Title: Cost effective analysis Long Lasting Insecticide Treated Nets in Nepal

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Acronyms

NMP	Nepal Malaria Program
API	Annual Parasite Incidence
DALY	Disability Adjusted Life years
EDCD	Epidemiology and Disease Control Division
HMIS	Health Management Information System
INGO	International Non-Governmental Organization
IRS	Indoor Residual Spraying
ITN	Insecticide Treated Nets
LLINs	Long –Lasting Insecticide Nets
MDG	Millennium Development Goal
MOHP	Ministry of Health and Population
NMP	Nepal Malaria Program
PSI	Population Services International
QUALY	Quality Adjusted Life Years
SEA	South East Asia
UNICEF	United Nation International Children's Education Fund
WHO	World Health Organization
WMR	World Malaria Report

Abstract

Mosquitos bite causes malaria. Death tolls due malaria is significant in Sub-Saharan countries. The effect of Malaria is huge burden to Nepal as well. There are various measures to control effect of it. One of the latest measure recommended by the WHO is Long-Lasting Insecticide Nets use in malaria infected area. This paper measures the cost-effectiveness of the LLINs use and life year saved due to the intervention in Nepal. Data were collected from various sources including published and unpublished papers. We have used Tree Age Pro software to measure cost and effectiveness of the LLINs intervention. Markov model is used to estimate repeated jump cycles from one states to another. Despites the geographical barriers, low level of sanitation, higher distribution cost and presence of malaria throughout the year, the intervention is cost effective and highly recommended for further continuation.

1. Introduction

1.1 Background

Malaria is caused by Plasmodium parasites. The parasites are spread to people through the bites of infected female *Anopheles* mosquitoes, called "malaria vectors." There are 5 parasite species that cause malaria in humans. It is found mainly in temperate zone such as sub-Saharan country, South Asia and some Latin America. More than 40 percent of the world's population lives in countries where malaria is rampant ("How Does Malaria Impact Communities?" 2016). But the impact malaria has on these countries gone beyond the health of its people – it costs billions of dollars in treatment and lost productivity each year and putting pressure in the national economy.

Malaria decreases gross domestic product in countries with high disease rates. Over the long term, these economic losses add up, resulting in substantial differences in GDP between countries with and without malaria, particularly in Africa. This presents an enormous challenge to efforts to lift people out of poverty.

According to World Malaria Report 2015, approximately 3.2 billion people – nearly half of the world's population – were at risk of malaria. Death due to malaria is accounted as 438,000 (World Health Organization, 2015) and mostly in Africa (88%). However, Asia, Latin America, and, to a lesser extent, the Middle East, are also at risk. It is found that 95 countries and territories had ongoing malaria transmission. Recent report reveals that mortality due to malaria is declined to 49% since 2000 in Africa. In the malaria affected countries, WHO has recommended a universally distributed long-lasting insecticide-treated bed nets (LLINs) and more than 56 % population has access to the LLINs compared to 2000 (WHO, 2016). 254 million

Insecticide Treated Nets, most of them LLINs are distributed in Sub-Saharan countries during 2008 and 2010 (Aregawi et al., 2010). An estimate further reveals that of 663 million cases averted due to malaria, 69% were attributed to use of LLINs. There is 75% reduction in malaria cases during the last 10 years among 57 countries (WHO,2016). Because of retreatment of net half yearly, new strategy is applied to reduce the cost of retirement of nets and WHO has recommended to use of LLINS.

During the 2000 – 2015, there is 55.3% decline in malaria cases (WHO, SEARO, 2015). Global Fund is supporting financially to malaria control program to offer services to 22.8 million people in 65 district in Nepal (WHO, SEARO, 2015)

1.2 Country Context and Burden of Malaria

Nepal is landlocked country with a population of nearly 28 million populations of which 80% live in rural area. By region it has Himal, Mountains and Terai. Mountans and Terai are mainly affected by malaria. Bulk of population (48.4%) live in Terai compared to 44 % in Hills and mountains. The hierarchical health system of Central, regional, district and local level is adopted within the MOHP in Nepal. The department of health services is responsible for preventive, curative and palliative health services. Under the department, the disease control section is responsible for vector-borne diseases such as malaria.

Out of 75 districts in Nepal, malaria is endemic in 65 district in and about 73% of the population are at malaria risk (Government of Nepal Ministry of Health and Population, n.d.). Over 5.9 million population live in high risk area of 13 districts. Age wise 73% cases were among people greater than 15 years old, however trend of malaria case is decreasing steadily due to various reasons among which LLINs is most efficient one. In 1985 there were 42, 321 laboratory confirmed malaria cases were recorded and heavily declined to 3,115 in 2010 (Nepal malaria Strategic Plan 2011-2016). The following table shows distribution of malaria throughout year.

Normally, spreading of mosquitos goes very fast in rainy season of summer, however mosquitos remains alive even in the winter and cause malaria. The following provides sufficient evidence that mosquitos can cause malaria even in the winter season in Nepal. The table shows mountains and hills are affected more than other reasons.

Table1: Distribution of malaria cases in any month

	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
Plain	43	43	50	50	84	88	128	123	81	87	68	38
Moderate	115	103	118	155	174	196	315	266	201	176	161	84
Highland	5	6	8	11	16	26	31	13	14	10	9	5
Country	163	152	176	216	273	310	475	403	295	273	238	127

Source: Nepal Strategic Plan 2011-2016 (MOHP)

One major cause of higher cases of malaria is that, there is higher population in the hills and higher temperature as well. Because of this, prevalence of malaria is higher in the hills and mountains.

Table 2: Population and level of malaria risk

Risk Level	High Risk	Moderate risk	Low Risk	No Risk	total
Population	5,984, 761	8,245,575	6,126,677	0	20, 357, 013

Source: Nepal Strategic Plan 2011-2016 (MOHP)

The bed net prevents individuals from mosquitos biting while, mostly sleeping inside it and reduces the chance of malaria. This paper tries to find cost- effectiveness of LLINs in Nepal by using Tree Age pro software. There are various types of bed nets in respect of lifespan but we are considering only LLINs for this paper keeping other as limitations to it, however some retreat able nets are available need to retreated in every 6-12 months which is not applicable in all region of Nepal. In some places Indoor Residual Spraying (IRS) is applied to reduce malaria compared to use of conventional bed nets in place. But again this is beyond the scope of this paper.

Cost Associated to Malaria

The health costs of malaria include both personal and public expenditures on prevention and treatment. In some malaria-endemic countries, the disease accounts only for preventive and in some countries it has taken account of curative treatment also. The following table shows malaria related cost in some affected countries.

Table 3: Expenditure Related to malaria program

Types of Expenditure	Percent
Public Health Expenditure	Up to 40
Inpatients Hospital Admission	30 to 50
Outpatients Health Clinic visits	Up to 60

- Source: ("How Does Malaria Impact Communities?" 2016)

According to a report from UNICEF, average cost of insecticide per annum is estimated as US$158, 646 in 2004. The LLINs distributed to 1209, 322 populations during 2006 – 2010, costing annually US$ 4.8 million approximately (unit price of LLINs US$4 (Bhatia, Fox-Rushby, & Mills, 2004). Malaria takes not only in lives lost, but also in medical costs associated to it and reduces economic outputs. The direct and indirect annual costs of malaria in Nepal are estimated to be more than US$2 billion, according to the WHO. In this way malaria is considered as one leading cause to poverty.

Therefore, Nepal has been fighting against malaria since long and has achieved the UN MDG target to reduce malaria morbidity by 2010. The LLINs seems cost effective at maximum of US$1600 per under -5 death averted (UNICEF Supply Division, 2013)

The Ministry of Health and Population, with the support of its partners, has implemented a strong malaria control program, steadily improving the coverage and introducing long lasting insecticide-treated nets. The National Malaria Control Program has launched long-lasting insecticidal nets (LLINs) to reduce the transmission of malaria as per WHO guidance and Global Fund financial support for Distribution and promotion of the use of LLINs. Since 2005, 3.3 million LLINs have been distributed. The national LLIN distribution policy 2005 recommended one LLIN per household in endemic district but it is changed as per two persons each house. By the end of 2013, the estimated LLIN coverage was 100% of target population in high- and moderate-risk areas (UNICEF, 2015)

The frequency of the malaria remains higher for people living in risk area and it is difficult to calculate cost related to it in simple way. There may be more than one transition chance of jump from a state such as from healthy to death or healthy to malaria. In this scenario, Markov mode take account of to calculate combined effect and cost related to each jump state. An individual can be in any of three states: healthy, sick or dead. In case of malaria, sick or healthy person can be in either states in any time and hence Markov model takes account of those state with associated transition probabilities. Malaria can occur at any time during the summer or start of summer till end of summer, we assume it will take place throughout the year. Insecticide-treated bed-nets have shown to reduce malaria cases by 50% (Folashade B. Agusto[a,,] ,et el) ; however, difficulty with them is to retreat and improper handling and human behavior can diminish their effectiveness. Even then they have positive impact in reducing malaria. The results show that if 75% of the population were to use bed-nets, malaria could be eliminated (Folashade B. Agusto[a,]) We are considering the life year averted as effectiveness and rest is beyond the limit of this paper. It is found that from a study in Congo that cost-effectiveness was found to be 15.70 per life year saved (Becker-Dreps et el). The use of LLINs or sleeping inside the bed nets not only save from malaria but also from the snake bite (Chappuis, François, et et)

Methodology

In order to complete this paper, we collected data from WHO; World Malaria Report, EDCD and INGO such as Population Services International (PSI), World Bank data-base, Health Management Information System (HMIS), Department of Health Services, Nepal Government, Population Monograph of Nepal (Central Bureau of Statistics). The data were collected for both conventional bed net and Long Lasting Insecticide Nets (LLINs). Cost is prorated to number of malaria infected population and compared with some other published and unpublished papers in respect of the LLINS and their effects in various countries. We calculated year of life saved due malaria using conventional bed nets against the LLINs in Nepal. The Potential Life Year (PLY) gained or saved due to use of the LLINs intervention is also calculated by using Tree Age software program. Similar method was applied to calculate the PYLL and due to conventional bed nets compared to LLINs in Nepal. People are suffering from malaria since long time, we are considering the project for 25 years and calculating cost effectiveness for over 25 years as we have assumed that there is regular distribution of LLINs throughout the year that constitutes 100 cycles where we have used Markov model. There is cost associated to conventional bed nets is lower than the cost attached to LLINs.

Since life span of LLINs is 3 years on average and malaria incidence is thought out the year (table 1), we assume that program distribute LLINs in each three months. Again we assume that there is no retreated net facility in the conventional bed nets, (which need 6-12 months retreated) (Pulkki-Brännström AM1 et el) and we just consider these nets as traditional nets only. We put all the cost from the literature review and some assumption in context of Nepal. For the cost we have taken cost from literature review and compared in country context. For effectiveness we are only consider life year saved even though there is chance of Disability Adjusted Life Year (DALY) averted or improve in Quality Adjusted Life Year (QUALY).

Further we are using a Markov chain (discrete-time Markov chain) for transitions from one state to another, among a finite or countable number of possible states. Since re-occurrence of malaria happens to those who are already recovered or can happen to those who are under recovery, Markov model take account of these under repeated number of cycles and calculate cost and effectiveness of the whole program for any number of cycles. In order to calculate cost, we multiply cost of intervention or event associated with any transition probabilities and sum them all up. Transition probabilities can be represented as in the table below. Suppose that we consider there are three state: Health, Sick and Dead due to malaria. The table below shows transition probability from one state to another state such as health to sick or healthy to dead. This is shown in the table below.

Table4: Transition states related to probabilities

Transition from one state to another			
Transition from State to state (per unit time)	**Healthy**	**Sick**	**Dead**
Healthy	Probability of being Healthy	Probability of being Healthy to sick	Probability of being Healthy to dead
Sick	Probability of being sick to healthy	Probability of being sick to sick	Probability of being sick to dead
Dead	Probability of being dead to healthy	Probability of being dead to sick	Probability of being dead to dead

Since this is a vector array, we use calculation as columns multiplied corresponding elements in the rows and sum them together as used multiplication of vectors in mathematics.

Valuing Outcomes

For valuing the program cost and effectiveness, cost is multiplied by corresponding different transition probabilities and sum them up together. Similar is case for the effectiveness. Under Markov Model, we assume that transition probability depends only on current health state residence and not on the past health states. The following formula is used to calculate cost and effectiveness.

Total Cost =Σ(ProbH*cH+(ProbS*cS) +(probD*cD)), Similarly for the effectiveness, where c= cost, H = healthy, S= Sick and D=dead.

Total Effectiveness(E) =Σ(ProbH*eH+(ProbS*eS) +(probD*eD)), where e= effectiveness.

Individuals are always in one of a finite number of states. Events are modeled as transitions from one state to another and time spent in each state determines overall expected outcomes. Living longer without disease yields higher life expectancy and quality of adjusted life expectancy and saves year of life. Therefore, bed-net prevent individuals from malarial death and increase life expectancy. During each cycle of the model, individuals may make a transition from one state to another. But if bed net is provided, there remains higher probability of remaining in healthy state as well as further recovery from clinical malaria and hence reduce death. Therefore, bed net program is found cost effective in Nepal as many countries in Sub Sahara. For sensitivity analysis, we have applied one-way sensitivity analysis, calculated by using coverage area and cost attached to it by using tree age software

Markov Tree

We designed Markov tree for LLINs bed net malaria. For this we defined the three health states (Healthy, Sick and Dead), define all the variables and probabilities and then assign unit cost for each state and corresponding outcomes in the tree diagram as shown in the Appendix. The defined variables, probabilities, cost per unit in the Markov Node and trench applied to Tree Age software to generate cost effective analysis result. Similarly, incremental cost and effectiveness is calculated and fitted in the Tree Age to run complete program and get sensitivity analysis. Again, we compare the cost effectiveness with GDP per capita. If cost effective ratio is less than 3 times of GDP it is considered to be cost effectiveness.

Result

Transition Probabilities for Status Quos - Conventional Bed Nets

The following table shows transitional probabilities for status –quos of using conventional bed nets available in Nepal and their effects again malaria. There is 60% chance of remaining in healthy state compared to jump into sick from healthy is 25% and into dead as 15%. Jump probability from sick to heathy is found as 70% compared to remain in the same sick state is 20% and there is 10% chance that people will die from malarial sickness.

Transition Probabilities

Table6: Transition probabilities for status-quos

Transition probabilities from	Healthy	Sick	Dead
Healthy	0.60	0.25	0.15
Sick	0.70	0.20	0.10
Dead	0.00	0.00	1.00

In comparison to status –quos, transition probabilities of the intervention of using LLINs is mentioned table below. There is 88% chance of remaining in healthy state compared to jump into sick from healthy is 8% and into dead as 4%. Jump probability from sick to heathy is found as 80% compared to remain in the same sick state is 15% and there is 5% chance that people will die from malarial sickness

Table6: Transition probabilities for the intervention (LLINs)

Transition probabilities from	Healthy	Sick	Dead
Healthy	0.88	0.08	0.04
Sick	0.80	0.15	0.05
Dead	0.00	0.00	1.00

Program Cost: We have found following cost in relation to intervention and status-quos.

Table 7: Program Cost for LLINs and Conventional bed nets

Items	Cost for Intervention	Cost for Status Quos
Net Cost	5.71	4
Transportation cost	1.05	0.50
Storage cost	0.5	0
Distribution	0.2	0
Monitoring cost	0.6	0
BCC cost	0.3	0
Training cost	1.2	0
Administrative cos t	0.1	0
Salary	2	0
Utility Cost	0.05	0
Mass Bidding cost	0.01	0
Total Cost per Bed Net **Difference = 6.51**	11.01	4.50

Previous studies show that the LLINs are cost effective if their net unit price is at most US$1.5 more than the conventional nets. On an average lifespan of net is of 3 years and each one-year life span increased is associated with US$1 is also cost effective. On an average conventional net costs US$4 and LLINs cost on average US$5, on top of this there is additional cost of transportation as US$1.5. Again use of net is reached to 80% coverage of population among 25 malaria affected countries, mostly used by under age-5. Price depends on various factors and countries so it is difficult to stick at the constant price. According to WHO Global Price list (WHO

WMR, 2015) provided by suppliers, it is estimated that on average the price of LLINs range from US$3.3 to US$7.9 for which conventional net cost is found range around US$4.50. Again this depends on the quantity and quality of the LLINs but we are considering on the average quality and quantity. In conclusion we are considering annual cost per LLINs is US$1.71 compared to base case as zero.

Effectiveness and Coverage

In community-wide trials in several African settings, ITNs have been shown to reduce under-5 deaths from all causes by about 20% [4-8]. A research from PubMed reveals that, there is 86% reduction in the incidence of malaria if we use LLINs.

Result from Tree Age

Table 8: Result of cost effective from Tree Age

Strategy	Cost	Incr Cost	Eff	Incr Eff	Incr C/E	NMB	C/E
Excluding dominated							
Status quo	7.76		1.56			-7.76	4.97
intervention	285.23	277.47	5.77	4.21	65.84	285.23	49.39
All							
Status quo	7.76	0	1.56	0	0	-7.76	4.97
intervention	285.23	277.47	5.77	4.21	65.84	285.23	49.39
All referencing common baseline							
Status quo	7.76		1.56			-7.76	4.97
intervention	285.23	277.47	5.77	4.21	65.84	285.23	49.39
All by Increasing effectiveness							
Status quo	7.76		1.56			-7.76	4.97
intervention	285.23		5.77			285.23	49.39

Fitting the above transition probabilities for both status-quos and intervention, related cost assuming, there are 100 cycles and no amortization but 3% discount rate applied to the calculation, we have following result. The result shows that there is higher cost and effectiveness. If there is any threshold for the for the LLINS say US$50 per life year saved, then the LLINs intervention is cost effective. Under the status-quo cost-effective ratio is only

US$4.97 but for the intervention it, is US$49.39 as mentioned in the following table

One study in Gambia shows that cost implementation, cost effective ratio per death averted was US$471 per death compared to cost per discounted life year gained was US$31.50.

Sensitivity Analysis

if we decrease the incremental cost to US$3 then the cost effective ration is $47.04 (decreased) for the intervention against the status-quos for which cost effective ration is found as $18. In similar fashion we can calculate other sensitivity. Other way of doing it is increase coverages.

4. Discussion

The paper shows the impact of the LLINs in reduction of chance of malarial cases and related death in Nepal. It also shows the effectiveness of LLINS in saving life years compared to conventional bed nets. The LLINs is cost effectiveness even for at the worst case scenario of 40 percent of the effectiveness level of the program. On the other hand, the program substantially has affected the overall malarial impact coverage. It is reported that 92 percent of the population is found covered with effectiveness level of up to 88% in some district (NMR, 2014) when the outcome level indicators of the malaria cases were compared with use of conventional bed nets. The intervention is remarkably significant in reducing malarial cases and more demand in use of the LLIN.

Since there are 6 transition probabilities associated with malaria cases and it is very difficult to find exact rate of increment in healthy life from either healthy state or from sick state. Therefore, it is hard to stick with the program result as there may be some other weakness to the previous report or other error to estimate. In relation to transition probabilities, costing is very high and again we can adjust cost to some extent in order to test effectiveness of the intervention. The cost we have assumed is worse case scenarios. We can set different reduced cost in relation to transportation and training cost. If this is going to happen then program cost is going to lower as well and there is lower cost effectiveness of intervention.

Because of the distribution channel and management there is increase in availability of LLINs This is one of the reason in significant change in use of LLINs. After running the Tree Age software, the LLINs intervention is highly cost effective as it is less than per capita GDP. There is only US$66 incremental cost per life gained due to use of LLINs in Nepal. From the cost-effectiveness point of view, any intervention with a cost less than three times the GDP per capita during the same period is considered as a cost effective (WHO). As GDP per capita is US$700 in Nepal during the same period, the intervention is highly cost effective

The limitations to the intervention includes; there may be other effects of the intervention in the community for example maternal health services than only averting deaths or saving life more years or saving malaria related cost.

The estimations of other effects of intervention like raise in awareness, improved quality of care etc. were outside of the scope of the study. Also, other associated costs which were not made available and any hidden costs are not included. Further there is economic benefits in the society by averting the death which is also not considered in the study.

If we reference of study in Congo, LLINs intervention is found cost effective at the UD415.70 life year saved. Then our study is highly cost effective.

5. Conclusion

The intervention is highly cost-effective at the higher effectiveness level of 88 successful in preventing from malarial compared to conventional bed nets. The intervention considerably has averted the malarial deaths. Indirectly it has improved quality of life to some extend as well. Also it has significantly improved awareness level on use of LLINs their utilization in order to be safe from malaria which further enhance the quality of life. This kind of intervention is highly recommended for preventing people from malaria cases and reducing mortality and related costing associated to it. The intervention is more effective for the hills and hence recommended to continue in the days to come unless malaria is completely eradicated from the globe. Taking reference, a study in Congo about LLINs, the intervention is highly cost effective at US$50 per life year saved.

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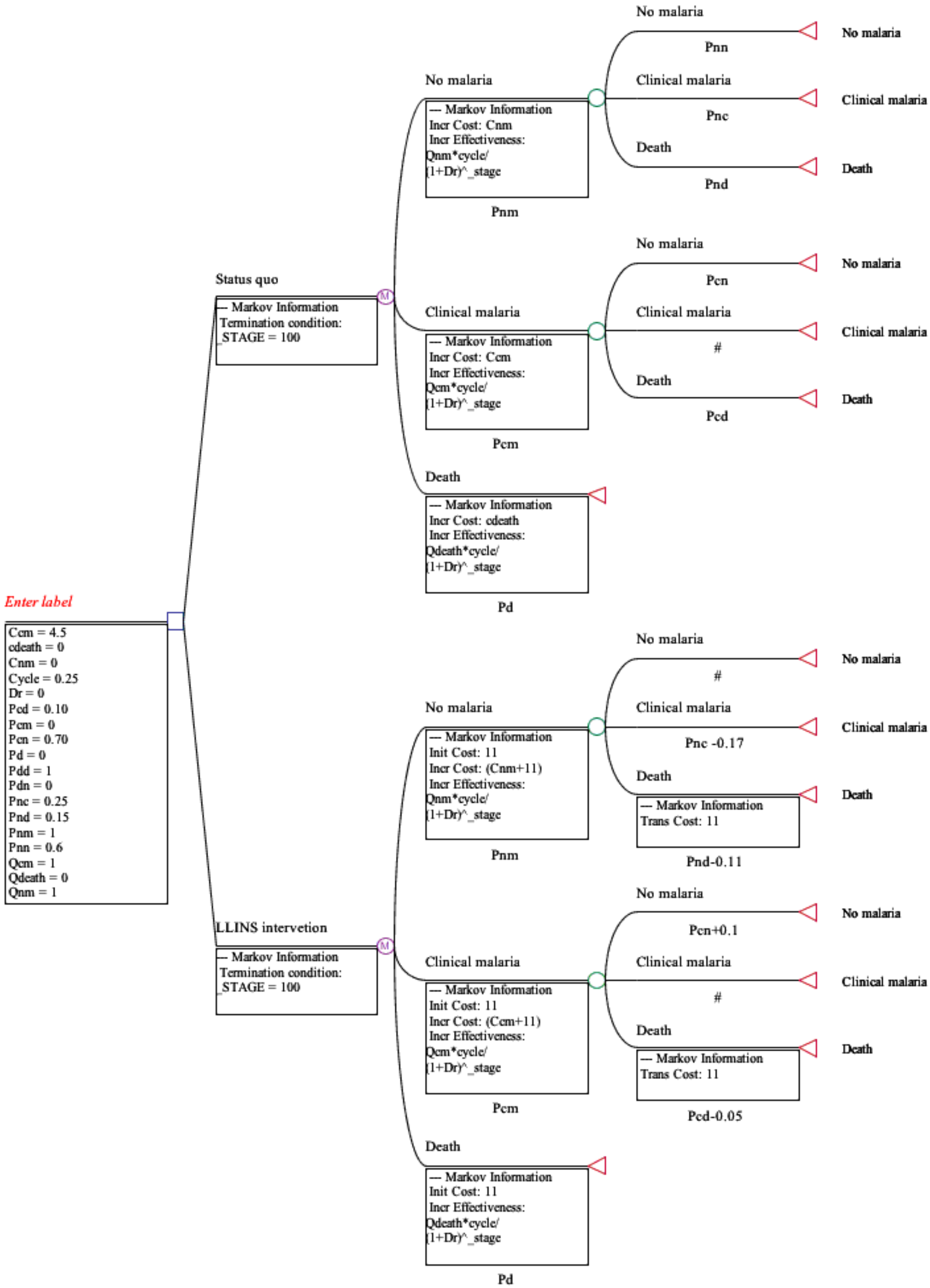
The cost effective analysis result from the Tree Age Pro is copied in Annex below.

Annex



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Status quo
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Termination condition:
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Incr Effectiveness:
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Pnm
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Pnn
Clinical malaria
Pnc
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Clinical malaria
Markov Information
Incr Cost: Ccm
Incr Effectiveness:
Qcm*cycle/
(1+Dr)^_stage
Pcm
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Incr Cost: cdeath
Incr Effectiveness:
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Pnd-0.11
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(1+Dr)^_stage
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Clinical malaria
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Clinical malaria
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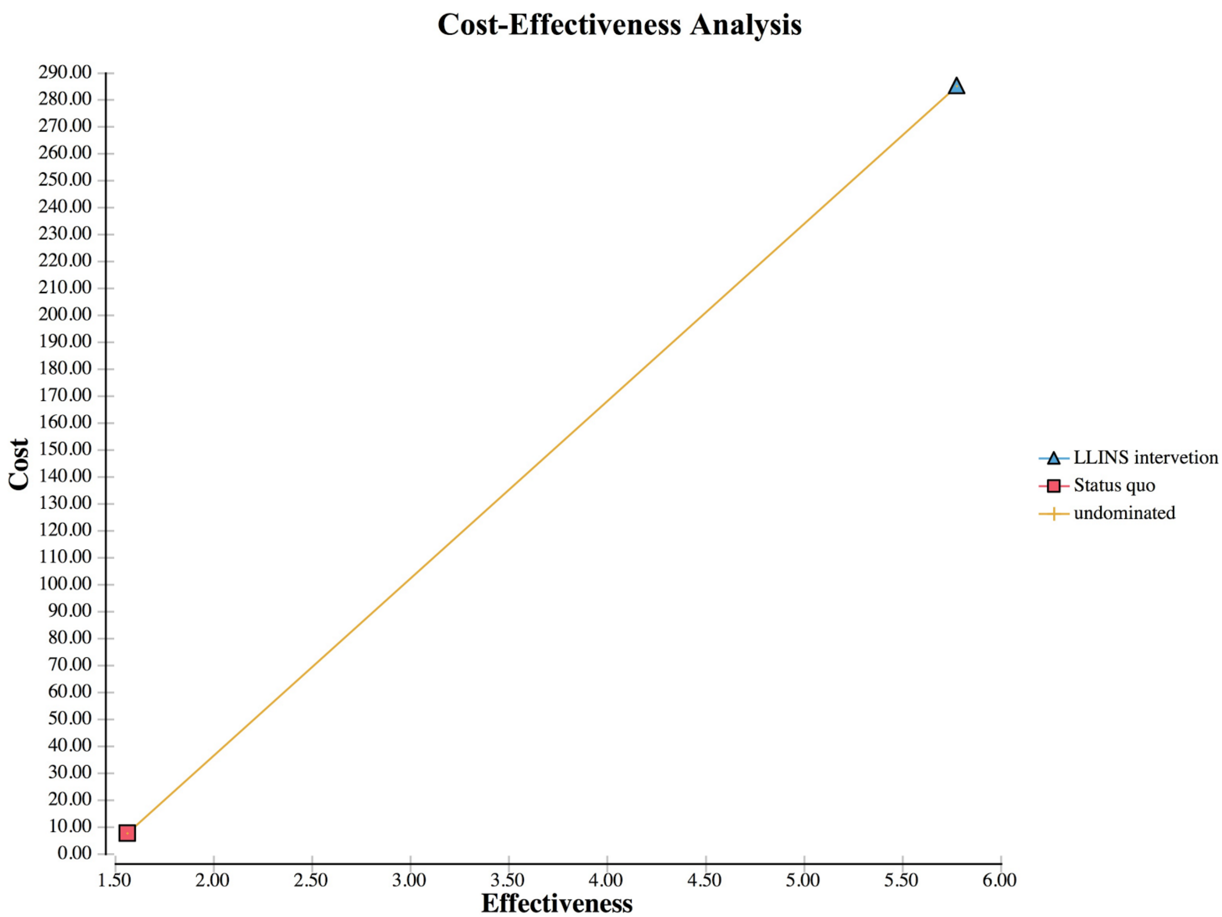
Cost-Effectiveness Analysis
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