The Cost-Effectiveness Analysis of Initiating HIV/AIDS Treatment with Efavirenz-Based Regimens Compared with Nevirapine-Based Regimens in Thailand

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Objectives: *The aim of this study is to evaluate the cost-utility of the treatment, starting with EFZ-based therapy, compared with NVP-based therapy in Thai HIV/AIDS patients.*
Material and Method: *The study adopted a health care provider perspective. A probabilistic Markov model was applied to Thai HIV/AIDS patients aged 15 to 65 years. Input parameters were extracted from a cohort study of four regional hospitals. The study explored the effects of uncertainty around input parameters.*
Results: *For those patients with a different baseline CD4, initial therapy using EFZ-based regimens was the preferable choice for all subgroups. Given a maximum acceptable willingness to pay (WTP) threshold of 300,000 Baht/DALY averted starting with EFZ-based regimens was cost-effective for patients with a baseline CD4 count less than 250 cells/mm^3 and in all patient age groups, except those who were 20 years old.*
Conclusions: *The results suggest that starting with EFZ-based regimens was the preferable choice and it should be used as the first line regimen for Thai HIV/AIDS patients.*

Keywords: *Cost-effectiveness, HIV/AIDS treatment, Efavirenz-based regimens, Nevirapine-based regimens, Thailand*

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Even though the introduction of highly active antiretroviral treatment (HAART) has dramatically reduced the number of deaths and AIDS-related opportunistic infections in developed world, the availability of antiretroviral therapy for HIV infected patients is still limited in developing settings[1]. The World Health Organization has estimated that more than 1 million people living with HIV/AIDS (PLWHA) in Asia are in need of HAART, but only 6-7% of them can access to this expensive therapeutic regimen[2]. In Thailand, despite the declining incidence of new HIV transmission, due to the efforts of the Thai government in the early 90's, including extensive and intensive campaigns to promote condom use and HIV education in susceptible populations, the estimated numbers of HIV-infected and AIDS cases were 600,000 and 70,000, respectively in 2005[3].

Although the accessibility to HAART among Thai PLWHA has dramatically improved since 2003, when the universal coverage to HAART was implemented[4], the negative consequences of the treatment raised concerns among health care providers. Six standard ARV regimens were approved for use in this program, including an NVP-based regimen, which was used as the first drug of choice, while an Efavirenz (EFZ)-based regimen and a Protease Inhibitor (PI)-based regimen were set as alternative regimens[5]. Empirical evidence revealed that NVP could cause serious

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and life-threatening adverse events such as cutaneous hypersensitivity reactions, including Steven Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN) and severe hepatic toxicity. These adverse events became an emerging cause of mortality in HIV-infected patients[6-10]. These serious adverse events not only affected the patients' quality of life and success of treatment, but also increased the budget of the program. Therefore, substitution with a less toxic alternative such as EFZ is warranted. EFZ was recommended as a substitute for NVP in the treatment regimen. It had less severe toxicity but was reserved for patients who had a severe adverse event because of its higher cost.

The purpose of this study is to appraise value for money, using the cost-effectiveness and cost-utility analyses, on initiating treatment with the NVP-based regimens compared with initiating treatment with EFZ-based regimens. It has developed an economic model to estimate long-term effects on both costs and outcomes of these two alternative treatment options.

Material and Method

Overview options

The standard antiretroviral treatment for eligible patients who had a baseline CD4 count less than 200 cells/mm^3 was to start with NVP-based regimens, which are composed of Nevirapine, Stavudine and Lamivudine. Switching to other combinations was allowed if the patients developed negative consequences, such as adverse events, drug resistance or major opportunistic infections. The second and third regimens were two nucleoside or reverse transcriptase inhibitors (NRTI) plus a non-nucleoside reverse transcriptase inhibitor (NNRTI) regimens and Protease Inhibitor (PI)-based regimens, respectively.

The other choice of treatment that was compared was starting with EFZ-based regimens instead of NVP-based regimens. Switching to other combinations was allowed if the patients developed negative consequences such as adverse events, drug resistance or major opportunistic infections. The second and third regimens were the 2NRTI+1NNRTI regimens and PI-based regimens, respectively.

Analyses and model

An economic model was created to estimate the long-term effects of the treatment of HIV disease progression. The main principle of the model was that, to be effective, antiretroviral regimens must not only reduce viral loads, but also be tolerated by patients who are willing to adhere to it over a long period of time. The model evaluated the effect of the initial choice of triple therapy on the progression of an HIV positive population through 4 states, starting with the naÔve to the treatment state (1st regimen), switching to the 2nd regimen, the 3rd regimen, and then death (Fig. 1).

The target population of this study was HIV/AIDS patients aged 15-65 years. The Markov model structure (shown in Fig. 1) illustrates the mutually exclusive health states that a patient commencing treatment from either NVP-based regimens or EFZ-based regimens might go through. Health states are denoted by the solid oval-lines. The model also includes sub-states (dotted oval lines) to reflect the difference in the rate of complications between the two treatment modalities. An arrow indicates that movement from one state to another is possible. The likelihood of movement between each state ("transition probability") was determined using data from a retrospective cohort study in four regional hospitals namely Lampang Hospital,

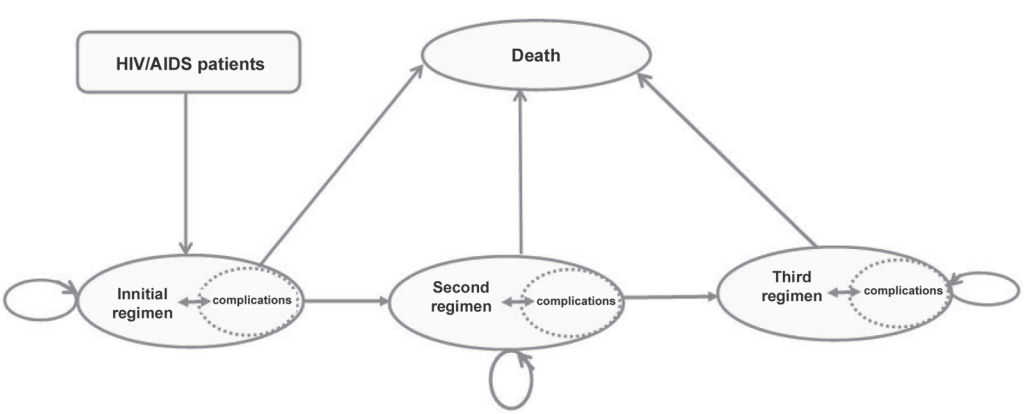


Fig. 1 Schematic diagram of the Markov model

Had-Yai Hospital, Chonburi Hospital and Sappasittiprasong Hospital. Initiating treatment with either NVP-based or EFZ-based ART was modeled for the remaining lifetime of the prevalence cohort. Cycle lengths of 1-year for the full health states and one or two months for the sub-states were used for the analysis.

The model was used to quantify the costs and effects of two long-term alternative treatments for HIV/AIDS patients in each age group and each baseline CD4 level. In the model, patients might start either with NVP-based or with EFZ-based ART and remain on the same treatment until the next cycle. Moving to other health states (second and third regimens) was dependent on the development of complications during treatment such as moderate or severe adverse drug reactions, opportunistic infections, or drug resistance. Moving to the final state (death) might or might not be related to the occurrence of complications since patients could die from non HIV/AIDS causes, such as cardiovascular disease. In each case, it was assumed that the event would only happen at the end of each cycle. The simulations were conducted to model cost and events over a 99-year period to cover the maximum total period over which the whole cohort could reasonably be expected to survive.

A probabilistic sensitivity analysis using a second-order Monte Carlo simulation was carried out. All input parameters were assigned a probability distribution to reflect the feasible range of values that each input parameter could attain. This process was repeated 1000 times to provide a range of possible values given the specified probability distributions. To comply with the Thai HTA guideline for conducting heath economic analyses, all costs and outcomes were discounted at a rate of 3 %[11].

Outcome measures

Probability of moving to next health states

The probabilities of moving to the next health state (from first regimen to second regimen, third regimen and death) were estimated using the survival analysis of a hypothetical cohort of patients from a retrospective cohort study of HIV/AIDS patients in 4 regional hospitals. To adjust the survival rate, CD4 at baseline, the age of patients and ordering of ARV regimens were used as covariates of disease progression.

This data consisted of 408 records of patients who started with NVP-based regimens and 116 records of patient who started with EFZ-based regimens. In the follow up period of 3 years, no one died in the group of patients who started with the EFZ-based regimens. Therefore, the existing data were not applicable to calculate the survival rate of the patients starting with the EFZ-based regimens. From a Cochrane review[12], the finding from a 2NN study, (a large randomized control trial), was that NVP-based regimens had a higher death rate compared with EFZ-based (RR [95%CI] = 1.33 [0.50, 3.53]). Thus, it was assumed that the HIV/AIDS patients who started with NVP-based regimens had 1.33 times (SE 0.49) higher death rate in the first health state compared with HIV/AIDS patients who started with EFZ-based regimens.

Using the statistical software package STATA (Stata Corp, College Station, TX), this study initially applied a non-parametric Kaplan-Meier approach[13] to fit Kaplan-Meier curves and plotted graphs of log against log (time) which were generally linear and indicated that a Weibull survival model would adequately fit the data[14]. The study consequently used the "streg" module of STATA to perform the maximum likelihood estimation for parametric regression of the Weibull survival models.

For the Weibull distribution, for example, the survival function, which describes the probability of survival as a function of age,[15] is:

$$S(t) = \exp[-H(t)]$$

and

$$H(t) = \lambda t^{\gamma}$$

Where H(t) is the cumulative hazard; λ (lambda) is the scale parameter; t is time in days; and γ (gamma) is the shape parameter that describes the instantaneous hazard rate h(t), which increases with age if $\gamma > 1$. The λ depends on the covariate and age, according to the formula:

$$\lambda = \exp[(\text{age\_coefficient} \times \text{age}) + \text{cons}]$$

The transitional probability of dying during the cycle, *tp(c)*, is therefore estimated from the following formula (where c is the number of cycles):

$$tp(c) = 1-\exp[H(t-c)-H(t)]$$

Disability-adjusted survival

This study measured outcomes in disability-adjustedlife years (DALY) by using the disability weight (DW) from Global Burden of Diseases (GBD)[16], an Australian study[17] and expert opinion. For co-morbidities in this model, such as AIDS patients who developed tuberculosis, the multiplicative adjustment method, which was used to calculate the disability weight for co-morbidities in Health-adjusted life expectancy (HALE) calculation[18], was applied. The concept of this is that it assumes that the increase in disability due to co-morbidity disability is proportional.

Total disability for an individual having more diseases could be written as:

$$w(1,2)=1-(1-w1)(1-w2)$$

$$w(d) = 1-\pi_d(1-wd)$$

Where: $w(1,2)$ disability weight of an individual with disease 1 and 2

$w(d)$ disability weight of an individual with d diseases

Costs

Using the health care provider perspective, the cost of treatment in this study was the direct health care cost. The costs of treatment in this study included the cost of ARV drugs, the cost of laboratory testing, the cost of medical services, the cost of hospital services and the cost of treating complications such as adverse events and opportunistic infections in out-patient and in-patient visits. The costs of treatment were derived based on the cost data from the retrospective cohort of HIV/AIDS patients in 4 regional hospitals. The costs of adverse events and opportunistic infections treatment were the average cost of treatment from the four hospitals. Only costs of ARV regimens were adjusted by the reference cost of ARV drugs from the Bureau of AIDS, Tuberculosis and Sexually Transmitted Infection, Ministry of Public Health and the Thai Government Pharmaceutical organization (GPO)[19,20] to minimize the variation of cost of ARV drugs. All costs were reported in 2006 Thai Baht, using the Consumer Price Index[21].

Uncertainty analysis

A probabilistic sensitivity analysis, with second-order Monte Carlo technique, was carried out using Microsoft Office Excel 2003[15]. All input parameters were assigned a probability distribution to reflect the feasible range of values that each input parameter could attain[22]. The beta-distribution was the choice of distribution for probability parameters which were bounded by zero and one. The gamma distribution, which ensured a positive value, was modeled for all rates and unit cost parameters. Normality, on the log-odds scale with a covariance matrix and using the Cholesky decomposition, was applied for survival parameters[23]. The simulation chose one value from each distribution simultaneously and calculated cost and effectiveness pairs. This process was repeated 1000 times to provide a range of possible values given the specified probability distributions. The means and standard error (SE) of input parameters are shown in Table 1. The incremental cost and incremental effects were represented visually by using a cost-effectiveness plane and cost-effectiveness acceptability curves based on the concept of net-benefit approach suggested by Stinnett and Mullahy[24] and Briggs *et al*[25]. To quantify the ceiling ratio for the Thai population, although there is no such accepted threshold for adopting health technologies in Thailand, we applied the threshold that is recommended by the commission on Macroeconomics and Health. This suggests the use of three times the gross domestic product (GDP) per capita as the threshold for consideration in developing countries[26]. In addition, this ceiling was used to assess the cost-effectiveness of HIV prevention in Thailand[27]. This would indicate a ceiling value in Thailand of 300,000 Baht per quality-adjusted life years (QALY) based on Thai GDP and population.

Results

Table 2 presents the lifetime-treatment costs and effectiveness of initiating the two different antiretroviral regimens using the health care provider perspective. The lifetime-treatment cost of the patients with baseline CD4 count of 200 cells/mm^3 that started with the EFZ-based regimens, was lower in all age groups compared with those treated by the NVP-base regimen, except for those patients aged 20 years old. It was shown that starting with NVP-based regimens for the patients with baseline CD4 at 200cell/mm^3 offered slightly more LYs gained in all age groups, except patients aged 20 years old, but offered less DALY averted in all age groups.

Table 3 presents the lifetime-treatment costs and effectiveness of initiating NVP-based and EFZ-based regimens for patients aged 38 years (average age of the Thai cohort) with a different baseline CD4 count. It can be seen that starting with EFZ-based regimens was cheaper in all baseline CD4 groups. In terms of effectiveness, starting with EFZ-based regimens offered more LY gained among the patients who initiated the regimen at a low CD4 count baseline (*i.e.* 50 to 100 cells/mm^3). In patients with higher baseline CD4 counts, starting with EFZ-based regimens offered slightly less LY gained compared to NVP-based regimens. However, starting with EFZ-based regimens provided more DALY averted compared to NVP-based regimens in all baseline CD4 groups.

Incremental cost-effectiveness ratios of initiating with EFZ-base regimens compared with NVP-based regimens were presented in Table 4. In patients with a baseline CD4 at 200 cells/mm^3, the incremental costs of providing the EFZ-based regimens as the first option ranged from 6,082,000 Baht per LY gained for

Table 1. Means and standard error (SE) of input parameters

Parameter description	Mean	SE	distribution	Data source
Weibull survival				
Weibull survival in NVP group: death				
Constant value for baseline hazard	-5.0534	1.1441	Lognormal	Thai cohort
CD4 baseline coefficient for baseline hazard	-0.019	0.0061	Lognormal	Thai cohort
Regimen coefficient for baseline hazard	-1.2305	0.5623	Lognormal	Thai cohort
Ln (g)	-0.3856	0.2024	Lognormal	Thai cohort
Weibull survival in NVP group: switching from Reg1 to Reg2				
Constant value for baseline hazard	-6.1716	0.525	Lognormal	Thai cohort
CD4 baseline coefficient for baseline hazard	0.0031	0.0011	Lognormal	Thai cohort
age coefficient for baseline hazard	0.0282	0.0106	Lognormal	Thai cohort
Ln (g)	-0.493	0.0715	Lognormal	Thai cohort
Weibull survival in NVP group: switching from Reg2 to Reg3				
Constant value for baseline hazard	-10.2941	1.2661	Lognormal	Thai cohort
age coefficient for baseline hazard	0.0602	0.0192	Lognormal	Thai cohort
Ln (g)	0.0127	0.1378	Lognormal	Thai cohort
Weibull survival in EFZ group: switching from Reg1 to Reg2				
Constant value for baseline hazard	-7.141	1.2231	Lognormal	Thai cohort
CD4 baseline coefficient for baseline hazard	0.0005	0.0022	Lognormal	Thai cohort
age coefficient for baseline hazard	-0.0021	0.0198	Lognormal	Thai cohort
Ln (g)	-0.1448	0.1524	Lognormal	Thai cohort
Weibull survival in EFZ group: switching from Reg2 to Reg3				
Constant value for baseline hazard	-6.8363	3.0088	Lognormal	Thai cohort
age coefficient for baseline hazard	0.0108	0.056	Lognormal	Thai cohort
Ln (g)	-0.4629	0.4716	Lognormal	Thai cohort
Transitional Probability				
Relative risk of NVP compared to EFZ: Outcome death				
Relative risk of EFZ-based compared with NVP based regimens	1.33	0.499	Gamma	Ref [12]
Annual rate of having complications				
Probability of Meningitis in 1st regimen in NVP-based regimens	0.0196	0.0069	Beta	Thai cohort
Probability of TB in 1st regimen in NVP-based regimens	0.0417	0.0099	Beta	Thai cohort
Probability of MAC in 1st regimen in NVP-based regimens	0.0098	0.0049	Beta	Thai cohort
Probability of Toxoplasmosis in 1st regimen in NVP-based regimens	0.0172	0.0064	Beta	Thai cohort
Probability of CMVR in 1st regimen in NVP-based regimens	0.0245	0.0076	Beta	Thai cohort
Probability of PCP in 1st regimen in NVP-based regimens	0.0294	0.0084	Beta	Thai cohort
Probability of skin reaction grade 2 in 1st regimen in NVP-based regimens	0.1299	0.0166	Beta	Thai cohort
Probability of SJS in 1st regimen in NVP-based regimens	0.0123	0.0054	Beta	Thai cohort
Probability of Hepatitis in 1st regimen in NVP-based regimens	0.0245	0.0076	Beta	Thai cohort
Probability of Hepatotoxicity in 1st regimen in NVP-based regimens	0.0221	0.0073	Beta	Thai cohort
Probability of HighTG in 1st regimen in NVP-based regimens	0.0294	0.0084	Beta	Thai cohort
Probability of Hepatotoxicity in 2nd regimen in NVP-based regimens	0.0025	0.0024	Beta	Thai cohort
Probability of HighTG in 2nd regimen in NVP-based regimens	0.0123	0.0054	Beta	Thai cohort
Probability of HighTG in 3rd regimen in NVP-based regimens	0.0025	0.0024	Beta	Thai cohort

Table 1. Means and standard error (SE) of input parameters (Cont.)

Parameter description	Mean	SE	distribution	Data source
Probability of TB in 1st regimen in EFZ-based regimens	0.0085	0.0085	Beta	Thai cohort
Probability of CMVR in 1st regimen in EFZ-based regimens	0.0085	0.0085	Beta	Thai cohort
Probability of skin reaction grade 2 in 1st regimen in EFZ-based regimens	0.0085	0.0085	Beta	Thai cohort
Probability of HighTG in 1st regimen in EFZ-based regimens	0.1624	0.034	Beta	Thai cohort
Resource cost parameter				
Direct medical care costs i.e. direct costs of treatment				
Monthly Cost of drug 1st regimen in NVP-based regimens	1750	519.221	Gamma	[19-20] and survey
Monthly Cost of drug 2nd regimen in NVP-based regimens	2657	732.8054	Gamma	[19-20] and survey
Monthly Cost of drug 3rd regimen in NVP-based regimens	9552	7000.449	Gamma	[19-20] and survey
Monthly Cost of drug 1st regimen in EFZ-based regimens	3067	537.373	Gamma	[19-20] and survey
Monthly Cost of drug 2nd regimen in EFZ-based regimens	4223	2280.822	Gamma	[19-20] and survey
Monthly Cost of drug 3rd regimen in EFZ-based regimens	9552	7000.449	Gamma	[19-20] and survey
Average cost of Meningitis treatment	14184.125	2199.5206	Gamma	Survey
Average cost of MAC treatment	20048.5	2213.2468	Gamma	Survey
Average cost of Tuberculosis treatment	9266.1538	1162.5913	Gamma	Survey
Average cost of CMV rhinitis treatment	25064	4213.4115	Gamma	Survey
Average cost of Toxoplasmosis treatment	5167.7143	2134.7126	Gamma	Survey
Average cost of PCP treatment	6506.7273	1245.32	Gamma	Survey
Average cost of ADR treatment(skin grade 2)	437.7925	184.1442	Gamma	Survey
Average cost of ADR treatment(SJS)	3420	346.1545	Gamma	Survey
Average cost of ADR treatment(Hepatitis)	1797.4	194.2507	Gamma	Survey
Average cost of ADR treatment (Hepatotoxicity)	6159.375	2402.079	Gamma	Survey
Average cost of ADR treatment (HighTG)	3650	1245.52	Gamma	Survey
Utility parameter				
Disability weight for AIDS without complications	0.5600			[17]
Disability weight for AIDS with meningitis & toxoplasmosis	0.9617			[17]
Disability weight for AIDS with TB	0.6898			[16]
Disability weight for AIDS with MAC and PCP	0.8064			Expert opinion
Disability weight for AIDS with CMVR	0.7492			[17]
Disability weight for AIDS with grade 2 skin reaction	0.6150			Expert opinion
Disability weight for AIDS with SJS&TEN	0.7593			Expert opinion
Disability weight for AIDS with Hepatitis	0.6524			[17]
Disability weight for AIDS with Hepatotoxic & cirrhosis	0.7092			[16]
Disability weight for AIDS with HighTG	0.6150			Expert opinion

patients aged 20 years to 28,772,000 Baht per LY gained for patients aged 30 years. However, in older patients, the incremental costs of providing the EFZ-based regimens as first option decreased from 7,967,000 to 15,510,000 Baht per LY gained. In terms of incremental costs per DALY averted, starting with EFZ-based regimens proved less costly with more DALY averted in all age groups except for those aged

Table 2. Lifetime cost and the effectiveness of starting with NVP-based and EFZ-based regimens classified by age-group (a baseline CD4 count at 200cell/mm^3)

Age (year)	Lifetime cost*		LY gained		DALY averted	
	NVP-based regimens	EFZ-based regimens	NVP-based regimens	EFZ-based regimens	NVP-based regimens	EFZ-based regimens
20	1,744,000	1,954,000	24.10	24.13	6.08	6.25
30	1,969,000	1,758,000	22.10	22.09	5.82	5.98
40	2,027,000	1,532,000	19.68	19.62	5.45	5.59
50	1,892,000	1,277,000	16.70	16.66	4.90	5.02
60	1,560,000	982,000	13.26	13.21	4.14	4.23

* Cost are given to nearest 1,000 baht, 2006 price level

Table 3. Lifetime cost of starting with NVP-based and EFZ-based regimens classified by baseline CD4 group (age at initial of treatment at 38 years-old)

Baseline CD4 count(cell/mm^3)	Lifetime cost*		LY gained		DALY averted	
	NVP-based regimens	EFZ-based regimens	NVP-based regimens	EFZ-based regimens	NVP-based regimens	EFZ-based regimens
50	1,521,000	1,349,000	17.12	17.25	4.80	4.95
100	1,736,000	1,514,000	19.07	19.08	5.26	5.41
150	1,882,000	1,535,000	19.82	19.81	5.45	5.59
200	2,051,000	1,595,000	20.22	20.19	5.54	5.69
250	2,130,000	1,624,000	20.37	20.34	5.58	5.72

* Cost are given to nearest 1,000 baht, 2006 price level

Table 4. Incremental cost-effectiveness ratio (ICER) of starting with EFZ-based regimens compared with NVP-based regimens classified by age group (baseline CD4 count at 200cell/mm^3)

Age (year)	Incremental cost-effectiveness ratio (ICER)	
	Baht per LY gained	Baht per DALY averted
20	6,082,000	1,200,000
30	28,772,000	Dominate (1,342,000)
40	7,967,000	Dominate (3,677,000)
50	15,510,000	Dominate (4,900,000)
60	10,578,000	Dominate (5,912,000)

( ) = negative ICER

20 years old.

On the other hand, the group of patients aged 38 years at initial treatment, at the low level of CD4 (50 and 100 cells/mm^3), starting with EFZ-based regimens, dominated NVP-based regimens in terms of baht per LY gained (Table 5). In patients with a high baseline CD4 level, the incremental costs of providing EFZ-based regimens as first option ranged from 33,509,000 baht per LY gained for patients with a baseline CD4 at 150 cell/mm^3 to 13,859,000 Baht per LY gained for patients with a baseline CD4 at 250 cells/mm^3. In terms of incremental costs per DALY averted, starting with EFZ-based regimens proved less costly with more DALY averted at all baseline CD4 levels (Table 5).

Uncertainty analysis

Uncertainty in cost-utility analysis classified by age-groups

The cost-effectiveness planes of the incremental costs and DALY averted for starting with EFZ-based regimens compared with NVP-based regimens, classified by age group, are presented in Fig. 2(a-e). The figures indicate that for patients who had CD4 200 cell/mm^3 at the baseline, starting with EFZ-based

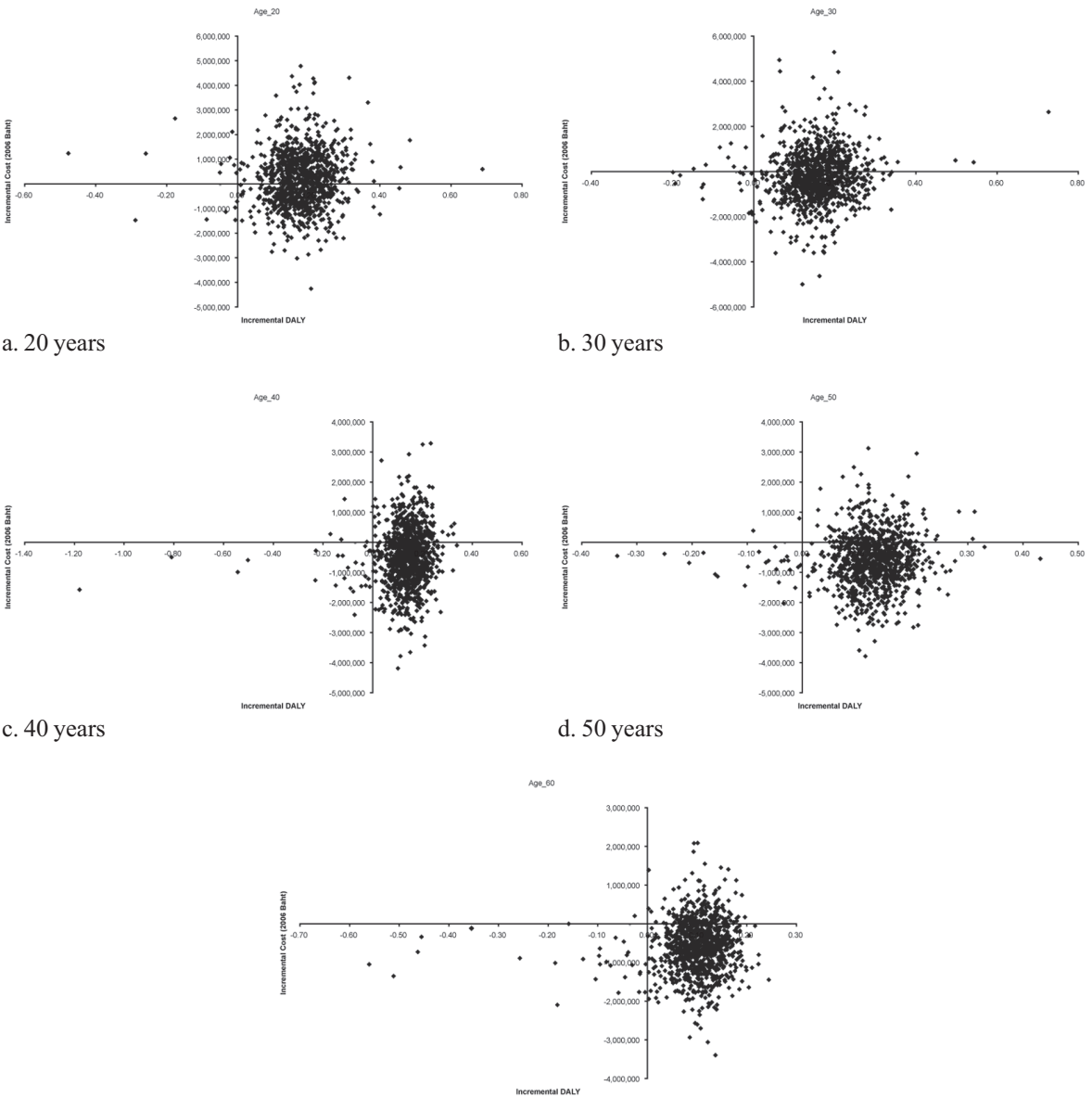


Fig. 2 Cost effectiveness plane of disability-adjusted life years (DALY) averted of EFZ-based regimens compared with NVP-based regimens classified by age group

regimens yielded more DALY averted than NVP-based regimens. However, the differences in the treatment costs between the two regimens depended on the patient's age. In younger age groups (*e.g.* 20 years old), introducing EFZ-based as first line regimens was more expensive than NVP-based regimens. In contrast, in middle to old age groups (*e.g.* 30 to 60 years old), introducing EFZ-based as first line regimens was cheaper than NVP-based regimens.

The cost effectiveness acceptability curve of DALY averted presented in Fig. 3 reveals that with no extra budget available it is more likely that starting with EFZ-based regimens is a preferable choice, except in patients aged 20 years. However, in this age-group, the higher the WTP threshold the lower the likelihood that an NVP-based regimen is still cost effective. Starting with

Table 5. Incremental cost-effectiveness ratio (ICER) of starting EFZ-based regimens compared with NVP-based regimens classified by baseline CD4 group (age at baseline treatment at 38 years)

Baseline CD4 count (cell/mm^3)	Incremental cost-effectiveness ratio (ICER)	
	Baht per LY saved	Baht per DALY averted
50	Dominate (3,133,000)	Dominate (1,144,000)
100	Dominate (19,454,000)	Dominate (1,460,000)
150	33,509,000	Dominate (2,344,000)
200	15,881,000	Dominate (3,149,000)
250	13,859,000	Dominate (3,603,000)

( ) = negative ICER

EFZ-based regimens in this age group is preferable when the WTP is above 1,200,000 Baht/DALY averted. Given a maximum acceptable WTP of 3 times per capita GDP or 300,000 Baht/DALY averted, starting with EFZ-based regimens is cost effective in all age groups except those who were 20 years old at baseline treatment when a NVP-based regimen is the preferred choice.

Uncertainty in cost-utility analysis classified by baseline CD4 groups

The incremental cost per DALY averted for those patients aged 38 years old indicated that starting with EFZ-based regimens yielded more DALY averted than NVP-based regimens in all age-groups (Fig. 4(a-e)). However, the differences in the treatment costs depended on the baseline CD4 count. With a low level of baseline CD4 (e.g. 50 cells/mm^3), introducing EFZ-based regimens as first regimens was more costly than NVP-based regimens. In contrast, with a higher level of baseline CD4 (*e.g.* 100 to 250 cells/mm^3) introducing EFZ-based regimens as first-line regimens was less costly than NVP-based regimens. The findings of the cost-effectiveness acceptability curve presented in Fig. 5 shows that for patients who were 38 years old at baseline treatment, starting with EFZ-based regimens dominated NVP-based regimens for all baseline CD4 counts.

Discussions and Conclusion

This study explored the value for money of initiating an EFZ-based regimen for the treatment of PLWHA at a CD4 count less than 250 cells/mm^3 compared to the current practice that uses an NVP-base regimen as the first line treatment. The patient's age and the levels of CD4 count were taken into account when considering additional costs and additional effectiveness in terms of DALY averted from the new regimen. Although the drug cost of initiating an EFZ-based regimen was higher in the model, the results indicated that starting with EFZ-based regimens was more cost effective for all baseline CD4 counts, and in

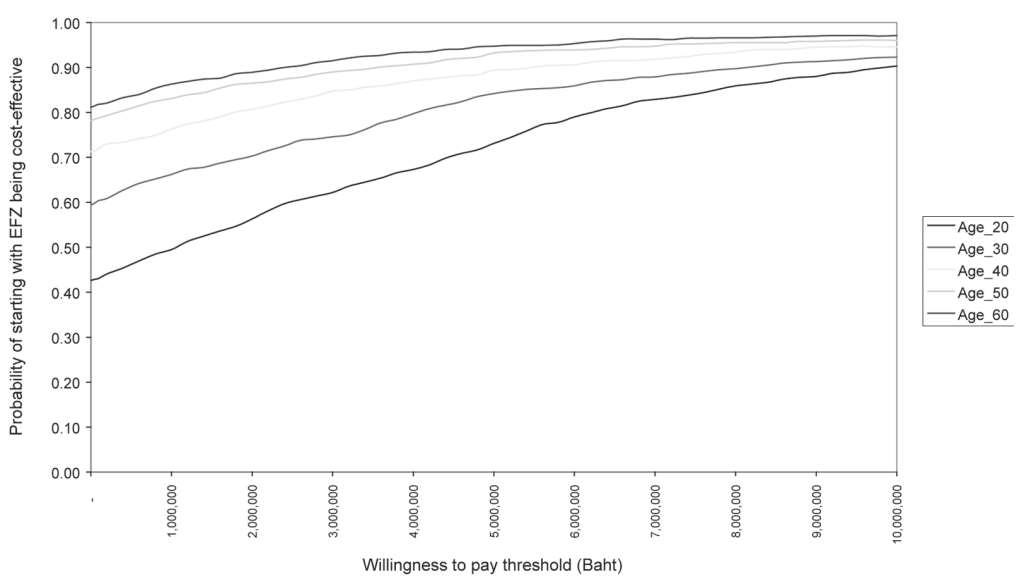
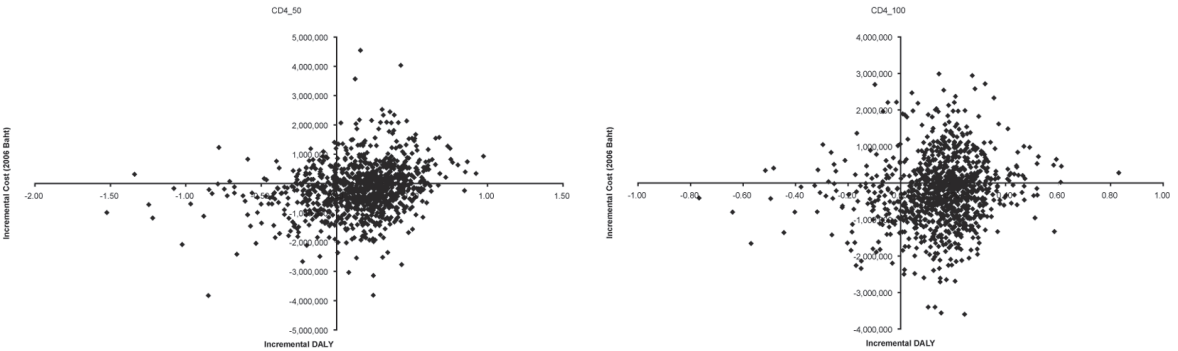
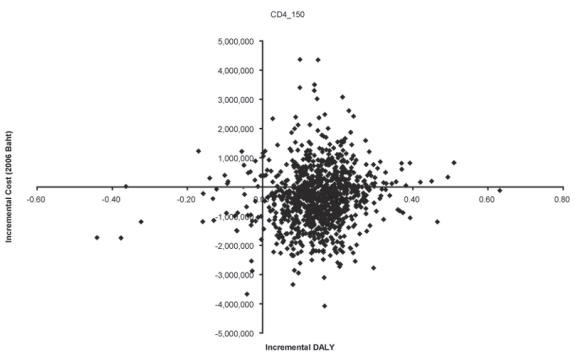


Fig. 3 Cost effectiveness acceptability curve of DALY averted of EFZ-based regimens compared with NVP-based regimens classified by age groups

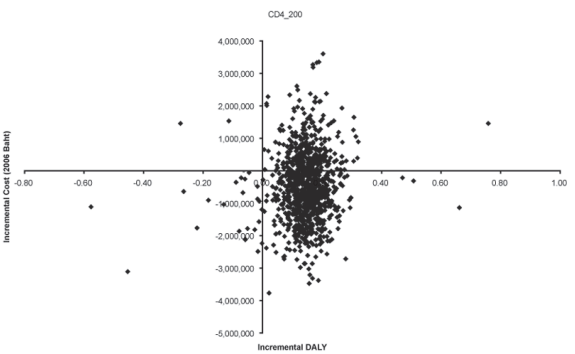


a. 50 cell/mm^3

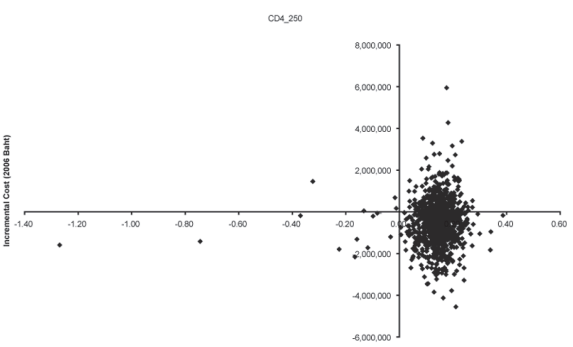
b. 100 cell/mm^3



c. 150 cell/mm^3



d. 200 cell/mm^3



e. 250 cell/mm^3

Fig. 4 Cost effectiveness plane of DALY averted of EFZ-based regimens compared with NVP-based regimens classified by baseline CD4 group

all age groups, except in the young patients i.e. those patients aged 20-29. These findings suggest that EFZ-based therapy should be used as the first line regimen for treating PLWHA.

These results are in agreement with the study conducted by Freedberg et al.[28]. The two studies found that the baseline CD4 cell count was the most important determinant concerning the costs, clinical outcomes, and cost effectiveness of HIV/AIDS treatment. Although the national guidelines for HIV/AIDS treatment stated that a patient with a CD4 count less than 200 cell/mm^3 must receive HAART, in reality many eligible patients do not have access to medications. The findings from this study showed that the higher initial CD4 cell count the better the effectiveness of the treatment in terms of LY gained, as well as DALY

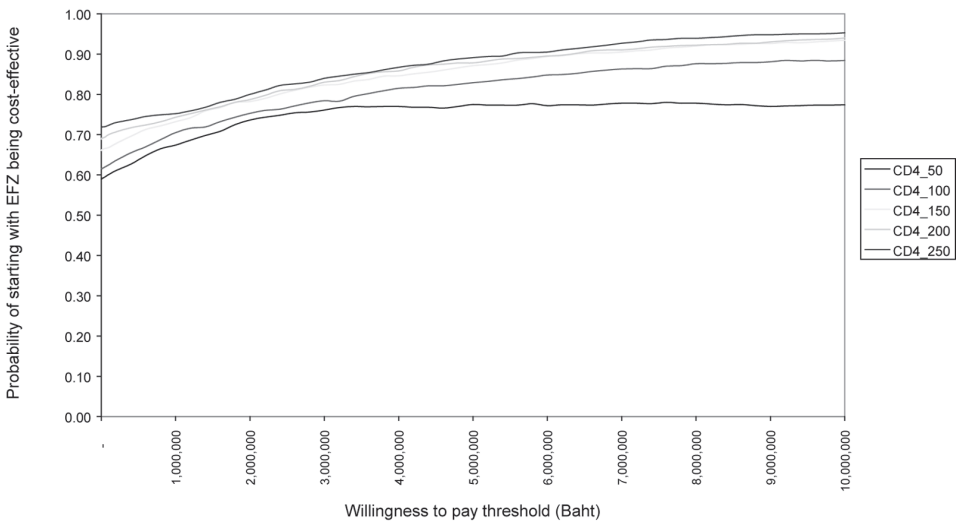


Fig.5 Cost effectiveness acceptability curve of DALY averted of EFZ-based regimens compared with NVP-based regimens classified by CD4 at baseline group

averted. Thus, the problem of the delay of treatment must be seriously considered by decision-makers. It also raised another question whether to start the treatment at an earlier stage, *i.e.* a CD4 cell count of 250 cells/mm^3, than that indicated in the current guidelines, a CD4 cell count of 200 cells/mm^3. It should be noted that the Thai government issued compulsory licensing (CL) for EFZ in November, 2006[29] which would substantially affect the treatment cost of EFZ-based regimens and might lead to a more preferable option to the initial treatment with an EFZ-based regimen.

There were some limitations regarding the availability of the data used in the model. This study intends to conduct subgroup analyses based on the level of CD4 cell count at the start of treatment and the patient's age. As a result, it was carried out by modelling CD4 level- and age-specific survival from the three-year cohort data, which was a relatively short period of the follow-up time, to determine the difference in mortality between the two treatment modalities. Based on the data, none of the patients who started with EFZ were dead within this follow-up period. The mortality rate of patients with EFZ-based regimen was, therefore, adjusted using the relative mortality between EFZ-based regimens and NVP-based regimens from the literature and the baseline mortality of the cohort patients with NVP-based regimens. It is also noteworthy that the relative mortality was derived from the Cochrane database, where the systematic search and meta-analysis were properly employed.

Furthermore, the disability weights used to estimate DALY gained from this study were derived from different sources[16-17] and where there was no disability weights available in the literature for some health states, e.g. Steven Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN) , expert opinions were sought to elicit the weights. This limitation should be treated with care, and future studies to determine the missing disability weights are welcome.

Competing interests

The authors declare that they have no competing interests.

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การประเมินต้นทุน-ประสิทธิผลของการเริ่มต้นใช้ยาต้านไวรัสเอดส์ด้วยสูตรที่มียาเอฟฟาวิเรนซเป็นองค์ประกอบเปรียบเทียบกับสูตรที่มียาเนวิราปีนเป็นองค์ประกอบในประเทศไทย

อุษาวดี มาลีวงศ์, วิทยา กุลสมบูรณ์, ยศ ตีระวัฒนานนท์

วัตถุประสงค์: *เพื่อประเมินต้นทุน-อรรถประโยชน์ของการเริ่มต้นการรักษาด้วยยาต้านไวรัสเอดส์สูตรที่มียาเอฟฟาวิเรนซเป็นองค์ประกอบเปรียบเทียบกับยาสูตรที่มียาเนวิราปีนเป็นองค์ประกอบสำหรับผู้ติดเชื้อและผู้ป่วยเอดส์ในประเทศไทย*
วัสดุและวิธีการ: *การศึกษานี้ใช้มุมมองของผู้ให้บริการ แบบจำลอง Markov ถูกพัฒนาขึ้นสำหรับผู้ติดเชื้อและผู้ป่วยเอดส์ในประเทศไทยที่มีอายุระหว่าง 15 ถึง 65 ปี ตัวแปรที่ใช้ในแบบจำลองมาจากการศึกษาไปข้างหน้าในโรงพยาบาลศูนย์ 4 แห่งในประเทศไทย ในการศึกษาทำการประเมินผลกระทบของความไม่แน่นอนของตัวแปรต่าง ๆ*
ผลการศึกษา: *สำหรับผู้ป่วยที่มีค่าซีดีโฟร์เริ่มต้นแตกต่างกันการเริ่มต้นการรักษาด้วยยาต้านไวรัสสูตรที่มียาเอฟฟาวิเรนซเป็นองค์ประกอบจะมีความคุ้มค่ามากกว่ายาต้านไวรัสสูตรที่มียาเนวิราปีนเป็นองค์ประกอบ ในทุก ๆ ค่าซีดีโฟร์ หากกำหนดให้ประเทศไทยมีค่าสูงสุดที่ยอมจ่ายเท่ากับ 300,000 บาทต่อ 1 ปีสุขภาวะที่ปรับด้วยความบกพร่องทางสุขภาพที่กลับคืนมา การเริ่มต้นการรักษาด้วยยาต้านไวรัสสูตรที่มียาเอฟฟาวิเรนซเป็นองค์ประกอบ จะมีความคุ้มค่ามากกว่ายาต้านไวรัสสูตรที่มียาเนวิราปีนเป็นองค์ประกอบ ในทุก ๆ ค่าซีดีโฟร์เริ่มต้นที่ต่ำกว่า 250 เซลล์ต่อมิลลิลิตร และในทุกกลุ่มอายุยกเว้นในกลุ่มอายุ 20 ถึง 29 ปี*
สรุป: *การศึกษานี้บ่งชี้ว่าการเริ่มต้นการรักษาด้วยยาต้านไวรัสสูตรที่มียาเอฟฟาวิเรนซเป็นองค์ประกอบจะมีความ คุ้มค่ามากกว่ายาต้านไวรัสสูตรที่มียาเนวิราปีนเป็นองค์ประกอบ และควรเสนอให้ใช้ยาต้านไวรัสสูตรที่มียาเอฟฟาวิเรนซเป็นองค์ประกอบเป็นยาสูตรเริ่มต้นในการรักษาผู้ติดเชื้อและผู้ป่วยเอดส์ในประเทศไทย*