Socioeconomic Factors and the Outcomes of Thailand's Prevention of Mother-To-Child Transmission program (PMTCT)

Wichsinee Wibulpolprasert¹

Professor Tracy A Falba, Faculty Adviser

Honor Thesis submitted in partial fulfillment of the requirements for Graduation with Distinction in Economics in Trinity College of Duke University

> Duke University Durham, North Carolina

> > April 14, 2008

¹ww18@duke.edu, P.O. Box 95678, Durham, NC, 27708

Acknowledgements

I would like to acknowledge and extend my gratitude to the following persons who have made the completion of this senior thesis possible. First, I would like to thank my father, for initially introducing me to health economics and who made possible collaboration with Thailand's Ministry of Public Health (MOPH); my faculty adviser, Professor Tracy Falba and my thesis adviser, Professor Michelle Connolly, for their useful comments and support. I would also like to thank Dr. Yot Teerawattananon, MD, for motivating the idea of this study and providing consistent encouragement and support; Dr. Thanarak Plipat, MD, and Ms. Niramon Rattanasuporn (both of the Bureau of Epidemiology, Department of Disease Control, Ministry of Public Health) for helping me acquire the data and the general background on the PHOMS. Last but not least, I would like to thank Dr. Viroj Tangcharoensatien, MD, for general advice and assistance in acquiring socio-economic data.

Abstract

Since its implementation in 2001, the national program for Prevention of Mother-To-Child Transmission (PMTCT) in Thailand has been successful in substantially reducing mother-to-child HIV transmission. In order to assess and improve the efficacy of the PMTCT program, it is important to identify relevant socio-demographic and biomedical factors associated with antiretroviral compliance and HIV transmission rates. In this paper, we attempt to measure the associations between province-specific socio-demographic characteristics, such as average income, education, average household size, and availability of health care providers, on the antiretroviral compliance rate. Then we measure how the antiretroviral completion rates and other biomedical factors affect the probability of mother-to-child HIV transmission among participants in Thailand's national PMTCT program. We find that education level, mother's nationality, family size, prenatal care, and the time the pregnant woman learned of her HIV status statistically affect the probability of completing the antiretroviral regimen. The sex of the infant, prenatal care, and the second antiretroviral regimen statistically affect the transmission rates.

1 Introduction

The first case of AIDS in Thailand was reported in September 1984. While the early AIDS cases in the country were reported predominantly among homosexual males, subsequently, the virus spread rapidly among injecting drug users, and to sex workers and their clients. The Joint United Nations Program on HIV/AIDS (UNAIDS) estimates that by the end of 2006 about 39.5 million people were living with HIV world-wide, including 7.8 million in South East Asia [UNAIDS, 2006a]. In Thailand, mother-to-child HIV transmission already infected 16,000 children under 14 years old in 2006 [UNAIDS, 2006b]. Without interventions, 4,000 children would likely become infected each year, about one seventh of all new HIV infections in Thailand [on HIV/AIDS Projection, 2001]. There are a growing number of households headed by grandparents and children in areas of high HIV prevalence. The physical and social welfare of children living with AIDS and of AIDS orphans in Thailand pose a major hindrance on the nation's development.

The HIV transmission from mother-to-child is an important economic phenomenon. That is, it represents a clear negative externality that the mother imposes on her child, either with or without intention. Transmission of mother-to-child HIV occurs prenatally in the intrauterine or intrapartum period, or postnatally through breast milk. Studies have shown that in the absence of breast feeding, about 30% of infant HIV infections occur in utero and 70% during labor and delivery [Bertolli J, 1996]. In Thailand, the perinatal transmission rate in untreated pregnant women ranges from 18.9% to 23% [Shaffer et al., 1999]; the additional risk from breastfeeding is shown to be as high as 12% [Fowler et al., 2000].

In 2001, Thailand's Ministry of Public Health (MOPH) began its national program for preventing mother-to-child HIV transmission (PMTCT). The program requires that all public hospitals provide free services (universal coverage) for voluntary HIV counseling and testing for all pregnant women. HIV infected pregnant women receive free antiretroviral prophylaxis (to prevent the transmission from mother-to-child) and breast milk substitutes. At the same time, the Ministry of Public Health collaborated with the US Centers for Disease Control and Prevention to es-

tablish a hospital-based surveillance system to collect information on infants born to HIV-infected pregnant women who were either born in or had their HIV status determined at an MOPH hospital, namely the Perinatal HIV Outcome Monitoring System (PHOMS). The PHOMS began in the first four pilot provinces in 2001 and expanded to cover 14 provinces in 2005.

The Ministry of Public Health has recommended two different antiretroviral regimens for preventing mother-to-child HIV transmission. The first regimen, recommended between 2001 and 2003, was the complete short-course AZT (Zidovudine). The current antiretroviral regimen is a combination of AZT and a single dose of Nevirapine (NVP) administered both to the mother during labor and to the newborn. Administering the first and second regimen in clinical settings resulted in transmission rates of 8.6% and 2% respectively [Lallemant et al., 2000, 2004]. Compared to the evidence from the clinical setting, the overall mother-to-child HIV transmission rate among PMTCT program participants between 2001 and 2004 were 6.8% (in case the mother completes the first antiretroviral regimen) and 4% (in case the mother completes second antiretroviral regimen) [Plipat Tanarak, 2007]. The deviations from the clinical trials suggest the role of some non-medical related factors not controlled in the studies. Thus, it is critical to identify and quantify these non-medical related factors in order to maximize the effectiveness of the PMTCT program in Thailand.

Non-medical factors can be broken down into two components: patients' adherence to treatment and the availability of health care providers. While socioeconomic status (age, income, education, race, social support) are thought to both directly and indirectly affect adherence to treatment, previous studies have reached inconclusive results about the impact of socioeconomic factors. Number of health care providers per capita is proved to enhance health outcomes in general, but there is no prior evidence associated with HIV cases. The present study aims to test the hypothesis that a) province-specific socioeconomic characteristics and the availability of health care providers affect the rate of antiretroviral completion, and b) medical compliance along with other socio-demographic and biomedical characteristics of the patient determine the mother-to-child transmission rate.

This paper is organized in eight sections. Section II provides a literature review on socioeconomic status and adherence to antiretroviral therapy. Section III presents a theoretical framework that explains the relationship between socioeconomic characteristics and the individual's decision to comply to treatment. Sections IV and V set up testable empirical models and describe the data. Sections VI and VII present empirical findings. Lastly, section VIII discusses the results, proposes conclusions, and comments on policy implications.

2 Literature Review

Keys to success in preventing mother-to-child HIV transmission are the availability of health care providers, patients' compliance (adherence) with antiretroviral therapy, and the medication's effectiveness. This section provides background knowledge on existing studies about the availability of health care providers on health outcomes, the socio-demographic characteristics associated with medication adherence, and the effectiveness of the two antiretroviral regimens used in Thailand. At the end of this section, the first study on mother-to-child HIV transmission in Thailand will be discussed, followed by the contributions of this study relative to these prior studies.

With respect to the availability of health care providers, none of the literature has specifically mentioned an association between health outcomes of patients with HIV/AIDS and availability of health care providers. Studies have, however, shown the positive correlation between human resources for health and the health outcomes of a population. Anand et al. show that in addition to other determinants, the density of human resources for health is important in accounting for the variation in rates of maternal mortality, infant mortality, and under-five mortality across countries [Anand and Barnighausen, 2004].

With respect to adherence behavior, a growing body of literature focuses on socioeconomic determinants of patient's adherence to antiretroviral therapy and to HIV-related treatment in general. A very relevant study by Ngamvithayapong et al. [Ngamvithayapong, 1997] measures the adherence to tuberculosis preventive therapy among HIV-infected persons in Chiang Rai province in Thailand. This study found that acceptance of HIV status, concern about family, and a good patient-provider relationship generally encourage the patients' adherence behavior.

The Ngamvithayapong study aimed to determine the level of adherence and reasons associated with adherence to the preventive therapy among HIV-infected individuals who did not demonstrate HIV-related symptoms. In the study, 412 HIV-infected patients were enrolled in a tuberculosis preventive therapy program in one hospital in Chiang Rai province, Thailand. Participants were prescribed a 9-month

tuberculosis treatment regimen and a pill count was used to determine adherence. At the end of the study, both participants who missed a scheduled appointment in more than one month (categorized as non-compliance) and participants who successfully completed the regimen were interviewed. By analyzing demographic characteristics of adherents and non-adherents, the study found that age, educational level, and distance from home to hospital were not associated with adherence. Married people, surviving spouses and self-employed people were more likely to be adherent. The adherence rate was 69.4% and the reasons reported for adherence were that the medication was recommended by physicians, that they were concerned about their family and that they experienced a good patient-provider relationship. On the other hand, out-migration, perceived side effects of the drug, and denial of HIV status were the most frequently cited reasons for non-adherence.

Besides the availability of health care providers and the patient's compliance to antiretroviral treatment, the major medical-related factor that determines motherto-child HIV transmission rates is the efficacy of the treatment regimen itself. The two main treatment regimens for HIV-infected pregnant women and their infants as recommended by the Ministry of Public Health were mainly influenced by the results of two clinical trials conducted by Lallemant et al. [Lallemant et al., 2000]. In the first trial, which lasted from 1997 to 1999, four regimens of short and longcourse Zidovudine(ZDV) drugs for HIV-positive pregnant women were compared. The demonstrated transmission rates ranged from 4.1 to 10.5%. The short-long regimen, which demonstrated a transmission rate of 8.6%, was used as the MOPH recommendation during 2000 to 2003. In the second trial lasting from 2001 to 2003, a single dose of Nevirapine was added to the oral Zidovudine starting at 28 weeks' gestation (12 weeks before child's birth) for pregnant women [Lallemant et al., 2004]. The study found that this new regimen, either with or without a single dose of Nevirapine to the infant, could reduce the mother-to-child HIV transmission rate to 1.9%. Eventually, the Ministry of Public Health adopted administration of Nevirapine to both mother and infant in addition to oral Zidovudine as a recommended treatment regimen from the end of 2003 onward.

The study that most closely resembles the present one is by Plipat et al. [Pli-

pat Tanarak, 2007]. Plipat's study is one of the first studies that measures the effectiveness of the prevention of the mother-to-child HIV transmission program in Thailand using the Perinatal HIV Outcome Monitoring System (PHOMS). The PHOMS is a population-based surveillance of the outcomes of children born to HIV-infected mothers in all public hospitals in fourteen pilot provinces in Thailand. The paper analyzes about 10% of all HIV-positive deliveries in Thailand in four provinces. The transmission rate was reported to be 6.8% among mother-infant pairs who completed the Zidovudine regimen alone (compared to 8.6% in Lallemant's study), and 3.9% among those who completed Zidovudine regimen combined with other antiretroviral medications, usually Nevirapine. Plipat found the overall transmission rate including all antiretroviral prophylaxis combinations to be 10.2%.

Lallemant's studies are conducted in controlled settings, all of which can comply with the overall study procedure. Therefore, the effectiveness of the treatment regimen might be different for the program at the national level. Furthermore, Lallemant's studies do not take into account external geography-specific, sociodemographic factors such as average household income, proportion of population who complete each education level, average family size, and availability of health care provider. In terms of compliance to medication, Ngamvithayapong's study describes compliance behaviors among a group of HIV-infected persons in Thailand to tuberculosis preventive therapy. However, since each type of therapy has its own cost and benefits to the patients, it might be inappropriate to deduce the same compliance pattern to apply to antiretroviral prophylaxis. Anand's study only evaluates the relationship between the availability of health care providers and health outcomes in general, but not the relationship between the availability of health care providers and HIV infection outcomes.

Relative to these prior studies, I will apply Lallemant's procedure in assessing transmission rates associated with each treatment regimen in real (as opposed to clinical) settings (with a much larger sample size) while also observing effects of compliance to antiretroviral prophylaxis and socio-demographic factors on transmission rates. My study uses samples from the same source as Plipat's study, namely the Perinatal HIV Outcome Monitoring System, but has a larger sample size and

more recent observations. The socio-demographic factors of interest include average household income, average household size, proportion of population completing each education level, and density (per capita) of health care providers. Relative to Ngamvithayapong's study, I will specifically examine compliance behaviors to antiretroviral prophylaxis, rather than tuberculosis therapy, among the HIV positive population. Altogether, this paper will provide policy makers with more information relevant to long-term intervention aimed at improving the effectiveness of the national PMTCT program in Thailand.

3 Theoretical Framework

Several studies indicate that medication failure rates increase dramatically as patients take their medication less often than their prescription requires. As a consequence, medicines are less likely to work if patients do not adhere to or comply with their treatment regimen [Paterson and Swindells, 2002]. Therefore, it is a concern that non-compliance with antiretroviral therapy can lead to an increasing probability of perinatal HIV transmission. Following this rationale, this study splits the empirical model into two parts. The first part measures the effects of different socio-demographic factors on the probability of complying with an antiretroviral regimen. The second part measures the effect of different factors, both medical and non-medical, on the likelihood of perinatal HIV transmission.

3.1 Expected Utility Model

An HIV-positive pregnant woman faces 4 different scenarios:

- receive treatment and infect her child: U_{TI}
- receive treatment and not infect her child: U_{TU}
- not receive treatment and infect her child: U_{NI}
- not receive treatment and not infect her child: U_{NU}

The probability of the child getting infected in each scenario is:

- $Pr(\text{infect}|\text{treatment})=p_1$
- $Pr(\text{not infect}|\text{treatment}) = 1 p_1$
- $Pr(\text{infect}|\text{no treatment})=p_2$
- $Pr(\text{not infect}|\text{no treatment}) = 1 p_2$

Thus, the expected utility of the treatment choices $E(U_{treat})$ vs. $E(U_{notreat})$ will be:

- $E(U_{treat}) = U_{TI}p_1 + U_{TU}(1-p_1)$ If the pregnant woman receives treatment and either infects or not infects her child.
- $E(U_{notreat}) = U_{NI}(p_2) + U_{NU}(1-p_2)$ if the pregnant woman does not receive treatment and either infects or not infects her child.

	infect	not infect
treatment	$U_{TI}p_1$	$U_{TU}(1-p_1)$
no treatment	$U_{NI}p_2$	$U_{NU}(1-p_2)$

Table 1: individual choice

Additional assumptions are:

- 1. The probability of infecting her child given that the mother receives treatment is always lower than if she does not receive treatment. That is, $p_1 < p_2$, which implies $1 p_2 < 1 p_1$.
- 2. Her utility if the child is not infected given the treatment is always greater than if the child is infected given the treatment: $U_{TU} > U_{TI}$.
- 3. Her utility if the child is infected given no treatment is always greater than if the child is infected given the treatment: $U_{NI} > U_{TI}$
- 4. Her utility if the child is not infected given no treatment is always greater than if the child is infected given no treatment: $U_{NU} > U_{NI}$
- 5. Her utility when the child is *not* infected given the treatment compared to the utility when the child is *not* infected given *no* treatment is ambiguous: $U_{NU} > U_{TU}$ if the negative side effects of the treatment outweigh the health benefits the mother gains from the treatment or $U_{NU} < U_{TU}$ if the contrary is true.

An HIV positive pregnant woman will choose to receive her treatment if the expected utility of receiving treatment, $E(U_{treat})$, is larger than the expected utility of not receiving treatment, $E(U_{notreat})$. As a result, there is a threshold function:

$$\Phi = (U_{TI}p_1 + U_{TU}(1 - p_1)) - (U_{NU}(1 - p_2) + U_{NI}p_2)$$

If $\Phi \geq 0$ the patient will receive treatment. If $\Phi \leq 0$ the patient will be better off without the treatment.

Several socio-demographic characteristics of a patient can influence the direction of the inequality sign, and thus, influence her decision to undertake the treatment. These characteristics are visits to prenatal care clinics, mother's nationality, gender of the infant, income, education, family size, and density of health care workers. These variables will be discussed in the next section.

4 Empirical Model

4.1 Part I: Compliance to treatment

This study defines compliance to a treatment regimen as either the completion of the Zidovudine regimen alone (recommended during 2000-2003), or the completion of the Zidovudine with additional Nevirapine (recommended after 2003). From this point onward, I will refer to the Zidovudine regimen as regimen1, and the Zidovudine with additional Nevirapine as regimen2.

This section determines compliance to antiretroviral prophylaxis by measuring the probability that an HIV positive pregnant woman will have completed either treatment regimen 1 or regimen 2 relative to having not completed the treatment (partial treatment). The status of completing treatment regimen 1 requires a pregnant woman to receive AZT beginning at 36 weeks' gestation and a single dose of AZT 3 hours before the delivery. It also requires an infant born to the pregnant woman to receive AZT for 6 weeks after birth. Additional requirements for completing treatment regimen 2 are that a pregnant woman receives AZT beginning at 28 weeks' gestation rather than at 36 weeks, a single dose of Nevirapine at labor, and a single dose of Nevirapine administered to the infant. Every woman in the sample received at least partial treatment. I specify the probability model of completing the antiretroviral treatment as:

Pr(Complete treament) = f(gender, prenatal care, income, education, family size, know HIV status, providers)

where *prenatal care* indicates whether or not the pregnant woman has received prenatal care; *know HIV status* indicates if the pregnant woman knows her HIV status prior or after receiving prenatal care, and *income*, *family size*, *education*, *providers* are the province-specific average income, household size, fraction of female population who complete each educational level, and physicians per 10,000 population respectively.

Since the probit regression will be used for this estimation, the model becomes:

$$Pr(\text{complete treatment}) = \Phi(\beta_0 + \beta_1 \vec{x} + \epsilon)$$

where \vec{x} is the vector of independent variables that could affect optimal choice.

4.2 Factors affecting optimal choice

- 1. Gender of the infant. Gender preference may influence the compliance behavior of an HIV-infected pregnant woman given that she knows the gender of her child before delivery. Unfortunately, we are unable to determine how many pregnant women in our sample know the gender of their infants before birth. Gender of the infant is included as a socio-demographic control for the compliance behavior of an HIV-infected pregnant woman.
- 2. Mother's nationality. The mother's nationality is included as a demographic control. Nationality is expected to correlate with other socio-economic factors such as income and education. Most of the pregnant women without Thai nationality are immigrants from Lao, Myanmar, Cambodia, Vietnam, and China. A pregnant woman with Thai nationality is more likely to receive governmental support and has higher socio-economic status than monorities and those with foreign nationalities. Therefore, we expect a higher treatment completion rate among pregnant women who are Thai.
- 3. Visits to prenatal care clinics. Visits to prenatal care clinics reflect the pregnant woman's level of risk-aversion. A risk-averse individual tends to prefer a low-risk choice over a high-risk one and thus her decision to seek prenatal care can be a predictor of medical compliance. Additionally, the prenatal clinic is the place where HIV positive pregnant women acquire more information about the costs and benefits of taking preventive measures and the costs of not taking them. This information can help pregnant women more accurately estimate the probability and severity of health outcomes in both cases—raising the expected utility of compliance while reducing the expected utility of non-compliance. Consequently, those who receive prenatal care are expected to have higher rates of medical compliance compared to those who do not.

In addition to the effect on medical compliance, visits to prenatal care clinics

can dramatically affect the HIV serostatus of the infants. The transmission rate among mothers who had prenatal care was significantly lower in a prior study [Plipat Tanarak, 2007]. This may be due to the increasing chance of completing the antiretroviral prophylaxis and having received proper care. Thus, receiving prenatal care increases the likelihood of early HIV detection in mothers and initiation of preventive actions. As a result it can significantly reduce the chance of HIV transmission to infants.

- 4. Income. Income enters into the decision making process of HIV positive pregnant women in terms of marginal utility gain or loss. Commuting to receive regular care requires effort and imposes an opportunity cost, thus lowering the expected utility of the individual. Assuming the standard property of diminishing marginal utility of income, a person with a higher income will experience a smaller utility loss from a 1 unit decrease in income than a person with a lower income. For lower income women, work time loss from going to seek regular care translates into a bigger loss in expected utility. Nonetheless, income could also have an countereffect on the decision to comply. The opportunity cost of receiving regular care (and not working) is higher for the high income person and lower for the low income person. In this case, high opportunity cost might discourage an HIV pregnant woman from completing the antiretroviral regimen. Therefore, we speculate that the effect of income on compliance behavior is ambiguous.
- 5. Education. Educational attainment relates to behavior in several ways. First, educated people tend to be more informed on the health issues; thus they are more likely to update their knowledge on the probability and severity of transmitting HIV to their children. Second, studies show that the higher-educated exhibit a stronger degree of risk aversion and more future-oriented behaviors than the less educated [Becker and Maiman, 1975]. This risk-averse preference attracts the higher-educated to a safer choice-compliance to medication. The future-oriented pregnant woman would choose the expected utility loss from completing the treatment over the future expected loss of infecting her child.

- Therefore, a more educated pregnant woman should exhibit a higher degree of medical compliance.
- 6. Family Size. Family size can influence compliance behavior in two ways. First, it can lower the expected utility loss from receiving treatment and regular care. Families with more members at working age can very well help mitigate the loss of income and therefore the expected utility loss of the patient. Additionally, help can be in the form of encouragement: an HIV positive pregnant woman who is supported by her family could have a higher psychological tolerance to the negative side effects of the medication. In the second scenario, however, having a larger family may indicate a more difficult situation for the HIV pregnant woman if other members are unable to help generate income. Having small children and elderly in the family means that limited resources need to be devoted to family members rather than to the pregnant woman to receive a complete antiretroviral treatment. In the first case, a pregnant woman who comes from a larger family is expected to comply with the treatment regimen, while in the second case she is not. Therefore, the effect of family size on the compliance behavior of an HIV positive pregnant woman is ambiguous.
- 7. Density of health care workers. A higher ratio of health care providers per patient could guarantee the allocation of the minimum necessary amount of health care to patients in a timely manner. Generally, by increasing the chance that a patient sees a physician, the cost of seeking medical care is lower. Once the expected cost and utility loss due to compliance and care go down, an HIV positive pregnant woman will be more likely to choose compliance to a regimen over non-compliance.

4.3 Part II: Infant HIV outcome

This section determines the probability that an infant born to an HIV positive mother will be infected given the characteristics of mother-infant pairs. These characteristics include compliance with antiretroviral prophylaxis, gender of the infant, place of delivery (e.g. hospital or other), mother's nationality, prenatal care visit, s, and delivery method. Note that we did not include the timing of when the mother learns about her HIV status in this regression. As illustrated later in the regression results, the time at which the mother learns her HIV status is a strong determinant of the probability that she completes the antiretroviral regimen. Therefore, the fact that a pregnant woman knew her HIV status early (prior to pregnancy or prior to receiving prenatal care) will be captured in the categorical variables indicating her medication completion status. The main outcome is the child's HIV diagnostic result. Thus, the model in the second part will be similar to the first part's and will be estimated using probit regression:

$$Pr(Infection|treatment status) = \Phi(\beta_0 + \beta_1 \vec{x} + \epsilon)$$

where \vec{x} is the vector of characteristics of the mother-infant pair described below.

4.4 Factors affecting the Transmission rate

- 1. Gender of the infant. Some studies found that HIV-infected infants are more likely to be girls than boys. However, none of these studies has established a clear explanation of why that is the case [Taha et al., 2005; Kuhn et al., 1994]. Therefore, we include sex here as a demographic control.
- 2. Place of delivery. Generally, the hospital setting guarantees optimal standards of hygiene, the availability of equipment and the availability of health care providers. Therefore, compared to other places of delivery, we expect infants born at the hospital to have a lower chance of mother-to-child HIV transmission.
- 3. Prenatal care. Prenatal care can be thought of as a part of the treatment along with receiving antiretroviral therapy itself. Therefore, we expect the probability of mother-to-child HIV transmission to decrease if the pregnant woman received prenatal care.

- 4. Breastmilk. The risk of HIV transmission through breastfeeding has been confirmed by many prior studies [Nduati et al., 2000; Miotti et al., 1999; D. T. Dunn and Peckham, 1992]. Even though breastfeeding is used as a biomedical control, we would still expect the probability of HIV transmission to increase among the mother-infant pair with breastfeeding.
- 5. Mode of delivery. The mode of delivery is used as a biomedical control. Cesarean section is shown to lower the mother-to-child HIV transmission rates in many studies [Kind, 1998; Study, 1994; Kuhn et al., 1994; Group, 1999] compared to vaginal delivery. However, there are some other studies that show that cesarean section could significantly reduce the transmission rate only if coupled with other biomedical factors. Therefore, we do not expect a strong effect of the mode of delivery on transmission rates.
- 6. Treatment completion. According to the Lallemant study discussed in the previous section, the completion of the antiretroviral prophylaxis decreases the chance of perinatal HIV transmission. In an attemp to assess the effectiveness of the two different antiretroviral regimens in real settings, the two treatment regimens, regimen1 and regimen2, will be our main focus for this part.

5 DATA and Descriptive Statistics

5.1 Perinatal HIV Outcome Monitoring System (PHOMS)

I will use data on individual PMTCT participats from the Perinatal HIV Outcome Monitoring System (PHOMS) which is under the Department of Communicable Disease Control of the Ministry of Public Health. The system is a hospital-based registry that collects information on children born to HIV-infected mothers in the Ministry of Public Health's hospitals in the 14 pilot provinces. The database records information on infants born during the first six months (January 1st to Jund 30th) of 2001, 2002, and so on, up to and including 2007, totaling 6,035 observations. Information reported is medical-related characteristics and socio-demographic characteristics of individual patients.

5.2 National Statistical Office (NSO)

Although the PHOMS data on individual participants are useful in terms of providing medical-related details, they do not provide sufficient socio-economic features of the participants. Therefore, to supplement the socio-demographic data from the PHOMS, additional socio-demographic characteristics of each mother-infant pair will be imputed from aggregate data from the National Statistical Office (NSO). The NSO database provides aggregated, province-level data on many socioeconomic indicators such as 1) number of physicians per capita, 2) average income per household, 3) average household size, 4) fraction of the population categorized by highest educational attainment, and 5) province-specific Gini coefficients.

This study analyzes the data using the STATA statistical package. The first part, a multivariate probit analysis, was performed using all the variables potentially related to the antiretroviral completion rates. The second part, also a multivariate probit analysis, was performed using all the factors potentially related to the mother-to-child HIV transmission rates.

5.3 Descriptive Statistics

Table 4 and 5 in the appendix display summary statistics for the characteristics of mother-infant pairs in the data set stratified by treatment level and infants' HIV diagnostic result. Although the overall sample consists of 6,035 individuals, there are a few individuals who report a different place of residence other than one of the 14 pilot provinces. These individuals are excluded from the analysis because the sample sizes from each of these non-pilot provinces are too small to be good representatives. Furthermore, for purposes of analysis, individuals who have missing observations for either dependent variables (treatment completion and diagnostic result) or one of the independent variables are excluded. The mother-infant pairs with inconclusive or unconfirmed infant's HIV outcomes are assumed to be systematic missings and excluded from the analysis because their bio-medical characteristics (as recorded in the PHOMS) are not different from those with the systematic missing HIV outcomes. Therefore, the sample used in the first regression will be slighly different from the one used in the second regression. In short, 70% (4,238 out of 6,035) of the overall observations were included in the first (on compliance rates) regression, while only 55% (3,298 out of 6,035) of the overall observations were included in the second regression (on transmission rates).

Overall, the transmission rate in this sample is 8%, compared to 10% in the Plipat study that uses data from the same Perinatal HIV Outcome Monitoring System. The transmission rate is 6.5% among the pregnant women who completed treatment regimen 1 and 1% among those who completed treatment regimen 2. These results are consistent with the prior studies by Plipat and Lallemant.

6 Probability of completing an antiretroviral regimen: Probit Results

Table 2 shows a probit estimation for the marginal probability of receiving complete antiretroviral treatment, whether regimen or regimen. Province-specific average family size turns out to have a negative effect on the probability that a pregnant women receives complete treatment. As predicted, the probability of completing antiretroviral therapy increases if the pregnant woman learned of her HIV status early (either before pregnancy or upon receiving prenatal care) and if the pregnant woman received prenatal care. It also increases for women who live in a province with a high physician per capita ratio. The effects of province-specific average family size and physician availability on the treatment completion are displayed in figure 1 and 2. Furthermore, an HIV-infected pregnant women who has Thai nationality is more likely to have completed the antiretroviral treatment than others. The fraction of the female population attaining each educational level turns out to play an important role in determining the probability of completing the therapy. However, the manner in which these education variables affect the therapy completion rate is not as straightforward as we have predicted. Omitting the fraction of the female population with no education (due to multicollinearity), our model predicts that the probability of completing antiretroviral treatment will rise as the fraction of the female population completing secondary and highschool education rise. On the other hand, it predicts that the probability of completing antiretroviral treatment will fall as the fraction of the female population completing college education rises.

The negative impact of a larger family size on compliance rate suggests an increasing economic burden of a larger family. A larger family size means that limited resource (time and income) will be allocated more to family members and less to the pregnant woman to receive regular treatment. In a larger family, the loss income due to the negative side effects of the treatment and the engagement in regular care translates into a larger disutility since it affects more members. Therefore, as the result suggests, having a larger family seems to impede the compliance to antiretroviral therapy rather than support it.

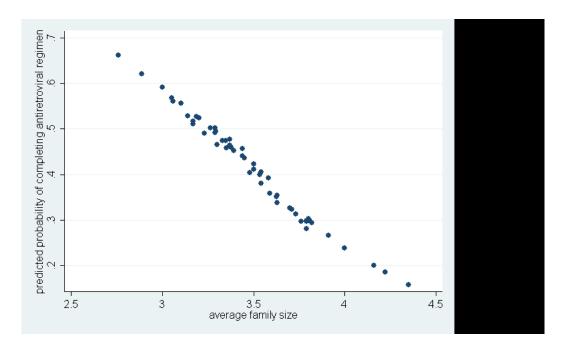


Figure 1: Province-specific family size and treatment completion

Having known her HIV status either before pregnancy or upon receiving the prenatal care increases the chance an HIV-infected pregnant woman initiates the antiretroviral prophylaxis early, which in turns make it more likely that she completed the regimen. Attending prenatal clinic not only reflects risk-aversion, but also reflect the increasing chance of completeing the treatment since most of the time the antiretroviral medication (specifically AZT) is allocated to the patients at the prenatal care visit. Note that the coefficients of both knowing HIV status early and receiving prenatal care are very large and significant because they almost perfectly predict the probability of treatment completion. As we can see in specification (2) of table 2, when these two variables are excluded from the regression the pseudo R-square drops dramatically while the magnitude of other coefficients do not change much. In table 4 in the appendix, almost 100% of the sample who completed treatment regimen 1 knew HIV status early and had prenatal care, while 100% of the sample who completed treatment regimen 2 knew HIV status early and had prenatal care. Higher physician per capita results in a much higher probabil-

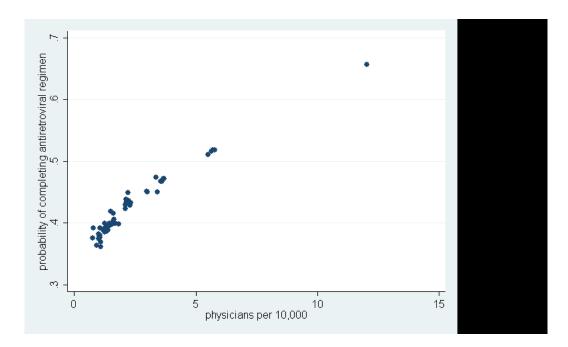


Figure 2: Physician availability and treatment completion

ity that a pregnant woman would complete the treatment because it indicates the availability of health resource to educate and administer antiretroviral prophylaxis to the patients.

Pregnant woman who is Thai demonstrates a higher completion rate than non-Thai. Most non-Thai individuals in our sample are immigrants from neighboring countries. These non-Thai pregnant women would face many socio-economic disadvantages that contribute to the lower probability of completing the treatment. For example, language can be an important barrier to the effective communications between these patients and the health care providers. This problem leads to misunderstanding about the costs, benefits, and the instruction to taking medication.

The impacts of province-specific education level contradict our hypothesis that higher education level would increase the chance of completing antiretroviral therapy. This unexpected result could have arisen from the fact that we utilize province-level data on education, rather than the individual-level data. This province-level aggregate data on the fraction of female population completing each education level

may also be related to intra-provincial education inequality, which in turn affects the probability that an HIV positive pregnant woman completes the therapy. We test this possibility by adding the province-specific gini index as a regressor. However, the estimation results turn out not to change much from the result without the gini index. This leaves us with a paradox about the effect of province-specific education on treatment completion rates.

Table 2: Marginal probability of completing antiretroviral therapy

Table 2. Warginar proba	(1)	(2)
	complete treatment	complete treatment
income	0.0000158	0.0000212
(Baht)	(0.86)	(1.24)
		, , ,
family size	-0.907***	-0.786***
	(-6.48)	(-6.01)
female	0.00780	-0.00634
	(0.18)	(-0.16)
	, ,	,
Thai	0.203*	0.307***
	(2.18)	(3.66)
% primary edu	-2.702**	-2.051*
70 primary cad	(-2.81)	(-2.28)
	,	,
% secondary edu	10.32***	7.847**
	(3.59)	(2.94)
% highschool edu	7.083*	9.192**
70 inglibelioor odd	(2.24)	(3.11)
	, ,	, ,
% college edu	-12.22***	-11.09***
	(-6.77)	(-6.66)
physician	0.0646**	0.0474*
(per 10,000)	(2.98)	(2.37)
	,	,
prenatal care	2.356***	
	(7.43)	
know HIV status early	2.166***	
miow iii v socious carry	(13.45)	
	(=3. =3)	
gini	-0.635	1.118
	(-0.78)	(1.48)
_cons	-1.059	1.57
_00116	(-0.72)	(1.18)
\overline{N}	4238	4238
pseudo R^2	0.180	0.032
Passace 20	0.200	

t statistics in parentheses

^{*} p < 0.05, ** p < 0.01, *** p < 0.001

7 Probability of perinatal HIV transmission: Probit Results

Table 3 displays the probit regression results for the probability of perinatal HIV transmission. The model predicts that female infants are more likely to be infected by HIV. As expected, the results from specification (2) show that having received prenatal care significantly reduces the chance of perinatal HIV transmission. Here, the effectiveness of the two antiretroviral regimens is tested. Only the completion of antiretroviral therapy regimen can significantly reduce the transmission rate.

There are three possible scenarios that could explain the higher transmission rates among female infants. First, the antiretroviral therapy is more effective in preventing the mother-to-child HIV transmission to the male infants than to the female infants. Second, knowing the gender of the infant might influence the compliance behavior of an HIV positive pregnant woman. In other words, HIV positive pregnant women who know their infants are female might exhibit lower compliance rates than those who know their infants are male. Third, it could be that HIV infected male infants are more likely to die before birth than are infected female infants. This would result in more HIV infected female infants being born than male infants being born.

By looking at specification (1) in table 3, we see that none of the interaction terms turns out to be statistically significant, which suggests no difference in treatment effectiveness between male infants and female infants. Also, recall from table 2 that the gender effect on compliance rate is not statistically significant. This means that the gender of the infant does not affect the compliance behavior of the HIV positive pregnant women. Lastly, since the ratio of female infants and male infants in our sample is approximately the same (female 49% and male 51%), the third scenario is unlikely to account for the higher transmission rate among female infants. Because none of the proposed explanations can explain the result, we speculate that female infants might be more susceptible to HIV infection than male infants. This susceptibility might involve several genetic and biological characteristics beyond the scope of this study. The result that female infants have a higher risk of getting

infected by HIV is consistent with many prior studies[Taha et al., 2005; Kuhn et al., 1994].

TD 11 0	T) 1 1 1111	c		TTTT 7	
Table 31	Probability	\circ t	perinatal	HIV	transmission

	001 111 7 010	011011111001011
	(1)	(2)
	diag1	diag1
female	0.285**	0.210**
	(2.83)	(2.80)
hospital delivery	0.107	0.109
	(0.38)	(0.39)
. 1	0 11 0 ***	0 41 5 4 4 4
prenatal care	-0.416***	-0.415***
	(-3.30)	(-3.31)
breastfeed	-0.109	-0.112
breasticed	(-0.40)	(-0.41)
	(-0.40)	(-0.41)
vaginal delivery	0.0837	0.0810
	(0.75)	(0.72)
	(0.10)	(0.12)
complete treatment regimen 1	-0.0135	-0.105
•	(-0.12)	(-1.30)
	,	,
complete treatment regimen 2	-0.591	-0.729**
	(-1.56)	(-2.69)
female*treatment regimen 1	-0.165	
	(-1.08)	
f1-*44	0.054	
female*treatment regimen 2	-0.254	
	(-0.47)	
_cons	-1.519***	-1.477***
	(-4.75)	(-4.65)
\overline{N}	3298	3298
pseudo R^2	0.028	0.027
Tarana 10		

t statistics in parentheses

^{*} p < 0.05, ** p < 0.01, *** p < 0.001

8 Conclusion and Policy Implications

Our analysis suggests strong relationships between the likelihood that an HIV positive pregnant woman will complete the antiretroviral therapy and the following features: province-specific education level, physician availability, nationality, prenatal care, the time when an HIV positive pregnant woman knows her HIV status and. However, the unexpected negative relationship between the percentage of the female population completing college education and the predicted treatment completion rate is still an unresolved paradox. In terms of the probability of mother-to-child HIV transmission, we found that the gender of the infant, prenatal care, and the completion of antiretroviral regimen 2 could significantly reduce the transmission rates. Interestingly, we found that female infant is more likely than male infant to get infected by HIV than being a male. This finding is consistent with some of the prior studies, but identifying the underlying cause is beyond the scope of this study.

Several policy implications for the PMTCT program in Thailand can be drawn from our analysis. Recall that physician availability, prenatal care, and knowing her HIV status early could significantly increase the antiretroviral completion rates. Additionally, receiving prenatal care and the completion of antiretroviral regimen 2 significantly reduce mother-to-child HIV transmission. Therefore, increasing human resources and infrastructure in health care, particularly for prenatal care, along with promoting health care equality should be important concerns for policy makers. Pregnant women and women at child bearing age should be encouraged to accept HIV testing to ensure that they take appropriate preventive measures against the mother-to-child HIV transmission. Messages about the costs and benefits of completing the antiretroviral prophylaxis should also be clearly and effectively conveyed to the target population. It is important to keep in mind that stigmas associated with being HIV-infected in Thailand still remain a challenging problem in promoting universal HIV testing and antiretroviral compliance among pregnant women. This suggests the multidimensional nature of the problem which needs a complete understanding in the social, cultural, and medical contexts in order to be overcome.

The major limitation of this study is the lack of individual level socio-demographic

characteristics such as income, education, and family size that influence the completion rates of antiretroviral regimens. That information was not solicited from the questionnaire used to collect data for the PHOMS database. Although using province-level data on these characteristics gives us rough approximations of the effect of each variable on compliance rates, it also induces several caveats. First, the province-level data cannot capture the intra-provincial variations among these characteristics which could account for a big part of the compliance behaviors. Second, using the province-level data greatly limits the number of observations, which in turn weakens the statistical power of our analysis. Lastly, the interpretation of each coefficient on province-level variables will not be as straightforward as using the individual-level data. Here we need to accommodate the fact that these province-level figures (income, education, and family size) can be proxies of several intra-provincial characteristics other than the average individual's income, education level, and family size.

The second limitation to this study is the incompleteness of the data. Almost half of the overall observations either had missing or inconclusive HIV outcomes. Minor fractions of the overall observations have missing data on one or more of the key variables. In addition, the data collected in the PHOMS include only the individuals who attended public hospitals, but not private hospitals.

In order to improve the estimation model for the completion rate of an antiretroviral regimen, future studies should focus on using individual-level socio-demographic characteristics along with more thorough records of medication adherence at every stage of pregnancy. Follow-up interview with members of the sample who exhibit full medication compliance and who did not will be useful to understanding the underlying cause of medical non-adherence among the PMTCT participants.

9 Appendix

9.1 Summary Statistics for the compliance analysis stratified by treatment levels

Table 4: Summary Statistics for the compliance analysis stratified by treatment levels

variable	statistics	Partial	Regimen 1	Regimen 2	Missing	Total
income	Mean	12263.16	12396.41	12916.64	13063	12404
	SD	2872.252	3079.990	3223.285	1607.199	2939.260
	N	2085	1861	292	244	4482
family size	Mean	3.49	3.386	3.384	3.719	3.453
	SD	0.347	0.331	0.394	0.253	0.349
	N	2085	1861	292	244	4482
% no education	Mean	0.068	0.068	0.073	0.061	0.068
	SD	0.039	0.034	0.045	0.037	0.037
	N	2085	1861	292	244	4482
% primary edu	Mean	0.577	0.567	0.548	0.599	0.572
	SD	0.079	0.073	0.075	0.088	0.077
	N	2085	1861	292	244	4482
% secondary edu	Mean	0.155	0.154	0.156	0.155	0.155
	SD	0.011	0.012	0.012	0.013	0.012
	N	2085	1861	292	244	4482
%highschool edu	Mean	0.106	0.112	0.115	0.098	0.109
	SD	0.021	0.021	0.021	0.017	0.021
	N	2085	1861	292	244	4482
%college edu	Mean	0.094	0.099	0.107	0.086	0.097
	SD	0.038	0.04	0.042	0.028	0.039
	N	2085	1861	292	244	4482
Continued on next page						next page

1 0

variable	statistics	Partial	Regimen 1	Regimen 2	Missing	Total
physician	Mean	2.157	2.411	2.860	2.471	2.325
(per 10,000)	SD	1.588	1.877	2.598	1.174	1.784
	N	2085	1861	292	244	4482
prenatal care	Mean	0.849	0.999	1.000	0.988	0.929
	SD	0.358	0.023	0.000	0.110	0.257
	N	2085	1861	292	244	4482
know HIV status early	Mean	0.763	0.996	1.000	0.975	0.887
	SD	0.425	0.061	0.000	0.155	0.317
	N	2085	1861	292	244	4482
female	Mean	0.475	0.477	0.466	0.475	0.475
	SD	0.499	0.500	0.500	0.500	0.499
	N	2085	1861	292	244	4482
gini	Mean	0.467	0.462	0.462	0.450	0.464
	SD	0.045	0.045	0.042	0.043	0.045
	N	2085	1861	292	244	4482

9.2 Summary Statistics for the transmission rate analysis stratified by infection outcomes

Table 5: Summary Statistics for the transmission rate analysis stratified by infection

outcomes

8				
variable	statistics	Not infected	Infected	Total
Female	mean	0.48	0.59	0.48
	SD	0.50	0.49	0.50
	N	3131	167	3298
Hospital delivery	mean	0.98	0.98	0.98
	SD	0.13	0.13	0.13
	N	3131	167	3298
prenatal care	mean	0.94	0.85	0.94
	SD	0.24	0.36	0.25
	N	3131	167	3298
breastfeed	mean	0.02	0.02	0.02
	SD	0.14	0.13	0.14
	N	3131	167	3298
vaginal delivery	mean	0.85	0.88	0.85
	SD	0.36	0.33	0.35
	N	3131	167	3298
partial treatment	mean	0.48	0.60	0.49
	SD	0.50	0.49	0.50
	N	3131	167	3298
complete regimen 1	mean	0.45	0.39	0.45
	SD	0.50	0.49	0.50
	N	3131	167	3298
complete regimen 2	mean	0.06	0.01	0.06
	SD	0.25	0.11	0.24
	N	3131	167	3298

References

- Anand, S. and Barnighausen, T. (2004). Human resources and health outcomes: cross-country econometric study. *The Lancet*, 364(9445):1603.
- Becker, M. H. and Maiman, L. A. (1975). Sociobehavioral determinants of compliance with health and medical care recommendations. *Medical Care*, 13(1):10–24.
- Bertolli J, Lee LM, S. P. (1996). Estimating the timing of mother-to-child transmission of human immunodeficiency virus in a breast-feeding population in kinshasa, zaire. *Journal of Infectious Disease*, pages 722–6.
- D. T. Dunn, M. L. Newell, A. E. A. and Peckham, C. S. (1992). Risk of human immunodeficiency virus type 1 transmission through breastfeeding. *The Lancet*, 340:585–588.
- Fowler, M. G., Simonds, R. J., and Roongpisuthipong, A. (2000). Update on perinatal hiv transmission. *Pediatr Clin North Am*, 47(1):21–38.
- Group, T. I. P. H. (1999). The Mode of Delivery and the Risk of Vertical Transmission of Human Immunodeficiency Virus Type 1 A Meta-Analysis of 15 Prospective Cohort Studies. *N Engl J Med*, 340(13):977–987.
- Kind, Christian 1, . R. C. . S. C.-A. . W. C.-A. . B. K. . L. U. . I. O. . S. J. . N. D. . S. N. H. S. G. . (1998). Prevention of vertical hiv transmission: additive protective effect of elective cesarean section and zidovudine prophylaxis. AIDS, 2(12):205–210.
- Kuhn, L., Stein, Z. A., Thomas, P. A., Singh, T., and Tsai, W. Y. (1994). Maternal-infant HIV transmission and circumstances of delivery. Am J Public Health, 84(7):1110–1115.
- Lallemant, M., Jourdain, G., Le Coeur, S., Kim, S., Koetsawang, S., Comeau, A. M., Phoolcharoen, W., Essex, M., McIntosh, K., Vithayasai, V., and Investigators, T. P. H. P. T. T. (2000). A Trial of Shortened Zidovudine Regimens to Prevent

- Mother-to-Child Transmission of Human Immunodeficiency Virus Type 1. N Engl J Med, 343(14):982-991.
- Lallemant, M., Jourdain, G., Le Coeur, S., Mary, J. Y., Ngo-Giang-Huong, N., Koetsawang, S., Kanshana, S., McIntosh, K., Thaineua, V., and the Perinatal HIV Prevention Trial (Thailand) Investigators (2004). Single-Dose Perinatal Nevirapine plus Standard Zidovudine to Prevent Mother-to-Child Transmission of HIV-1 in Thailand. N Engl J Med, 351(3):217–228.
- Miotti, P. G., Taha, T. E. T., Kumwenda, N. I., Broadhead, R., Mtimavalye, L. A. R., Van der Hoeven, L., Chiphangwi, J. D., Liomba, G., and Biggar, R. J. (1999). HIV Transmission Through Breastfeeding: A Study in Malawi. *JAMA*, 282(8):744–749.
- Nduati, R., John, G., Mbori-Ngacha, D., Richardson, B., Overbaugh, J., Mwatha, A., Ndinya-Achola, J., Bwayo, J., Onyango, F. E., Hughes, J., and Kreiss, J. (2000). Effect of Breastfeeding and Formula Feeding on Transmission of HIV-1: A Randomized Clinical Trial. *JAMA*, 283(9):1167–1174.
- Ngamvithayapong, Jintana; Uthaivoravit, W. Y. H. A. P. S. P. (1997). Adherence to tuberculosis preventive therapy among hiv-infected person in chiang rai, thailand. *AIDS*, pages 107–112.
- on HIV/AIDS Projection, T. T. W. G. (2001). Projections for hiv/aids in thailand: 2000-2020.
- Paterson, D. L. and Swindells, S. (2002). Adherence to protease inhibitor therapy and outcomes in patients with hiv infection.. *Annals of Internal Medicine*, 133(1):p21 –.
- Plipat Tanarak, e. a. (2007). Reduction in mother-to-child transmission of hiv in thailand, 2001-2003: results from population-based surveillance in six provinces. *AIDS*, 21:145–151.

- Shaffer, N., Chuachoowong, R., Mock, P. A., Bhadrakom, C., Siriwasin, W., Young, N. L., Chotpitayasunondh, T., Chearskul, S., Roongpisuthipong, A., Chinayon, P., Karon, J., Mastro, T. D., and Simonds, R. J. (1999). Short-course zidovudine for perinatal hiv-1 transmission in bangkok, thailand: a randomised controlled trial. *The Lancet*, 353(9155):773–780.
- Study, T. E. C. (1994). Caesarean section and risk of vertical transmission of hiv-1 infection. *Lancet*, 343:1464–1467.
- Taha, T. E., Nour, S., Kumwenda, N. I., Broadhead, R. L., Fiscus, S. A., Kafulafula, G., Nkhoma, C., Chen, S., and Hoover, D. R. (2005). Gender Differences in Perinatal HIV Acquisition Among African Infants. *Pediatrics*, 115(2):e167–172.
- UNAIDS (2006a). Aids epidemic update: December 2006. UNAIDS Web site. Available at:http://data.unaids.org/pub/EpiReport/2006/2006EpiUpdateen.pdf.
- UNAIDS (2006b). Country situation analysis: Thailand. UNAIDS Web site. Available at:http://www.unaids.org/en/Regions_countries/Countries/thailand.asp.