequity in HIV testing in Malawi. These results highlight the paucity of evidence on inequity in HIV testing uptake in Malawi.

This study aims to assess horizontal inequity in HIV testing at the national level in Malawi.

3.2 Literature review

A literature review was carried out regarding the topic of 'HIV test in Malawi' and 'equity in HIV test'. No restriction on published year was imposed, and only English-language articles were taken into consideration. The literature review was conducted using 2 databases: Web of Science and PubMed. Studies were retrieved through Web of Science with following terms: Malawi, HIV test, socioeconomic, and equity. The keywords *Malawi* and *HIV test* identified 583 studies. After refining the search result with *equity,* only 5 studies remained (Appendix 1). Expanding the result with the keyword *socioeconomic,* 13 studies obtained. After combining with previous result and excluding duplicated results, 16 studies remained. Considering relevance to the purpose of the chapter (2 articles from other country, 6 articles not about HIV test) excluded 8 more. Among the 8 that were left, 2 were about costs of HIV (148) and identifying risk group (149). One was about socioeconomic status and HIV prevalence (150) and 1 was based on a qualitative interview (151). Hence, from the 8 studies, 4 articles were chosen (147,152–154).

Eleven articles were identified with same keywords through PubMed (Appendix 2). However, all of these were irrelevant to the research topic. Among them, 2 were duplicates identified by Web of Science (149,153), and so eliminated. 3 by Streatfield et al. (155–157) were not about HIV test or Malawi. Two were just overviews about HIV (158,159). One was qualitative research (160) and 3 were about other disease such as mental health, food security, and paediatric care (161–163).

Finally hand search on Google Scholar using identical keywords to the above added 5 (40,41,78,143,164). In total, 9 articles from Web of Science and Google Scholar were included.

Among the identified papers, 4 focused on the gender inequity in HIV testing. Conroy (152) examined how relationships between men and women in families affect young people's decisions to test for HIV in rural Malawi. They found women's testing were more strongly influenced by perceptions of a partner's risk on HIV than their women's own decision while men decided HIV testing based on self-assessments.

Makwiza et al. (154) carried out the synthesis of published and unpublished reports to see equity on voluntary counselling and testing (VCT) in Malawi. They found an urban bias in provision of HIV testing and counselling, which more women than men used.

Weinreb et al. (41) examined women's access to HIV test using the data of Malawi Diffusion and Ideation Change Project (MDICP). They argued that substituting home-based for clinic-based testing may reduce the gap in inequality between those tested and those who cannot be. They also found less demand for HIV testing from the poorer and less educated in Malawi.

Obare et al. (40) examined the acceptance of repeat population-based voluntary counselling and testing (VCT) for HIV in rural Malawi. They argued that women are more likely to be stigmatised about seeking to be tested for HIV than men.

Two papers studied equity in rural areas of Malawi. Helleringer et al. (147) measured uptake of home-based HIV testing and counselling and estimated HIV

prevalence for residents of 6 villages of Likoma Island, Malawi. They found that HIV testing and counselling uptake was high during a home-based HIV testing and counselling campaign on Likoma Island, particularly among the poorest groups.

Thornton et al. (79) found that only 8% of rural Malawians received voluntary counselling and testing (VCT), while 74% had never been tested for VCT, using the data from the Malawi Diffusion and Ideational Change Project (MDICP). This study implies the equity study of HIV patients in African countries encounters fundamental issues.

Mitchell et al. (153) conducted a household survey of 24,069 people regarding HIV testing and access in African countries: Botswana, Lesotho, Malawi, Mozambique, Namibia, South Africa, Swaziland, Tanzania, Zambia, and Zimbabwe. They found males received significantly more HIV test than females in Malawi, South Africa and Tanzania.

Yoder et al. (78) carried out demographic research regarding HIV test in Malawi using Demographic and Health Survey (DHS) data; however, this research focuses on neither equity nor geographical variation of access.

Ziwa et al. (164) evaluated whether and technical support provided by Umoyo Network to Malawi AIDS Counselling & Resource Organization (MACRO) has significantly increased the quality and availability of voluntary counselling and testing at MACRO in Malawi. They concluded that the overall institutional capacity and quality of voluntary counselling and testing service delivery at Malawi AIDS Counselling & Resource Organization (MACRO) was improved but raised concerns about privacy and confidentiality, clients having to travel long distances for voluntary counselling and testing services, and insufficient funds.

In summary, these studies show an evidence gap. They did not approach the equity in HIV test using needs and non-needs variables to see horizontal equity in Malawi. It would be appropriate to carry out an analysis on socioeconomic inequity in HIV test at Malawi using concentration index to estimate the inequity related to HIV testing and to make up this limitation.

3.3 Methods

This study calculates a decomposed concentration index (39) of access to HIV testing in Malawi. While the concentration index quantifies the extent of any inequity, the decomposition method explores the determinants of inequity; that is, the contribution of different health need and non-need factors to any inequity identified in the concentration index. Common indicators of non-need variation in the literature include socio-economic status such as income (165). In this study, need factors include symptoms of sexually transmitted infections, while non-need factors include wealth, education, literacy, and marriage status. 'Need factors' here reflect the need for health service use. Common indicators of need used in other studies include demographic variables such as age and gender, and measures of health status (165). As the variable measuring uptake of HIV testing is binary ("Have you ever been tested for HIV?"), a probit model is used in the regression stage within the concentration index (39).

A standard decomposition index (39) is not sufficient to measure horizontal inequity in HIV test uptake in sub-Saharan African settings such as Malawi because of the complex relationship between HIV risk and socio-economic status. In this context, as mentioned previously, wealthier groups have higher HIV prevalence (166,167). This appears to contradict findings from other settings, that poorer groups are more at risk of HIV (146,166,168) and may be a consequence of the fact that prevalence estimates are derived from testing outcomes, and access to testing may be skewed towards higher wealth groups (41). As such, a standard (pooled) concentration index for HIV testing is likely to non-randomly underestimate need and

thus inequity between wealth groups as it does not properly capture different need in different wealth groups (86).

This paper therefore applies a decomposition index method developed by Van de Poel et al. (86) in which the contribution of need variables in a decomposition index is broken up into two parts, labelled 'corrected need' and 'discrimination', respectively. Corrected need explores whether corrected, need adjusted horizontal inequity is underestimated or not, given the pooled group. Discrimination explores how the health service use for a given need in a group compares with a reference group.

This method for estimating corrected need is distinguished from traditional decomposition methods by the use of a reference group that is expected to realise vertical equity (86). Vertical equity implies individuals with different levels of needs 'appropriately' consuming different amounts of health care (140). Van de poel et al. (86) suggest that the highest wealth quintile is the reference group, while the pooled group is the whole population. Accordingly, this method captures variation in need and health service use between the reference and pooled groups - horizontal inequity - enabling us to extract the hidden vertical inequity that cannot be seen with conventional decomposition methods.

3.3.1 Calculation of the concentration index, corrected need and horizontal inequity

A concentration index is generally calculated as

$$CI_y = \frac{2Cov(y_i, R_i)}{\mu} \quad (1)$$

where CI_y is the concentration index for health service use y, y_i is health service use for individual i, μ is the mean of health service use, and R_i is individual i's fractional socio-economic rank.

We assume that health service use is determined by a set of k independent variables (x_k)

$$y = \alpha + \sum_k \beta_k x_k + \varepsilon \quad (2)$$

where β_k is a vector of coefficients and ε is the error term. Then the concentration index for health service use can be expressed as

$$CI = \sum_k \frac{\beta_k \bar{x}_k}{\mu} C_k + GC_\varepsilon/\mu \quad (3)$$

where $\bar{x}_k$ is the mean of the independent variable x_k and C_k is the concentration index of x_k. GC_ε is the generalized concentration index for the error term, which is the remaining unexplained socioeconomic inequality in the model (39).

Equation (3) consists of two parts: the explained part and the unexplained part. The explained part is made up of two elements: the concentration index for the independent variable (C_k) and a measure of elasticity ($\frac{\beta_k \bar{x}_k}{\mu}$). Elasticity ($\frac{\beta_k \bar{x}_k}{\mu}$) is the impact of each independent variable on health service use. That is to say, elasticity shows how much the dependent variable changes when one unit of the independent variable is changed. The CI in equation (3) represents the extent to which the determinants of health service use are unequally distributed across wealth groups.

Bearing this in mind, the standard decomposition index including need and non-need variables is as follows.

$$CI = \sum_k \frac{\beta_k^p \bar{x}_k C_k}{\mu} + \sum_m \frac{r_m^p \bar{z}_m C_m}{\mu} + GC_u/\mu \quad (4)$$

where x_k and z_m are vectors of independent need and non-need variables, respectively. β_k^p and r_m^p are the regression coefficients of x_k and z_m for the pooled group on health service use from (2). $\bar{x}_k$ and $\bar{z}_m$ are the means of x_k and z_m respectively. GC_u is again the generalized concentration index for the error term and μ is the mean of health service use. Conceptually, the first term on the right-hand side is the contribution of need variables ($\bar{x}_k$) to the whole CI ("need contribution"), and the second term is the contribution of non-need variables ($\bar{z}_m$) to the whole CI ("non-need contribution"), taking into account both the elasticity and the concentration index of the independent variables. This is an extension of equation (3) above.

Jones and Ropez (169) then introduced another form of standard decomposition based on equation (4) as follows.

$$CI = \sum_k \frac{\beta_k^p \bar{x}_k C_k}{\mu} + \frac{2}{\mu N} \sum_k \sum_i x_{ik} \left(\beta_{kg} - \beta_k{}^p\right)\left(R_i - \frac{1}{2}\right) \tag{5}$$

$$+ \sum_m \frac{r_m^p \bar{z}_m C_m}{\mu} + \frac{2}{\mu N} \sum_m \sum_i Z_m \left(r_{mg} - r_m{}^p\right)\left(R_i - \frac{1}{2}\right)$$

$$+ \frac{2}{\mu} cov(\alpha_g, R_i) + \frac{2}{\mu} cov(u_i, R_i)$$

In this specification, the first and third terms are referred to as the homogeneous contributions, and the second and fourth terms as the heterogeneous contributions, of need and non-need variables to the CI, respectively. The homogeneous contribution terms assume that the effects are the same across wealth groups. The second and fourth terms are the covariance between the regression coefficients and the socioeconomic rank (R_i) of individual i in wealth group g. These terms represent the heterogeneous contribution of the coefficient of the pooled values for need and non-need variables, respectively. The fifth term corresponds to the covariance

between the fractional rank and group intercepts, and means the contribution of group differences in health service use to SES associated inequality. The sixth term is the remaining unexplained inequality in health service use (169).

3.3.2 Corrected need and horizontal inequity

Van de Poel et al. (86) split the second term in equation (5) into two parts and label them ‘corrected need’ and ‘discrimination’, respectively. This method is distinguished from traditional decomposition methods by employing a reference group as a way of incorporating normative choice.

In this method, an asset index is used to split the population into wealth groups, and coefficient estimates from a pooled regression are compared with coefficient estimates from a regression using only the highest wealth group. The highest wealth group is expected to achieve higher levels of access in a use-need relationship (86). The ‘corrected need’ component of the CI can then be obtained after splitting the heterogeneous contributions of need and non-need variables into two parts: the corrected need effect, and discrimination (86). The decomposition index can thus be disaggregated as follows:

$$\begin{aligned} \mathrm{CI} = \sum_{\mathrm{k}} \frac{\beta_k^p \bar{x}_k C_k}{\mu} + \frac{2}{\mu N} \sum_k \left(\beta_{kgr} - {\beta_k}^p\right) \sum_i x_{ik} \left(R_i - \frac{1}{2}\right) \\ + \frac{2}{\mu N} \sum_k \sum_i x_{ik} \left(\beta_{kg} - \beta_{kgr}\right) \left(R_i - \frac{1}{2}\right) \\ + \sum_m \frac{r_m^p \bar{z}_m C_m}{\mu} + \frac{2}{\mu N} \sum_m \sum_i z_m \left(r_{mg} - {r_m}^p\right) \left(R_i - \frac{1}{2}\right) \\ + \frac{2}{\mu} cov(\alpha_g, R_i) + \frac{2}{\mu} cov(u_i, R_i) \end{aligned} \tag{6}$$

Where ${\beta_k}^p$, ${r_m}^p$ are the parameters from the original model (4). β_{kgr} is the coefficient from the reference (high wealth) group. β_{kg} is the coefficient from a wealth

quintile subgroup other than the reference group. The first and fourth terms are the homogeneous contributions from the standard decomposition and identical to the first and third terms in (5), respectively. As previously explained, the second and third terms are referred to as ‘corrected need’ and ‘discrimination’, respectively. These terms are the main difference from equation (5).

The second term of equation (6) is the contribution of corrected need to the CI:

$$\frac{2}{\mu N} \sum_{k} \left(\beta_{kgr} - {\beta_k}^{p}\right) \sum_{i} x_{ik} \left(R_i - \frac{1}{2}\right) \tag{7}$$

Where $\beta_{kgr} - {\beta_k}^{p}$ is the difference between the parameter estimates from the reference group and the pooled population regressions respectively, x_{ik} is a need variable of individual i, and μ is the mean of health service use. N is the total population and R_i is the fractional rank of individual i. Corrected need will be positive if the reference group uses more health services and need is also concentrated more on this group. Likewise, corrected need will be negative if the highest wealth group uses more health services but need is more concentrated on the poorest wealth group.

In general, unstandardized horizontal inequity (HI) is estimated by subtracting the contribution of need variables from the concentration index:

$$HI = C - \sum_{k=1}^{k} \frac{\beta_k^p \bar{x}_k C_k}{\mu} \tag{8}$$

So, horizontal inequity is higher, the higher is the contribution of non-need variables to the concentration index.

Corrected need-adjusted horizontal inequity (86) is calculated by subtracting the contributions of both need and corrected need from CI:

$$HI = CI - \sum_{k=1}^{k} \frac{\beta_k^p \bar{x}_k C_k}{\mu} - \frac{2}{\mu N} \sum_k \left(\beta_{kgr} - {\beta_k}^p\right) \sum_i x_{ik} \left(R_i - \frac{1}{2}\right) \quad (9)$$

Horizontal inequity will be lower if corrected need is positive, and vice versa. We do not have to consider Van de Poel's discrimination term because discrimination is effectively captured on the right-hand side of equation (9) as a result of the estimation of horizontal inequity, given equation (6).

Wealth, as measured by an asset index, is included as a non-need variable in the decomposition approach. The decomposition analysis shows the contribution of each need and non-need factor to the pooled CI as shown in equations (1) and (2). The concentration index depends on the relationship between the rank of socioeconomic status and the health or other non-need variable, and not on the variation in the socio-economic status variable itself (39). When a socio-economic or wealth variable is included, as shown in equation (4), the CI of wealth is calculated using the covariance between the individual's level of wealth and their wealth rank R_i (see (1)). Based on the given sample weight, individuals with the same level of wealth may have a different rank in DHS data (170). By definition, the CI of richer wealth quintiles are positive while the CI of poorer quintiles are negative (86). In practice, when equity studies using decomposition analysis include the CI of 'wealth' in the non-need factors (39,86,146,171), the focus is on the contribution of the wealth variable to the total CI, rather than on interpreting the CI of the wealth variable itself. For example, Wagstaff et al. (171) calculated a CI with the covariance between stunting and household consumption expenditure. In that study, the CI of household consumption expenditure was included as a non-need factor in the decomposition analysis. Once the CI of a 'wealth' variable is calculated, it is possible to estimate the contribution of wealth to the pooled CI because the contribution is the product of

elasticity and the CI of each variable. Therefore, the inclusion of wealth in the decomposition analysis does not constitute ‘double counting’.

Rural-urban inequality can be measured using a method similar to that described above. For the purposes of this study, a regional concentration index was calculated using the standard decomposition method, following steps in the equations (1) - (4). To compare rural and urban areas, a concentration index was calculated by estimating the covariance between each need variable, non-need variable, and the wealth rank of people living in the area. A single asset index comprising five quintiles was developed for the whole of Malawi, without distinguishing between rural and urban areas (172).

To estimate the coefficients used in the decomposed concentration index, a probit model was used (39). A probit model allows the estimation of probabilities or marginal effects, imposing a normal distribution on the data (173). The mean of need variables and coefficents of the probit model were compared using a t test for continuous variables and a chi-2 test for categorical variables. All tests were conducted at the 95% confidence level.

3.3.3 Data

Demographic and Health Surveys (DHS) are designed to collect national health and demographic data (172). Topics in the survey include fertility, contraception, breastfeeding, family planning, nutritional status of mothers and children, childhood illnesses and mortality, use of maternal and child health services, maternal mortality, and domestic violence (88,172). In addition, DHS 2004 and DHS 2010 in Malawi collected detailed HIV-related data including knowledge of and attitudes towards HIV/AIDS, receipt of an HIV test, HIV-related behavioural Indicators, HIV status and symptoms of sexually transmitted infections (STIs). The DHS in Malawi also tested a sub sample of respondents for HIV. The age of the respondents ranges from 15 to 49 for women and from 15 to 54 for men (88).

This study uses data from two rounds of the DHS survey in Malawi – the 2004 round, and the 2010 round. This enables the calculation of within year inequity and a comparison of trends in inequity between these two periods. Then 2004 data used in this study includes 15,091 households, 11,698 women aged 15- 49 and 3,261 men aged 15-54. The 2010 dataset includes 27,000 households, 24,000 women and 7,000 men. Both samples were drawn over 522 clusters: 458 in rural areas and 64 in urban areas (172). Malawi is divided into 11 districts in the DHS: Blantyre, Kasungu, Machinga, Mangochi, Mzimba, Salima, Thyolo, Zomba, Lilongwe, Mulanje, and other districts. Based on the FAO classification (174), Lilongwe, Mzimba, Blantyre, and Zomba were classified as urban areas in the DHS.

A probability sample, which is defined as one in which the units are selected randomly with known and nonzero probabilities, was used in the DHS data collection (175). Households were pre-selected in the central office before the start of data collection (175). Trained field staff conducted interviews only the pre- selected households to avoid bias. Sample size was determined based on the calculation of sample size using relative standard error. Further details on the DHS sampling methodology can be found elsewhere (175).

The dependent variable in these analyses is ‘Ever tested for HIV’. This takes the value of ‘1’ if the respondent has ever tested for HIV and ‘0’ if they have never tested. Three questions on experience of STI symptoms in DHS 2010 and DHS 2004 are used as need variables in the analysis: 1) a diagnosed STI in the last 12 months; 2) a genital sore or ulcer in the last 12 months; or 3) genital discharge in the last 12 months. A number of previous studies have used symptoms as need indicators in empirical analyses of equity (176,177). The symptoms used in this study may be indicators of HIV infection (178) and patients should be referred for an HIV test when these symptoms are observed (178,179). The presence of STIs also increases the possibility of transmitting HIV (142). Socioeconomic status variables were selected

as non-need variables including wealth as measured by an asset index, literacy, education, and marital status.

No ethical approval was needed for the conduct of this study as it makes use of open-access secondary data.

3.4 Results

3.4.1 HIV test uptake in 2010

Table 6 describes HIV test uptake by socioeconomic status in 2010. The data reveal significant differences in HIV testing by socioeconomic status, especially among men. Three-quarters (74.5%) of women and over half (53.7%) of all men report that they have been tested for HIV. In terms of region, literacy, education, marriage and wealth, those who have been tested are significantly different from those who have not been tested ($P < 0.05$). Testing is about 10 percentage points more common in the Northern region (79.2% among women and 61.6% among men) than in the Central region, and men in the Southern region are also lagging behind (52.3%). Literate women and men have more often been tested, but the gap is small for women, while it is relatively large for men: 43.4% of illiterate men and 57.1% of men who can read a whole sentence have received an HIV test. The difference between primary and secondary education is relatively small for women (73.5% vs. 79.3%) but large for men (48.3% vs. 67.7%). The gap in HIV testing by wealth quintile is smaller than the gap by education: 72.1% of the poorest women and 49.7% of the poorest men have been tested, compared with 76% of the richest women and 59.9% of the richest men. There is very little difference between never married (mostly young) women and men (40.2% and 42.5% respectively); however, the difference between married and never married women is much larger (43 percentage points) than the difference between married and never married men (18 percentage points). Widowed and divorced women report lower levels of testing than women in a relationship (whether married, living together or not living together). Few men are divorced, widowed or not living together in this context. These results show that higher SES and the uptake of HIV testing have a positive association.

TABLE 6: HIV TESTING BY SOCIO-ECONOMIC STATUS (DHS 2010)

		Women			Men		
		Not Tested (N=5788) (% not tested)	Tested (N=16928) (% tested)	P value	Not Tested (N=3293) (% not tested)	Tested (N=3821) (% tested)	P value
Region	**Northern**	858(20.8)	3275(79.2)	<0.001	491(38.4)	789(61.6)	<0.001
	Central	2360(30.4)	5399(69.6)		1248(48.4)	1329(51.6)	
	Southern	2570(23.7)	8254(76.3)		1554(47.7)	1703(52.3)	
Literacy	**Cannot read at all**	1930(26.7)	5305(73.3)	0.014	788(56.6)	604(43.4)	<0.001
	Able to read only parts of sentence	544(25.6)	1585(74.4)		284(52.2)	260(47.8)	
	Able to read whole sentence	3314(24.8)	10038(75.2)		2221(42.9)	2957(57.1)	
Education	**No education**	912(27.3)	2431(72.7)	<0.001	257(58)	186(42)	<0.001
	Primary	4007(26.5)	11104(73.5)		2371(51.7)	2213(48.3)	
	Secondary	817(20.7)	3125(79.3)		608(32.3)	1275(67.7)	
	Higher	52(16.3)	268(83.8)		57(27.9)	147(72.1)	
Marriage	**Never married**	2676(59.8)	1801(40.2)	<0.001	1542(57.5)	1142(42.5)	<0.001
	Married	2212(16.6)	11099(83.4)		1407(39.5)	2158(60.5)	
	Living together	306(16)	1612(84)		239(39.1)	373(60.9)	
	Widowed	190(22.4)	660(77.6)		14(48.3)	15(51.7)	
	Divorced	244(20.9)	924(79.1)		53(41.7)	74(58.3)	

	not living together	160(16.1)	832(83.9)		38(39.2)	59(60.8)	
Wealth	**Poorest**	1248(27.9)	3229(72.1)	0.001	568(50.3)	562(49.7)	<0.001
	Poorer	1137(25.6)	3305(74.4)		730(50.6)	713(49.4)	
	Middle	1166(25)	3491(75)		695(47.5)	768(52.5)	
	Richer	1155(24.9)	3479(75.1)		680(44.4)	851(55.6)	
	Richest	1082(24)	3424(76)		620(40.1)	927(59.9)	

Notes to Table 6: P value was calculated using chi-2 test. No reply was excluded.

Table 7 presents the mean values and concentration indices for the need and non-need variables. Genital sore or ulcer is the most commonly reported of the three indicators of need (6.9% of women and 3.4% of men). Among women, the CI for need is zero. Among men, the CI is also very small, but negative, indicating that need is concentrated among the relatively poor. The equitable distribution of need is surprising given that HIV prevalence is higher among the relatively wealthy in Malawi.

TABLE 7: DESCRIPTIVE SUMMARY OF NEED AND NON-NEED VARIABLES AND THEIR CONCENTRATION INDICES, DHS 2010

		Women (N=22716)					Men (N=7114)				
Variable		N	Mean	CI	S.D	P value §	N	Mean	CI	S.D	P value §
Test	Ever tested for HIV	22,716	0.745		0.436		7,114	0.537		0.499	
N1	Any std in last 12 months	377	0.016	0.003	0.127	<0.001	113	0.016	-0.034	0.124	0.1341
N2	Genital sore/ulcer in last 12 months	1594	0.069	0.002	0.253	<0.001	245	0.034	-0.045	0.182	0.0062
N3	Genital discharge in last 12 months	860	0.037	0.002	0.189	<0.001	183	0.025	-0.006	0.156	0.9266
wealth	Pooled	22,716	3.011	0.264	1.408	0.001	7,114	3.130	0.249	1.381	<0.001
	Lowest wealth quintile	4,477	0.197		0.398		1,130	0.159		0.366	
	Second lowest wealth quintile	4,442	0.196		0.397		1,443	0.203		0.402	
	Middle wealth quintile	4,657	0.205		0.404		1,463	0.206		0.404	
	Second upper wealth quintile	4,634	0.204		0.403		1,531	0.215		0.411	
	Upper wealth quintile	4,506	0.198		0.399		1,547	0.217		0.413	
literacy	Pooled	22,716	1.269	0.127	0.913	0.014	7,114	1.532	0.075	0.800	<0.001
	Cannot read at all	7,235	0.318		0.466		1,392	0.196		0.397	
	Able to read only parts of sentence	2,129	0.094		0.291		544	0.076		0.266	
	Able to read whole sentence	13,352	0.588		0.492		5,178	0.728		0.445	
education	Pooled	22,716	1.055	0.129	0.612	<0.001	7,114	1.260	0.116	0.612	<0.001
	No education	3,343	0.147		0.354		443	0.062		0.242	
	Primary	15,111	0.665		0.472		4,584	0.644		0.479	

		Secondary	3,942	0.174		0.379		1,883	0.265		0.441	
		Higher	320	0.014		0.118		204	0.029		0.167	
	marriage	Pooled	22,716	1.291	-0.076	1.228	<0.001	7,114	0.825	-0.044	0.910	<0.001
		Never married	4,477	0.197		0.398		2,684	0.377		0.485	
		Married	13,311	0.586		0.493		3,565	0.501		0.500	
		Living together	1,918	0.084		0.278		612	0.086		0.280	
		Widowed	850	0.037		0.190		29	0.004		0.064	
		Divorced	1,168	0.051		0.221		127	0.018		0.132	
		not living together	992	0.044		0.204		97	0.014		0.116	

Notes: 1) Variables Test, N1, N2 and N3 take the value 1 for “yes” and 0 for “no”.2) CI: Concentration index 3) S.D : standard deviation 4) § : Calculated using t test for need variables and chi-2 test for non-need variables.

Table 8 presents the results of decomposing the CI for HIV test uptake in DHS 2010. It also shows the contributions of the need and non-need variables to the estimated socio-economic inequity in HIV testing. The sum of the homogeneous contributions of the need variables from the standard decomposition is approximately zero for both women and men. The sum of the contributions of corrected need is also approximately zero for both women and men. This means that non-need variables explain all of the existing inequity in HIV testing in 2010.

Horizontal inequity among both women and men is positive (0.008 and 0.040 respectively), indicating that for a given need, the relatively wealthy are more likely to access HIV testing in Malawi. However, the degree of horizontal inequity is small, especially for women. There is no difference between horizontal inequity and corrected need adjusted inequity.

Figure 4 illustrates the contributions of the different non-need factors to the inequity in HIV testing. For both women and men in 2010, education is the most important non-need contributor to the concentration index. However, in 2004, wealth was a significant contributor for both women and men.

3.4.2 Comparison of 2010 with 2004

The results from DHS 2010 contrast significantly with the data for 2004 in terms of access to HIV testing and inequity. Appendix 5 describes HIV testing by socio-economic status in 2004. Access to HIV testing has dramatically increased in the intervening period. In 2004, only 14.7% of women and 16.0% of men had been tested, compared with 74.5% of women and 53.7% of men in 2010. The pattern of socio-economic differences in 2004 was similar to 2010. However, one difference is worth noting; in 2004, socio-economic differences tended to be similar in magnitude

among both women and men, while in 2010, the differences were more pronounced among men than among women. For example, the gap in testing between illiterate and fully literate decreased from 6 to 2 percentage points among women but increased from 7 to 14 percentage points among men. However, the gap in testing between married and never married women was more pronounced in 2010 than in 2004 (43 vs. 7 percentage points). The difference between the highest and the second highest wealth quintiles was relatively large in 2004 (8 and 11 percentage points among women and men respectively) but relatively small in 2010 (1 and 4 percentage points respectively).

The concentration indices for the need variables for women were negative but close to zero in 2004 (Appendix 6). On the other hand, for men, the CIs for the need variables were positive. This suggests that in 2004, need for HIV testing among men was concentrated among the relatively rich, but by 2010 the need for testing was equitably distributed.

Table 8 shows the decomposition of the CI for HIV testing in 2004. Horizontal inequity has fallen significantly between 2004 and 2010 from 0.152 to 0.008 for women, and from 0.185 to 0.04 for men. In 2010, there was no difference between horizontal inequity and corrected need adjusted inequity in 2004.

TABLE 8: DECOMPOSITION OF THE CONCENTRATION INDEX FOR HIV TESTING, DHS 2010 AND 2004

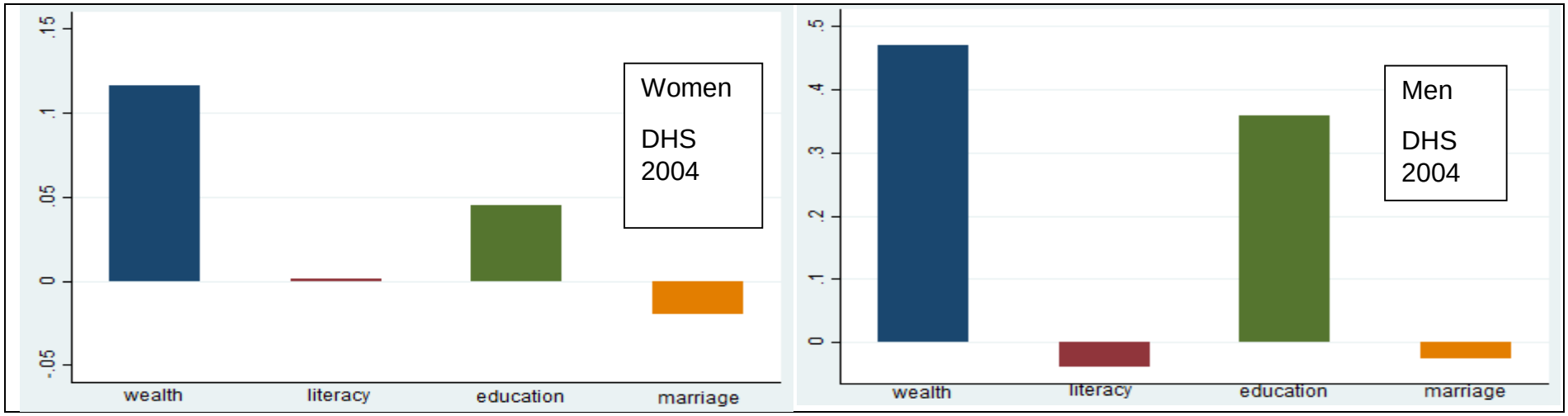
DHS 2010	Women					Men				
Need	**Coefficient**	**P value†**	**Homogeneous**	**Corrected need**	**P value††**	**Coefficient**	**P value†**	**Homogeneous**	**Corrected need**	**P value††**
N1(had any std in last 12 months)	0.097	0.000	0.000	0.000	0.915	0.022	0.667	0.000	0.000	0.560
N2(had genital sore/ulcer in last 12 months)	0.065	0.000	0.000	0.000	0.900	0.077	0.028	-0.001	0.000	0.225
N3(had genital discharge in last 12 months)	0.037	0.029	0.000	0.000	0.931	-0.001	0.990	0.000	0.000	0.119
Sum of need contribution			0.000	0.000				-0.001	0.000	
Non- need										
Wealth	0.009	0.000	0.010			0.002	0.707	0.003		
Literacy	-0.001	0.723	0.000			0.023	0.007	0.005		
Education	0.056	0.000	0.010			0.150	0.000	0.041		
Marriage‡	0.079	0.000	-0.002			0.081	0.000	-0.009		
Sum of non-need contribution			0.018					0.040		
Horizontal inequity (HI)			0.008	0.008				0.04	0.04	
DHS 2004	**Women**					**Men**				
Need	**Coefficient**	**P value†**	**Homogeneous**	**Corrected need**	**P value††**	**Coefficient**	**P value†**	**Homogeneous**	**Corrected need**	**P value††**
N1(had any std in last 12 months)	0.067	0.074	-0.001	0.000	0.528	0.026	0.718	0.002	0.000	0.065

N2(had genital sore/ulcer in last 12 months)	-0.003	0.831	0.000	0.000	0.166	0.041	0.300	0.002	0.000	0.118
N3(had genital discharge in last 12 months)	0.042	0.052	-0.003	0.000	0.003	0.000	0.992	0.000	-0.001	0.229
Sum of need contribution			-0.004	0.000				0.004	-0.001	
Non- need										
Wealth	0.022	0.000	0.116			0.023	0.000	0.109		
Literacy	0.001	0.817	0.001			-0.012	0.213	-0.009		
Education	0.049	0.000	0.045			0.101	0.000	0.082		
Marriage‡	0.023	0.000	-0.001			0.027	0.000	-0.012		
Sum of non-need contribution			0.161					0.17		
Horizontal inequity (HI)			0.152	0.152				0.185	0.186	

Notes to Table 8: The contribution of homogeneous need corresponds to the first term in equation (6). Corrected need correspond to the second term in equation (6). *Horizontal inequity is calculated by subtracting the need contribution from the unstandardized concentration index. P value††: calculated using t-test comparing corrected need with zero. ‡: calculated using not married (divorced, widowed, never married and not living together) and living together (married and living together)

Figure 4 illustrates that in 2004, wealth was the largest contributor to the concentration index for women and also accounted for a great part of the contribution to the concentration index for men. This implies that as the extent of inequity in HIV testing has fallen between 2004 and 2010, the main contributor to inequity has also changed from wealth to education over this time.

FIGURE 4: CONTRIBUTION OF NON-NEED FACTORS TO THE INEQUALITY IN HIV TESTING UPTAKE IN MEN AND WOMEN IN MALAWI, DHS 2010 AND DHS 2004


Women
DHS
2004
.15
.1
.05
0
-.05
wealth
literacy
education
marriage
Men
DHS
2004
.5
.4
.3
.2
.1
0
wealth
literacy
education
marriage

3.4.3 Decomposition analysis: Rural-urban inequality

Rural-urban inequality in HIV testing was also examined. The results show that there exists little rural-urban inequality in HIV testing in 2010 (Table 9). Horizontal inequity among women living in rural areas was 0.005 compared with 0.014 among women living in urban areas, and 0.041 among men living in rural areas compared with 0.007 among men in urban areas. This means that access to HIV testing is more pro-rich among men in rural areas. In 2004, however, horizontal inequity among women and men living in urban areas was higher (0.18 and 0.211, respectively) than among women and men living in rural areas (0.111 and 0.146 respectively). This result suggests that while access to HIV testing was more affected by socioeconomic factors in urban areas in 2004, men in rural areas are somewhat less affected by socioeconomic factors in 2010. Figure 5 illustrates regional variation in horizontal inequity in 2004 and in 2010.

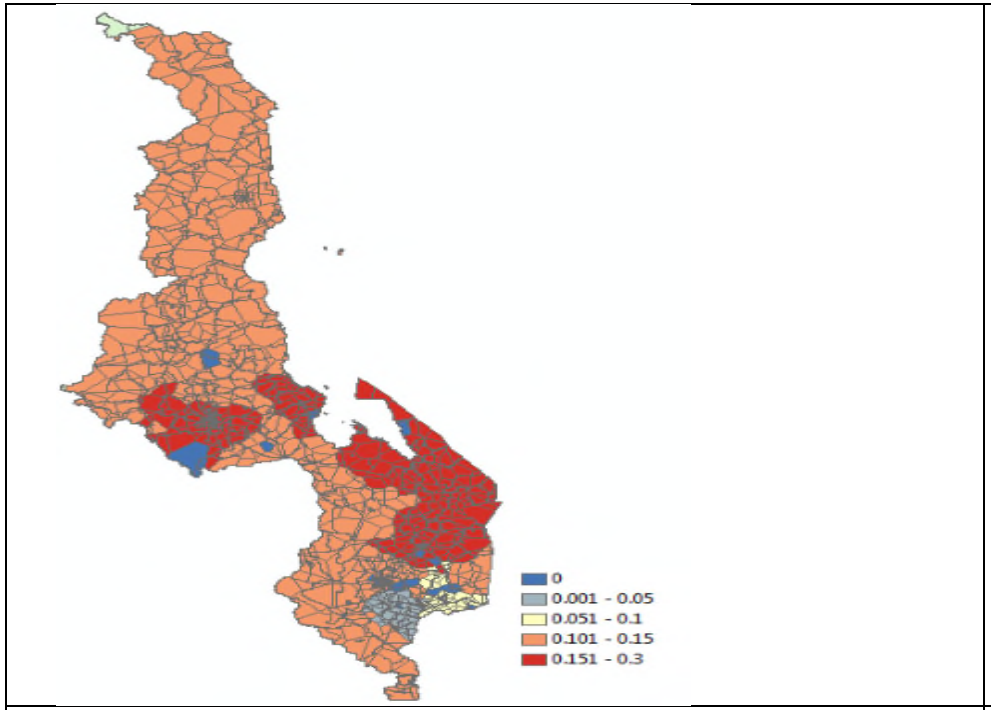
TABLE 9: RURAL URBAN INEQUALITY IN HIV TESTING IN MALAWI , DHS 2010 AND 2004

Urban total(2010)				**Rural total(2010)**			
Women		**Men**		**Women**		**Men**	
	CI		**CI**		**CI**		**CI**
Wealth	0.218	**Wealth**	0.203	**Wealth**	0.268	**Wealth**	0.253
Literacy	0.113	**Literacy**	0.066	**Literacy**	0.123	**Literacy**	0.070
Education	0.145	**Education**	0.124	**Education**	0.115	**Education**	0.102
Marriage	-0.040	**Marriage**	-0.083	**Marriage**	-0.001	**Marriage**	-0.030
	Contribution		**Contribution**		**Contribution**		
Need	-0.001	**Need**	0.002	**Need**	0.000	**Need**	-0.001
Non Need	0.012	**Non Need**	0.025	**Non Need**	0.007	**Non Need**	0.043
HI	0.014	**HI**	0.007	**HI**	0.005	**HI**	0.041
Urban total(2004)				**Rural total(2004)**			
Women		**Men**		**Women**		**Men**	
	CI		**CI**		**CI**		**CI**
Wealth	0.217	**Wealth**	0.206	**Wealth**	0.259	**Wealth**	0.237
Literacy	0.118	**Literacy**	0.086	**Literacy**	0.143	**Literacy**	0.072
Education	0.137	**Education**	0.111	**Education**	0.128	**Education**	0.103
Marriage	-0.035	**Marriage**	-0.062	**Marriage**	0.009	**Marriage**	-0.032
	Contribution				**Contribution**		
Need	-0.002	**Need**	0.000	**Need**	-0.003	**Need**	0.009

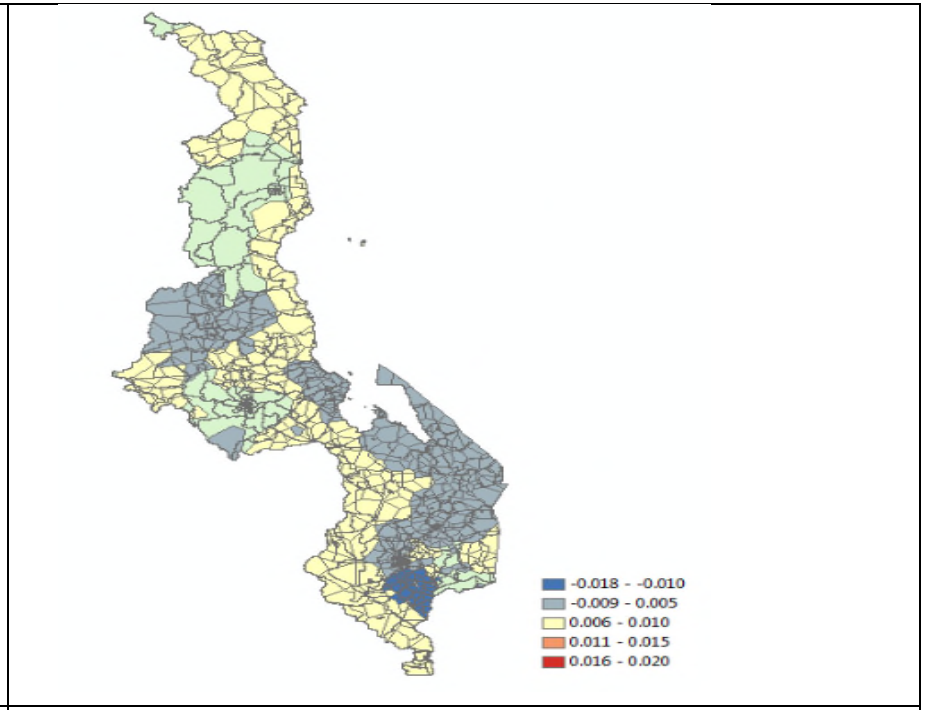
Non Need	0.178	**Non Need**	0.210	**Non Need**	0.105	**Non Need**	0.143
HI	0.180	**HI**	0.211	**HI**	0.111	**HI**	0.146

Note to table 9: 1) CI : concentration index

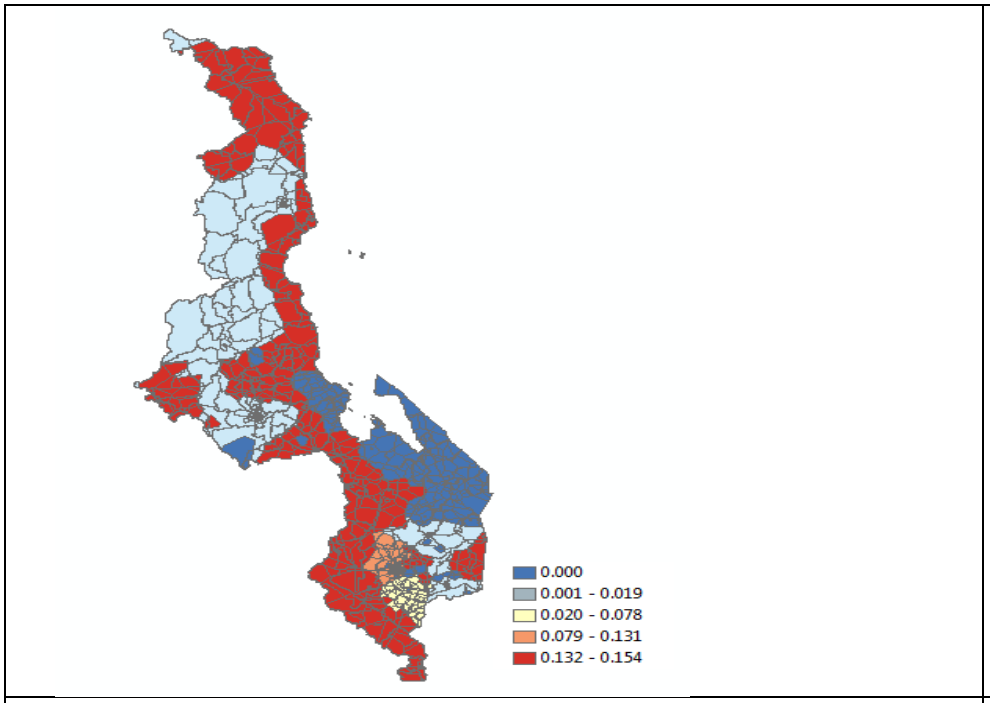
FIGURE 5: MAP OF HORIZONTAL INEQUITY IN MALAWI



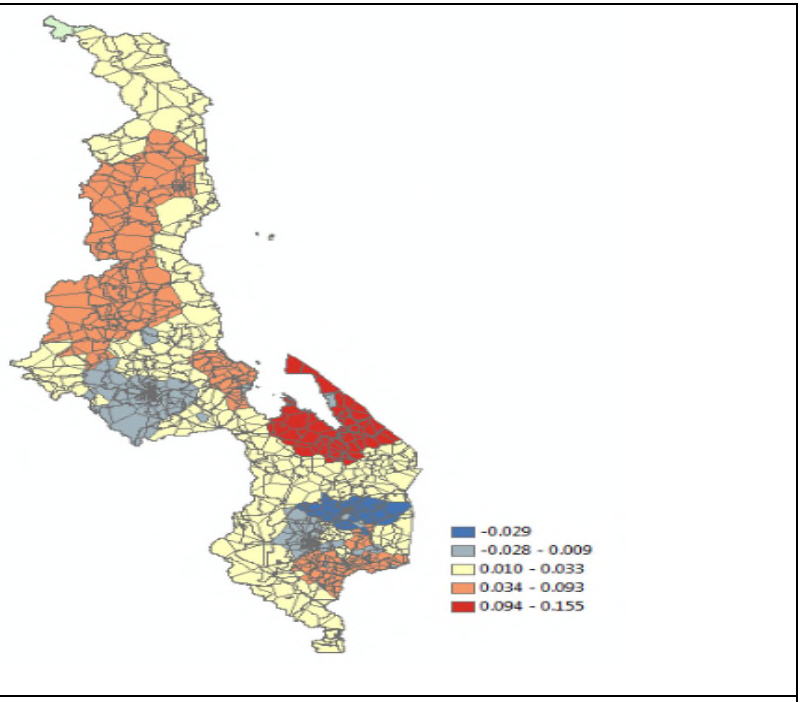
Horizontal inequity of women (2004)



Horizontal inequity of women (2010)



Horizontal inequity of men (2004)



Horizontal inequity of men (2010)

Note to Figure 5: Horizontal inequity was calculated based on conventional concentration index.

3.5 Discussion

This study measures horizontal inequity in access to HIV testing in Malawi, using a decomposed concentration index. The approach of Van de Poel et al. (86) was applied to capture differences in need in Malawi. Rural-urban inequity was also examined using decomposition analysis. Inequity is explored using the 2010 Malawi DHS data to describe current access to HIV testing. This is compared with inequity calculated using the 2004 DHS data in order to reflect on possible trends in access to HIV treatment.

Within the 2010 data, the need for HIV testing was equitably distributed, as reflected in equality between the standard index of horizontal inequity and corrected, need-adjusted inequity. In other words, the reference group of high-wealth men and women did not receive more HIV testing than the whole population. This finding may seem surprising, given that HIV prevalence is higher for higher SES groups in Malawi, as in the majority of sub- Saharan African countries (180). As described earlier however, prevalence estimates are themselves affected by access to testing in a previous time period. Need in this statement refers to the need for testing, which does not suffer from the same bias, and the variables we use to estimate this need – while potentially imperfect - are not subject to those barriers to access that may affect estimates of HIV prevalence.

Comparing 2010 data with 2004 data, the first notable observation is the total increase in access to HIV testing in the Malawian context. This increase in testing has also been accompanied by a significant reduction in horizontal inequities in HIV testing. These changes may in part be due to the significant financial support for HIV programmes in Malawi by global donors (8,72). For instance, the Global Fund disbursed US$ 41 million for implementation of HIV treatment activities, including HIV testing, in 2005 (181). The number of HIV testing facilities as well as outreach programmes have increased, and national testing and counselling campaigns have been conducted (182). In 2008, a national programme offering HIV counselling and testing to 500,000 pregnant women was implemented at more than 500 sites (82).

As a result, there has been a shift from facility-based testing to mobile and door-to-door testing, which appears to have had a net positive impact on testing access, and also a positive impact on the equity of access to treatment – overcoming previous non-need barriers to HIV test access (82).

In short, the strategies adopted for expanding access to HIV testing in Malawi have been successful in reducing inequity and expanding access. That reduction has taken place in both urban and rural areas. However, some degree of inequity remains among men living in rural areas, despite substantial investments in mobile clinics and door-to-door testing. A number of studies have found that distance is one of the biggest barriers to obtaining access to HIV testing and treatment in sub-Saharan Africa (183–185) and that transport costs constitute a substantial burden for patients in Malawi. In general, mobile testing is deemed a useful tool for offering HIV testing to low SES groups living in rural areas (147).

The reduced inequity observed in this study is of particular interest as global donors have been criticised for having a short term results focus, with a need to attributed outcomes to their funding or support (186). Critics are concerned that programs carried out by global health initiatives may create vertical service delivery structures that, to some extent, exacerbate health system problems (187). This seems not to have been the case in the Malawian context over the period from 2004-2010.

While these findings advance our understanding of inequity in HIV test uptake in Malawi and comparable contexts, the analysis has known limitations. Trends in the uptake of HIV testing since 2010 cannot be measured as no more recent data are available. DHS Malawi 2014 is being prepared but is not currently available at the moment. When DHS 2014 becomes available, it will be possible to study whether the equity trends identified in this study have also continued since 2010 and this is identified as a priority area for future study. Moreover, only three variables on STI symptoms were available within the DHS datasets. As a result, the need for HIV

testing may be conservatively estimated in these analyses. The addition of further need variables in future analyses may enable a more nuanced or sensitive analysis of inequity in HIV testing in the Malawian context.

3.6 Conclusion

Measuring inequity in HIV test uptake is important to improve access to care and inform health policy. While global stakeholders in HIV financing and care are embracing the 90-90-90 agenda, there has been a paucity of evidence on inequity in HIV test uptake in local sites which could highlight important barriers to care and that may constitute barriers to the attainment of these goals.

In resource-limited countries, expansion in access does not always result in improved equity in access. The findings of this study show that access to HIV testing has significantly expanded in the Malawian context, and socioeconomic inequity in HIV test access has significantly reduced between 2004 and 2010. This may be attributed not only to increases in donor funding in this period, but also to the strategies that donor used to expand testing access to the rural population. It remains to be seen whether the observed low degree of inequity can be sustained as global priorities and funding patterns change. Finally, as education persists as the remaining contributor to horizontal inequity, the question of how to further increase testing among men and reduce the residual inequity among rural men in particular, remains a priority area for further study.

4 Can Voluntary Pooled Procurement Reduce the Price of Antiretroviral Drugs? A case study of Efavirenz[6]

[6] This chapter has been accepted in *Health policy and planning* as of 13th Nov 2016. This chapter reflected the recommendations and this chapter is a revised version. The decision letter is in Appendix 15.

4.1 Introduction

Global health initiatives and international non-government organisations (NGOs) such as the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM), the President's Emergency Plan for AIDS Relief (PEPFAR) and the Clinton HIV/AIDS Initiative (CHAI) have used a number of strategies to procure antiretroviral therapy (ARV) at lower prices. Common strategies include negotiation (188,189) and a range of procurement mechanisms (94).

Historically, the funding mechanism of GFATM was based on the country coordination mechanism (CCM), which was initiated after receiving a grant proposal from the government. Within this system, medicine procurement was effectively left to each principal recipient (PR) (71,92,94), and Ripin et al. (45) refer to this as a 'distributed country-led' model. Under this arrangement, each country was free to select its own supply chain and procurement companies, and to set policies to manage tendering, purchasing and ordering (45). GFATM would then disburse the funds for the procurement once the country's proposal was approved. Finally, each principal recipient (PR) would procure the ARV drugs. Under CCM, the Ministry of Health or another implementing body may negotiate 'directly' with manufacturers or contract with logistics companies using GFATM funding (71).

There are a number of price reduction strategies available for HIV drugs: pooled procurement, differential pricing and generic competition;

a) Pooled procurement involves purchasing drugs in bulk for multiple buyers, to reduce the cost of the drugs and is based on the principles of economies of scale (94). Multiple buyers are grouped into a single group to obtain the benefits of pooled procurement.

b) Price differentiation based on the income of consumers, can maximize profits for manufacturers. In this instance, price differentiation or differential pricing occurs when low and middle income countries are sold the drugs at lower prices than high income countries (190).

c) Generic competition is a strategy where price is reduced by supplying multiple generic versions of drugs after the patent for the branded equivalent drug has expired. Perez-Casas (191) showed that the price of a branded drug can be reduced by generic competition. In Brazil, generic competition lowered the branded price of Stavudine, Lamivudine and Nevirapine from $10,439 to $631, while the generic price dropped to $800 from $2,767.

In 2009, GFATM commenced voluntary pooled procurement (VPP), wherein purchases were pooled at the national level, increasing the negotiating power of purchasers (93). Under the VPP system, each PR country may volunteer to join the procurement programme, but are not obligated to do so. Between 2009 and 2011, 47 countries joined the scheme, usually to purchase one or more of five key health products: ARVs for HIV, artemisinin-based combination therapy (ACTs) for malaria, long-lasting insecticidal bed nets (LLINs), rapid diagnostic tests (RDTs) for Tuberculosis (TB), and condoms. Overall, 307 million daily doses of antiretroviral drugs were procured and approximately 336,000 people received ARV therapy with drugs purchased through voluntary pooled procurement (97).

The VPP mechanism is mainly implemented by a procurement services agent (PSA), working on behalf of a principal recipient country.[7] Although the GFATM may facilitate communications between the principal recipient and the procurement services agents (PSA), the GFATM does not act as an agent (192). The principle recipient sends a request with product specifications, quantities and delivery dates to the Procurement Services Support (PSS) team. The PSA invites bids from manufacturers and submits price quotations to the principle recipient (192). The principle recipient then decides whether they accept the price quoted. The PSA can act for multiple principles in a single transaction, thus effectively 'bulk buying' for a number of purchasers. In theory, bulk purchasing of this sort is expected to lead to price reductions in commodities (92,193).

[7] The Global Fund hires local fund agents (LFA) such as Price Waterhouse Coopers (PWC) and KPMG who monitor and oversee grant performance. Their role is different from PSA (71,246).

Pooling procurement would be expected to increase procurement efficiency and reduce transaction costs (93), further reducing the cost of drugs purchased. Pooled procurement is a form of cooperation between buyers and suppliers using the purchasing power that buyers have (194). The purpose of pooled procurement is to provide sustainable supply of commodities, reduce transaction costs and the total price paid for ARV (195). Therefore, appropriately conducted pooled procurement is likely to help low income countries access to ARV.

However, there is a paucity of evidence regarding the effect of bulk purchasing and VPP on procurement prices in practise. Waning et al. (94) tried to estimate the impact of global strategies such as large volume purchasing and the Clinton Health Access Initiative's (CHAI) price negotiation on antiretroviral drug prices, using the global price purchasing mechanism (GPRM) database. They carried out an analysis using bulk purchase as a proxy for pooled procurement. They concluded that large purchase volumes did not necessarily reduce drug prices. While their study found no beneficial price effect in the case of a single buyer, a study of VPP would enable the exploration of a potential price effect when bulk purchasing is conducted on behalf of multiple buyers. Wafula et al. (193) studied procurement prices after the introduction of VPP, using 115 completed questionnaires from 69 countries. In that study, two-thirds of those who had used the VPP system replied that VPP made procurement cheaper, although that reduction was not quantified as this study was based on the interviews. Wafula et al. (196), in a separate study, also analysed regional and temporal trends in the costs of malaria-related commodities using procurement data from 79 countries. They concluded that VPP resulted in significant declines in the cost of malaria rapid diagnostic tests (RDTs) and long-lasting insecticide-treated nets (LLINs). The impact of VPP on antiretroviral drugs was, however, not explored.

In addition to the studies already cited above, other studies have explored drug prices using procurement data. Danzon et al. (197) examined the effect of income and competition on drug prices using GPRM data and IMS health[8] data for the

[8] IMS health is a private company offering information regarding health care.

period 2004–2008. GPRM data was used to compare procurement prices, while IMS data was used to compare retail prices. The authors found that the income of a country was not associated with the drug prices and the availability of generic competition did not reduce the price of drugs. However, they also found that procurement based on tendering that stimulates price competition can reduce the prices of ARVs. Lucchini et al. (198) studied ARV price variation in Africa and Brazil. They used an econometric analysis with multiple linear regressions for 13 sub Saharan African countries in their study of price variation, using data from Medecines Sans Frontiers (MSF). As with Danzon et al. (197), they found no clear relationship between basic indicators like GDP per capita and the ex-manufacturer prices for generic and original drugs across countries. Wirtz et al. (199) carried out a study of price comparison of ARV drugs in order to identify factors related to lower drug prices. In contrast with Danzon et al. (197) and Lucchini et al. (198), they concluded that countries defined as 'lower-middle income' and 'upper-middle income' tended to pay significantly more for ARVs than 'low-income countries'. They did not focus on compulsory licensing but demonstrated that differential pricing is not applied in proportion to the income per capita of country. No study has yet, to our knowledge, formally explored the impact of VPP on antiretroviral drug prices.

To fill this gap in the evidence, this study aims to estimate the effect of VPP on the price of antiretroviral drugs, using difference-in-difference (DID) analysis of WHO GPRM data. The drug Efavirenz is chosen as a case study given the emphasis on fixed dose combination (FDC) therapy in the WHO HIV treatment guidelines (200).

A significant proportion of patients are currently on Efavirenz. In 2012, approximately 16% of children were using Efavirenz based first-line regimens in low and middle income countries (201). One study conducted in Sweden reported that among 276 HIV patients, 61% (168 patients) were given EFV as part of the initial regimen (202). In 2008, the number of people using Efavirenz was less than 2 million but expected to rise to more than 9 million by 2016 (201). Given the expectation that approximately 16.8 million people will be using anti-retroviral therapy by 2016 (201), and Efavirenz is increasingly being used as part of ARV administration, demand for the drug is likely to remain high.

Antiretroviral therapy generally requires a large number of tablets every day. In contrast, fixed-dose combinations (FDCs) need only once or twice daily doses, significantly simplifying the process of antiretroviral therapy (203). Fixed-dose combination therapy tends also to be cheaper than more complex treatment schedules (204) and is more easily preserved, as it does not need refrigeration. As a result, FDC therapy is especially useful in resource-limited countries in which cold storage may be absent or unreliable. Perhaps unsurprisingly, global organisations are increasing their commitment to FDC (205) and non-nucleoside reverse-transcriptase inhibitors (NNRTI) such as Efavirenz or Nevirapine, which have a pivotal role in FDC therapy. Of these drugs, Efavirenz is widely held to have a smaller risk of virologic failure (206). Considering that the wider uptake of FDC therapy may, in itself, have lowered ARV prices in the procurement market (92), it becomes important to adopt a methodology that can isolate any additional price effects of voluntary pooled procurement.

4.2 Literature review

Literature review was carried out regarding the impact of voluntary pooled procurement on ARV of GFATM using the keywords: *global fund* and *voluntary pooled procurement.* The search result clearly shows that this topic was substantially less highlighted. Eight articles contained those terms on the Web of Science and PubMed. This result was narrowed down to 4 when refined with *voluntary* (Appendix 3). Each was chosen for relevance to the research question (92,193,196,207). Three identical articles by Wafula et al. were identified (Appendix 4). These were de-duplicated and 4 articles were finally included.

Waning et al. (92) analysed price trends in ARV drugs using several data sources based on ARV purchase transaction. They found that purchase volumes for HIV drugs such as emtricitabine and tenofovir substantially increased from 2006 to 2008. Based on the findings, they argued that GFATM VPP will introduce large-scale purchasers, which will aggregate the number of buyers.

Wafula et al. (196) analysed for the three most widely procured commodities such as long-lasting insecticide-treated nets (LLINs), malaria rapid diagnostic tests (RDTs) and the artemether/lumefantrine (AL) combination treatment. They concluded that the cost of RDT was lowest in West and Central Africa (US$ 0.57), and highest in Latin America (US$ 1.1.) For the period between 2005 and 2012, VPP costs showed significant declines for RDTs.

Wafula et al. (193) analysed GFATM procurement data for 3 commodities: male condoms, HIV rapid tests, and ARV combination of lamivudine, nevirapine, and zidovudine. They concluded that pooled procurement lowered costs for condoms but not for other commodities included in the study.

Wafula et al. (207) carried out an internet-based survey on 315 principal recipients to identify their perception on the procurement programme of GFATM. Sixty-nine African countries replied and most PRs thought that the voluntary pooled procurement by GFATM was effective to simplify the procurement process.

To sum up, the result of literature search reveals that the assessment on the effort of GFATM to supply HIV drugs received less attention. Although these studies attempted to estimate or evaluate the effect of VPP, the result is limited, as they focused merely on time trends in procurement costs using a simple OLS rather than estimating the policy impact. Therefore, one needs to conduct analysis using a more elaborated econometric method, such as difference-in-difference analysis, to precisely estimate the impact of the programme.

4.3 Data

This analysis uses WHO Global Price Report Mechanism (GPRM) data from 2004 to 2013. This is a panel data set of information on transaction prices for

antiretroviral drugs purchased by international donors and programmes in low- and middle-income countries. GPRM is an umbrella term for procurement data. It was developed from an earlier version of the Price and Quality Report (PQR), and the price data included in the Price and Quality Report is automatically fed into the GPRM (208). Procurement services agents (PSAs) are responsible for entering data into the price and quality report (PQR) system, and therefore also into the GPRM. Grant funded purchases conducted using voluntary pooled procurement, are similarly reported to the PQR system by the procurement services agents (PSA) and so need not be entered by principal recipient (PR) countries (209). As the aim of this study is to estimate the overall impact of VPP on the mean change in a particular drug's price in all locations, rather than any country-specific impact on prices, GPRM data appears to be appropriate for the purpose of this analysis.

GPRM data contain two types of prices: *ex-works* prices and International Commercial Terms (*incoterms*) prices. *Ex-works* prices refer to the wholesale price at the manufacturer's site, while *incoterms* prices reflect which side, either seller or buyer, covers payment and risks (210). *Incoterms* prices are expected to reflect real procurement prices because the procurement process involves shipping charges such as freight and transport fees, which are not appropriately reflected in *ex-works* prices. *Incoterms* includes *ex-works* price and other 10 rules : FCA(Free Carrier) ; CPT(Carriage Paid To) ; CIP (Carriage And Insurance Paid To) ; DAT (Delivered At Terminal) ; DAP (Delivered At Place) ; DDP (Delivered Duty Paid) ; FAS (Free Alongside Ship) ; FOB (Free On Board) ; CFR (Cost and Freight) ; CIF (Cost, Insurance and Freight) ; EXW(Ex works) (211).

The main Incoterms rules applied for VPP countries from 2009 to 2013 were: EXW (Ex works: 68%), CIP (Carriage And Insurance Paid To:14%), and FCA (Free Carrier: 13%). Those for non VPP countries for the same period were; CIP (Carriage And Insurance Paid To: 27%), FCA (Free Carrier: 25%), and EXW (Ex works :15%). This text has also been inserted in the appendices (Appendix 12).

Information as to whether a country procured ARVs through VPP was obtained from the Price and Quality Reporting System (PQR) data (Appendix 7). A total of 25 out of 107 countries volunteered for VPP to procure generic Efavirenz between 2009 and 2011 (Appendix 7). GPRM data specify country, dosage, *incoterms* and *ex-works* unit prices, number of units, and manufacturer. Under VPP, Efavirenz was procured by only one logistics company, the Partnership for Supply Chain Management (PFSCM) (Appendix 8). This study focuses on 600mg Efavirenz, given that the 600mg dosage makes up more than 60% of all procured Efavirenz (appendix 9). A total of 25 out of 107 countries volunteered for VPP to procure generic Efavirenz between 2009 and 2011 (Appendix 7), however, countries may procure Efavirenz through VPP or other programmes. To include only Efavirenz procured by VPP, observed data was dropped if the manufacturers in the GPRM data and price quality reporting (PQR) data did not match. 121 observations over 10 years were retained for a treatment group of 25 countries, while 482 were from a control group of 82 countries.

4.4 Methods

Difference in difference estimation of the impact of voluntary pooled procurement on drug prices in this study can be expressed using Equation (1) (101,173).

$$y_{it} = \beta_1 VPP + \beta_2 Year + \beta_3 VPP \times Year + \beta_4 transaction\ volume + \beta_5 HIV\ prevalence + \beta_6 GNI + \beta_7 CPI + \beta_8 Expenditure + \beta_9 Tax + \beta_{10} Generic\ competition + \beta_{11} Country + \varepsilon_{it} \quad (1)$$

where, VPP is a dummy variable equalling 1 for those countries that utilised VPP and 0 for those not using VPP. $Year$ is a set of year dummy variables representing years with the label/name corresponding to the relevant year, spanning 2004 to 2013 and generated from a reference year of 2004. Since VPP was implemented in different countries for different periods from 2009, the interaction term of VPP (Treatment) $\times$ Year (Post) is the main variable of interest, and the coefficient of this term is the effect of VPP on procurement prices (173). Subscripts *t* and *i* refer to year and country, respectively, while ε_{it} is the error term.

Due to the highly skewed distribution of drug prices, a generalised linear model (GLM) was employed in the estimations. GLM is an estimation strategy well suited to modelling skewed data (212). Several other models have been suggested for skewed data including ordinary least square (OLS) on log transformed data, and a GLM with a log link and Gamma or Poisson distributions. The first approach using log transformation has the challenge of necessitating a smearing factor. Exponentiation of the mean of the logs generates the geometric mean of the skewed dependent variable (in this case costs), which is a downward-biased estimate of the arithmetic mean (212). To avoid this problem, a smearing factor, $\emptyset = 1/N \sum_{i=1}^{N} e^{(z_i - \hat{z}_i)}$ should be used where z_i corresponds to the log of cost and $\hat{z}_i$ corresponds to the treatment-group-specific mean of the log. However, results using

this smearing factor can be inconsistent. In contrast, GLM predicts the mean of the log without using a smearing factor and thus tends to yield more consistent results.

GLM does however, entail assumptions about the underlying distribution (101,213). The modified park test for the data suggests the choice of the Gamma distribution for the GLM, presenting the coefficient of 2.037 (P-value= 0.7374). When the coefficient is approximately 2, Gamma distribution is recommended whereas Poisson is chosen when the coefficient is 1. In addition, high p-value presents that Gamma distribution cannot be rejected. As a result, a GLM with a log link and Gamma distribution was chosen for this study. All analyses were carried out with Stata, Version 12 (StataCorp, College Station, Texas, USA).

To capture country-level heterogeneity, a fixed-effects model was used in the analysis. In practice, it is hard to assume that it was only VPP that affected the procurement prices. The fixed-effects model is a good method to control the endogeneity owing to a time-invariant omitted variable (101). In other words, the fixed-effects model is robust to unobserved time-invariant omitted variables. As commands in STATA (version 12) for GLM do not fully support fixed effects, country dummies were included as subject-specific intercepts for fixed effects. We implemented the Hausman test with the null hypothesis that the preferred model is random effects(RE) vs. the fixed effects(FE): Chi2(16)=61.75 (P value<0.001). Therefore, the more appropriate model for the data in the study is confirmed as a FE model.

Considering the literatures for factors associated with prices for HIV drugs (94,190,191,197–199,214–222) and the panel data of a drug price that will be used in this study, seven independent variables at country level were included in the model (Table 10): transaction volume of 600mg Efavirenz, HIV prevalence, tax revenue as percentage of GDP, gross national income (GNI), consumer price index (CPI), public health expenditure as % of total health expenditure, and number of generic manufacturers. Transaction volume is the sum of the product of quantity per

package and the number of packages, and it is obtained from WHO GPRM. The number of generic manufacturers presents a generic competition in the market, which is in line with the study by Danzon et al. (197). Among the studies identifying the importance of these independent variables in analyses of drug prices, only four carried out their analyses using procurement data (94,197–199). Consequently, the association between procurement and these likely independent variables will be investigated further in this study.

4.4.1 Sample size

This study uses a sample size of 25 treatment countries and 82 control countries. There is no general guideline on the minimum treatment group size for country level difference in difference analysis. Jones and Schneider (223) explored the association between global inequality in income and national average IQ using 23 countries of treatment group and 63 comparisons. Slaughter (224) performed difference in difference analysis at country level with four countries belonging to the European Economic Community (EEC) as a treatment group and 54 countries in the control group, in order to see how trade liberalisation contributes to per capita income convergence across countries. These examples demonstrate that country level difference in difference analysis is generally based on unbalanced data. Considering also the sample size norms established by these studies, the sample size proposed for this study is likely to be acceptable.

Nevertheless, to compensate for the relatively small number of observations for VPP attending countries and further bolster the results of this analysis, a simulation using wild cluster bootstrap was conducted. This simulation technique, based on re-sampling, is widely used in DID analysis to check the robustness of the result (225,226). It has been shown that wild cluster bootstrap can work well in providing conservative p-values even for 3 treated groups and 27 control groups (227). A further advantage of using the wild cluster bootstrap, is to reduce the risk of over-rejection by adjusting the size of standard error (228). The key idea of using the wild

cluster bootstrap is to rely on the fact that model errors of a given cluster are correlated over time, preserving the observed correlation in errors by drawing errors on the basis of original errors (228).

4.5 Results

Table 10 presents the descriptive statistics for this study. Means of *incoterms* prices and *ex-works* prices are substantially and significantly different between the treatment group and the control group (p-value <0.001). Among the covariates, GNI (p-value=0.0033) and CPI (p-value<0.001) were statistically different between the treatment group and the control group. These results show the possibility that VPP has an impact on the reduction of drug prices and that GNI and CPI will be significantly different between VPP attending countries and others.

In Table 10, the mean incoterms price for pre-intervention and post intervention for VPP and non VPP countries are 0.56 and 0.65, respectively. These fall to 0.15 and 0.2 after intervention. Therefore, there is a 73% reduction in the price for VPP countries and a 69% reduction for non-VPP countries. Likewise, for ex-works prices, VPP have a mean of 0.52 and 0.14 pre- and post- intervention respectively, amounting to a 73% price reduction. In non-VPP countries, ex-works prices are 0.6 and 0.18 pre- and post- intervention respectively, amounting to a 70% price reduction. In both cases the price reduction is higher for VPP countries.

TABLE 10: DESCRIPTIVE STATISTICS: 2004-2013

			Pre intervention (N=98)				*Post intervention (N=107)*				P value
			VPP countries(N=24)		Non VPP countries (N=74)		VPP countries (N=25)		Non VPP countries (N=82)		
Variable	**Definition**	**Source**	**Mean**	**S.D**	**Mean**	**S.D**	**Mean**	**S.D**	**Mean**	**S.D**	
Inconterms price	Mean unit cost of 600mg Efavirenz(incoterms applied)	WHO GPRM(229)	0.56	0.18	0.65	0.29	0.15	0.08	0.20	0.12	<0.001
Ex works price	Mean unit cost of 600mg Efavirenz(ex works applied)	WHO GPRM(229)	0.52	0.17	0.60	0.26	0.14	0.06	0.18	0.10	<0.001
Transaction volume	Sum of quantity*package of transaction per year	WHO GPRM(229)	1589175	3633073	2258281	6172162	3941418	9965920	6050612	14200000	0.8325
Market competition	Number of generic manufacturers	WHO GPRM(229)	1.94	0.91	2.00	1.08	1.86	0.97	1.71	1.06	0.8931
HIV prevalence	Prevalence of HIV, total (% of population ages 15-49)	World Bank(230)	2.60	3.51	3.63	6.15	2.42	3.50	2.83	5.30	0.3264
GNI	GNI per capita, PPP (current international $)	World Bank(230)	2357.21	1785.72	5109.83	7098.11	2884.95	2514.82	6256.06	8050.83	0.0033
CPI	Consumer price index (reference year=2010)	World Bank(230)	73.04	12.20	64.89	22.21	90.75	14.90	87.02	29.25	<0.001
Public health expenditure	Health expenditure, public (% of total health expenditure)	World Bank(230)	39.44	14.60	44.93	19.50	42.50	15.20	45.80	21.64	0.6621
Tax	Tax revenue (% of GDP)	World Bank(230)	7.89	6.73	10.58	11.78	8.78	7.45	7.69	8.45	0.8653
Treatment X Post	Interaction term of treatment*post period	WHO GPRM(229) GFATM PQR(231)	0	0	0	0	0.85	0.36	0	0	
Treatment	=1 if joined VPP	GFATM	1	0	0	0	1	0	0	0	

Year (2004 is the reference category)									
2005	=1 if year=2005	0.08	0.27	0.12	0.32	0	0	0	0
2006	=1 if year=2006	0.22	0.42	0.24	0.43	0	0	0	0
2007	=1 if year=2007	0.36	0.48	0.27	0.45	0	0	0	0
2008	=1 if year=2008	0.34	0.48	0.33	0.47	0	0	0	0
2009	=1 if year=2009	0	0	0	0	0.19	0.39	0.21	0.41
2010	=1 if year=2010	0	0	0	0	0.22	0.41	0.20	0.40
2011	=1 if year=2011	0	0	0	0	0.22	0.41	0.20	0.40
2012	=1 if year=2012	0	0	0	0	0.17	0.38	0.20	0.40
2013	=1 if year=2013	0	0	0	0	0.20	0.40	0.19	0.39

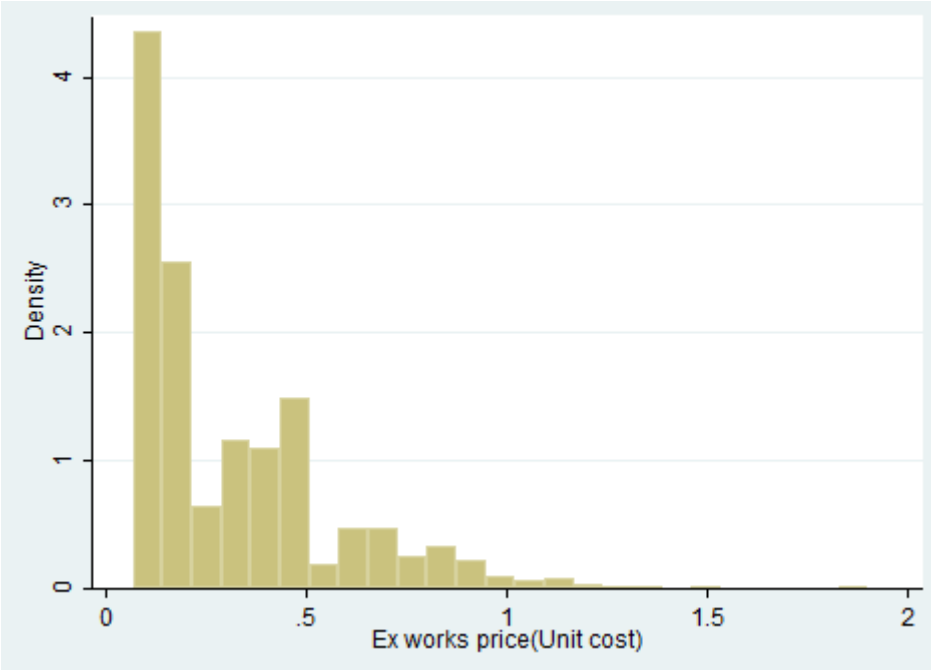
* P value was calculated using t-test with the interaction term comparing a treatment group with a control group

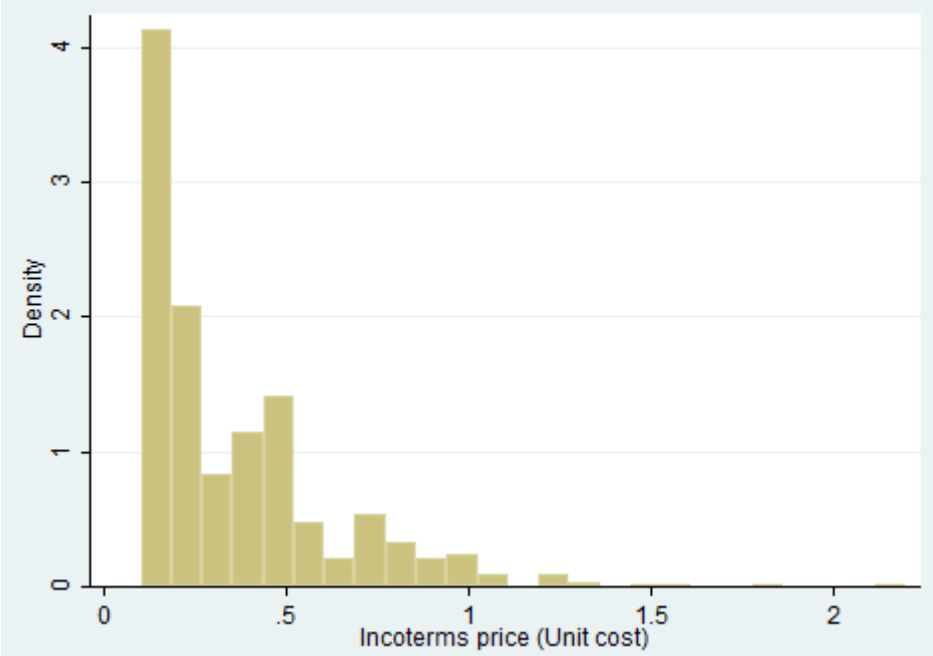
*N=number of countries

4.5.1 Distribution of drug prices

The histogram of *ex-works* price and *incoterms* price presents the skewed distribution of drug prices (Figure 6). This histogram shows that using GLM would be appropriate for this study.

FIGURE 6: HISTOGRAM OF EX WORKS PRICE AND INCOTERMS PRICE





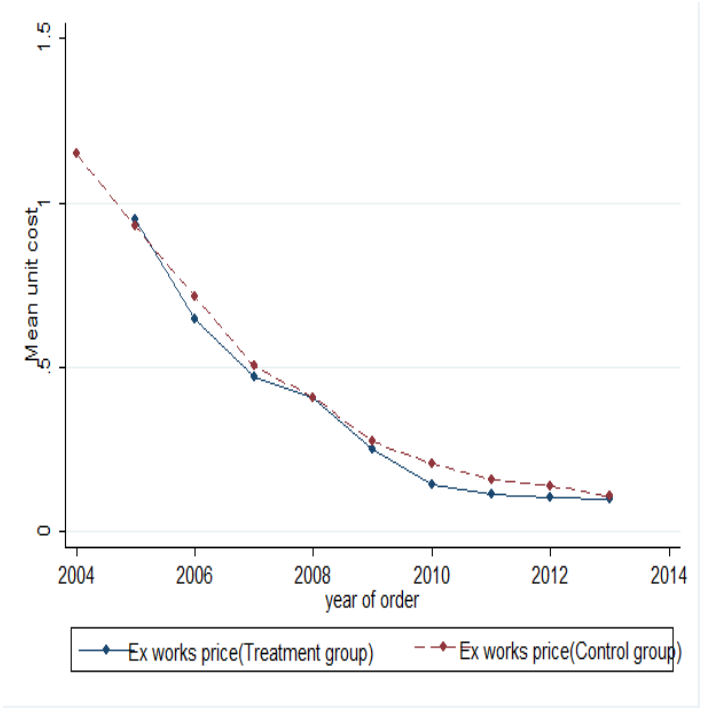
*Mean unit cost(US $) of 600 mg Efavirenz for ex works price and incoterms price.

4.5.2 The assumption of a common trend

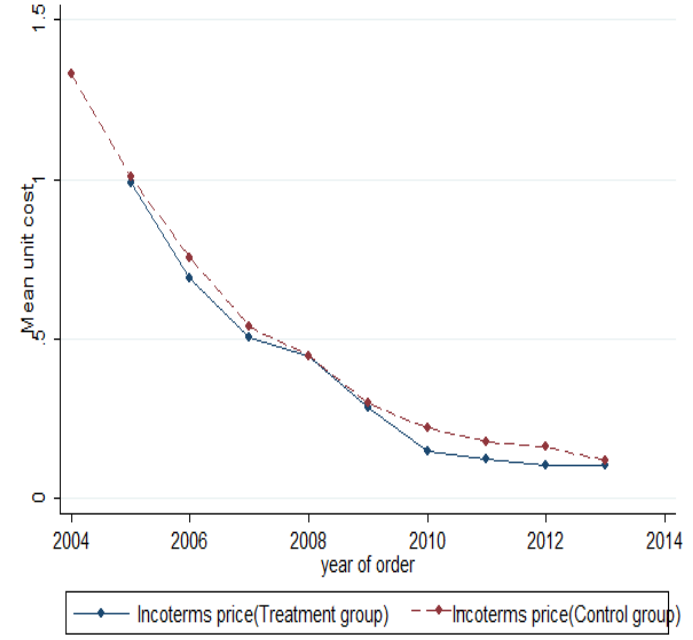
A critical assumption of using a DID estimator is to check whether common time trends hold (101,232,233). The availability of the DID estimator relies on the assumption that the underlying 'trends' in the outcome variable are similar for both treated and untreated groups in a pre-treatment period. In other words, the dependent variable should present a common trend before treatment in both the treatment and control groups. Although visually checking the trend with a graph is still recommended (233), Autor (234) developed an econometric method to check a common trend assumption using lagged and lead variables.

From figure 7, it appears that the common trend assumption holds for both *incoterms* prices and *ex-works* prices. In addition, this graph shows that there was no external shock, or so-called 'Ashenfelter's dip', before treatment (235). This assumption was again checked with the Autor (234)'s method. This method establishes whether the treatment effect exists before and after the treatment using lag and lead variables. If lead and lag variables are significant, it implies that the effect of treatment existed before and after the treatment. If that is the case, the common trend assumption will not hold.

FIGURE 7: THE ASSUMPTION OF A COMMON TREND - GRAPHICAL APPROACH



Ex works price(Mean unit cost 600mg Efavirenz)



Incoterms price(Mean unit cost of 600mg Efavirenz)

TABLE 11: THE ASSUMPTION OF A COMMON TREND– REGRESSION APPROACH

	GLM			
	Ex works price		Incoterms price	
	Coefficient(95% CI)	P value	Coefficient(95% CI)	P value
Transaction volume	0 (0 : 0)	0.106	0 (0 : 0)	0.264
HIV prevalence	0.04 (-0.014 : 0.093)	0.145	0.041 (-0.015 : 0.097)	0.150
GNI	0 (0 : 0)	0.982	0 (0 : 0)	0.878
CPI	-0.001 (-0.002 : 0.001)	0.555	-0.001 (-0.003 : 0.001)	0.183
health expenditure	-0.003 (-0.006 : 0)	0.081	-0.002 (-0.006 : 0.001)	0.133
tax revenue	0.003 (-0.001 : 0.007)	0.089	0.001 (-0.003 : 0.005)	0.629
Generic competition(Manufacturers)	-0.012 (-0.041 : 0.017)	0.402	-0.015 (-0.045 : 0.016)	0.342
Year:2005	-0.031 (-0.259 : 0.197)	0.791	-0.05 (-0.29 : 0.19)	0.682
Year:2006	-0.343 (-0.562 : -0.124)	0.002	-0.371 (-0.601 : -0.14)	0.002
Year:2007	-0.667 (-0.886 : -0.447)	0.000	-0.675 (-0.906 : -0.443)	0.000
Year:2008	-0.863 (-1.081 : -0.645)	0.000	-0.837 (-1.067 : -0.607)	0.000
Year:2009	-1.283 (-1.503 : -1.063)	0.000	-1.256 (-1.488 : -1.024)	0.000
Year:2010	-1.615 (-1.838 : -1.392)	0.000	-1.635 (-1.87 : -1.4)	0.000
Year:2011	-1.915 (-2.14 : -1.69)	0.000	-1.85 (-2.087 : -1.613)	0.000
Year:2012	-2.031 (-2.26 : -1.803)	0.000	-1.998 (-2.239 : -1.757)	0.000

Year:2013	-2.122 (-2.355 : -1.89)	0.000	-2.132 (-2.377 : -1.887)	0.000
Lag 2(Treatment X Post)	0.027 (-0.063 : 0.116)	0.560	0.033 (-0.061 : 0.127)	0.493
Lag 1(Treatment X Post)	-0.012 (-0.116 : 0.092)	0.818	-0.003 (-0.112 : 0.106)	0.954
lead1(Treatment X Post)	-0.015 (-0.119 : 0.088)	0.770	-0.023 (-0.132 : 0.086)	0.684
Lead2 (Treatment X Post)	-0.001 (-0.099 : 0.097)	0.980	0.033 (-0.071 : 0.136)	0.536
Treatment X Post	-0.173 (-0.291 : -0.055)	0.004	-0.209 (-0.333 : -0.085)	0.001
treated	-0.405 (-1.251 : 0.441)	0.348	-0.365 (-1.255 : 0.525)	0.422

* Treatment X Post is the term of interaction showing difference-in-difference.

* Lag 1 and lag 2 are the coefficients of lagged variable of interaction term 'Treatment X Post', while lead1 and lead2 are the coefficients of the lead variable of interaction term 'Treatment X Post'.

*95% CI in parentheses

Table 11 shows the result of testing for the assumption of a common trend based on Autor's method. Other things being constant, GLM regression including lag and lead variables was carried out. Country effects estimated from this regression using leads and lags for the common trend can be seen in Appendix 10. Lag 1 and lag 2 are the coefficients of the lagged variable of interaction term 'Treatment X Post', while lead1 and lead2 are the coefficients of the lead variable of interaction term 'Treatment X Post'. The p-value of the lead variables in the table 11 is statistically insignificant, showing that the effect of VPP before treatment is close to zero. If the trends between treatment and control group are sufficiently similar, then lead2 and lead1 will be insignificant. In other words, DID is not significantly different between treatment and control group in the pre-treatment period. Synthetic control method, which synthesises hypothetical counterfactuals with the weighted average of other control groups, was not used because the common trend holds (236). In sum, this result implies that the effect was not happening in the pre-post period, and so it can be concluded that the common trend assumption holds.

4.5.3 Difference-in-difference analysis

Table 12 presents the result of difference-in-difference analysis on VPP. The regression result of GLM shows that the 'Treatment X Post' term was statistically significant at the 0.1% level for each price. Country dummies were used for fixed effects as aforementioned in the method section and the result is included in appendix 11 due to the large volume. The results of both *ex-works* prices and *incoterms* prices in GLM were -0.177 (95% confidence interval: -0.247 to -0.107; p-value<0.001) and -0.213 (95% confidence interval : -0.287 to -0.139; p-value<0.001), respectively. This suggests that VPP has an effect of reducing the *ex-works* prices of generic Efavirenz by 16.2% and *incoterms* prices by 19.1%, respectively, after taking the exponential of the interaction term. It is also noted that year dummies were also statistically significant from 2006 to 2013. On the other hand, it can be seen that the magnitude of year dummies is gradually increasing. In 2006, *ex-works* prices decreased by approximately 29.3% and *incoterms* prices by 31.8% after taking the exponential of the year 2006 dummy. However, in 2013, the results of GLM regression show that *ex-works* prices decreased by approximately 88.0% and *incoterms* prices by 88.3%, compared with when the year is not 2013, after taking the exponential of the year 2013 dummy. Other independent variables were statistically insignificant in GLM.

TABLE 12: DIFFERENCE-IN-DIFFERENCE ANALYSIS- REGRESSION APPROACH

	GLM		GLM	
	Ex works price	**P value**	**Incoterms price**	**p value**
Transaction_volume	0 (0 : 0)	0.147	0 (0 : 0)	0.352
HIV prevalence	0.037 (0.004 : 0.07)	0.029	0.035 (-0.001 : 0.071)	0.055
GNI	0 (0 : 0)	0.965	0 (0 : 0)	0.761
CPI	0 (-0.002 : 0.001)	0.4	-0.001 (-0.002 : 0)	0.063
health expenditure	-0.003 (-0.005 : 0)	0.016	-0.002 (-0.004 : 0)	0.017
tax revenue	0.004 (0 : 0.007)	0.054	0.001 (-0.002 : 0.004)	0.543
Generic competition(Manufacturers)	-0.012 (-0.037 : 0.012)	0.324	-0.015 (-0.043 : 0.012)	0.276
Year:2005	-0.032 (-0.183 : 0.118)	0.673	-0.057 (-0.228 : 0.115)	0.517
Year:2006	-0.347 (-0.497 : -0.197)	0.000	-0.383 (-0.551 : -0.215)	0.000
Year:2007	-0.673 (-0.821 : -0.525)	0.000	-0.688 (-0.854 : -0.522)	0.000
Year:2008	-0.871 (-1.025 : -0.718)	0.000	-0.851 (-1.019 : -0.683)	0.000
Year:2009	-1.294 (-1.445 : -1.143)	0.000	-1.273 (-1.438 : -1.108)	0.000
Year:2010	-1.635 (-1.796 : -1.475)	0.000	-1.664 (-1.842 : -1.485)	0.000
Year:2011	-1.928 (-2.098 : -1.758)	0.000	-1.87 (-2.054 : -1.686)	0.000
Year:2012	-2.031 (-2.213 : -1.849)	0.000	-2.007 (-2.2 : -1.815)	0.000
Year:2013	-2.125 (-2.296 : -1.954)	0.000	-2.148 (-2.333 : -1.964)	0.000
Treatment X Post	-0.177 (-0.247 : -0.107)	0.000	-0.213 (-0.287 : -0.139)	0.000
treated	-0.511 (-1.168 : 0.147)	0.128	-0.598 (-1.43 : 0.233)	0.159
DID effect (mean(SD)) †	-0.162		-0.191	

Note: 1) Treatment X Post is an interaction term showing the effect of difference-in-difference.

2) 95% CI in parentheses

† :This was calculated by taking the exponential of Treatment X Post and compare it with when Treatment X Post=0

Table 13 presents the result of bootstrap simulation on the impact of VPP with the standard DID model described in equation 1. An identical interaction term of Treatment X Post in table 12 was used. On the basis of 1,000 times bootstrap re-sampling, this result shows that the coefficient of interaction term of 'Treatment X Post' was consistently negative, -0.174 (95% confidence interval: -0.272 to -0.063, p-value<0.001) for *ex-works* price and -0.217 (95% confidence interval: -0.320 to -0.117, p-value<0.001) for *incoterms* price, respectively. Based on this result, VPP reduced the mean unit cost of Efavirenz by approximately 16 % for *ex-works* price and by approximately 19 % for *incoterms* price. Bias was as small as 0.0048 for *ex-works* price and 0.0055 for *incoterms* price, presenting no substantial difference from the result of GLM model in table 12. Wild cluster bootstrap was conducted separately with the identical model in equation 1, and the result is incorporated in table 13. The P-values based on the wild cluster bootstrap for both *ex-works* price and *incoterms* price in table 13 are increased compared with p-values estimated using cluster robust standard error in table 12 (*ex-works* price: p<0.001; *incoterms* price: p<0.001). However, the p-values were 0.028 and 0.01, which are still statistically significant at 5 % level. In brief, this result of simulation supports the result of the difference-in-difference analysis and the impact of VPP.

TABLE 13: BOOTSTRAP SIMULATION ON INTERACTION TERM

Variable	Replication		Difference-in-difference	Bias	95% confidence interval	P value(Cluster)†	P value(wild cluster bootstrap)††
TreatmentXPost	1000	Ex works price	-0.174	0.0048	-0.272 : -0.063	<0.001	0.0280
TreatmentXPost	1000	Incoterms price	-0.217	0.0055	-0.320 : -0.117	<0.001	0.0100

*Replication : 1000 times.

†P value was calculated with cluster robust error.

††P value was calculated with wild cluster bootstrap error.

4.6 Discussion

This study examined the effect of VPP on the procurement prices of ARV. Efavirenz was chosen as a case study given the frequent use of Efavirenz in fixed dose combination (FDC) therapy for HIV. A difference-in-difference (DID) estimator in regression form was used to estimate the effect of VPP. The assumption of a common trend was confirmed with graphs and a regression model using lags and leads of the interaction term. To the best of our knowledge, this is the first study estimating the impact of VPP on ARV procurement prices adopting a formal econometric method.

The analyses found VPP significantly reduced the procurement price of 600mg generic Efavirenz. The coefficient of the DID estimator was significant at the 0.1% level for both *ex-works* prices and *incoterms* prices. Simulation using 1,000 times bootstrap re-sampling and p-values calculated by a wild cluster bootstrap strongly supported the results of the DID analysis.

A strong decreasing trend in the ARV price over 8 years was also found. Year dummies were significant for all years aside from 2005. The finding of decreasing ARV costs over 8 years is consistent with the results of Wafula et al.(196) and with the trend of consistently decreasing ARV prices more widely observed. The median procurement price per treatment year for adult first-line regimens in low- and middle-income countries decreased from $US 499 to $122 between 2003 and 2013 (237,238). In 2006, UNITAID was launched to supply drugs at lower prices (239). Also in 2006, Generic FDCs were available to PEPFAR recipients after FDA approval (92). Donor funding for HIV increased from $1.6 billion to $8.7 billion largely due to PEPFAR and GFATM from 2002 to 2008 (240). The GAVI alliance (GAVI) committed US $500 million for a 5-year period from 2006 to 2010 (241). Therefore, the decreasing trend in ARV prices may be associated with increased funding for ARV procurement, the emergence of powerful global donors, and the introduction of

generic drugs. These analyses demonstrate that the use of VPP can further reduce drug prices.

In addition, it was found that HIV prevalence was not associated with drug prices. This is consistent with Danzon et al. (197) and Wirtz et al. (199). Transaction volume was not associated with the drug price. This too is consistent with results from Wirtz et al. (199). They found that transaction volume does not have an effect on the price reduction using GPRM data. This fact confirms that GPRM data do not support our common assumption that large procurement volume reduce procurement prices. Generic competition was not statistically significant and again, this is consistent with results from Danzon et al. (197) and is plausible because there is little incentive to reduce ARV prices in generic markets.

While VPP may improve access to HIV drugs, it is difficult to say whether or not improved procurement arrangements have the ability to strengthen the health systems of low and middle income countries more generally. It has been pointed out that the long term dependence of principal recipients (PR) countries on external funding bodies can weaken the health systems of these countries (242). On the contrary, PR countries could turn this challenge into an opportunity if they use the experience to develop the capacity to forecast, budget and plan independently.

Mills (243) argued that the strengthening of public systems of supply such as transport infrastructure could be an alternate solution for improving drug supply. In particular, a landlocked country may need additional time for transportation from the nearest port (192). This argument suggests that improving drug procurement processes may be an important starting point but would not be sufficient to improve drug access without a concurrent expansion of public facilities and qualified health to ensure those drugs reach the patients most in need (243). Thus while VPP may not strengthen health systems more broadly, health systems strengthening seems a necessary precursor to maximising the gains of a VPP scheme.

The quality of the data used in the study has been continuously improved through the use of rigorous data management and updating with new information. This includes; Individual transactions in GPRM showing a price of US$0 and duplications being removed (244), missing data being replaced with updated price data compared to the previous version of the dataset a few years ago, the recent inclusion of Incoterms prices in the dataset (244), and the fact that GFATM periodically report the transaction prices so that the data is constantly updated. Moreover, as procurement services agents (PSA) rather than recipient countries have the responsibility for data entry (209) , data is transparently managed. However, these data do not have components of retail prices such as mark-up. Therefore, analysis of retail drug prices would not be possible with this dataset.

The strengths of this study are, firstly, that it used the International Chamber of Commerce standard trade definition (*Incoterms*) price as a dependent variable. The majority of studies on procurement prices could not consider the *incoterms* prices due to data unavailability. However, excluding *incoterms* can strongly bias the results regarding procurement prices because procurement processes include the variable cost of freight and shipping. This study attempted to reduce this bias by employing *incoterms* price as the dependent variable. Secondly, this study is based on the recently updated GPRM data. The update made this data richer compared with the previous version of GPRM data; hence, the analysis carried out in this study did not have to rely on multiple imputation (MI) to supplement missing data. Thirdly, adopting fixed effects to GLM by including country dummies, which work as subject-specific slopes, this study tried to control endogeneity arising from time-invariant unobservables such as national policies. Instrumental variables were not used in this study as it was hard to find an appropriate instrument for the procurement price of ARVs, especially the price of *incoterms*, given the scarcity of literature on the procurement prices of ARVs. However, this study attempted to reduce the endogeneity caused by omitted variables (101) by including a proxy variable of generic competition such as the number of manufacturers and by using a fixed-effects model.

A few limitations of these analyses should be noted. Firstly, this analysis targeted only one ARV, Efavirenz. Therefore, the given result needs to be carefully interpreted and may not be generalizable to other types of drugs. Further research expanding the result of this study to other ARVs will be needed. Secondly, the timeline of analysis was limited to 2013 due to data unavailability, even though VPP is still being implemented.

4.7 Conclusion

This study provides robust economic evidence about the effect of voluntary pooled procurement on antiretroviral drug prices and highlights a clear agenda for further work in this area. Voluntary pooled procurement significantly reduced the price of 600mg generic Efavirenz between 2009 and 2013. Voluntary pooled procurement can be a potentially effective strategy for the reduction in HIV drug prices and the improvement of technical efficiency in HIV drug procurement. The findings of this case study suggest that further work in this area is needed. Future work should aim to explore a more generalizable or multi-context analysis of the impact of voluntary pooled procurement. It would also be possible and potentially worthwhile, to carry out a difference-in-difference analysis on a basket of various HIV drugs rather than focusing on a single drug such as Efavirenz as in this study.

5 Conclusion

The main purpose of this thesis is to assess whether the activities of global donors for HIV programmes improved technical, productive and allocative efficiency, using the relevant empirical studies. The topics dealt with in this thesis—harm reduction intervention, HIV testing, and ARV procurement—are all main activities being conducted by global health initiatives all over the world. What they have in common is to target socially deprived people or low-income countries; that is, the main target of these activities is a vulnerable group less likely to have access to health services related to HIV. For the purpose mentioned above, a literature review was conducted, revealing an evidence gap regarding the activities of global donors. Then an empirical analysis was performed in each chapter with respect to the gap found from the literature reviews. This analysis not only evaluated the results of interventions conducted by global donors such as cost-effectiveness and equity of global donors' intervention but also provide implications for policy on the procurement process of HIV drugs conducted by the global donors.

The main contributions of this thesis are that the analyses attempted to assess the activities of global donors, which have received less attention, to enhance the population health of people living with HIV worldwide. It estimated the cost-effectiveness of combined NSPs and OST using the example of Ukraine. And equity analysis was conducted using the HIV testing service in Malawi. It was also attempted to evaluate the effect of voluntary pooled procurement on HIV drug of Efavirenz. To the best of our knowledge, all of these case studies were first attempt to analysis on the issues.

The main findings of this thesis could be summarised as follows. First, in Chapter 2, the analysis found that all interventions were cost-effective in terms of QALYs gained and HIV infections averted. NSPs alone were the most cost-effective and OST alone was the least cost-effective option. Either single therapy—NSPs alone or OST alone—and the combined intervention were all cost-effective in Ukraine. However, the combined intervention gained more effectiveness at more cost. While it

did not have the lowest cost-effectiveness ratio, it was significantly more effective than any alternative. Second, from Chapter 3, comparing DHS 2004 data with DHS 2010 shows how equity and HIV uptake in Malawi depending on socioeconomic status has varied. It was notable that horizontal inequity dropped between 2004 and 2010 although pro-rich horizontal inequity exists in receiving HIV test in Malawi. The portion of the population that has ever been tested for HIV increased from 15% among women and 16% among men in 2004 to 75% among women and 54% among men in 2010. Horizontal inequity (HI) was 0.152 among women and 0.186 among men in 2004, which indicates that testing was concentrated among the relatively wealthy. In 2010, there is only a marginal degree of inequity in HIV testing among women (HI 0.008) and although testing remains pro-rich among men (HI 0.040), the degree of inequity is much smaller than in 2004. HIV test uptake is associated with socioeconomic factors such as wealth, education, and literacy, and a main contributor to the horizontal inequity in 2010 was education rather than wealth. Third, Chapter 4 found that voluntary pooled procurement effectively reduced the procurement price of 600 mg generic Efavirenz. Voluntary pooled procurement reduced both the ex-works price of generic Efavirenz and the incoterms price by 16.2% and 19.1%, respectively. The coefficient of DID estimator was significant at 0.1% level for ex-works prices and incoterms prices. Simulation using 1,000 times bootstrap re-sampling and a wild cluster bootstrap strongly supported the results of DID analysis.

Considering the research questions raised in the introduction of this thesis, some recommendations for global donors are possible based on the results of each analytical chapter.

It could be recommended from the findings in Chapter 2 that medical interventions, such as harm reduction interventions, should consider the affordability of treatment in the recipient country in accordance with GDP per capita and an appropriate level of cost-effectiveness threshold. The combined intervention of NSPs and OST was found to be cost-effective given the GDP per capita of Ukraine. However, it is doubtful whether this intervention is still deemed cost-effective if conducted in sub-

Saharan countries, which usually have much lower GDP per capita than Ukraine. Given the result, combined intervention of harm reduction may be too expensive to be accepted for the low income countries unless adjustment on cost-effectiveness threshold and affordability is done.

This is important because it is highly likely that a recipient country will ask GFATM for funding based on the result of CEA. Likewise, GFATM may refer to the result of CEA when it disburses funding for recipient countries. In line with the recent trend of adjustment on a cost-effectiveness threshold, global donors need to think about whether current level of threshold limits the best level of HIV treatment and whether cost-effectiveness threshold based on GDP per capita is an appropriate standard to make a decision on their clinical intervention and antiretroviral therapy.

In Chapter 3, it could be concluded that global donors' support of HIV testing may reduce the level of inequity in HIV test uptake. The strategy of global donors shifting from facility-based HIV testing to mobile and door-to-door testing appears successful. The important thing is that it served two ends: access and equity.

Based on this finding, we suggest that global health initiatives to pay more attention on education sector in Malawi. In DHS 2010, education was the main contributor to the horizontal inequity rather than financial status of people. To improve the uptake of HIV testing for less educated people would decrease inequity.

Based on the finding in Chapter 4, we recommend a current procurement strategy such as VPP for more countries to join the programme. If it is not feasible to increase the affordability of HIV patients or low income countries in a short period of time, to supply HIV drugs with lower costs using VPP can be an appropriate and an effective alternative to enhance HIV treatment uptake.

The analyses in this thesis have several limitations. First, the cost-effectiveness analysis in Chapter 2 in this thesis relies on secondary data rather than trial based data. Therefore, it makes more assumptions regarding study setting such as intervention periods or drop-out rate. Probabilistic sensitivity analysis handled any uncertainties generated from these assumptions. Second, Chapter 3 did not reflect geographical development such as modernisation and improved transportation. Although region CI analysis observes geographical variation, this analysis may not sufficiently reflect recent trends of HIV testing in Malawi. Third, Chapter 4 targeted only one ARV, Efavirenz. Therefore, the given result needs to be carefully interpreted and is not generalisable to other types of drugs. Further research expanding the analysis of this study to other ARVs will be needed.

There are a few interesting issues to develop our analyses further. With respect to the cost-effectiveness analysis of harm reduction intervention, it would be interesting to carry out a study using a clinical data, considering a new cost-effectiveness threshold rather than WHO CHOICE threshold (Chapter 2). With respect to HIV test in Malawi, as education has become the main contributor to horizontal inequity, the questions of how to further increase testing among men and how to reduce the remaining inequity among rural men in particular remains for further study (Chapter 3). The difference in testing between women and men is massive, so inequity around gender needs to be highlighted. Lastly, with regards to voluntary pooled procurement, to obtain a generalisable result, it would be possible to perform a difference-in-difference analysis on a basket of various HIV drugs rather than focusing on a single drug and then the coefficients of each DID analysis can be aggregated with a meta-regression or a hierarchical model (Chapter 4).

The findings of empirical studies in this thesis confirm that the efforts of global donors successfully improved the efficiency of HIV programmes in terms of global health. It is highly likely that their activities are not only improving productive and technical efficiency but also promoting allocative efficiency. VPP can be maintained for the near future, lowering procurement prices of drugs. Based on these assessments, this thesis urges that global donors continuously support people living

with HIV in low-income countries and disadvantaged groups. Most people living with HIV still heavily rely on the support of global donors.

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7 Appendices

APPENDIX 1 : SEARCH RESULT ON EQUITY IN HIV TESTING IN MALAWI (WEB OF SCIENCE)

Set	Result	Term
# 7	**16**	#6 OR #4 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH Timespan=All years*
# 6	**13**	#5 AND #3 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH Timespan=All years*
# 5	**78,102**	**TOPIC:** (socioeconomic) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH Timespan=All years*
# 4	**5**	**TOPIC:** (Malawi) **Refined by:TOPIC:** (HIV) AND **TOPIC:** (test) AND **TOPIC:** (equity) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH Timespan=All years*
# 3	**583**	**TOPIC:** (Malawi) **Refined by:TOPIC:** (HIV) AND **TOPIC:** (test) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH Timespan=All years*
# 2	**1,868**	**TOPIC:** (Malawi) **Refined by:TOPIC:** (HIV) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH Timespan=All years*
# 1	**8,597**	**TOPIC:** (Malawi) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH Timespan=All years*

16 articles identified using the strategy of Web of Science (# 7).

Author	Year	Title
Hargreaves et al.	2015	Trends in Socioeconomic Inequalities in HIV Prevalence among Young People in Seven Countries in Eastern and Southern Africa
Conroy et al.	2015	The Influence of Relationship Power Dynamics on HIV Testing in Rural Malawi
Skeen et al.	2014	Mental health of carers of children affected by HIV attending community-based programmes in South Africa and Malawi
Nyondo et al.	2014	Stakeholders' perceptions on factors influencing male involvement in prevention of mother to child transmission of HIV services in Blantyre, Malawi
Pinto et al.	2013	Patient costs associated with accessing HIV/AIDS care in Malawi
Emina et al.	2013	Identifying HIV most-at-risk groups in Malawi for targeted interventions. A classification tree model
Sartorius et al.	2010	Young and vulnerable: Spatial-temporal trends and risk factors for infant mortality in rural South Africa (Agincourt), 1992-2007
Mitchell et al.	2010	Equity in HIV testing: evidence from a cross-sectional study in ten Southern African countries
Helleringer et al.	2009	Increasing Uptake of HIV Testing and Counseling Among the Poorest in Sub-Saharan Countries Through Home-Based Service Provision
Makwiza et al.	2009	Who has access to counseling and testing and anti-retroviral therapy in Malawi - an equity analysis
Kwiek et al.	2008	Socio-demographic characteristics associated with HIV and syphilis seroreactivity among pregnant women in Blantyre, Malawi, 2000-2004
Crampin et al.	2008	Use of antenatal clinic surveillance to assess the effect of sexual behavior on HIV prevalence in young women in Karonga district, Malawi
Hong et al.	2007	Effect of maternal HIV infection on child survival in Ghana
Taha et al.	1999	HIV infection and disturbances of vaginal flora during pregnancy

Slutsker et al.	1994	HIV-1 infection among women of reproductive age in a rural district in Malawi
Miotti et al.	1992	A retrospective study of childhood mortality and spontaneous abortion in HIV-1 infected women in urban Malawi

APPENDIX 2:SEARCH RESULT ON EQUITY IN HIV TESTING IN MALAWI (PUBMED)

Search: ((malawi) AND HIV test) AND (equity OR equality)

PubMed Results

Items 1 - 11 of 11 (Display the 11 citations in PubMed)

1 Barriers to using eHealth data for clinical performance feedback in Malawi: A case study.

Landis-Lewis Z, Manjomo R, Gadabu OJ, Kam M, Simwaka BN, Zickmund SL, Chimbwandira F, Douglas GP, Jacobson RS.

Int J Med Inform. 2015 Oct;84(10):868-75. doi: 10.1016/j.ijmedinf.2015.07.003. Epub 2015 Jul 19.

PMID: 26238704 [PubMed - in process]

Similar articles

2. HIV/AIDS-related mortality in Africa and Asia: evidence from INDEPTH health and demographic surveillance system sites.

Streatfield PK, Khan WA, Bhuiya A, Hanifi SM, Alam N, Millogo O, Sié A, Zabré P, Rossier C, Soura AB, Bonfoh B, Kone S, Ngoran EK, Utzinger J, Abera SF, Melaku YA, Weldearegawi B, Gomez P, Jasseh M, Ansah P, Azongo D, Kondayire F, Oduro A, Amu A, Gyapong M, Kwarteng O, Kant S, Pandav CS, Rai SK, Juvekar S, Muralidharan V, Wahab A, Wilopo S, Bauni E, Mochamah G, Ndila C, Williams TN, Khagayi S, Laserson KF, Nyaguara A, Van Eijk AM, Ezeh A, Kyobutungi C, Wamukoya M, Chihana M, Crampin A, Price A, Delaunay V, Diallo A, Douillot L, Sokhna C, Gómez-Olivé FX, Mee P, Tollman SM, Herbst K, Mossong J, Chuc NT, Arthur SS, Sankoh OA, Byass P.

Glob Health Action. 2014 Oct 29;7:25370. doi: 10.3402/gha.v7.25370. eCollection 2014.

PMID: 25377330 [PubMed - indexed for MEDLINE] **Free PMC Article**

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3. Adult non-communicable disease mortality in Africa and Asia: evidence from INDEPTH Health and Demographic Surveillance System sites.

Streatfield PK, Khan WA, Bhuiya A, Hanifi SM, Alam N, Bagagnan CH, Sié A, Zabré P, Lankoandé B, Rossier C, Soura AB, Bonfoh B, Kone S, Ngoran EK, Utzinger J, Haile F, Melaku YA, Weldearegawi B, Gomez P,

Jasseh M, Ansah P, Debpuur C, Oduro A, Wak G, Adjei A, Gyapong M, Sarpong D, Kant S, Misra P, Rai SK, Juvekar S, Lele P, Bauni E, Mochamah G, Ndila C, Williams TN, Laserson KF, Nyaguara A, Odhiambo FO, Phillips-Howard P, Ezeh A, Kyobutungi C, Oti S, Crampin A, Nyirenda M, Price A, Delaunay V, Diallo A, Douillot L, Sokhna C, Gómez-Olivé FX, Kahn K, Tollman SM, Herbst K, Mossong J, Chuc NT, Bangha M, Sankoh OA, Byass P.

Glob Health Action. 2014 Oct 29;7:25365. doi: 10.3402/gha.v7.25365. eCollection 2014.

PMID: 25377326 [PubMed - indexed for MEDLINE] **Free PMC Article**

Similar articles

4. Cause-specific mortality in Africa and Asia: evidence from INDEPTH health and demographic surveillance system sites.

Streatfield PK, Khan WA, Bhuiya A, Alam N, Sié A, Soura AB, Bonfoh B, Ngoran EK, Weldearegawi B, Jasseh M, Oduro A, Gyapong M, Kant S, Juvekar S, Wilopo S, Williams TN, Odhiambo FO, Beguy D, Ezeh A, Kyobutungi C, Crampin A, Delaunay V, Tollman SM, Herbst K, Chuc NT, Sankoh OA, Tanner M, Byass P.

Glob Health Action. 2014 Oct 29;7:25362. doi: 10.3402/gha.v7.25362. eCollection 2014.

PMID: 25377324 [PubMed - indexed for MEDLINE] **Free PMC Article**

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5. Methods and protocol of a mixed method quasi-experiment to evaluate the effects of a structural economic and food security intervention on HIV vulnerability in rural Malawi: The SAGE4Health Study.

Weinhardt LS, Galvao LW, Mwenyekonde T, Grande KM, Stevens P, Yan AF, Mkandawire-Valhmu L, Masanjala W, Kibicho J, Ngui E, Emer L, Watkins SC.

Springerplus. 2014 Jun 12;3:296. doi: 10.1186/2193-1801-3-296. eCollection 2014.

PMID: 25019044 [PubMed] **Free PMC Article**

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6. Gender equity and sexual and reproductive health in Eastern and Southern Africa: a critical overview of the literature.

MacPherson EE, Richards E, Namakhoma I, Theobald S.

Glob Health Action. 2014 Jun 26;7:23717. doi: 10.3402/gha.v7.23717. eCollection 2014. Review.

PMID: 24972916 [PubMed - indexed for MEDLINE] **Free PMC Article**

Similar articles

7. Mental health of carers of children affected by HIV attending community-based programmes in South Africa and Malawi.

Skeen S, Tomlinson M, Macedo A, Croome N, Sherr L.

AIDS Care. 2014;26Suppl 1:S11-20. doi: 10.1080/09540121.2014.906559. Epub 2014 Apr 25.

PMID: 24766642 [PubMed - indexed for MEDLINE]

Similar articles

8. Delivering pediatric HIV care in resource-limited settings: cost considerations in an expanded response.

Tolle MA, Phelps BR, Desmond C, Sugandhi N, Omeogu C, Jamieson D, Ahmed S, Reuben E, Muhe L, Kellerman SE; Child Survival Working Group of the Interagency Task Team on the Prevention and Treatment of HIV infection in Pregnant Women, Mothers and Children.

AIDS. 2013 Nov;27Suppl 2:S179-86. doi: 10.1097/QAD.0000000000000105. Review.

PMID: 24361627 [PubMed - indexed for MEDLINE]

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9. Identifying HIV most-at-risk groups in Malawi for targeted interventions. A classification tree model.

Emina JB, Madise N, Kuepie M, Zulu EM, Ye Y.

BMJ Open. 2013 May 28;3(5). pii: e002459. doi: 10.1136/bmjopen-2012-002459.

PMID: 23793677 [PubMed] **Free PMC Article**

Similar articles

10. Test and treat in HIV: success could depend on rapid detection.

Cohen T, Corbett EL.

Lancet. 2011 Jul 16;378(9787):204-6. doi: 10.1016/S0140-6736(11)60896-

9. No abstract available.

PMID: 21684592 [PubMed - indexed for MEDLINE]

Similar articles

11. Equity in HIV testing: evidence from a cross-sectional study in ten Southern African countries.

Mitchell S, Cockcroft A, Lamothe G, Andersson N.

BMC Int Health Hum Rights. 2010 Sep 13;10:23. doi: 10.1186/1472-698X-10-23.

PMID: 20836859 [PubMed] **Free PMC Article**

Similar articles

Appendix 2-1: Search result on the location of HIV testing facilities in Malawi(Web of Science)

# 7	**27**	#6 OR #3 *Timespan=All years* *Search language=Auto*	Select to combine sets. ☐	Select to delete this set. ☐
# 6	**11**	**TOPIC:** (HIV testing) **Refined by:TOPIC:** (location) AND **TOPIC:** (malawi) *Timespan=All years* *Search language=Auto*	Select to combine sets. ☐	Select to delete this set. ☐
# 5	**875**	**TOPIC:** (HIV testing) **Refined by:TOPIC:** (location) *Timespan=All years* *Search language=Auto*	Select to combine sets. ☐	Select to delete this set. ☐
# 4	**Approximately 162,160**	**TOPIC:** (HIV testing) *Timespan=All years* *Search language=Auto*	Select to combine sets. ☐	Select to delete this set. ☐
# 3	**17**	**TOPIC:** (HIV testing facilities) **Refined by:TOPIC:** (malawi) AND **TOPIC:** (policy) *Timespan=All years* *Search language=Auto*	Select to combine sets. ☐	Select to delete this set. ☐
# 2	**93**	**TOPIC:** (HIV testing facilities) **Refined by:TOPIC:** (malawi) *Timespan=All years* *Search language=Auto*	Select to combine sets. ☐	Select to delete this set. ☐
# 1	**2,484**	**TOPIC:** (HIV testing facilities) *Timespan=All years* *Search language=Auto*	Select to combine sets. ☐	Select to delete this set. ☐

24 articles (excluding duplicates) identified **using the strategy of Web of Science.**

Author	Year	Title
Meehan et al.	2015	Availability and acceptability of HIV counselling and testing services. A qualitative study comparing clients' experiences of accessing HIV testing at public sector primary health care facilities or non-governmental mobile services in Cape Town, South Africa
Bott et al.	2015	Rewards and challenges of providing HIV testing and counselling services: health worker perspectives from Burkina Faso, Kenya and Uganda
Makusha et al.	2015	HIV Self-Testing Could "Revolutionize Testing in South Africa, but It Has Got to Be Done Properly": Perceptions of Key Stakeholders
Van Rooyen et al.	2015	What are the constraints and opportunities for HIVST scale-up in Africa? Evidence from Kenya, Malawi and South Africa
Van Lettow et al.	2014	Towards elimination of mother-to-child transmission of HIV: performance of different models of care for initiating lifelong antiretroviral therapy for pregnant women in Malawi (Option B plus)
Price et al.	2014	Uptake of prevention of mother-to-child-transmission using Option B plus in northern rural Malawi: a retrospective cohort study
Denno et al.	2012	Reaching Youth With Out-of-Facility HIV and Reproductive Health Services: A Systematic Review
Deo et al.	2012	Modeling the Impact of Integrating HIV and Outpatient Health Services on Patient Waiting Times in an Urban Health Clinic in Zambia
Van den Akker et al.	2012	HIV care need not hamper maternity care: a descriptive analysis of integration of services in rural Malawi
Hardon et al.	2012	Women's views on consent, counseling and confidentiality in PMTCT: a mixed-methods study in four African countries
Sartorius et al.	2010	Young and vulnerable: Spatial-temporal trends and risk factors for infant mortality in rural South Africa (Agincourt), 1992-2007

Israels et al.	2010	Strategies to improve care for children with cancer in Sub-Saharan Africa
Kasenga	2010	Making it happen: prevention of mother to child transmission of HIV in rural Malawi
Hardon et al.	2009	Preventing mother-to-child transmission of HIV in Vietnam and Indonesia: Diverging care dynamics
Bisika	2009	Sexual and reproductive health and HIV/AIDS risk perception in the Malawi tourism industry
Day et al.	2014	CryptoDex: A randomised, double-blind, placebo-controlled phase III trial of adjunctive dexamethasone in HIV-infected adults with cryptococcal meningitis: study protocol for a randomised control trial
Bedell et al.	2014	Women's choices regarding HIV testing, disclosure and partner involvement in infant feeding and care in a rural district of Malawi with high HIV prevalence
Phiri et al.	2014	Etiology of Genital Ulcer Disease and Association With HIV Infection in Malawi
Park et al.	2011	Designing a genome-based HIV incidence assay with high sensitivity and specificity
Thorsen et al.	2008	Potential initiators of HIV-related stigmatization: Ethical and programmatic challenges for PMTCT programs
terKuile et al.	2007	Effect of sulfadoxine-pyrimethamine resistance on the efficacy of intermittent preventive therapy for malaria control during pregnancy - A systematic review
Wyss et al.	2007	Reaching disenfranchised youth and mobile populations in Ghana through voluntary counselling testing services for HIV
deGraft-Johnson et al.	2005	HIV voluntary counseling and testing service preferences in a rural Malawi population
Misiri et al.	2004	Attitudes towards premarital testing on human immunodeficiency virus infection among Malawians

APPENDIX 3:SEARCH RESULT ON VOLUNTARY POOLED PROCUREMENT BY GFATM (WEB OF SCIENCE)

# 3	**4**	**TOPIC:** (global fund) **Refined by:TOPIC:** (pooled procurement) AND **TOPIC:** (voluntary) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*	Select to combine sets. ☐	Select to delete this set. ☐
# 2	**8**	**TOPIC:** (global fund) **Refined by:TOPIC:** (pooled procurement) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH Timespan=All years*	Select to combine sets. ☐	Select to delete this set. ☐
# 1	**6,042**	**TOPIC:** (global fund) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH Timespan=All years*		

8 **articles identified usingthestrategy of Web of Science.**

Author	Year	Title
Wafula et al.	2014	Trends in Procurement Costs for HIV Commodities: A 7-Year Retrospective Analysis of Global Fund Data Across 125 Countries
Wafula et al.	2014	Implementing Global Fund programs: a survey of opinions and experiences of the Principal Recipients across 69 countries
Wafula et al.	2013	Regional and temporal trends in malaria commodity costs: an analysis of Global Fund data for 79 countries
Glassman et al.	2013	Global Health and the New Bottom Billion: What do Shifts in Global Poverty and Disease Burden Mean for Donor Agencies?
Shretta et al.	2012	Stabilizing supply of artemisinin and artemisinin-based combination therapy in an era of wide-spread scale-up
Rudge et al.	2010	Critical interactions between Global Fund-supported programmes and health systems: a case study in Papua New Guinea
Waning et al.	2009	Global strategies to reduce the price of antiretroviral medicines: evidence from transactional databases
Price et al.	1999	How the World Trade Organisation is shaping domestic policies in health care

APPENDIX 4: THE RESULT OF LITERATURE REVIEW USING PUBMED (KEYWORD: GLOBAL FUND, VOLUNTARY POOLED PROCUREMENT)

Sent on: Mon Oct 5 19:22:34 2015

Search: (global fund) AND voluntary pooled procurement

PubMed Results

Items 1 - 3 of 3 (**Display the 3 citations in PubMed**)

1. Implementing Global Fund programs: a survey of opinions and experiences of the Principal Recipients across 69 countries.

   Wafula F, Marwa C, McCoy D.

   Global Health. 2014 Mar 24;10:15. doi: 10.1186/1744-8603-10-15.

   PMID: 24661793 [PubMed - indexed for MEDLINE] **Free PMC Article**

   Similar articles

2. Regional and temporal trends in malaria commodity costs: an analysis of Global Fund data for 79 countries.

   Wafula F, Agweyu A, Macintyre K.

   Malar J. 2013 Dec 30;12:466. doi: 10.1186/1475-2875-12-466.

   PMID: 24373527 [PubMed - indexed for MEDLINE] **Free PMC Article**

Similar articles

3. Trends in procurement costs for HIV commodities: a 7-year retrospective analysis of global fund data across 125 countries.

Wafula F, Agweyu A, Macintyre K.

J Acquir Immune DeficSyndr. 2014 Apr 1;65(4):e134-9. doi: 10.1097/QAI.0000000000000053.

PMID: 24189152 [PubMed - indexed for MEDLINE]

Similar articles

APPENDIX 5: HIV TESTING BY SOCIO-ECONOMIC STATUS (DHS 2004)

		Women			Men		
		Not Tested (N=9692) (% not tested)	Tested (N=1670) (% tested)	P value	Not Tested (N=2696) (% not tested)	Tested (N=513) (% tested)	P value
Region	Northern	1308(83)	268(17)	<0.001	352(78)	99(22)	0.001
	Central	3604(89.3)	431(10.7)		1056(85.2)	183(14.8)	
	Southern	4780(83.1)	971(16.9)		1288(84.8)	231(15.2)	
Literacy	Cannot read at all	3848(88.7)	492(11.3)	<0.001	604(89.5)	71(10.5)	<0.001
	Able to read only parts of sentence	833(85.9)	137(14.1)		157(86.3)	25(13.7)	

	Able to read whole sentence	5011(82.8)	1041(17.2)		1935(82.3)	417(17.7)	
Education	No education	2325(89)	288(11)	<0.001	323(91)	32(9)	<0.001
	Primary	6121(86.4)	960(13.6)		1793(87.7)	251(12.3)	
	Secondary	1205(75.3)	395(24.7)		554(73.7)	198(26.3)	
	Higher	41(60.3)	27(39.7)		26(44.8)	32(55.2)	
Marriage	Never married	1679(91.1)	165(8.9)	<0.001	882(87.1)	131(12.9)	0.057
	Married	6438(84.4)	1188(15.6)		1700(82.6)	358(17.4)	
	Living together	447(82.9)	92(17.1)		29(82.9)	6(17.1)	
	Widowed	348(85.7)	58(14.3)		13(86.7)	2(13.3)	
	Divorced	487(84.3)	91(15.7)		36(80)	9(20)	
	not living together	293(79.4)	76(20.6)		36(83.7)	7(16.3)	
Wealth	Poorest	1773(89.4)	211(10.6)	<0.001	363(87.9)	50(12.1)	<0.001
	Poorer	1984(87.9)	273(12.1)		602(90.7)	62(9.3)	
	Middle	2145(87.6)	305(12.4)		632(85.9)	104(14.1)	
	Richer	2032(85.2)	353(14.8)		614(84.1)	116(15.9)	
	Richest	1758(76.9)	528(23.1)		485(72.8)	181(27.2)	

NOTES : P VALUE WAS CALCULATED USING CHI-2 TEST. NO REPLY WAS EXCLUDED.

APPENDIX 6: DESCRIPTIVE SUMMARY OF NEED, NON-NEED VARIABLES AND THEIR CONCENTRATION INDICES, DHS 2004

		Women (N=11362)					Men (N=3209)				
Variable		**N**	**Mean**	**CI**	**S.D**	**P value §**	**N**	**Mean**	**CI**	**S.D**	**P value §**
Test	**Ever tested for HIV**	11362	0.147		0.354		3,209	0.16		0.367	
N1	**Any std in last 12 months**	106	0.009	-0.036	0.094	0.0058	25	0.008	0.217	0.088	0.2725
N2	**Genital sore/ulcer in last 12 months**	614	0.052	-0.033	0.223	0.3599	99	0.03	0.08	0.17	0.1884
N3	**Genital discharge in last 12 months**	346	0.029	-0.099	0.168	0.0168	64	0.019	0.093	0.137	0.7034
wealth	**Pooled**	11362		0.255		<0.001	3,209	0.13	0.235	0.336	<0.001
	Lowest wealth quintile	1,984	0.177		0.381		413	0.13		0.336	
	Second lowest wealth quintile	2,257	0.2		0.4		664	0.207		0.405	
	Middle wealth quintile	2,450	0.215		0.411		736	0.229		0.42	
	Second upper wealth quintile	2,385	0.209		0.406		730	0.227		0.419	
	Upper wealth quintile	2,286	0.199		0.4		666	0.207		0.405	
literacy	**Pooled**	11362	1.142	0.151	0.946	<0.001	3,209	1.519	0.079	0.821	<0.001
	Cannot read at all	4,340	0.387		0.487		675	0.212		0.409	
	Able to read only parts of sentence	970	0.085		0.279		182	0.057		0.232	
	Able to read whole sentence	6,052	0.528		0.499		2,352	0.731		0.444	
education	**Pooled**	11362	0.918	0.148	0.624	<0.001	3,209	1.158	0.113	0.625	<0.001
	No education	2,613	0.233		0.423		355	0.111		0.314	
	Primary	7,081	0.622		0.485		2,044	0.638		0.481	
	Secondary	1,600	0.139		0.346		752	0.233		0.423	
	Higher	68	0.006		0.077		58	0.018		0.133	
marriage	**Pooled**	11362	1.238	-0.099	1.128	<0.001	3,209	0.798	-0.045	0.803	0.057
	Never married	1,844	0.163		0.369		1,013	0.163		0.369	
	Married	7,626	0.671		0.47		2,058	0.671		0.47	
	Living together	539	0.047		0.212		35	0.047		0.212	
	Widowed	406	0.036		0.185		15	0.036		0.185	
	Divorced	578	0.051		0.219		45	0.051		0.219	

not living together	369	0.033	0.177	43	0.033	0.177

Notes : Variables Test, N1, N2 and N3 take the value 1 for “yes” and 0 for “no”.

APPENDIX 7: *COUNTRIES ATTENDED VPP PROGRAMME*

Year	Country	Year	Country	Year	Country	Year	Country
2009	Armenia	**2010**	Armenia	**2011**	Armenia	**2009-2011**	Armenia
	Guinea-Bissau		Cambodia		Cambodia		Cambodia
	Haiti		Comoros		Central African Republic		Central African Republic
	Lao People's Democratic Republic		Congo		Comoros		Comoros
	Mozambique		Djibouti		Congo		Congo
	Nicaragua		Gambia		Côte d'Ivoire		Côte d'Ivoire
	The former Yugoslav Republic of Macedonia		Haiti		Djibouti		Djibouti
	Zambia		Honduras		Gambia		Gambia
			Indonesia		Guinea		Guinea
			Lao People's Democratic Republic		Guinea-Bissau		Guinea-Bissau
			Liberia		Honduras		Haiti
			Mongolia		Lao People's Democratic Republic		Honduras
			Mozambique		Liberia		Indonesia
			Nicaragua		Mali		Lao People's Democratic Republic
			Niger		Mongolia		Liberia
			Philippines		Nicaragua		Mali
			The former Yugoslav Republic of Macedonia		Niger		Mongolia
			Togo		Philippines		Mozambique
					Viet nam		Nicaragua

			Zambia	Niger Philippines The former Yugoslav Republic of Macedonia Togo Viet Nam Zambia
Total	8	18	20	25

Source: the Global Fund the Price and Quality Reporting PQR (2015)

APPENDIX 8: SUPPLIER AND AGENTS

Supplier / Agent / Intermediary	Freq.	Percent
CHMP- Centrale Humanitaire Médico-Pharm	5	0.19
Central Medical Stores	550	21.33
Centrale d'Achat des Médicaments Essent	19	0.74
Clinton Foundation	14	0.54
Crown Agents Limited	10	0.39
Direct from manufacturer	1,063	41.22
The Deutsche Gesellschaft für Internationale Zusammenarbeit(GIZ) (formerly: GTZ)	3	0.12
IDA Foundation	144	5.58
IMRES	3	0.12
Medical Export Group (MEG)	1	0.04
Médecins sans Frontières (MSF)	11	0.43
Other n/s	13	0.5
Pan American Health Organization (PAHO)	7	0.27
Partnership for Supply Chain Management	4	0.16
UN Population Fund	1	0.04
UNICEF Supply Division	291	11.28
VPP, through The Partnership for Supply Chain Management	426	16.52
WHO Procurement Department	1	0.04

i+ Solutions	13	0.5
Total	2,579	100

Source: the Global Fund PQR(2015).

Note: *This data is from 2007 to 2013 for Efavirenz.

APPENDIX 9: STRENGTH OF PROCURED EFAVIRENZ THROUGH VOLUNTARY POOLED PROCUREMENT(VPP)

	Freq.	**Percent**
100 mg	1	0.04
200 mg	628	24.35
30 ml	50	1.94
300 mg	2	0.08
50 mg	323	12.52
600 mg	1,575	61.07
Total	2,579	100

Source: the Global Fund the Price and Quality Reporting PQR (2015)

*mg= milligram**/***ml = millilitre

APPENDIX 10: COUNTRY EFFECTS ESTIMATED FROM THE REGRESSION USING LEADS AND LAGS FOR COMMON TREND IN THE TABLE 11

	GLM			
	Ex works price		Incoterms price	
	Coefficient(95% CI)	P value	Coefficient(95% CI)	P value
Albania	0.248 (-0.282 : 0.777)	0.359	0.234 (-0.323 : 0.792)	0.410
Angola	0.033 (-0.49 : 0.556)	0.902	0.1 (-0.451 : 0.651)	0.721
Armenia	0.564 (-0.191 : 1.318)	0.143	0.631 (-0.163 : 1.426)	0.119
Azerbaijan	0.189 (-0.354 : 0.732)	0.494	0.267 (-0.305 : 0.839)	0.361
Bangladesh	0.15 (-0.364 : 0.664)	0.567	0.414 (-0.128 : 0.955)	0.134
Belarus	0.278 (-0.289 : 0.845)	0.337	0.357 (-0.24 : 0.954)	0.241
Benin	0.104 (-0.416 : 0.623)	0.695	0.286 (-0.26 : 0.832)	0.305
Bolivia (Plurinational State of)	0.169 (-0.361 : 0.7)	0.531	0.304 (-0.255 : 0.863)	0.287
Brazil	0.036 (-0.537 : 0.608)	0.903	0.07 (-0.532 : 0.672)	0.820
Burkina Faso	0.178 (-0.339 : 0.694)	0.500	0.273 (-0.271 : 0.817)	0.326
Burundi	-0.049 (-0.565 : 0.466)	0.852	0.088 (-0.455 : 0.631)	0.751
Cambodia	0.338 (-0.349 : 1.024)	0.335	0.414 (-0.308 : 1.135)	0.261
Cameroon	0.3 (-0.258 : 0.859)	0.292	0.281 (-0.307 : 0.868)	0.349
Central African Republic	0.493 (-0.003 : 0.99)	0.051	0.509 (-0.012 : 1.029)	0.055
Chad	0.558 (0.022 : 1.093)	0.041	0.693 (0.13 : 1.257)	0.016
Colombia	1.155 (0.564 : 1.747)	0.000	1.65 (1.026 : 2.274)	0.000
Comoros (the)	0.649 (-0.133 : 1.43)	0.104	0.773 (-0.049 : 1.595)	0.065
Cuba	0.08 (-0.57 : 0.731)	0.809	-0.032 (-0.717 : 0.654)	0.927

Cote d'Ivoire	0.353 (-0.182 : 0.889)	0.196	0.437 (-0.129 : 1.003)	0.130
Democratic Republic of the Congo	0.035 (-0.483 : 0.553)	0.895	0.08 (-0.466 : 0.625)	0.774
Denmark	0.384 (-0.432 : 1.201)	0.356	0.457 (-0.399 : 1.312)	0.295
Djibouti	0.673 (-0.013 : 1.359)	0.055	0.712 (-0.01 : 1.433)	0.053
Dominican Republic (the)	0.408 (-0.14 : 0.955)	0.145	0.431 (-0.145 : 1.008)	0.143
Ecuador	0.132 (-0.403 : 0.667)	0.629	0.137 (-0.427 : 0.7)	0.635
Egypt	0.219 (-0.314 : 0.752)	0.421	0.137 (-0.424 : 0.697)	0.632
El Salvador	0.043 (-0.496 : 0.583)	0.875	0.148 (-0.421 : 0.716)	0.611
Equatorial Guinea	0.356 (-0.312 : 1.024)	0.297	0.393 (-0.306 : 1.092)	0.271
Ethiopia	-0.053 (-0.576 : 0.47)	0.843	-0.037 (-0.588 : 0.514)	0.896
Gambia	0.695 (-0.012 : 1.401)	0.054	0.651 (-0.093 : 1.394)	0.086
Ghana	-0.024 (-0.547 : 0.499)	0.929	0.047 (-0.504 : 0.598)	0.867
Guatemala	0.064 (-0.461 : 0.59)	0.810	0.231 (-0.322 : 0.784)	0.413
Guinea	0.475 (-0.192 : 1.142)	0.163	0.544 (-0.156 : 1.244)	0.128
Guinea-Bissau	0.481 (-0.081 : 1.043)	0.093	0.493 (-0.098 : 1.084)	0.102
Haiti	0.603 (-0.028 : 1.233)	0.061	0.569 (-0.093 : 1.232)	0.092
Honduras	0.495 (-0.244 : 1.233)	0.189	0.505 (-0.272 : 1.282)	0.202
India	-0.063 (-0.572 : 0.447)	0.809	0.074 (-0.462 : 0.611)	0.785
Indonesia	0.535 (-0.224 : 1.293)	0.167	0.498 (-0.3 : 1.295)	0.221
Iran (Islamic Republic of)	0.216 (-0.383 : 0.816)	0.480	0.234 (-0.397 : 0.865)	0.467
Iraq	0.39 (-0.216 : 0.996)	0.207	0.368 (-0.27 : 1.007)	0.258
Israel	0.158 (-0.577 : 0.894)	0.673	0.168 (-0.603 : 0.939)	0.669

Jamaica	0.241 (-0.291 : 0.773)	0.375	0.416 (-0.145 : 0.977)	0.146
Kenya	-0.185 (-0.776 : 0.406)	0.540	-0.096 (-0.717 : 0.526)	0.763
Kyrgyzstan	0.924 (0.393 : 1.454)	0.001	1.054 (0.495 : 1.613)	0.000
Lao People's Democratic Republic	0.477 (-0.267 : 1.22)	0.209	0.482 (-0.3 : 1.264)	0.227
Lesotho	-0.906 (-2.145 : 0.333)	0.152	-0.702 (-2.004 : 0.6)	0.291
Liberia	0.484 (-0.171 : 1.14)	0.148	0.401 (-0.288 : 1.09)	0.254
Libya	0.264 (-0.438 : 0.966)	0.461	0.226 (-0.513 : 0.964)	0.549
Madagascar	0.279 (-0.238 : 0.796)	0.290	0.385 (-0.159 : 0.93)	0.166
Malawi	-0.329 (-1.16 : 0.501)	0.437	-0.382 (-1.255 : 0.492)	0.391
Mali	0.552 (-0.147 : 1.252)	0.122	0.593 (-0.142 : 1.329)	0.114
Mauritania	0.586 (0.06 : 1.112)	0.029	0.662 (0.108 : 1.216)	0.019
Mongolia	0.487 (-0.298 : 1.272)	0.224	0.44 (-0.385 : 1.265)	0.296
Morocco	0.442 (-0.122 : 1.007)	0.125	0.612 (0.018 : 1.206)	0.043
Mozambique	0.263 (-0.03 : 0.556)	0.079	0.167 (-0.141 : 0.475)	0.287
Myanmar	0.135 (-0.369 : 0.639)	0.599	0.188 (-0.342 : 0.719)	0.487
Namibia	-0.509 (-1.426 : 0.408)	0.276	-0.447 (-1.411 : 0.517)	0.363
Nepal	0.167 (-0.338 : 0.673)	0.516	0.165 (-0.367 : 0.697)	0.544
Nicaragua	0.508 (-0.253 : 1.268)	0.191	0.553 (-0.247 : 1.353)	0.176
Niger	0.752 (0.037 : 1.467)	0.039	0.749 (-0.002 : 1.5)	0.051
Nigeria	-0.047 (-0.578 : 0.484)	0.863	-0.043 (-0.602 : 0.515)	0.879
Pakistan	0.265 (-0.242 : 0.772)	0.306	0.232 (-0.302 : 0.766)	0.394
Papua New Guinea	0.41 (-0.123 : 0.944)	0.132	0.384 (-0.179 : 0.946)	0.182

Paraguay	0.187 (-0.335 : 0.708)	0.483	0.161 (-0.388 : 0.71)	0.566
Philippines	0.607 (-0.151 : 1.365)	0.117	0.596 (-0.201 : 1.393)	0.143
Republic of Moldova	0.25 (-0.262 : 0.761)	0.339	0.451 (-0.087 : 0.99)	0.100
Rwanda	-0.159 (-0.677 : 0.359)	0.548	-0.128 (-0.674 : 0.418)	0.646
Senegal	0.46 (-0.057 : 0.976)	0.081	0.636 (0.091 : 1.18)	0.022
Sierra Leone	-0.05 (-0.563 : 0.462)	0.847	0.082 (-0.457 : 0.622)	0.765
Somalia	0.114 (-0.403 : 0.632)	0.665	0.051 (-0.494 : 0.595)	0.855
South Africa	0.07 (-1.029 : 1.17)	0.900	0.235 (-0.921 : 1.391)	0.691
South Sudan	-0.154 (-0.707 : 0.399)	0.585	-0.105 (-0.688 : 0.478)	0.724
Sri Lanka	0.098 (-0.427 : 0.624)	0.714	0.243 (-0.311 : 0.796)	0.390
Sudan	0.17 (-0.342 : 0.681)	0.515	0.162 (-0.376 : 0.701)	0.555
Suriname	0.172 (-0.396 : 0.741)	0.552	0.258 (-0.34 : 0.856)	0.397
Swaziland	-0.79 (-2.232 : 0.652)	0.283	-0.749 (-2.264 : 0.767)	0.333
Switzerland	0.429 (-0.49 : 1.348)	0.360	0.479 (-0.484 : 1.442)	0.330
Tajikistan	0.187 (-0.318 : 0.692)	0.468	0.191 (-0.34 : 0.723)	0.481
Thailand	0.218 (-0.366 : 0.802)	0.465	0.276 (-0.339 : 0.891)	0.380
The former Yugoslav Republic of Macedonia	0.783 (-0.017 : 1.583)	0.055	0.784 (-0.057 : 1.624)	0.068
Timor-Leste	0.547 (-0.096 : 1.191)	0.096	0.472 (-0.207 : 1.151)	0.173
Togo	0.359 (-0.224 : 0.941)	0.228	0.465 (-0.149 : 1.078)	0.138
Uganda	-0.11 (-0.71 : 0.491)	0.720	-0.071 (-0.702 : 0.561)	0.827
Ukraine	0.276 (-0.259 : 0.81)	0.312	0.447 (-0.116 : 1.01)	0.120
United States of America	0.289 (-0.629 : 1.207)	0.538	0.325 (-0.638 : 1.288)	0.508

Uzbekistan	0.185 (-0.342 : 0.711)	0.492	0.196 (-0.358 : 0.75)	0.488
Viet Nam	0.527 (-0.212 : 1.267)	0.162	0.438 (-0.339 : 1.215)	0.269
Yemen	0.139 (-0.373 : 0.651)	0.594	0.023 (-0.516 : 0.563)	0.932
Zambia	(omitted)		(omitted)	
Zimbabwe	-0.791 (-1.867 : 0.284)	0.149	-0.882 (-2.014 : 0.249)	0.126

Notes: 95% CI is in parentheses. 1) Zambia was omitted because of collinearity 2)Ex works price refers to the initial price at the manufacturer's sites while incoterms prices reflect which side, either seller or buyer, covers payment and risks (210). 3) Incoterms includes ex-works price and other 10 rules : FCA(Free Carrier) ; CPT(Carriage Paid To) ; CIP (Carriage And Insurance Paid To) ; DAT (Delivered At Terminal) ; DAP (Delivered At Place) ; DDP (Delivered Duty Paid) ; FAS (Free Alongside Ship) ; FOB (Free On Board) ; CFR (Cost and Freight) ; CIF (Cost, Insurance and Freight) ; EXW(Ex works).

APPENDIX 114: THE RESULT OF GENERALIZED LINEAR MODEL (GLM) WITH COUNTRY FIXED EFFECTS IN THE TABLE 12

	GLM		GLM	
	Ex works price (95% CI)	**P value**	**Incoterms price (95% CI)**	**p value**
Albania	0.109 (-0.425 : 0.643)	0.690	-0.102 (-0.82 : 0.617)	0.782
Angola	-0.101 (-0.622 : 0.419)	0.703	-0.223 (-0.928 : 0.483)	0.536

Armenia	0.526 (0.042 : 1.009)	0.033	0.551 (0.024 : 1.077)	0.040
Azerbaijan	0.063 (-0.493 : 0.62)	0.824	-0.05 (-0.758 : 0.657)	0.889
Bangladesh	0.011 (-0.579 : 0.6)	0.971	0.078 (-0.652 : 0.809)	0.833
Belarus	0.137 (-0.441 : 0.715)	0.642	0.021 (-0.73 : 0.773)	0.956
Benin	-0.034 (-0.55 : 0.482)	0.897	-0.047 (-0.782 : 0.688)	0.901
Bolivia (Plurinational State of)	0.031 (-0.496 : 0.558)	0.907	-0.03 (-0.747 : 0.686)	0.934
Brazil	-0.101 (-0.644 : 0.441)	0.715	-0.262 (-0.986 : 0.462)	0.479
Burkina Faso	0.04 (-0.494 : 0.574)	0.882	-0.06 (-0.775 : 0.655)	0.870
Burundi	-0.187 (-0.704 : 0.331)	0.479	-0.241 (-0.961 : 0.479)	0.511
Cambodia	0.303 (-0.139 : 0.745)	0.179	0.332 (-0.146 : 0.809)	0.173
Cameroon	0.182 (-0.389 : 0.753)	0.533	-0.018 (-0.766 : 0.731)	0.963
Central African Republic	0.469 (0.125 : 0.814)	0.008	0.447 (0.096 : 0.799)	0.013
Chad	0.432 (-0.118 : 0.983)	0.124	0.384 (-0.366 : 1.134)	0.316
Colombia	1.01 (0.33 : 1.69)	0.004	1.313 (0.467 : 2.158)	0.002
Comoros (the)	0.609 (0.087 : 1.131)	0.022	0.679 (0.09 : 1.269)	0.024
Cuba	-0.048 (-0.615 : 0.519)	0.868	-0.34 (-1.085 : 0.404)	0.370
Cote d'Ivoire	0.327 (0.004 : 0.65)	0.048	0.37 (0.022 : 0.718)	0.037
Democratic Republic of the Congo	-0.092 (-0.605 : 0.421)	0.724	-0.233 (-0.935 : 0.47)	0.517
Denmark	0.246 (-0.432 : 0.925)	0.477	0.132 (-0.68 : 0.945)	0.750
Djibouti	0.64 (0.176 : 1.104)	0.007	0.636 (0.127 : 1.145)	0.014
Dominican Republic (the)	0.278 (-0.265 : 0.822)	0.316	0.118 (-0.602 : 0.838)	0.747
Ecuador	-0.005 (-0.531 : 0.521)	0.986	-0.195 (-0.91 : 0.52)	0.593

Egypt	0.081 (-0.453 : 0.615)	0.766	-0.194 (-0.926 : 0.537)	0.602
El Salvador	-0.092 (-0.617 : 0.434)	0.733	-0.182 (-0.886 : 0.521)	0.612
Equatorial Guinea	0.216 (-0.383 : 0.815)	0.480	0.062 (-0.696 : 0.819)	0.873
Ethiopia	-0.188 (-0.716 : 0.339)	0.485	-0.364 (-1.078 : 0.35)	0.317
Gambia	0.659 (0.185 : 1.132)	0.006	0.57 (0.065 : 1.074)	0.027
Ghana	-0.156 (-0.679 : 0.367)	0.559	-0.275 (-0.986 : 0.437)	0.449
Guatemala	-0.072 (-0.603 : 0.46)	0.791	-0.1 (-0.823 : 0.624)	0.787
Guinea	0.442 (-0.014 : 0.898)	0.057	0.468 (-0.013 : 0.948)	0.056
Guinea-Bissau	0.462 (0.1 : 0.825)	0.012	0.447 (0.037 : 0.856)	0.032
Haiti	0.571 (0.165 : 0.977)	0.006	0.498 (0.059 : 0.937)	0.026
Honduras	0.465 (0.002 : 0.928)	0.049	0.427 (-0.071 : 0.924)	0.093
India	-0.196 (-0.719 : 0.327)	0.462	-0.25 (-0.974 : 0.473)	0.498
Indonesia	0.495 (0.006 : 0.984)	0.047	0.402 (-0.116 : 0.921)	0.128
Iran (Islamic Republic of)	0.094 (-0.488 : 0.676)	0.751	-0.074 (-0.809 : 0.66)	0.842
Iraq	0.253 (-0.297 : 0.803)	0.367	0.037 (-0.695 : 0.768)	0.921
Israel	0.021 (-0.626 : 0.668)	0.950	-0.161 (-0.973 : 0.65)	0.697
Jamaica	0.104 (-0.445 : 0.653)	0.711	0.091 (-0.623 : 0.805)	0.802
Kenya	-0.306 (-0.858 : 0.246)	0.278	-0.392 (-1.13 : 0.346)	0.298
Kyrgyzstan	0.789 (0.092 : 1.485)	0.026	0.722 (-0.178 : 1.622)	0.116
Lao People's Democratic Republic	0.44 (-0.031 : 0.911)	0.067	0.401 (-0.112 : 0.914)	0.125
Lesotho	-0.98 (-1.83 : -0.131)	0.024	-0.899 (-1.917 : 0.12)	0.084
Liberia	0.451 (0.006 : 0.897)	0.047	0.321 (-0.149 : 0.792)	0.181

Libya	0.142 (-0.544 : 0.828)	0.685	-0.08 (-0.93 : 0.77)	0.854
Madagascar	0.141 (-0.418 : 0.7)	0.621	0.052 (-0.676 : 0.78)	0.889
Malawi	-0.43 (-1.081 : 0.22)	0.195	-0.637 (-1.457 : 0.183)	0.128
Mali	0.515 (0.074 : 0.955)	0.022	0.503 (0.018 : 0.987)	0.042
Mauritania	0.452 (-0.318 : 1.222)	0.250	0.332 (-0.584 : 1.249)	0.477
Mongolia	0.451 (-0.053 : 0.954)	0.079	0.361 (-0.189 : 0.91)	0.198
Morocco	0.317 (-0.42 : 1.054)	0.399	0.299 (-0.536 : 1.134)	0.483
Mozambique	0.257 (0.079 : 0.434)	0.005	0.155 (-0.033 : 0.344)	0.106
Myanmar	-0.002 (-0.516 : 0.512)	0.994	-0.144 (-0.847 : 0.559)	0.689
Namibia	-0.606 (-1.291 : 0.079)	0.083	-0.688 (-1.551 : 0.174)	0.118
Nepal	0.028 (-0.493 : 0.549)	0.916	-0.172 (-0.89 : 0.547)	0.640
Nicaragua	0.471 (-0.017 : 0.959)	0.059	0.471 (-0.056 : 0.998)	0.080
Niger	0.722 (0.268 : 1.177)	0.002	0.673 (0.176 : 1.169)	0.008
Nigeria	-0.172 (-0.691 : 0.347)	0.517	-0.35 (-1.058 : 0.358)	0.333
Pakistan	0.126 (-0.421 : 0.673)	0.651	-0.102 (-0.833 : 0.629)	0.784
Papua New Guinea	0.274 (-0.258 : 0.806)	0.313	0.05 (-0.662 : 0.762)	0.890
Paraguay	0.047 (-0.549 : 0.644)	0.876	-0.174 (-0.935 : 0.587)	0.654
Philippines	0.568 (0.075 : 1.06)	0.024	0.511 (-0.016 : 1.038)	0.057
Republic of Moldova	0.114 (-0.444 : 0.672)	0.690	0.121 (-0.611 : 0.853)	0.746
Rwanda	-0.291 (-0.804 : 0.223)	0.267	-0.449 (-1.152 : 0.255)	0.212
Senegal	0.321 (-0.221 : 0.863)	0.246	0.299 (-0.406 : 1.004)	0.406
Sierra Leone	-0.186 (-0.706 : 0.334)	0.483	-0.242 (-0.952 : 0.467)	0.503

Somalia	-0.021 (-0.533 : 0.491)	0.937	-0.274 (-0.974 : 0.427)	0.444
South Africa	-0.016 (-0.966 : 0.933)	0.973	0.018 (-1.101 : 1.136)	0.975
South Sudan	-0.283 (-0.816 : 0.25)	0.298	-0.417 (-1.154 : 0.321)	0.268
Sri Lanka	-0.039 (-0.575 : 0.496)	0.885	-0.089 (-0.803 : 0.624)	0.806
Sudan	0.032 (-0.485 : 0.549)	0.903	-0.172 (-0.877 : 0.534)	0.634
Suriname	0.039 (-0.512 : 0.589)	0.891	-0.067 (-0.81 : 0.677)	0.861
Swaziland	-0.848 (-1.785 : 0.088)	0.076	-0.918 (-2.027 : 0.191)	0.105
Switzerland	0.289 (-0.453 : 1.03)	0.445	0.153 (-0.707 : 1.013)	0.727
Tajikistan	0.049 (-0.476 : 0.575)	0.854	-0.143 (-0.848 : 0.563)	0.692
Thailand	0.078 (-0.462 : 0.618)	0.777	-0.053 (-0.777 : 0.671)	0.885
The former Yugoslav Republic of Macedonia	0.744 (0.21 : 1.277)	0.006	0.701 (0.126 : 1.276)	0.017
Timor-Leste	0.43 (-0.118 : 0.978)	0.124	0.166 (-0.56 : 0.891)	0.655
Togo	0.33 (-0.04 : 0.7)	0.081	0.396 (-0.001 : 0.793)	0.051
Uganda	-0.226 (-0.775 : 0.322)	0.418	-0.36 (-1.091 : 0.371)	0.334
Ukraine	0.142 (-0.433 : 0.717)	0.629	0.123 (-0.63 : 0.876)	0.749
United States of America	0.145 (-0.602 : 0.893)	0.703	-0.002 (-0.859 : 0.856)	0.997
Uzbekistan	0.048 (-0.479 : 0.575)	0.859	-0.131 (-0.844 : 0.582)	0.719
Viet Nam	0.49 (0.018 : 0.962)	0.042	0.345 (-0.176 : 0.866)	0.194
Yemen	0.008 (-0.516 : 0.532)	0.977	-0.3 (-1.012 : 0.412)	0.409
Zambia	(omitted)		(omitted)	
Zimbabwe	-0.853 (-1.6 : -0.107)	0.025	-1.063 (-1.98 : -0.145)	0.023

Notes: 95% CI is in parentheses. 1) Zambia was omitted because of collinearity 2)Ex works price refers to the initial price at the manufacturer's sites while incoterms prices reflect which side, either seller or buyer, covers payment and risks (210). 3) Incoterms includes ex-works price and other 10 rules : FCA(Free Carrier) ; CPT(Carriage Paid To) ; CIP (Carriage And Insurance Paid To) ; DAT (Delivered At Terminal) ; DAP (Delivered At Place) ; DDP (Delivered Duty Paid) ; FAS (Free Alongside Ship) ; FOB (Free On Board) ; CFR (Cost and Freight) ; CIF (Cost, Insurance and Freight) ; EXW(Ex works).

APPENDIX 12 : INCOTERMS PRICE FOR VPP COUNTRIES AND NON VPP COUNTRIES

VPP countries from 2009 to 2013			Non VPP countries from 2009 to 2013		
INCO	**Freq.**	**Percent**	**INCO**	**Freq.**	**Percent**
CIF	1	1	**CFR**	6	2
CIP	13	14	**CIF**	47	15
DAP	1	1	**CIP**	86	27
DDP	3	3	**CPT**	4	1
EXW	63	68	**DDP**	15	5
FCA	12	13	**DDU**	12	4
			EXW	48	15
			FCA	78	25
			FOB	19	6
Total	93	100	**Total**	315	100

APPENDIX 13: CHAPTER 2- PUBLISHED PAPER (THIS PART HAS BEEN REMOVED DUE TO THE PERMISSION)

APPENDIX 14: CHAPTER 3- PUBLISHED PAPER (THIS PART HAS BEEN REMOVED DUE TO THE PERMISSION)

APPENDIX 15: CHAPTER 4- DECISION LETTER

Kim, Sungwook

From: onbehalfof+hpp.editorialoffice+oup.com@manuscriptcentral.com on behalf of Health Policy and Planning <onbehalfof+hpp.editorialoffice+oup.com@manuscriptcentral.com>
Sent: 13 November 2016 17:31
To: Kim, Sungwook
Subject: Health Policy and Planning - Decision on Manuscript ID HEAPOL-2015-Nov-0583.R2

13-Nov-2016

Dear Mr. Kim,

It is a pleasure to accept your revised manuscript entitled "Can Voluntary Pooled Procurement Reduce the Price of Antiretroviral Drugs?: A case study of Efavirenz" for publication in Health Policy and Planning. The comments of the reviewer(s) on your manuscript are included at the foot of this letter.

Thank you for your fine contribution. We look forward to your continued contributions to the Journal.

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Yours sincerely,
Dr. Virginia Wiseman
Virginia Wiseman
Co-Editor-in-Chief
Health Policy and Planning

Reviewer(s)' Comments to Author: