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Antiretroviral therapy adherence in Quang Ninh, Vietnam

- Analyzing results on adherence from a randomized controlled trial

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Programme: The Public Health Science Programme with Health Economics 180 hec Bachelor Thesis 2010

Extent: 15 higher education credits

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Sammanfattning

Introduktion: God följsamhet till antiretroviral behandling (ARV) av human immunodeficiency virus (HIV) är avgörande för en framgångsrik behandling. En gynnsam behandling ger HIV/AIDS patienten ökad livskvalitet och mindre risk för utvecklande av medicinsk resistans. Kamratstöd är en vedertagen metod som kan hjälpa patienten till en god följsamhet. För att nå framgång i behandlingen av HIV patienter är det ur ett folkhälso- policy perspektiv av stor vikt att studera de ekonomiska och sociala aspekter som inbegriper behandlingen och metoden kamratstöd. **Syfte**: Att undersöka om det fanns skillnader i följsamhet till antiretroviral behandling för patienter som fick kamratstöd och patienter som inte fick kamratstöd i DOTARV projektet i Quang Ninh, Vietnam. Syftet var att undersöka följsamhet till ARV i relation till kön och patienter med tidigare drogmissbruk. **Metod**: Data analyserades från den randomiserade kontrollerade studien DOTARV projektet. Projektets intervention var kamratstöd. En grupp av 641 patienter randomiserades till två olika behandlingskohorter; optimal kontrollerad behandling (OCR), som innebär att patienten får kamratstöd och själv bevakad behandling (SST), som innebär att patienten själv kontrollerar sin behandling utan kamratstöd. Kohorterna följdes upp under två år via självrapportering. En epidemiologisk och statistisk metod applicerades för att undersöka effekten av interventionen kamratstöd i relation till kön och tidigare drogmissbruk. **Resultat:** Frekvensen av icke-följsamhet bland män och kvinnor, tidigare drogmissbrukare och icke drogmissbrukare jämfördes, men gav inte några signifikanta skillnader mellan gruppen med kamratstöd och gruppen utan kamratstöd. Emellertid rapporterade tidigare drogmissbrukare och manliga patienter inom gruppen med kamratstöd en signifikant högre icke-följsamhet jämfört med patienter utan drogmissbruk och kvinnor. Regressionsanalysen visade på att gruppen med kamratstöd hade mindre association

med icke-följsamhet än gruppen utan kamratstöd. **Diskussion**: Till skillnad från andra studier av följsamhet i antiretroviral behandling och kamratstöd i relation till kön och drogmissbruk visade resultaten inga signifikanta skillnader i följsamhet mellan patientgruppen med kamratstöd och patienter som tillhörde gruppen utan kamratstöd. Resultatet kan bero på att confounders i studien eller bias i själv rapporteringsmätningarna påverkat utfallet. Dock var det en signifikant association till icke- följsamhet för kamratstödgruppen jämfört med gruppen utan kamratstöd, som kan visa på att kamratstöd är associerat med följsamhet. Resultaten från denna studie kan skilja sig från de slutliga resultaten från DOTARV projektet, eftersom projektet fortfarande pågår.

Sökord: HIV, Följsamhet, Antiretroviral behandling, Kamratstöd, Quang Ninh

Abstract

Introduction: Adherence to antiretroviral therapy for patients with human immunodeficiency virus (HIV) is important to obtain a successful treatment, increased quality of life and to decrease drug resistance development in patients. Peer-support is a well-known method, which can help HIV/AIDS patients to improve adherence. Moreover, to improve the therapy for patients living with HIV it is from a public health policy perspective important to study the economical and social benefits of adherence for the treatment and the method peer support. **Aim/objective:** To assess if there were differences in ART adherence among patients receiving peer support and those who do not in the DOTARV project in Quang Ninh, Vietnam. An additional aim is to investigate adherence in relation to sex and former drug use. **Method**: Data was extracted from the randomized controlled trial, the DOTARV project. The intervention of the project was peer support. A treatment cohort of 641 patients was randomized into two different treatment cohorts; optimally controlled treatment (OCR) receiving peer support, which means that patients get peer support and self-supervised treatment (SST), which means that patients controlled the treatment without help from a peer supporter. The cohorts were followed up during two years with self-report measures of adherence. An epidemiological and statistical method was applied to investigate the effect of the peer support intervention in relation to gender and IDU´s. **Results:** Comparison of frequencies for non-adherence among men and women, former injection drug users and patients without drug use, revealed no significant differences between the support group and the non-support group. However, drug users and male patients within the support group reported a significantly higher non-adherence than patients without a former drug use and women. The regression analysis showed that the support group had less association with non-adherence than the non-support group. **Discussion**: In contrast to former studies on ART adherence and peer support, the results showed no significant differences in adherence between the patients receiving peer support and the patients without support. This could be due to confounders in the study or bias in the self-report measurements. There was a significant association with non-adherence for the support group compared to the non-support group, which could indicate that peer

support is associated with adherence. The results from this study may differ from the final results of the DOTARV project, which has not ended yet.

Keywords: HIV, Adherence, ART, Peer support, Quang Ninh

Preface

In the months of February 2010 to mid May 2010 we participated in an exchange program sponsored by Sida, between Gothenburg University and Hanoi Medical University in Hanoi, Vietnam. Part of the exchange program was to write our bachelor thesis in the context of Vietnam and with help from tutors related to Hanoi Medical University. For this thesis we had the unique opportunity to experience and investigate the randomized controlled trial; the DOTARV project, which takes place in the Quang Ninh province. We worked closely with the staff from DOTARV and received help and advice from the staff at Hanoi Medical University. It was a very challenging and educative period in which we learned a lot about Vietnamese work ethics, administration practices, and Vietnamese culture.

We thank our tutor in Vietnam, Mattias Larsson for giving us access to the DOTARV data material. We would also like to extend a heartfelt thanks to DOTARV's statistician Tran Thanh Do, for taking time to help us with the statistical calculations. Finally, we would like to thank our tutor in Sweden, Lena Andersson for constructive and helpful advice.

List of Abbreviations

AIDS- Acquired immunodeficiency syndrome

ART- Antiretroviral treatment or therapy

ARV- Antiretroviral

DOTARV- Direct observed treatment antiretroviral treatment

FSW- Female sex worker

HAART- Highly active antiretroviral therapy

HIV- Human immunodeficiency virus

IDU- Intravenous drug user

PEPFAR- The United States president's emergency plan for AIDS relief

PLWHA- People living with HIV/AIDS

RCT- Randomized controlled trial

OCR- Optimally controlled treatment

SST- Self-supervised treatment

Conceptual explanations

Adherence	Here defined as following the physician's guidelines for the prescribed drug regimen.
CD4 count	A test used to determine when a HIV patient should start treatment (Avert, 2010c)
Combination therapy	Taking two or more antiretroviral drugs at a time. Reduces the rate of resistance (Avert, 2010b).
First line therapies	Combination of drugs that a HIV patient is given in the initial treatment phase (Avert, 2010b).
Opportunistic infections	Infection caused by different pathogens that would usually not cause disease in a person with a healthy immune system, i.e. tuberculosis, fungal diseases etc. (Seeley, Stephens & Tate, 2008).
Second line therapies	ARV drugs used when the patient has developed resistance to first line therapies, or if adverse side effects occur (Avert, 2010b).
Viral load	The number of viral RNA molecules in a mL blood. High viral load can be an indicator of development of AIDS or viral resistance (Seeley, Stephens & Tate, 2008).
Peer support	Is meant to be understood as: social support provided to a patient by a person with the same disease

Contents

1. Introduction

For the first time since the discovery of human immunodeficiency virus (HIV)/ acquired immunodeficiency syndrome (AIDS) there are signs of progress and the HIV transmission rate is actually decreasing globally. Nevertheless, the HIV epidemic remains an urgent public health problem. In 2007 there were an estimated 33 million people living with HIV, the incidence was 2.7 million, and 2 million people died globally from AIDS (UNAIDS, 2008). About 300.000 people are living with HIV/AIDS in Vietnam, which is less than 1% of the overall population. However, the HIV epidemic in Vietnam is increasing as well as the need for treatment (WHO, 2009a). There are large geographical differences in HIV prevalence and the highest rate is found in the north, in the province of Quang Ninh. The highest concentration of HIV positive people is seen among intravenous drug users (IDU's) (Thanh, Moland & Fylkesnes, 2009). In Vietnam as a whole, the HIV epidemic is predominantly among IDU's and female sex workers (FSW's). The prevalence has reached 50-60% among IDU's and 16% among FSW's in a number of provinces (WHO, 2005). This is a cause of grave concern because there is a high transmission risk from HIV infected IDU's and FSW's to the general population (Thanh et al., 2008).

Antiretroviral therapy (ART) is well documented as an effective treatment for people living with HIV/AIDS (PLWHA). However, the effectiveness of the treatment is dependent on patient adherence (Paterson et al., 2000). Non-adherence to ART is a multi-factorial problem that includes patient, treatment and contextual factors (Remien, Hirky, Johnson, Weinhardt, Whitter & Minh Le, 2002). Studies have indicated that non-adherence is associated with drug resistance, opportunistic infections and higher risk of developing AIDS (Bangsberg et al. 2003; Paterson et al., 2000). For low income countries like Vietnam, discovering ways to increase adherence in HIV/AIDS patients could be an important issue in relation to improving patient health, and being able to afford optimal treatment regimens for patients in the future.

2. Background

In Vietnam the HIV epidemic is concentrated to different areas as well as different groups of people, however the transmission risk is high at the moment and the need for treatment is increasing (Thanh, Moland & Fylkesnes, 2009; Thanh et al., 2008). At present only an estimated 30% of PLWHA receive treatment in Vietnam (WHO 2009b). The Vietnamese government has implemented several programs with health promotional aims to address the HIV/AIDS epidemic as a whole. As an example, the Prime Minister of Vietnam approved a National Strategy on HIV/AIDS in 2003 which adopted international practices on prevention, care, support and treatment of HIV/AIDS. The strategy also included harm reduction for drug users and sex workers (WHO, 2005). Furthermore, the goal of the National Strategy of HIV/AIDS Prevention and Control in Vietnam has in recent years been to expand voluntary counseling and testing services in provinces and districts. Another goal has been to increase access to ART

through price reduction and local production of medicine. Moreover, the development of a comprehensive care, treatment and support system has been an objective (WHO, 2005). The national guidelines recommend a first line combination Antiretroviral therapy consisting of the drugs Stavudine (or Zidovudine) together with Lamivudine and Nevirapine (or Efavirenz). This kind of therapy cost about US$ 260 per patient per year for a locally produced Vietnamese drug, and US$ 545 for a branded product approved by the World Health Organization (WHO). Branded drugs are more than twice as expensive as locally produced drugs. For a low-income county like Vietnam with a gross national income per capita of 2.310 purchasing-power-parity international dollars, the prices are not really affordable for patients without financial help. The gross national income per capita in Vietnam can be compared to Sweden that has 34.310 purchasing-power-parity international dollars (WHO, 2010a, 2010b). The gross national income shows the average income by a country's citizens. In recent years, the Vietnamese government has begun to distribute locally produced ARV drugs. Branded® ARV drugs have been distributed with the support from the United States President's Emergency Plan for AIDS Relief (PEPFAR), and generic ARV medicine has been dispersed with support from Ensemble pour une Solidarité Thérapeutique Hospitalière En Réseau (ESTHER) and Global Fund to Fight AIDS, Tuberculosis and Malaria. These and other organisations provide support to Vietnam, working with the Vietnam Ministry of Health, bilateral organisations, United Nation agencies and non-governmental organizations (NGO's) (WHO, 2005). These collaborations have been necessary to increase access to drugs for patients. In line with the national strategy, services for testing, and care and support for PLWHA are available in the national and provincial hospitals. However, the services are deemed poor in number and capacity (WHO, 2005). WHO estimates that effective interventions for harm reductions that reach vulnerable groups like FSW's, or IDU's should be implemented to a larger degree and be linked to health services (WHO, 2005). This paper will focus on HIV/AIDS patients in the context of Northern Vietnam, in the Quang Ninh province where the highest prevalence of PLWHA is seen, and the main risk group is IDU's. Furthermore, it will focus on ARV treatment of these patients, and the problems relating to this treatment.

2.1 Antiretroviral treatment

The use of combination antiretroviral therapy for the treatment of HIV patients and the use of primary prevention for opportunistic infections like tuberculosis or fungal infections have had a significant effect on the global HIV/AIDS epidemic (Moyle et al., 2008). ART suppresses the viral load in patients and improves the strength of the immune system, thereby decreasing the amount of opportunistic infections and improving the quality of life for the patient (Moyle et al., 2008). Effective ART regimens have improved the prognosis of HIV patients (Moyle et al., 2008), and the disease is at present considered a chronic disease (Bartlett, 2002). HIV/AIDS patients have to take the treatment for the rest of their life and this can represent several problems. These include for example, the availability and financial costs of the

medicine, the treatment of side effects and the problem with patients not following the treatment guidelines.

2.2 Cost and availability of antiretroviral treatment

Generally, low-income countries have had difficulties in procuring life saving medications like ART because of excessive drug costs. Drug prices have been and are presently high due to long enduring drug patents and low price-competition on the drug markets. This condition is due to larger drug companies' monopoly on medicines (Avert, 2010a). Recent expiry of patents on first line therapies for HIV and pressure on the larger drug companies by independent agencies, NGO's and even governments to lower the price of ART drugs, have resulted in low income countries being able to procure low cost treatment for HIV patients. A positive development is that several drug companies in low-income countries have begun producing and distributing affordable ARV drugs (Avert, 2010a). In Vietnam, agencies like UNITAID, the Clinton Foundation and PEPFAR are providing increased coverage for HIV positive patients (Avert, 2010a; Castelli, Pietra, Diallo, Schumacher & Simpore, 2010). The positive developments in production and decreased prices for drugs are still mostly seen for first line drug therapies, and not for second line therapies, which are often newly developed drugs. Second line therapies are therefore often more expensive, because patents for new drugs will run for a longer period (Avert, 2010a). This is problematic because second line therapies can be more efficient and have fewer side effects (Avert, 2010a). Moreover, an increased demand for second line therapies could arise in the future, if resistance development to ARV increases in patients. A number of studies have shown that non-adherence is related to patient drug resistance development, development of opportunistic infections and admission to hospital (Bangsberg et al., 2003; Bartlett, 2002; Moyle et al., 2008). The object of ARV treatment is to obtain sustained suppression of viral load, which requires adherence to more than 95% of treatment doses (Bartlett, 2002; Moyle et al., 2008; Visnegarwala, Rodriguez-Barradass, Graviss, Caprio, Nykyforchyn, & Laufman, 2006). Resistance development to ART limits the range of treatment options (Bartlett, 2002; Peltzer, Friend-du Preez, Ramlagan & Andersson, 2010). In relation to the expense of second line therapies, procuring treatment for HIV positive patients may become problematic with increased resistance. This is especially true for low-income countries like Vietnam that rely on international funding to obtain drug coverage for HIV/AIDS patients. In this respect it is important for Vietnam to discover cost-effective ways to improve adherence and integrate this in policies for national and local health promotional programs.

2.3 Obstacles to adherence

There can be many obstacles present for the patient regarding adherence to a medical regimen. Most studies that has investigated adherence, defines adherence as missing medication doses. However, non-adherence can also be not taking the medicine

correctly, i.e. at the wrong time, or not taking it with meals. It is often necessary to take ART at specific times and with meals, and to store the medication at specific temperatures (Bartlett, 2002; Moyle et al., 2008). These prescriptions can be an obstacle to the patient. Furthermore ART regimens often have quite a few side-effects such as vomiting, headache and diarrhea (Remien et al., 2002). Also, structural, biological, social, behavioral, demographic or economic reasons for non-adherence could be relevant issues for a patient (Silva et al., 2009). Several studies have investigated these and other possible reasons for non-adherence. For example, Silva et al. (2009) found variables like daily dose, use of alcohol or former drug use to be significantly associated with non-adherence to ART. They found no association between adherence and demographic variables like gender, age, marital status, educational level and sexual orientation. Another study has also shown worse adherence among active drug users and alcohol users (Wang et al., 2008). However, the relationship between gender and adherence to ART has not been properly established yet. Berg et al. (2004) showed that there are differences between men and women's social and behavioral patterns that lead to different factors associated with adherence. In Vietnam, where the HIV epidemic is concentrated in vulnerable groups like IDU's and FSW's adherence should be investigated further to discover adherence patterns for these risk groups. This is important because improving adherence could require different strategies for different risk groups. One strategy that has proven to be feasible and effective in other contexts is the intervention of peer support.

2.4 Improving adherence through peer support

Understanding the adherence patterns and methods to meet high adherence in patients is a complex matter. Bartlett (2002) has suggested that to increase adherence, it is necessary to make an effort to motivate and educate the patient. Peer support is a form of social support, which has been shown to affect adherence for patients. The intervention peer support as a part of HIV treatment has been used since the beginning of the HIV epidemic, and interventions based on peer support have been indicated to be feasible, practical, cost-effective and exportable (Simoni et al., 2007). One study conducted in South Africa, using self-report measures, found that social support showed higher adherence (Peltzer, Friend-du Preez, Ramlagan, & Andersson, 2010). Moreover, high adherence was found among people who received information about the treatment, and among people with high behavior skills. Peer support related to adherence and gender and drug use has also been investigated. One study, conducted by Visnegarwala et al. (2006), found a positive effect on adherence in women by weekly delivery of medications by a HIV positive peer supporter. Another study by Sharma et al. (2007) found that for former drug users not attending counseling about ART in the last six months influenced adherence negatively. In a study cohort of present and former opioid drug users, worse adherence was found in people that did not belong to a HIV support group and people with current use of crack or cocaine (Berg et al., 2004). Further, Remien et al. (2002) found that substance addiction is likely to influence adherence. The authors suggest that specialized support with clinical intervention can help patients with a history of substance use (Remien et al., 2002).

2.5 Health promotion and health policy

Adherence improvements are important to the Vietnamese government, as well as for the sponsor organisations that it collaborates with and further for PLWHA. As explained earlier, resistance development in patients can create considerable financial problems as well as decrease patient health and well-being. In public health the perspective on health is multidimensional, meaning that health is not simply absence of disease. Health is seen as a resource that can be strengthened on societal level as well as the individual level (Andersson, 2006). A health promotional model that includes systematic preventive and promotional measures to improve health is often used (Janlert, 2000). In health promotion, the individual is given the tools and support to take command of their own life situation and the problems they are facing in everyday life (Andersson, 2006).

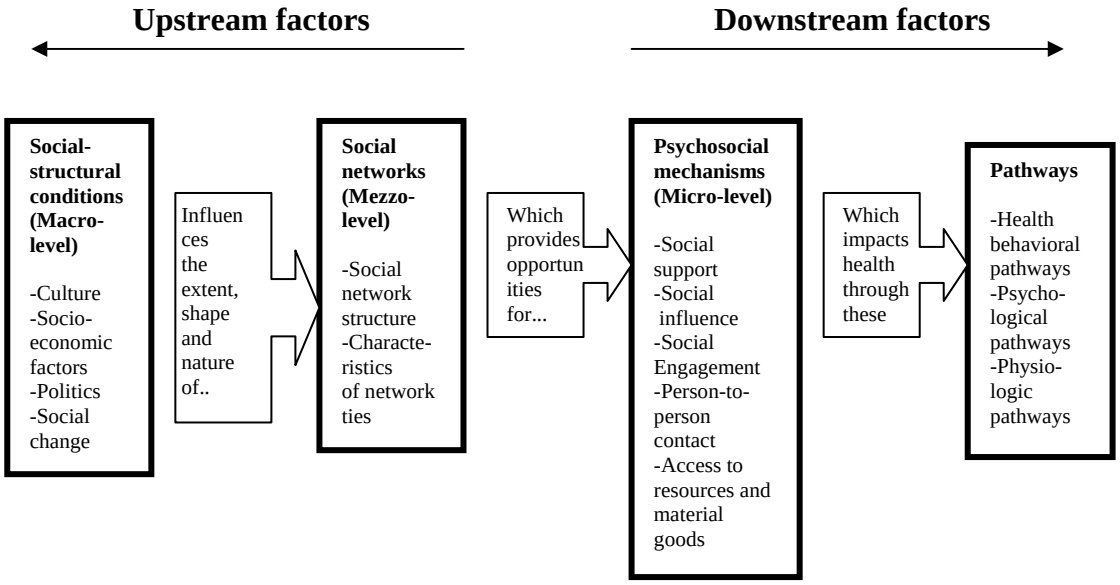
In Vietnam, the government has implemented several national programs with preventive objectives, and instigated projects with international agencies targeting ART availability. Health policies and health promotional programs are therefore well used in Vietnam. In the field of health policy, epidemiological data is often used in health promotion planning (Ferraz- Nunes, Karlberg & Bergström, 2007). Taking an evidence-based approach to policy making is important to have a sound foundation for decisions. What constitutes as evidence can be argued. An evidence based approach does not mean that one method has privilege over another or that there is only one hierarchy of evidence. Best evidence and best practice depends on the fitness for purpose and being able to explain choices (Kelly, Morgan, Bonnefoy, Butt & Bergman, 2007). A scientific basis for decision-making is unarguably a necessary approach to health promotion and preventive measure in the field of health policy. Health policy measures, as well as health promotional measures can be instigated at different levels of society, depending on the objective and target group. Using peer support with a health promotional objective would require a scientific basis indicating that this kind of intervention is feasible and effective. In behavioral science several theories have been developed to explain how social support affects the health of individuals, and where interventions containing social support should be instigated in society (Dahlgren & Whitehead, 2007).

2.6 Peer support, sense of coherence and empowerment of patients

Poor health such as living with HIV/AIDS, has many consequences for an individual. These are for example loss of earnings from employment, unemployment, social isolation or exclusion (Dahlgren & Whitehead, 2007). Stigmatization creates these forms of exclusions in society. In order to prevent such outcomes, empowerment and sense of coherence are important factors for a greater health. The purpose of empowerment at the individual level is to give the person possibilities to increase control over their life situation and to make decisions for themselves (Janlert, 2000). Different types of social networks, participation and supportive relationships have been indicated to have positive effect on a person's health (Dahlgren & Whitehead, 2007). Visnegarwala et al. (2006) believed that peer support empowered women in their study,

which lead to greater adherence. Moreover, Bartlett (2002) suggests that patients need to understand the treatment and the effect of non-adherence on their health. He also believes that the patient should be given a motivational goal for the treatment. These strategies can all be said to give empowerment to the patients and they can be implemented in clinical settings; however, they can also be implemented via peer support. Overall such strategies will help empower the patients to understand their situation and make beneficial choices for themselves. In addition, peer support can increase the sense of coherence for HIV/AIDS patients. Sense of coherence includes understanding, coping and meaning in life (Janlert, 2000). Understanding means that the individual can understand and predict the signals of the surroundings and the body. Coping implies that an individual has the resources to meet the demands that the signals send, and meaning in life signifies that these demands are worth meeting for the individual (Janlert, 2000). Peer supporters can help the patient cope with their situation, understand their situation and find meaning in life by providing emotional, informational, instrumental, appraisal support (Uchino, 2004). Emotional support means that the peer supporter listens, cares and shows empathy towards the patient. Informational support implies that the peer supporter provide the patient with facts and guidelines. Instrumental support means help with day-to-day tasks and practical issues, such as remembering to take the medication. Finally, appraisal support suggests that the peer supporter acknowledges the patients efforts in a constructive way (Uchino, 2004).

Figure 1. Conceptual framework of the impact of social networks on health



Source: Adapted from Berkman, Glass, Brissette and Seeman (2000).

Figure 1. depicts a conceptual framework of the impact of social networks on health. The positive and protective effects of peer support on the patients all occur at the micro-level of the model, which can impact health through for example psychological pathways (Dahlgren & Whitehead, 2007). Dahlgren and Whitehead (2007) who have adapted the model believe that the model helps to suggest entry points for policy

measures from the macro- to the micro-level. Positive and protective effects on the psychosocial mechanisms can have an impact on health behavior pathways. Adherence is a health behavior and could as such be an outcome of positive or protective effects of peer support on psychosocial mechanisms. Peer support interventions happen at the micro-level, however it may affect the other levels, influencing both upstream factors and downstream factors. According to Dahlgren and Whitehead (2007) a successful intervention needs to consider both upstream and downstream factors as depicted in figure 1. Policies including action in both directions, for example; educations in the downstream to legislation in the upstream have been seen to be successful (Dahlgren &Whitehead, 2007).

2.7 Gender inequalities in health

That there are gender differences in health is a well-established fact. There are global gender inequalities in health as well as national, and the gap is increasing in low-income countries (Dahlgren & Whitehead, 2007). The inequalities between men and women should be seen from a social, cultural and economical perspective, as well as a biological perspective. Moreover, the social constructed inequalities should, if possible, be analyzed separately because the causes and size of the problem may differ between men and women (Dahlgren & Whitehead, 2007). In this way it is possible to investigate differences. Health promotion policies and sensitivity to gender issues in health are important in achieving optimal health with optimal measures (Doyal, 2001). When applying a gender perspective on the model, the different levels can be seen as being ingrained with socially constructed power distributions between the sexes. These power distributions manifests through gender disparities in the social networks and social ties of the individual, as well as the societal structure. The manifestations affect the psychosocial mechanisms of the individual, and thereby also the pathways. On understanding the gender inequalities ingrained at the different levels, the model could further be used to see health behavior from a gender perspective.

2.8 Adherence and public health

From a public health perspective, discovering effective measures of improving adherence is relevant not only to improve the health of HIV positive patients, but also to investigate if such interventions are practically and economically feasible in a low-income country. As mentioned earlier, studies have shown promising results for peer support in improving adherence for ART. Peer support has even shown beneficial in improving adherence for gender and indeed even for former drug users. From a health economic perspective, improving adherence could lead to decreased hospitalization, increased productivity in patients and decreased need for second line therapies. Moreover, peer support is a cheap intervention option that could be cost effective (Simoni et al., 2007). Policies on increasing ART availability needs to consider adherence, and in relation to this also peer support. However, the effects of peer support

on adherence need to be studied further in contextualized settings, to serve as a basis for policymaking and health promotional program development. In light of this, the following objectives were developed for a randomized controlled trial (RCT) on the effects of peer support on adherence, in the Quang Ninh province of Vietnam where the HIV/AIDS epidemic is mainly concentrated among IDU's.

3. Aim/Objective

To assess if there are differences in ART adherence among patients receiving peer support and those who do not in the DOTARV-project in Quang Ninh, Vietnam. An additional aim is to investigate adherence in relation to sex and former drug use.

4. Method

In the following, part of a data set from the Direct Observed Treatment of Antiretroviral Treatment (DOTARV) project was analyzed using epidemiological and statistical methods. The DOTARV project will be described in relation to the study design, the intervention and the data-collection methods. Lastly, the method of analysis for this paper will be presented, together with the ethical considerations of the study.

4.1 Description of study

The data for this analysis was made available from the DOTARV project, which is a randomized controlled trial (RCT) including 641 patients at present. The project was initiated in 2007 in the Quang Ninh province in Vietnam mainly because of the large HIV prevalence in this area. It is supported by PEPFAR, the Global Fund to Fight AIDS, Tuberculosis and Malaria and the Swedish International Development Cooperation Agency (Sida). The project is part of the collaborative efforts between these organisations and the Vietnamese government to improve access to ARV drugs in Vietnam. It has been running for two years and will continue for an estimated one and a half year more. The main aim of the project is to assess different ARV treatment strategies in the specific setting of Quang Ninh, Vietnam, and look at drug resistance and treatment failure. The different treatment strategies will eventually be evaluated and compared in relation to adherence of the patients, drug resistance development and treatment failure as a primary endpoint. In the following, the period considered will be from baseline and two years onwards (2007-2009). Thus the information mentioned from the project is preliminary and the final results from the trial may differ from the ones in this paper.

4.1.1 Inclusion criteria

Inclusion criteria for patients in the DOTARV project were HIV positive patients aged 18-59 years. The patients had to be clinically adequate for therapy based on CD4 count, and not be institutionalized elsewhere. Moreover, the patient should not have been treated with ARV drugs previously. The patient should not have developed tuberculosis when entering the project. The patient should have revealed his or her HIV status to a supporter and lastly a patient should be prepared to receive combination ART.

4.1.2 Exclusion criteria

People below 15 and above 60 years old were excluded in the study, as well as patients with current severe opportunistic infections, active tuberculoses, institutionalized patients and pregnant women.

4.1.3 Study population

The study population consisted of HIV/AIDS patients from the Quang Ninh province in Vietnam. The patients were randomized into two different treatment cohorts; optimally controlled treatment (OCR) through direct observation of the treatment, and self-supervised treatment (SST) as recommended by the Vietnamese National AIDS Control Program. These treatment cohorts will hereafter be referred to as the support group and non-support group.

4.1.4 Sample size

A total of 641 patients were recruited from baseline and the patients entered the project at different points in time. There were a total of 332 patients in the intervention group and 309 patients in the non-support group that were recruited in the period from July 2007 to December 2009. Eventually, 26 of the patients were arrested, 22 dropped out of the study and 54 died. Unfortunately, we have no information on whether the characteristics of the drop outs where different for the non-support group compared to the support group. Patients that had missed visits to the health centre were excluded from the analysis. The analysis was done on a study population of 606 patients, including both patients from the support and the non-support group. The exclusion of patients in the analysis resulted in data from 383 patients in the support group, and 223 from the non-support group. Patients are recruited every month to the DOTARV project, which explains the increase of patients in the data used for analysis. In the support group there were 272 men and 111 women. Moreover, there were 166 intravenous drug users out of the 383 patients in the support group. In the non-support group there were 149 men and 74 women and 128 IDU’s and 95 non- IDU’s. This means that there were a higher proportion of intravenous drug users in the non-support group, and that there were more men than women in both the support group and the non-support group.

4.1.5 Age distribution

The age distribution was as follows; around 40% were between 18-29 years old. A little over 50% were between 30-39 years old and the rest between 40-49 years old. A very little proportion was 50 years old or older.

4.1.6 Socioeconomic and marital status

A large proportion of the study population were temporary workers or unemployed. The rest were either drivers, in the service sector, miners, farmers, government officers or other. The education level of the study population was quite high with only 1% being illiterate. Around 40 % had finished secondary school and high school. Most people had finished secondary school and around 40% went to high school. A little under half of the study population were married, around 30% single and the rest either divorced or widowed. Almost half of the women were widowers and almost half of the men were single. There were no significant differences between the support group and the non-support group regarding education, occupation and marital status.

4.1.7 HIV transmission and intravenous drug use

All the patients were asked about the route of HIV transmission at baseline. About half of the patients answered injection drug use and the other half answered through sexual intercourse. The patients were also asked about their history of heroin use. Around half of the study population had used heroin and the other half answered never. 70% of the men had a history of drug use. A little proportion of patients chose not to answer. When asked if they had used heroin in the last 6 months, around 20% answered in the affirmative. There was no information from baseline about whether the female patients had been or where sex workers.

4.1.8 Clinical condition of patients

Most of the patients that entered the project had quite a low CD4 count and were therefore clinically adequate for therapy. In addition many of the patients had one or several opportunistic infections, due to a large part of them being in the later stages of HIV, where HIV is symptomatic, or when HIV has progressed to AIDS.

4.2 Description of intervention

Now that the inclusion criteria and characteristics of the study population have been described, we move on to the intervention itself. First and foremost, all DOTARV

patients received free combination ART and health checks on a monthly basis. The patients were required to pick up their medicine themselves at their assigned health centre every month. Moreover, all patients attended a health clinic at a quarterly basis to undergo a clinical examination, routine laboratory tests and have their well being assessed. At these visits, the health centre personnel performed adherence questionnaires. During the study period the patients were monitored for resistance development, or side effects of the medicine. If any adverse side-effects occurred, i.e. if the patient developed resistance or if the treatment did not show any effect, the treatment regimen was changed to attain optimal effect and well-being for the patient.

4.2.1 Peer support to improve adherence

The main intervention in the DOTARV project was the peer support intervention. This was what distinguished the support group and the non-support during the study. The Optimally Controlled Treatment (OCR) group, or the support group had weekly visits from a peer supporter, and the non-support group had no additional help, other than what they received at the health centre according to national guidelines on treatment of HIV patients. Peer supporters conducted weekly visits to the support group, and recorded changes in the patient's condition or adherence to ART. Five to ten percent of the peer supporters' recordings of information about the patients were controlled by a peer supporter supervisor every month. The supporter would ask the patient about side effects, count pills, and discuss barriers to taking ART and how to overcome these barriers. During the first two months, the supporter visited the HIV positive patient's household or met the patient at an appointed place twice a week. Some patients preferred not to meet the supporter at their home because of fear of disclosure of their HIV status to their surroundings. Due to stigma the supporters did not have a work outfit. In this way, the supporters tried to minimize the patient's fear of stigma from their surroundings.

4.2.2 Selection and training of peer supporters

At the outset, a total of 14 peer supporters were selected for the intervention. The supporters were all PLWHA, selected using the snowball effect method. This method entailed that the supporters asked friends, family or fellow patients that they found eligible to become a peer supporter. The supporters had to show good adherence to ART, have good communication skills, and have transportation opportunities like a motorbike or bicycle. The supporters were trained in peer support and educated about HIV/AIDS. They received basic information on HIV/AIDS, including transmission routes and opportunistic infections. Moreover, they received information about ART, the importance of adherence and the possible side effects of the therapy. The supporters also learned about stigma, how to perform patient visits and how to conduct the interviews in order to collect the data. In this way, the supporters were equipped to provide peer support to patients. Through the supporters' own HIV status the level of understanding for the patient's situation should theoretically be higher. The supporters had experience of the consequences of HIV themselves both regarding problems in the

social context relating to the stigma surrounding HIV, and the physical and emotional consequences of the disease. The training that the DOTARV project provided enabled the supporters to deal with occurrences of frustration, confusion, fear or other emotions that the HIV patient may have experienced during the study period. Additionally, the supporters gained information and support through participating in the DOTARV training, which could have helped them in coping with their own situation.

4.2.3 Internal supporters

The family or friends of the patient were included in the intervention as internal supporters. Internal meaning that they were in the internal part of the patient's social network. Family members or friends acted as internal supporters in the daily life for the HIV positive patient. It was important that another person supervised every dose of ARV drug intake. The internal supporters helped the patient to remember to take the medicine and to answer questions about adherence at the peer support meetings. The peer supporters only visited the patient once a week and could not observe all dose intakes. Therefore a family member or another person close to the patient was supposed to observe all doses the patient needed to take during the study period.

4.2.4 The non-support group

In contrast, the patients in the self supervised treatment (SST) group, or non-support group, were responsible for their own treatment. However, they received treatment according to the National guidelines.

4.3 How to collect data and measure adherence

In the following the data collection and how to measure adherence in the DOTARV project will be described.

4.3.1 Self-report measures on adherence

The DOTARV project had several areas of data collection; assessment of adherence was one of them. There is no gold standard for measuring adherence, and several different strategies, i.e. pill counts, electronic monitors of pills, diaries and interviewer administered self-report questionnaires. Self-report measures can overestimate adherence, however this way of measuring adherence is inexpensive and is easy to distribute. In addition, self-report measures have been shown to be associated with HIV concentration in the blood (Chesney et al., 2000), meaning that low reported adherence has been shown to correlate with higher HIV concentration in the blood. For the DOTARV project, adherence assessment measures were developed using Adult Clinical Trials Group (AACTG) Adherence Instruments (Chesney et al., 2000). There are two

adherence questionnaires in this approach. The first is a baseline assessment of adherence, and the second is for follow up visits. The questionnaires were developed according to these, and carried out uniformly for both the support and non-support group. At baseline the patients were required to give consent to participation, and informed consent was ensured before data collection. Table 1. provides an overview of the data collection about information on adherence in the DOTARV project.

Table 1. Types of data collection to investigate patients' adherence to ART

Data collection	Time	Collector
Questionnaires on; Baseline information, patient adherence, stigma, socioeconomic status, patient history, lab results, symptoms and quality of life. All self reported by patient	Before entering the project and use of ART	Peer-supporter & health staff
Questionnaire on adherence to ART	The first two months - twice a week, thereafter once a week	Peer-supporter
Questionnaire on adherence to ART and collection of information about side effects, lab results and symptoms	Every third month	Health staff

4.3.2 Pill counting to measure adherence

Another adherence measure in the project was pill counting. All the patients in the two treatment cohorts were required to bring their pill bottles to the monthly visits to the health centers. The health staff counted remaining pills during these visits. In the support group, the supporter also counted pills during their visits.

4.3.3 Data used for the analysis

The data that were used in this analysis derived from the self-report measures only- i.e. the data came from the questionnaires about adherence that were distributed every third month by the health staff. These were chosen as the questions were posed uniformly for both the support and the non-support patient group and therefore were suitable for comparison between the treatment cohorts. Furthermore, the baseline information that was collected about the patient was used in the analysis.

4.4 Method of analysis

The statistical program SPSS version 16 was used to analyze the data. In corporation with the statistician at DOTARV the following methods of analysis were chosen to

explore the data material in relation to the aims of this thesis. Frequency of non-adherence was investigated in relation to the independent variables gender and former drug use. Moreover, nominal logistic regression analyses were performed to investigate associations between variables. For statistical significance Pearson's Chi Square Test was performed for P-values. The DOTARV study design was that two study cohorts were followed from baseline and two years forward. For this reason it was possible to investigate causality, meaning whether peer support had an effect on self-reported adherence in the two different cohorts.

4.4.1 Variables in the analysis

Non-adherence was investigated in relation to the variables sex, former drug use and whether the patient was in the support or non-support group. The variables in the statistical analysis of the data were built by using the adherence information from the adherence questionnaires and the baseline data on the patients.

4.4.2 The dependent variable

Non-adherence was the dependent variable for the statistical analysis. Because of limited self-report data, the questions on adherence with the highest prevalence of answers were selected and later grouped. The patient was first informed: "The question below is about ART taken in the last four days", thereafter the follow up questions displayed in table 2 were asked. The possible answers were categorized into the patient either having "adherence" or "non-adherence". Following this, three groups were built for the coding of the data. These were: "adherence and not forgetting", "non-adherence and forgetting" and "non-adherence or forgetting". If the patient was categorized as adherent in the first and in the second question the patient was coded as adherent (Adherence and not forgetting). If a patient was categorized as non-adherent in the first question and non-adherent in the second question, the patient was coded as non-adherent (Non-adherence and forgetting). If a patient was categorized as non-adherent in the first question and adherent in the second question, the patient was coded as non-adherent (non-adherence only or forgetting only). In this way the dependent variable: non- adherence was built.

Table 2. Data coding on adherence and non-adherence from the adherence questionnaires

Questions	Answers	Category
How many days did you forget to take ARV in total?	1 day 2 days 3 days 4 days	**Non-adherence**
	Did not forget	**Adherence**
What is your adherence level according to your doctor's guidelines?	Total adherence	**Adherence**
	Almost all the time	
	Half of the time Some of the time	**Non-adherence**
	No adherence	

4.4.3 Independent variables

The independent variables for the frequency analysis were sex and drug-use. Information about these variables was procured from the baseline questionnaire. Patients were asked about former drug use at baseline, and how they used drugs. If the patient had answered that they had used intravenous injection in the past, they were labeled as intravenous drug users (IDU's) in the dataset. For the nominal regression analysis the independent variable, cohort, was additionally investigated, meaning the support group and the non-support group.

4.5 Ethical considerations

The international guidelines for ethical considerations regarding epidemiologic studies include; informed consent, confidentiality, benificience and nonmaleficience. Beneficience relates to an ethical obligation to maximize benefits for the participants, and nonmaleficience means that the study should not inflict harm on the participants (Andersson, 2006). Randomized controlled trials often carry more ethical problems compared to other study types (Andersson, 2006). For this study, randomization to the control group could mean that the patients were possibly reprieved of an effective means of increasing adherence, depending on the outcome of the study. However, for RCTs it is necessary to weigh up the advantages to the study outcomes, to the potential disadvantages for the control group. If the possible positive effect of the new kind of treatment or intervention measure is effective, this may benefit the larger patient group. For this study, no patient was deprived of the medicine itself, and the control group received the medicine according to the Vietnamese National Guidelines on treatment of HIV/AIDS patients. Additionally, all patients were treated for any opportunistic

infections that occurred. The peer supporters were all PLWHA and had to face their own disease as well as that of the patients they were visiting, giving many kinds of social support; emotional, instrumental, appraisal and informational. This called for a surplus of psychological strength on the supporters' side and could have constituted a psychological burden for the supporters. Nevertheless, the meeting between patients with similar experiences could have increased a sense of coherence on both sides. There may possibly have been a two-way effect where the supporter also benefited from the exchange. Informed consent was obtained by informing the patients about what the self-report measures was going to be used for, that all information given was confidential, and that the patient would remain anonymous. In this way, the patients were fully aware of the objectives of the study. HIV is a stigmatized disease in many societies around the world, and disclosure of HIV status to the surrounding environment can be a sensitive subject to a patient. This was also taken into account during the DOTARV project through the supporters not having a uniform or anything that would disclose to others, that they were affiliated with an HIV program. It was up to the patient to decide the place where they would meet with the supporter for the weekly meeting. Moreover, education about stigma was given to the peer supporters during their training.

5. Results

The frequency of non-adherence was investigated in the patient cohort receiving peer support in relation to sex and former drug use. There was a significant difference in non-adherence between intravenous drug users (IDU's) and non-drug users (non-IDU's). Intravenous drug users reported more non-adherence (31.3%) than patients without a former drug use (19.9%) (p=0.012, see table 3.). Moreover there was a significant difference in self- reported non-adherence between women and men. Men reported almost double as much non-adherence (30.9%) compared to women (15.3%) (p=0.002, see table 3.). The frequency of non-adherence was also investigated in the non-support regarding sex and former drug use. There were no significant differences in this group in self-reported non-adherence between men and women or intravenous drug users compared to non-drug users. To sum up, the only significant differences in non-adherence were found in the support group, and these displayed higher non-adherence among intravenous drug users and to a certain extent among men.

Table 3. Self reported non-adherence in patients receiving peer support among women and men, intravenous drug users (IDU's) and non-drug users (non- IDU's)

Patients with peer support								
	Male (n=), %	**Female (n=), %**	**Total (n=), %**	**p-value**	**IDU (n=), %**	**Non-IDU (n=),%**	**Total (n=),%**	**p-value**
Non-adherence	84 (30.9%)	17 (15.3%)	101 (26.4%)		68 (31.3%)	33 (19.9%)	101 (26.4%)	
Adherence	188 (69.1%)	94 (84.7%)	282 (73.6%)		149 (68.7%)	133 (80,1%)	282 (73.6%)	
Total	272 (100%)	111 (100%)	383 (100%)	* **0.002**	166 (100%)	217 (100%)	383 (100%)	* **0.012**

***** Comparison between frequencies

Table 4. Self reported non-adherence patients without peer support among women and men, Intravenous drug users (IDU's) and non-drug users (non- IDU's**)**

Patients without peer support								
	Male (n=), %	**Female (n=), %**	**Total (n=), %**	**p-value**	**IDU (n=),%**	**Non-IDU (n=), %**	**Total (n=), %**	**p-value**
Non-adherence	46 (30.9%)	18 (24.3%)	64 (28.7%)		37 (28.9%)	27 (28.4%)	64 (28.7%)	
Adherence	103 (69.1%)	56 (75.7%)	159 (71.3%)		91 (71.1%)	68 (71.6%)	159 (71.3%)	
Total	149 (100%)	74 (100%)	223 (100%)	* **0.309**	128 (100%)	95 (100%)	223 (100%)	* **0.937**

***Comparison between frequencies

Because the object of interest was to assess differences in non-adherence between the support group and the non-support these groups were compared in relation to sex and former drug use. Women receiving peer support were compared with women not receiving peer support. There were no significant differences in self-reported non-adherence between the women (p=0.125, table 5). It was the same case for men receiving peer support and men not receiving peer support (p=0.998, table 5).

Table 5. Comparison of non-adherence in women in support group with women in non-support and between men in the support group and men in the non-support group

	Female patients				**Male patients**			
	Non-adherence (n=), %	**Adherence (n=), %**	**Total (n=), %**	**P-value**	**Non-adherence (n=), %**	**Adherence (n=), %**	**Total (n=), %**	**P-value**
Non-support group	18 (24.3%)	56 (75.7%)	74 (100%)		46 (30.9%)	103 (69.1%)	149 (100%)	
Support group	17 (15.3%)	94 (84.7%)	111 (100%)		84 (30.9%)	188 (69.1%)	272 (100%)	
Total	35 (18.9%)	150 (81.1%)	185 (100%)	* **0.125**	130 (30.9%)	291 (69.1%)	421 (100%)	* **0.998**

*Comparison of women with women, and men with men

Furthermore, comparison of intravenous drug users in the support group with intravenous drug users in the non-support group did not reveal a significant difference in non-adherence (see table 6.).

Table 6. Comparison of non-adherence between intravenous drug users (IDU's) with patients without a drug use (non-IDU's)

	IDU's				**Non- IDU's**			
	Non-adherence (n=), %	**Adherence (n=), %**	**Total**	**P-value**	**Non-adherence (n=), %**	**Adherence (n=), %**	**Total (n=), %**	**P-value**
Non-support group	37 (28.9%)	91 (71.1%)	128 (100%)		27 (28.4%)	68 (71.6%)	95 (100%)	
Support group	68 (31.3%)	149 (68.7%)	217 (100%)		33 (19.9%)	133 (80.1%)	166 (100%)	
Total	105 (30.4%)	240 (69.6%)	345 (100%)	* **0.636**	60 (19.2%)	201 (80.8%)	261 (100%)	* **0.115**

*Comparison of IDU's with IDU's, and non- IDU's with non- IDU's

Table 7. displays the associations between non-adherence in the two groups. It was not possible to combine the questions to one variable of non-adherence, which meant that the variable non-adherence and forgetting had very small samples in each subgroup; male-female, support-non-support, IDU-non-IDU. This produced very large values for the confidence intervals as shown in table 7, and no significant values. Nevertheless, the variable where patients who had answered that they had been non-adherent or forgot, showed significant results. Male patients receiving peer support had more than double odds of reporting non-adherence in the support group compared to women (CI (1.02-5.08), table 7). This concurs with the significant result within the support group where male patients reported more non-adherence than female patients. The patients in the support group had about half the odds of reporting non-adherence, compared to the patients not receiving peer support (CI (0.34-0.97), table 7). In plain words this means that receiving peer support was associated with reporting less non-adherence.

Table 7. Associations between non-adherence and cohort, gender and drug use. Associations presented as odds ratios (OR) with Confidence Intervals (CI).

Odds ratio for non-adherence in the entire patient group				
			95% Confidence Interval	
Variables		**OR**	**Lower Bound**	**Upper Bound**
Non-adherence only or forgetting only	Male	2.277	1.02	5.08
	Female	1	.	.
	Support	0.572	0.34	0.97
	Non-support	1	.	.
	IDU	1.539	0.76	3.12
	Non-IDU	1	.	.
Non-adherence and forgetting	Male	2.806	0.42	18.75
	Female	1	.	.
	Support	1.446	0.55	3.84
	Non-support	1	.	.
	IDU	0.509	0.12	2.14
	Non-IDU	1	.	.

6. Discussion

6.1 Discussion of method

The DOTARV project is a randomized controlled trial with nearly 600 patients; however, self-report data on adherence were scarce, and is therefore seen as a weakness in the study. The method of the analysis is considered applicable according to the objective of this paper; to investigate differences in non-adherence in relation to gender and former drug use between the support group and the non-support group. Further, it was possible to sort the data in groups in order to analyze gender, IDU's, non-IDU's and compare the frequency of non-adherence in these groups according to the support group and the non-support group. It was not possible to perform a statistical analysis on the trend of the data, which is usually performed on longitudinal data. In addition, from a health policy perspective, a randomized controlled trial represents a sound evidence base from which to make policy. However as Kelly et al. (2007) argue, a randomized controlled trial does not mean that the best results will be found, or that it is automatically the best method. One needs to consider which method is best for the study question at hand. As an example, a qualitative study embedded within the trial could have been of use in order to investigate reasons for adherence among HIV positive patients in the DOTARV project.

6.1.1 Strengths of the study

The data from the DOTARV project is quite unique for Vietnam and there have been no similar trials on adherence before it. This can be seen as strength of the study. The sample size provided statistical power to the calculations, which strengthened the study results. The randomization reduced the chance of systematic bias in the study, as well as confounding factors (Andersson, 2006). The follow-ups on the patients throughout the study were a considerable strength of the study. There was a high amount of control and knowledge about the patient's life situations as well as clinical situation, mainly through the peer supporter who recorded information about the patients every week. This information was further strengthened by checkups by the peer supporters' supervisor. Also the health staff recorded considerable amounts of information about the health of the patient, and the baseline information about patient characteristics was extensive. The study was additionally strengthened by the DOTARV project's several areas of data collection, meaning that adherence was investigated with different measures. First of all there were the self-report measures of adherence, which have proven effective in other studies, yet with a tendency to overestimation. There were not strong results of the effects of peer support from these measures; however, the trial has not ended yet. We may still see a difference in adherence in the support and non-support group measured via self-report. Furthermore, the viral load of the patients was checked, as well as the CD-4 count. These measures will help to see adherence patterns in the patients, and also it will be possible to correlate these results with the ones from the self-report measures.

Lastly, the drop out was low during the study period; 26 of the patients were arrested, 22 dropped out of the study and 54 died. These low numbers can be considered strength of the study.

6.1.2 Limitations of the study

As mentioned earlier there was a certain amount of uncertainty in the adherence measurements, and there was not a lot of data on non-adherence from the self-report measures. As earlier mentioned self-report measures have a tendency to overestimate adherence. Moreover, self-report measures inherently carry a certain amount of response bias and recall bias from the patient. Moreover, the fact that the patient received expensive medications for free would have been an incentive to answer positively to questions on adherence. Fear of being denied further treatment plays a role here. Furthermore, counting pills is not an accurate measure of adherence because patients could have emptied their pill bottles before coming to the health centre, or where the support group is considered, before the arrival of the supporter. Patients could have done this for fear of not receiving new medicine, fear of disclosing non-adherence to the treatment regimen or other reasons. The pill counting in this respect should perhaps rather be seen as having been a mean for the supporter to help the patient remember the pills. For the health staff pill counting may have served as a reminder for the patient to remember to bring the pill bottle to the health centre. Finally, the data collection done by the health staff was not controlled, which could mean that there was bias in the collection.

6.1.3 Validity, reliability in the study

In the DOTARV project the validity and the reliability were controlled in several ways. Through randomization the variation was guaranteed in the study groups that were to be compared. Moreover, systematic and random errors were minimized with a longitudinal design, which also increases the possibility of stating causality (Andersson, 2006). When examining the quality of the study, except from confounders and random errors it is important to identify the validity and the reliability. Validity means how the method is constructed to measure what is meant to be measured. Validity includes both internal and external validity. Internal validity means thoroughness and external validity refers to the generalizability of the study results. Reliability means the dependability and precision of the study (Andersson, 2006). The data collection methods were developed according to former studies and guidelines. This means that the content validity was strengthened. Content validity signifies that an instrument measures what experts believe to be included in the concept that is to be measured (Andersson, 2006). Moreover, the use of peer support for improving adherence has been tested in earlier studies with positive results. This is a further strengthening of the internal validity. The reliability of the study can be questioned regarding the data collection done by the health personnel at the quarterly visits at the health centers. The questionnaires that were filled in by the nurses were not controlled like the supporters' data collection was.

This means that there could be some bias in the data, if the data was not entered correctly, or if the health staff did not administer the self-report measure properly.

6.1.4 External validity of the study

The focus of the analysis was on intravenous drug users due to the high proportion of intravenous drug users in the area of Quang Ninh in Vietnam. The study results are highly contextualized to the setting that it was performed in. This means that it is not possible to generalize the results to all HIV /AIDS patients in other contexts. The results have relevance first and foremost for Vietnam and for the specific group of patients that the study included. Because the study population mainly consisted of intravenous drug users, the interpretation of the study results will have to relate to this fact. Nevertheless, intravenous drug use is the main HIV transmission route in Asia, and the results may have relevance for other areas where the HIV/AIDS epidemic is concentrated in this particular patient group.

6.2 Discussion of results

About 300.000 people are living with HIV/AIDS in Vietnam, which is less than 1% of the overall population. Nevertheless, the HIV epidemic in Vietnam is increasing as well as the need for treatment (WHO, 2009a). Adherence to antiretroviral therapy for HIV patients is essential to obtain a successful treatment. A successful treatment can increase a patient's quality of life and decrease drug resistance development. In Vietnam the epidemic is predominantly among intravenous drug users and female sex workers. The government has instilled several measures to address the HIV epidemic, among other things to increase access to ARV treatment. To increase access will increase the need for interventions that will improve adherence in patients. Non-adherence to treatment can have detrimental effects on treatment effects and patient health. Moreover there is a risk of resistance development. The DOTARV project investigates peer support as a way of improving adherence to ARV treatment. The main findings of this thesis using data from the DOTARV project were that peer support did not show a particular improvement in self-reported adherence to antiretroviral treatment in relation to gender and former drug use. However, in the nominal regression analysis, male patients reported more non-adherence than female patients, and the support group had less odds of reporting non-adherence than the patients in the non-support group.

6.2.1 Characteristics of the study sample and obstacles to adherence

The study sample of the DOTARV project can be said to be representative for that particular region. However, the characteristics of that sample are probably transferable to other parts of Vietnam because the epidemic is spreading among former drug users and sex workers in all of the country. The patients from the Quang Ninh province were mainly former drug users and either temporary workers, unemployed or otherwise financially and socially speaking not in the upper layers of society. This represents

obstacles to adherence. As mentioned, former drug use has earlier been shown to have association to non-adherence (Silva et al., 2009). Taking medicine at specific times of the day can represent problems for patients that are working as for example truck drivers, or patients whose work routine changes within a short period like temporary workers. Moreover there are the side effects of the treatment, which can be quite severe (Remien et al., 2002), and represent problems for patients needing to adapt to new work situations. These obstacles to adherence would have been present for both the support group as well as the non-support group, and are important to take notice of.

6.2.2 The support group and the non-support group

Within the groups the only significant differences in self-reported non-adherence were found in the support group. Drug users reported more non-adherence compared to patients with no drug use. Remien et al. (2002) found that substance use is likely to influence adherence negatively, which correlates with our findings in the support group. Male patients receiving peer support reported significantly less adherence than female patients receiving support. This could relate to the fact that the main part of the intravenous drug users in the study cohorts was male. Drug users report reported more non-adherence and drug users were more often men in the sample. This could be a reason to why male patients reported more non-adherence. As earlier mentioned the relationship between gender and adherence has not been properly established yet, but drug use has been shown to be associated with non-adherence. For example, Silva et al. (2009) found that former drug use was significantly associated with non-adherence to ART. Nevertheless, the non-support group did not show significant differences in non-adherence for neither drug users nor male patients. Whether peer support produced these differences in non-adherence within the support group is hard to establish. This was why the peer support group and the non-support group were compared.

6.2.3 Sex, peer support and non-adherence

Visnegarwala et al. (2006) found self-reported adherence improvements for women receiving peer support compared to women receiving standard care. Contrary to their findings, the results in this thesis showed no differences in self-reported adherence between female patients receiving support and female patients that did not. There were no differences among the male patients either. However, Silva et al. (2009) also found that sex is not a factor for non-adherence, which correlated with our results. In relation to this, it should be mentioned that the DOTARV project has not yet finished and the final end results may differ from our results. Furthermore, there is a large amount of HIV/AIDS interventions by other non-governmental organizations in the Quang Ninh province. As an example the organisation Pact has several ongoing interventions. One of these interventions is cooperation between CARE, PEPFAR and Global Fund and targets community health based care and support for HIV/AIDS patients. This means that there were other interventions working in different ways to improve the situation for PLWHA during the study period. The patients not receiving peer support in the DOTARV project could easily have been a member of these groups or partaken in networks related to them. This would have been a bias of the study, because the non-

support patients would have received support through these other groups, which could have affected adherence. However, it would have been very difficult to control for this bias. Furthermore, the samples were small in the different subgroups, and a larger sample may have revealed different results. To sum up, peer support did not seem to have an effect on self-reported adherence in relation to sex. The reasons for this could be that peer support simply has no differentiated effect on non-adherence and sex, that confounding factors in the surroundings of the patients influenced the results or that the study has not ended yet, and the end results will differ. Moreover, there is the question of self-report as data collection method, which was discussed earlier.

The results can also be seen in relation to health policy and the Berkman Glass, Brissette and Seeman (2000) framework described earlier. From a gender perspective the framework of social networks on health is ingrained with gender inequities. The framework shows that policies have impacts on different levels, and therefore also on the different inequities on the different levels. The peer support intervention was done on the micro-level, which is the individual level. Because the results did not produce any differences in self-reported adherence according to sex, one cannot say from this study that there is a need to direct peer support interventions differently to address gender differences in non-adherence. Policies addressing gender disparities in health are nevertheless important, which is why it was important to investigate sex and non-adherence in relation to peer support.

6.2.4 Intravenous drug users

Berg et al. (2004) and Sharma et al. (2007) found that peer support influenced adherence positively among former drug users. Our results showed no particular difference in adherence between former drug users receiving support, and those who did not. Within the peer support group former drug users had higher non-adherence than non-drug users. From these results it is not possible to say that peer support has a beneficial effect on self-reported adherence in former drug users. Nevertheless, there may be further beneficial effects that peer support can achieve in patients that are not dealt with in this paper. These effects could be an increased quality of life, increased sense of coherence and empowerment of the patient. Both patients with former drug use as well as patients without could achieve these effects from peer support.

6.2.5 The results from the nominal regression analysis

In the regression analysis, male patients reported significantly more non-adherence than female patients, and the support group had significantly less association with non-adherence than the patients in the non-support group. This result concurs with earlier studies on the effect of peer support on adherence, where peer support was shown to have a positive effect on adherence in patients (Berg et al., 2004; Peltzer, Friend-du Preez, Ramlagan, & Andersson, 2010). That there were differences in adherence for the support group is a quite positive result for peer support as an intervention option to improve adherence in patients. The results could indicate that peer support is a viable

intervention option. However, again it should be taken into consideration that the DOTARV project will continue for one and a half years more, and that the final result could be different from the results of this thesis. Moreover, the results from the frequency analysis showed that there was no difference in adherence between men and women, and former drug users and patients with no former drug use could indicate that these particular subgroups does not benefit especially from peer support. However, as there were confounders in the study, and perhaps overestimation of adherence from the self-report measures, this is hard to establish with any certainty.

6.2.6 Health policy options for Vietnam

Expiring patents have enabled several low-income countries, among them Vietnam, to produce and distribute ARV medication. Vietnam still relies on funding from outside parties to be able to supply HIV patients with branded and generic drugs. It is not likely that Vietnam will be able to afford the more newly produced medications in the near future when looking at their current status as a low-income country. In all probability focus on decreasing resistance development in patients will become increasingly important because Vietnam is now able to produce the first line therapies and distribute these to a larger degree. More patients will therefore have the probability of resistance development, and therefore also the need for second line therapies. Instilling policies at the micro-level in the Berkman, Glass, Brissette and Seeman (2000) framework, is another step for the Vietnamese government, because it has already made policies at the macro-level to improve access to treatment. Dahlgren and Whitehead (2007) said that policies including action in both directions have been seen to be successful. Including an intervention at the micro-level may therefore be just what is needed to obtain the goal of improving access. If patients develop less drug resistance due to less non-adherence, then there will be less need for more expensive second line therapies. However, this is of course only an assumption.

Peer support could be a health policy option for the Vietnamese government to reach its goal of increasing access to ART for HIV patients and obtaining harm reduction for intravenous drug users and female sex workers. Other studies have shown beneficial effects and peer support has been shown to be cost-effective, feasible, practical and exportable (Simoni et al., 2007). These aspects of peer support in the context of Vietnam, however, need to be further explored, before peer support is chosen as an intervention option. Moreover, the presence of other projects in the Quang Ninh province may have affected the results to a significant degree, as mentioned earlier. The DOTARV projects measures adherence via viral load in patients as well, and this data may also reveal a different result from the self-report measures. There are furthermore the beneficial effects of increased quality of life, sense of coherence and empowerment to be taken into consideration. Stigma reduction could be a further benefit of peer support, and this needs to be studied further in the Vietnamese context, and in relation to gender and drug use. Health policies should consider the intervention in light of these positive health effects as well. This is especially the case for a province like Quang Ninh, where the HIV infected population is mainly intravenous drug users and female sex workers. Targeting marginalized HIV infected subpopulations with an intervention

that could improve the general quality of life and reduce stigma would be in line with a public health perspective. Non-adherence creating resistance development in patients could increase the financial burden of providing patients with treatment.

6.3 Suggestions for further research

Additional research is needed to investigate HIV positive people's adherence to antiretroviral treatment and how the adherence to the treatment can be improved. A qualitative study on the effects of peer support on the quality of life status of the patients is already being conducted in the DOTARV project. A further qualitative study could focus on the four different forms of social support; emotional, informational, instrumental and appraisal support which Uchino (2004) mentions as the four forms of social support. Such a study could examine which kinds of support the patients appreciate the most, and which forms of support that contributes the most to improving adherence. A qualitative study on the knowledge and attitude of the patients towards adherence to ARV treatment could reveal reasons for a patient not being adherent. Also, a study on stigma related obstacles to adherence in the Vietnamese context would be of use to see how peer supporters should address these issues. Furthermore, a cost-effectiveness analysis is crucial when developing global, national and local policies for HIV prevention and care. Peer support may be an implementation option for IDU's specifically, which national and local policymakers in Vietnam need to take into consideration. More knowledge is needed on the cost-effectiveness of peer support in the contextualized settings that the trial was carried out in, and the applicability to national policies.

7. Conclusion

Within the peer support group there was a significant difference between men and women and between former drug users and patients with no former drug use. In the regression analysis, male patients had a larger association with non-adherence than female patients, and the support group had less odds of reporting non-adherence than the patients in the non-support group. There were however, some confounders that could have disrupted the results, like other interventions in the study area that could have meant higher adherence in the non-support group caused by support form a different source than the DOTARV project. Moreover, there could have been collection bias as well as recall bias in the self-report data. When the DOTARV project ends in one and a half years time, the results could differ from the ones in this paper. Finally, there were other measurements in the project that may reveal different results on adherence levels in patients. From a public health perspective, peer support as an intervention could be a policy option that the Vietnamese government should consider in reaching their goal of providing more patients with antiretroviral treatment.

8. References

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