Cost-effectiveness Model Technical Report

Long-lasting insecticide-nets for the prevention of malaria in rural and urban malarious areas

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Executive summary

GiveWell is a non-profit organisation, dedicated to finding outstanding giving opportunities for donors. As of December 2017, GiveWell recommends the Against Malaria Foundation (AMF) as a top rated charity, which provides long-lasting insecticide-treated nets (LLINs) for the protection against malaria in developing countries. FIECON is a health economics consultancy, and has conducted an independent audit to evaluate the cost-effectiveness of LLINs for the prevention of malaria in adults and children from rural and urban malarious areas.

A cost-effectiveness model (CEM) has been developed to compare the costs and quality adjusted life years (QALYs) of preventing malaria with LLINs, untreated nets (UTNs) and no nets (NNs). Three populations enter the model; children aged less than 5 years old, children aged between 5 and 18 years old, and adults and children of any age. The model adopts a UK net provider perspective, i.e. all costs borne from the donor (AMF). A 3 year time horizon with yearly cycles is used, and a discount rate of costs and outcomes is applied at 3% per annum.

A Markov model structure is adopted with health states based on an individual's malaria diagnosis. Health states are defined as 'Alive and healthy' and 'Alive with malaria', and 'Dead'. The probability of transitioning between states is based on published literature obtained from a systematic literature review (SLR) and targeted literature searches. Cost categories included in the model are acquisition costs, implementation costs and retreatment costs. Utilities are based on published literature. Sensitivity analyses are performed to explore the level of uncertainty in the model results.

The base case results found that LLINs are cost-effective in comparison to UTNs and NNs with an incremental cost-effectiveness ratio (ICER) below £1,000 per QALY in all populations. Despite the fact that the analysis uses an entirely different model structure compared to GiveWell, a variety of different sources to derive clinical effects, and a broader population scope, it is reassuring to observe that the cost-effectiveness results calculated by GiveWell are similar to those calculated in this analysis. It can be confidently concluded that LLINs for the prevention of malaria are a cost-effective intervention in all populations where malaria is at high risk.

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Abbreviations

AH	Alive healthy
AMF	Against Malaria Foundation
AWM	Alive with malaria
CEA	Cost-effectiveness analyses
CEAC	Cost-effectiveness acceptability curve
CEAF	Cost-effectiveness acceptability frontier
CEM	Cost-effectiveness model
GBP	Great British Pounds
HR	Hazard ratio
ICEP	Incremental cost-effectiveness plane
ICER	Incremental cost-effectiveness ratio
LLIN	Long-lasting insecticide net
M&E	Management and evaluation
Mm	Millimetres
NN	No net
OWSA	One-way sensitivity analyses
PSA	Probabilistic sensitivity analyses
QALY	Quality adjusted life year
RCT	Randomised controlled trial
SLR	Systematic literature review
USD	United States Dollars
UTN	Untreated net
WHO	World Health Organisation
WTP	Willingness to pay

1. Background

GiveWell is a non-profit organisation, dedicated to finding outstanding giving opportunities for donors. To achieve this, GiveWell conduct in-house economic analyses to evaluate the cost-effectiveness of various charities. As of December 2017, GiveWell recommends the Against Malaria Foundation (AMF) as a top rated charity, which provides long-lasting insecticide-treated nets (LLINs) for the protection against malaria in developing countries.

FIECON is a health economics consultancy and has offered to audit the findings published by GiveWell. This report details the methods, results and conclusions of an independent cost-effectiveness analysis developed by FIECON evaluating the use of long-lasting insecticide-treated nets (LLINs) for the protection against malaria in developing countries.

The lead investigators for the analysis at FIECON are Mark Fisher and Lydia Walder, for further information please contact: mark.fisher@fiecon.com or lydia.walder@fiecon.com.

2. Methods

2.1. Population

The population entering the cost-effectiveness model (CEM) are adults (excluding pregnant women) and children living in rural and urban malarious areas. Based on the evidence available in the literature, the population is split by age group, and results are considered for:

- Children aged less than 5 years old
- Children aged between 5 and 18 years old
- Adults and children of any age

2.2. Comparator

A systematic literature review (SLR) of randomised controlled studies (RCTs) and observational trials was conducted to identify studies evaluating the use of LLINs by children and adults in rural and urban malarious areas (Appendix 1). The SLR found that populations either used treated nets, UTNs or NNs. Therefore, the model evaluates two comparators; UTNs and NNs.

2.3. Perspective

The model adopts a UK net provider perspective, i.e. all costs borne from the donor, AMF.

2.4. Discounting

Cost and outcomes are discounted at 3% per annum in line with World Health Organisation (WHO) guidelines.[1] Scenario analyses explore the impact of varying the discount rate level.

2.5. Time horizon

The time horizon for estimating clinical and cost-effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. LLINs are said to remain effective for an average of 3 years;[2] after which the net must be retreated to regain its optimum insecticide dosage and maintain effectiveness. For this reason the CEM adopts a 3 year time horizon. The impact of a shorter time horizon is explored in a scenario analysis.

2.6. Model structure

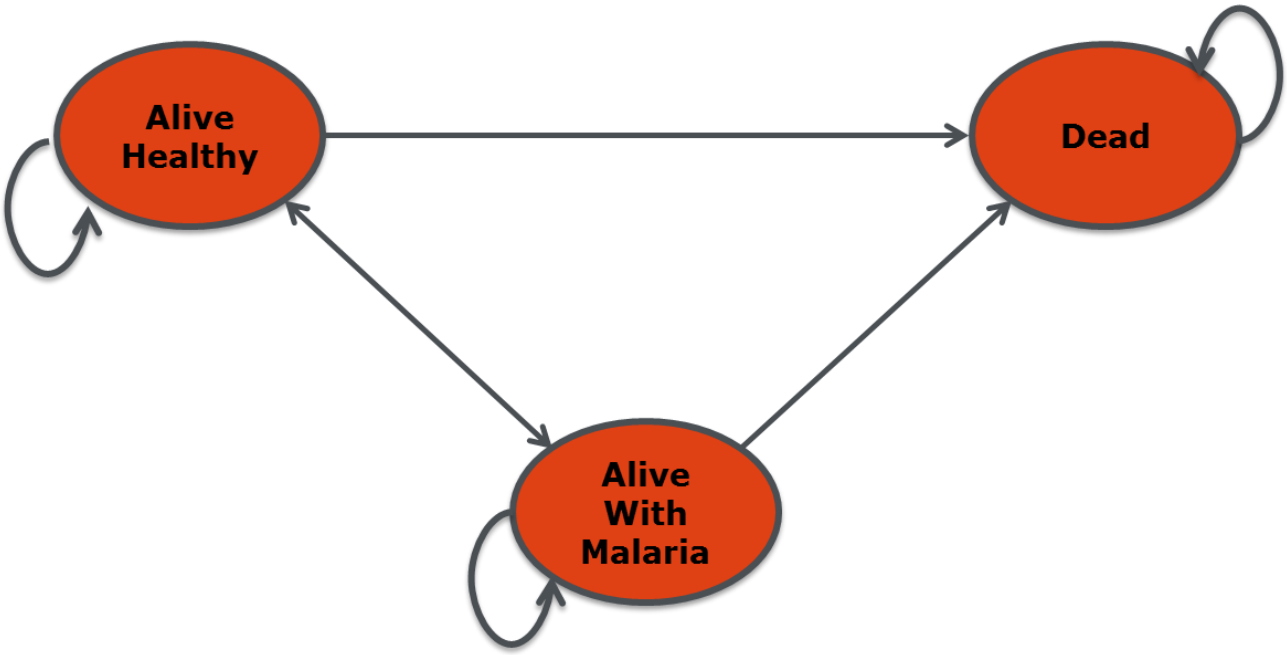
A targeted cost-effectiveness literature search identified a selection of models that evaluated the cost of insecticide treated nets (not specifically LLINs) for the prevention of malaria. Based on the results of this search, the model for this analysis adopts a multistate Markov structure with health states based on an individual's malaria diagnosis (Figure 1).

The model structure has three health states; 'Alive healthy' (AH), 'Alive with malaria' (AWM), and 'Dead'. Patients enter the model in AH, and can either remain in this

health state, transition to AWM or Dead. Patients in AWM can either remain in this health state, transition to AH or Dead. Once transitioned to 'Dead', patients remain there for the remainder of the time horizon.

Four studies identified in the SLR collected data over 12 months, whilst twelve studies collected data over 24 months; therefore an annual cycle length is used in the model (Appendix 1).

Figure 1: Model structure



2.6.1. Baseline demographics

The three populations are assigned baseline ages that are appropriate to the demographic they are describing (Table 1). Children aged less than 5 years enter the model with a mean age of 3 years, children aged between 5 and 18 years enter the model with a mean age of 12 years, and adults and children of any age enter the model with a mean age of 21 years.

Table 1: Baseline age by population

Population	Mean (years)	Source
Children aged less than 5 years of age	3	Assumption
Children aged between 5 and 18 years old	12	Assumption
Adults and children of any age	21	Kamolratanakul 2001[19]

2.7. Clinical effectiveness

The clinical effectiveness of LLINs, UTNs and NNs is based on the SLR of RCTs and observational trials evaluating the use of these interventions in children and adults (Appendix 1). The effectiveness of each intervention is quantified by the percentage of individuals becoming infected with malaria and the percentage of these individuals who go on to die. Appendix 2 provides all transition matrices used in the model.

2.7.1. Children aged less than 5 years of old

To capture the percentage of children aged less than 5 years old that became infected with malaria, data are sourced and extrapolated from a cluster randomised controlled trial of LLINs versus NNs in the Kilifi District of Kenya[9]. LLINs and NNs were randomly assigned to 56 clusters and the effectiveness was measured over 24 months. Out of 11,566 children in the LLIN arm, 322 children were reported to have had a primary diagnosis malaria admission. These data are converted into a 1 year probability for LLINs to inform the clinical transition from 'Alive healthy' to 'Alive with malaria' in children aged less than 5 years old (Table 2).

The 1 year probability is used to determine how individuals transition between 'Alive healthy' and 'Alive with malaria'. As such, remaining in 'Alive healthy' is calculated as 100%-1.4% = 98.6%. In the NN arm, 579 out of a total of 11,432 children were recorded to have had a primary diagnosis malaria admission. Based on this, a 1 year probability of transitioning from AH to AWM is calculated as 2.6% (Table 2) and hence the probability of remaining in AH is 97.4%. No data were available to inform the UTN arm, therefore the relative effective of UTNs is assumed such that UTNs are 50% less effective compared to LLINs. Hence, the probability of remaining in AH is 98.0%. Scenario analyses explore the impact of varying the relative effectiveness assumption.

Table 2: Probability for AH-AWM transition for children aged less than 5 years old

		LLIN	UTN	NN
Neville 1996[9]	N	11,566	N/A	11,432
AH – AWM	Primary diagnosis malaria admissions	322	N/A	579
	2 year probability*	2.8%	N/A	5.1%
	Rate*	1.4%	N/A	2.6%
	1 year probability*	1.4%	2.0%	2.6%
AH – Alive healthy; AWM – alive with malaria; LLIN – long-lasting insecticide net; NN – no net;				

UTN – untreated net
*calculated using Briggs 2006[15]

Transitions to the Dead state for patients in the AH state are based on all-cause mortality statistics split by age and gender, provided by the World Health Organisation (WHO) mortality database.[13] Individuals in AWM have an increased risk of death, which is calculated based on a study that reported a 16% overall case fatality rate of children admitted to hospital with severe malaria. Based on this study, a mortality hazard ratio (HR) of 2.31 [(0.16/all-cause mortality probability)-1] is applied to the WHO all-cause mortality statistics to adjust the risk of mortality in patients in AWM.[14]

2.7.2. Children aged between 5 and 18 years of old

One observational trial is used to estimate the clinical effectiveness of LLINs, UTNs and NNs in children aged between 5 and 18 years old.[16] The study was an observational trial that investigated the effect of permethrin treated LLINs in the prevention of malaria and anaemia in adolescent school girls in western Kenya. Two types of malaria were defined in the study:

1. Clinical malaria: a positive blood smear in concurrent axillary template of 37.5°C
2. Malaria: the presence of asexual blood stage parasites of any species in the blood (high density - ≥500/mm^3)

The transitions are calculated using both definitions (Table 3). A scenario analysis explores the effect of removing the second definition.

Of 339 children who received an LLIN, 2 were diagnosed with clinical malaria and 19 were reported to have had high density parasitaemia over the 2 year observation time. Therefore, a 1 year probability of transitioning from AH to AWM is calculated as 3.1%, and hence the probability of remaining in AH is 96.9%. Of the 305 children who received NN, 6 were diagnosed with clinical malaria and 20 were reported to have had high density parasitaemia over the 2 year observation time. Therefore, a 1 year probability of transitioning from AH to AWM is calculated as 4.4%, and hence the probability of remaining in AH is 95.6%. No data were available to inform the UTN arm, therefore the relative effective of UTNs is assumed such that UTNs are 50% less effective compared to LLINs, and hence the probability of remaining in AH is 96.2%. Scenario analyses explore the impact of varying the relative effectiveness assumption.

Table 3: Probability for AH-AWM transition in children aged between 5 and 18 years old

		LLIN	UTN	NN
Leenstra 2003[16]	N	339	N/A	305
AH - AWM	Clinical malaria	2	N/A	6
	High density parasitaemia (≥500/mm^3)	19	N/A	20
	2 year probability*	6.2%	N/A	8.5%
	Rate*	3.2%	N/A	4.5%
	1 year probability*	3.1%	3.8%	4.4%
AH – Alive healthy; AWM – alive with malaria; LLIN – long-lasting insecticide net; NN – no net; UTN – untreated net				

*calculated using Briggs 2006[15]

Transitions to the Dead state for patients in AH state are based on all-cause mortality statistics split by age and gender, provided by the WHO mortality database.[13] Individuals in AWM have an increased risk of death, which is assumed to be 25% lower than the risk of death in children less than 5 years old; 1.73 (0.75*AWM mortality hazard ratio for children aged less than 5 years old).

2.7.3. Adults and children of any age

Results from two trials are pooled to estimate the clinical effectiveness of LLINs in adults and children of any age: Sedlmayr 2013 and Sochantha 2006[14, 15] (see Table 4 to Table 6). Sedlmayr 2013 evaluated the health impact and cost-effectiveness of a private sector bed net distribution in Zambia. Sochantha 2006 was a cluster randomised trial that evaluated the effectiveness of ITNs for the prevention of *Plasmodium falciparum* in Cambodia.[14, 15]

Sedlmayr 2013 recorded the number of presumed malaria cases in the LLIN and NN arms over 6 months. Of the 2,744 individuals who received an LLIN, 178 were reported to have presumed malaria over the observation period. From these figures a 1 year probability of transitioning from AH to AWM is calculated as 12.6% and hence, the probability of remaining in AH is 87.4%. Of the 2,968 individuals who received NN, 476 presumed malaria cases were recorded. From this a 1 year probability of transitioning from AH to AWM is calculated as 22.2% and hence, the probability of remaining in AH is 77.8%.

Sochantha 2006 recorded the number of individuals who were diagnosed with *Plasmodium falciparum* parasitaemia. Of the 2,748 individuals who received an LLIN, 440 had *Plasmodium falciparum* parasitaemia over 1 year. From these figures a 1 year

probability for the transition from AH to AWM is calculated as 14.8% and hence, the probability for remaining in AH is 85.2%. Of the 2,646 individuals who received NN, 476 cases of *Plasmodium falciparum* parasitaemia were reported over 1 year. From these figures a 1 year probability for the transition from AH to AWM is calculated as 16.5% and hence, the probability of remaining in AH is 83.5%.

No data were available to inform the UTN arm, therefore the relative effectiveness of UTNs is assumed such that UTNs are 50% less effective compared to LLINs. Scenario analyses explore the impact of varying the relative effectiveness assumption.

Table 4: Probability for AH-AWM transition in adult and children of any ages[14]

		LLIN	UTN	NN
Sedlmayr 2013	N	2744	N/A	2968
AH – AWM	Presumed malaria cases	178	N/A	350
	0.5 year probability	6.5%	N/A	11.8%
	1 year rate*	13.4%	N/A	25.1%
	1 year probability	12.6%	N/A	22.2%
AH – Alive healthy; AWM – Alive with malaria; LLIN – long-lasting insecticide net; NN – no net; UTN – untreated net				

*calculated using Briggs 2006[15]

Table 5: Probability for AH-AWM transition in adult and children of any ages[15]

		LLIN	UTN	NN
Sochantha 2006	N	2748	N/A	2646
AH – AWM	Plasmodium *falciparum prevalence*	440	N/A	476
	1 year rate*	16.0%	N/A	18.0%
	1 year probability	14.8%	N/A	16.5%
AH – Alive healthy; AWM – Alive with malaria; LLIN – long-lasting insecticide net; NN – no net; UTN – untreated net				

*calculated using Briggs 2006[15]

Table 6: Pooled results from Sedlmayr 2013 and Sochantha 2006

		LLIN	UTN	NN
Pooled	N	5492	N/A	5614
AH - AWM	1 year probability*	13.7%	16.6%	19.5%
AH – Alive healthy; AWM – Alive with malaria; LLIN – long-lasting insecticide net; NN – no net; UTN – untreated net				

*Weighted average

Transitions to the Dead state for patients in AH state are based on all-cause mortality statistics split by age and gender, provided by the WHO mortality database.[13] Individuals in AWM have an increased risk of death, which is assumed to be 50% lower than the risk of death in children less than 5 years old; 1.16 (0.50*AWM mortality hazard ratio for children aged less than 5 years old).

2.8. Insecticide resistance

Published literature reports an increase in mosquito insecticide resistance from the use of insecticide-treated nets.[11] Insecticide resistance is a growing problem for programme distributors as it causes the effectiveness of the nets to be reduced. The SLR identified no definitive way to relate the development of insecticide resistance to the effectiveness of LLINs. However, a separate targeted literature search identified a mathematical model. The model described how resistance could be modelled instantaneously; after X years mosquitoes develop a level of resistance to the insecticides used and therefore the effectiveness of the net is reduced by Y%.[12] In GiveWell's existing CEA, a 33% reduction in the effectiveness of LLINs due to insecticide resistance is assumed. In addition to insecticide resistance, the effectiveness of LLINs could be affected by wear and tear, misuse and compliance (all of which are particularly difficult to quantify). Therefore, it is assumed that the effectiveness of LLINs is reduced by 50% each year across all three populations. Scenario analyses explore how varying this figure impacts the results.

2.9. Costs and resource use

The base case cost categories included in the model are: acquisition costs, implementation costs and retreatment costs. In a scenario analysis, health state costs and resource use are also included. The categories included are a visit to the health care facility resulting in the diagnosis of positive *Plasmodium falciparum*, diagnosis of positive *Plasmodium vivax,* or a negative diagnosis.

A 2016 price year and GBP currency are used. Where costs were reported in USD, they were first inflated if necessary to 2016 using the Consumer Price Index (CPI) medical inflation rates for the US, and then converted using a conversion rate of 0.694 USD = 1 GBP (Table 7).[19]

Targeted literature searches were performed to provide cost and resource use data to inform the model. In addition, the GiveWell cost-effectiveness model was used to inform specific costs regarding the acquisition and implementation of nets.

Table 7: Health care and medical consumer price index (CPI) inflation rates[19]

Year	CPI	Multiplier to 2016
1994	220.0	160%
1995	225.3	157%
1996	231.3	152%
1997	236.3	149%
1998	239.6	147%
1999	244.6	144%
2000	252.9	139%
2001	260.0	136%
2002	264.2	133%
2003	270.3	130%
2004	277.5	127%
2005	286.9	123%
2006	296.1	119%
2007	304.6	116%
2008	316.2	112%
2009	315.2	112%
2010	320.4	110%
2011	330.4	107%
2012	337.3	105%
2013	342.2	103%
2014	347.8	101%
2015	348.2	101%
2016	352.6	100%
CPI - Consumer Price Index		

2.9.1. Equipment costs

Based on the GiveWell cost-effectiveness model, the basic acquisition cost of an LLIN is £1.87. In addition, the cost of shipping, warehousing, distribution, training, microplanning, social mobilisation, and monitoring and evaluation (including supervision) are £0.69, £0.15, £0.28, £0.21, £0.10, £0.10 and £0.21 respectively. Therefore the total cost of acquisition and implementation of an LLIN is £3.76 (Table 8). LLINs are said to remain effective for 3 years on average;[2] therefore it is assumed that 1 net is given for a 3 year time span. Based on an existing cost-effectiveness study, retreatment occurs annually at a cost of £0.46 (Table 8). [23]

It is assumed that the cost of a UTN was the cost of an LLIN minus the cost for retreatment: £1.41 (£1.87-£0.46). The cost of shipping, warehousing, distribution, training, microplanning, social mobilisation, and monitoring and evaluation (including supervision) are assumed to be the same for a UTN as an LLIN. Therefore the total

cost of acquisition and implementation of one UTN is £3.30 (Table 8). No acquisition or implementation costs are assigned to NNs.

Large net distributions usually take place across a big geographical area; nets are distributed over a period of a few weeks. Therefore, for simplicity it was assumed that all nets are distributed at approximately the same time. Net insecticide dosage will vary from the optimum dose, and if nets are retreated this variation will only increase. To simplify calculations, an average dosage and hence effectiveness is assumed. The base case analysis assumes that one net is distributed to one individual; however it is known that in large populations this is not always the case. Therefore, a scenario analysis investigates how the results would change if the number the of nets per person is reduced to 0.67 (i.e. 2 nets could be used effectively for three people).[21]

Table 8: Acquisition, implementation and retreatment costs of an LLIN and UTN

Acquisition, distribution and follow-up		$	Year	Converted to £	Source
LLIN	Shipping	$1.00	2016	£0.69	[21]
	Warehousing	$0.21	2016	£0.15	[21]
	Distribution	$0.40	2016	£0.28	[21]
	Training	$0.30	2016	£0.21	[21]
	Microplanning	$0.14	2016	£0.10	[21]
	Social mobilisation	$0.15	2016	£0.10	[21]
	M&E, includes supervision	$0.30	2016	£0.21	[21]
	Cost of net	$2.70	2016	£1.87	[21]
	LLIN retreatment	$0.64	2012	£0.46	[23]
UTN	Shipping	$1.00	2016	£0.69	[21]
	Warehousing	$0.21	2016	£0.15	[21]
	Distribution	$0.40	2016	£0.28	[21]
	Training	$0.30	2016	£0.21	[21]
	Microplanning	$0.14	2016	£0.10	[21]
	Social mobilisation	$0.15	2016	£0.10	[21]
	M&E, includes supervision	$0.30	2016	£0.21	[21]
	Cost of net			£1.41	Assumption*

M&E – management and evaluation; N/A – not applicable

*Cost of LLIN – cost or LLIN retreatment

2.9.2. Health state cost and resource use inputs

Health state costs are not included in the base case analysis; however, a scenario analysis investigates the impact of including these costs. The same unit resource costs are applied across all three interventions; LLINs, UTNs and NNs. The three resource inputs are; visit to a health care facility resulting in a diagnosis of positive *plasmodium falciparum*, visit to a health care facility resulting in a diagnosis of positive *plasmodium vivax*, and a visit to a health care facility resulting negative diagnosis.

The unit costs are £4.70, £3.08 and £1.57 respectively (Table 9). No sources were identified to provide resource use inputs therefore it is assumed that individuals within the AH health state visited the health care facility once and received a negative diagnosis. Individuals in the AWM health state had one visit to the health care facility that was proportioned equally across a *Plasmodium falciparum* diagnosis and a *Plasmodium vivax* diagnosis.

Table 9: Health state cost and resource use

Intervention	Unit cost (£)	Health state	Resource use (per cycle)	Total costs (£)
Visit to health care facility resulting in a diagnosis of positive *plasmodium falciparum* [19]	4.70	Alive healthy	0	£0.00
		Alive with malaria	0.5	£2.35
Visit to health care facility resulting in a diagnosis of positive *plasmodium vivax* [19]	3.08	Alive healthy	0	£0.00
		Alive with malaria	0.5	£1.54
Visit to health care facility resulting in a negative diagnosis [19]	1.57	Alive healthy	1	£1.57
		Alive with malaria	0	£0.00
Total		Alive healthy		£1.57
		Alive with malaria		£2.16

2.10. Quality of life

Targeted literature searches were performed to identify quality of life data to inform the model. McCarthy 2010 provided a utility score of 0.73 for a population of low income individuals living in Bangladesh; this is assigned to AH.[23] Sultana 2016 provided two utility scores of 0.54 and 0.09 for complicated and uncomplicated malaria, respectively.[25] These two scores are used to determine the overall utility applied to the AWM health state. *Plasmodium falcipar*um causes a more serious infection than *Plasmodium vivax*, therefore a diagnosis of *Plasmodium falciparum* is assumed to be complicated malaria and a diagnosis of *Plasmodium vivax* is assumed to be uncomplicated malaria.[25] Kamolratanakul 2001 reported the proportion of individuals who contracted uncomplicated malaria and complicated malaria as 24.1%

and 75.9%, respectively.[19] In order to calculate the utility for AWM, a weighted average is taken between the proportion of uncomplicated and complicated malaria reported by Kamolratanakul 2001 and the respective utility scores reported by Sultana 2016. The base case utilities are therefore 0.73 for AH and 0.60 for AWH (Table 10). In addition, the base case analysis assumes that an average individual has malaria for 3 months. A scenario analysis explores how varying this time period affects the results.

Table 10: Utility scores applied in the cost-effectiveness analysis

Health state	Utility
AH	0.73
AWM	0.60*
AH – Alive healthy; AWM – Alive with malaria	

*Weighted average

2.11. Uncertainty

Deterministic and probabilistic sensitivity analyses are performed to explore the level of uncertainty in the model results.

2.11.1. Deterministic sensitivity analyses

Deterministic sensitivity analyses consisted of scenario analyses to test structural uncertainty of the model and one-way sensitivity analysis (OWSA) to test parameter uncertainty of the model. Table 11 details the scenario analyses conducted. OWSA considered +/- 20% of the mean value. A tornado diagram for each population and comparator (Figure 2 - Figure 7) illustrates the level of uncertainty considering the incremental net monetary benefit of upper and lower bounds.

Table 11: Scenario analyses

Parameter	Scenario	Justification
Discount rate	Discounting costs and outcomes at 0%, 1.5% and 6% per annum	Explore impact of discounting
Time horizon	Applying shorter time horizon of 1 year	Explore impact of shorter duration
UTN relative effectiveness	Varying the relative	Explore impact of UTN

efficacy	effectiveness of UTNs compared to LLINs from 25% to 75%	effectiveness assumption
Waning of effectiveness of UTNs and LLINs over time	Varying the annual decrease in effectiveness with LLINs and UTNs from 33% to 67%	GiveWell estimate of effectiveness reduction is 33%
Number of nets per person	Applying the observed net to person ratio as 0.67	Alaii 2003[21]
The definition of malaria in children aged between 5 and 18 years old	Do not include parasitaemia ≥500m^3 in the definition of malaria	Explore the impact of the definition of malaria
Average time with malaria	Varying the average time an individual has malaria from 1.5 months to 6 months	Explore the impact of malaria duration
Health state costs	Include health state costs	Explore the impact of broadening the model perspective
LLIN – long-lasting insecticide net; UTN – untreated net		

2.11.2. Probabilistic sensitivity analyses

Probabilistic sensitivity analysis (PSA) assigned distributions to the model parameters and ran 10,000 simulations to further explore parameter uncertainty. The cohort size, time horizon, discount rates, price of an LLIN and UTN were kept fixed. Beta distributions were used for the proportion male, annual probability of malaria with LLINs, UTNs and NNs, AH utility, AWM utility, decreased in effectiveness of LLINs due to insecticide resistance and relative effectiveness of UTNs. Gamma distributions were used for age, mortality HR, resource use, costs and average time with malaria.

Mean incremental results were recorded and illustrated through an incremental cost-effectiveness plane (ICEP). In addition, a cost-effectiveness acceptability curve (CEAC) and cost-effectiveness acceptability frontier (CEAF) was plotted.

3. Results

3.1. Base case

3.1.1. Children aged less than 5 years old

Base case results of LLINs versus UTNs and NNs in children aged less than 5 years old are presented in Table 12. Over a 3 year time horizon, children who received LLINs accrued 2.061 quality adjusted life years (QALYs) at a cost of £4.76. Children who received UTNs accrued 2.058 QALYs at a cost of £2.14. Children who received NNs accrued 2.055 QALYs at no cost. The incremental cost per QALY of LLINs versus NNs is £795. The incremental cost per QALY of LLINs versus UTNs is £875. Base case results presented in USD can be found in Appendix 3.

Disaggregated QALYs by health state and costs by health state are presented in

Table 13 to Table 14, respectively. The disaggregated QALYs are very close in magnitude, whilst the disaggregated costs results show that the costs attributed to LLIN acquisition and implementation drive the differences between costs.

Table 12: Base case results for children aged less than 5 years

	Total Costs (£)	Total QALYs	Incremental Costs (£)	Incremental QALYs	ICER (£) versus baseline (QALYs)	ICER (£) incremental (QALYS)
NN	0.00	2.055	-	-	-	-
UTN	2.14	2.058	2.14	0.003	715	715
LLIN	4.76	2.061	2.62	0.003	795	875
ICER – incremental cost-effectiveness ratio; LLIN – long-lasting insecticide net; NN – no net; UTN – untreated net; QALY – quality adjusted life year						

Table 13: Disaggregated QALY by health state for children aged less than 5 years

Health state	QALY LLIN	QALY UTN	QALY NN
AH	2.03	2.01	2.00
AWM	0.03	0.04	0.05
Total QALYs	2.06	2.06	2.05
AH – Alive healthy; AWM – Alive with malaria; LLIN – long-lasting insecticide net; NN			

– no net; UTN – untreated net

Table 14: Disaggregated cost by health state for children aged less than 5 years

Health state	LLIN	UTN	NN
AH	£4.60	£1.93	£0.00
AWM	£0.16	£0.20	£0.00
Total costs (£)	£4.76	£2.14	£0.00
AH – Alive healthy; AWM – Alive with malaria; LLIN – long-lasting insecticide net; NN – no net; UTN – untreated net;			

3.1.2. Children aged between 5 and 18 years old

Base case results of LLINs versus UTNs and NNs in children aged between 5 and 18 years old are presented in Table 15. Over a 3 year time horizon, children who received LLINs accrued 2.084 QALYs at a cost of £4.94. Children who received UTNs accrued 2.081 QALYs at a cost of £2.32. Children who received NNs accrued 2.078 QALYs at no cost. The incremental cost per QALY of LLINs versus NNs is £915. The incremental cost per QALY of LLINs versus UTNs is £969. Base case results presented in USD can be found in Appendix 3.

Disaggregated QALYs by health state and costs by health state are presented in Table 16 to Table 17, respectively. The disaggregated QALYs are very close in magnitude, whilst the disaggregated costs results show that the costs attributed to LLIN acquisition and implementation drive the differences between costs.

Table 15: Base case results for children aged between 5 and 18 years old

	Total Costs (£)	Total QALYs	Incremental Costs (£)	Incremental QALYs	ICER (£) versus baseline (QALYs)	ICER (£) incremental (QALYS)
NN	0.00	2.078	-	-	-	-
UTN	2.32	2.081	2.32	0.003	861	861
LLIN	4.94	2.084	2.62	0.003	915	969
ICER – incremental cost-effectiveness ratio; LLIN – long-lasting insecticide net; NN – no net; UTN – untreated net						

Table 16: Disaggregated QALYs gains by health state for children aged between 5 and 18 years old

Health state	QALY LLIN	QALY UTN	QALY NN

AH	2.01	2.00	1.98
AWM	0.07	0.08	0.09
Total QALYs	2.08	2.08	2.08
AH – Alive healthy; AWM – Alive with malaria; LLIN – long-lasting insecticide net; NN – no net; UTN – untreated net; QALY – quality adjusted life year			

Table 17: Disaggregated costs by health state for children aged between 5 and 18 years old

Health state	LLIN	UTN	NN
AH	£4.60	£1.93	£0.00
AWM	£0.34	£0.40	£0.00
Total cost	£4.94	£2.32	£0.00
AH – Alive healthy; AWM – Alive with malaria; LLIN – long-lasting insecticide net; NN – no net; UTN – untreated net; QALY – quality adjusted life year			

3.1.3. Adults and child of all ages

Base case results of LLINs versus UTNs and NNs for adults and children of any age are presented in Table 18. Over a 3 year time horizon, individuals who received LLINs accrued 2.002 QALYs at a cost of £5.89. Individuals who received UTNs accrued 1.991 QALYs at a cost of £3.42. Individuals who received NNs accrued 1.981 QALYs at no cost. The incremental cost per QALY of LLINs versus NNs is £277. The incremental cost per QALY of LLINs versus UTNs is £230. Base case results presented in USD can be found in Appendix 3.

Disaggregated QALYs by health state and costs by health state are presented in Table 19 to Table 20, respectively. The disaggregated QALYs vary with more AH patients in LLINs compared to comparators. The disaggregated costs results show that the costs attributed to LLIN acquisition and implementation drive the differences between costs.

Table 18: Base case results for adults and children of any age

	Total Costs (£)	Total QALYs	Incremental Costs (£)	Incremental QALYs	ICER (£) versus baseline (QALYs)	ICER (£) incremental (QALYs)
NN	0.00	1.981	-	-	-	-
UTN	3.42	1.991	3.42	0.011	324	324
LLIN	5.89	2.002	2.46	0.011	277	230
ICER – incremental cost-effectiveness ratio; LLIN – long-lasting insecticide net; NN – no net; UTN – untreated net						

Table 19: Disaggregated QALYs by health state for adults and children of any age

Health state	QALY LLIN	QALY UTN	QALY NN
AH	1.70	1.64	1.58
AWM	0.31	0.35	0.40
Total QALYs	2.00	1.99	1.98
AH – Alive healthy; AWM – Alive with malaria; LLIN – long-lasting insecticide net; NN – no net; UTN – untreated net; QALY – quality adjusted life year			

Table 20: Disaggregated costs by health state for adults and children of any age

Health state	LLIN	UTN	NN
AH	£4.45	£1.76	£0.00
AWM	£1.44	£1.66	£0.00
Total costs	£5.89	£3.42	£0.00
AH – Alive healthy; AWM – Alive with malaria; LLIN – long-lasting insecticide net; NN – no net; UTN – untreated net; QALY – quality adjusted life year			

3.2. Sensitivity analyses

3.2.1. Scenario analyses

3.2.1.1. Children aged less than 5 years old

Table 21 shows the scenario analysis results for children aged less than 5 years old for LLINs versus UTNs. Results are most sensitive to shorter time horizons, varying the average time a child has malaria and UTN relative effectiveness. Results are also sensitive to the number of nets per person. Results are relatively insensitive to other scenarios.

Table 21: Scenario analyses results for children aged less than 5 years old

Parameter	Scenario		ICER vs. NN	ICER vs. UTN
Base case			795	875
Discount rate	Discounting costs and	0%	771	839

	outcomes.	6%	819	910
Time horizon	Applying shorter time horizon.	1 year	4,992	1,232
UTN relative effectiveness	Varying the relative effective of UTNs compared to LLINs	25%	795	1,763
		75%	795	579
Decreased in effectiveness due to insecticide resistance	Varying the percentage the LLINs effectiveness reduction	33%	750	825
		67%	846	932
Number of nets per person	Applying the observed net to person ratio	0.67	586	612
Average time with malaria	Varying the average time an individual has malaria to 1.5 months and 6 months	1.5	1,239	1,364
		6	463	510
Health state costs	Include health state costs	Yes	793	872
ICER – incremental cost-effectiveness ratio; LLIN – long-lasting insecticide net; UTN – untreated net				

3.2.1.2. Children aged between 5 and 18 years old

Table 22 shows the scenario analysis results for children aged between 5 and 18 years old for LLINs versus UTNs. Results are most sensitive to shorter time horizons, varying the average time a child has malaria and UTN relative effectiveness. Results are also sensitive to the number of nets per person. Results are relatively insensitive to other scenarios.

Table 22: Scenario analyses for children aged between 5 and 18 years old

Parameter	**Scenario**		**ICER vs. NN**	**ICER vs. UTN**
Base case			915	969
Discount rate	Discounting costs and outcomes.	0%	890	931
		6%	941	1,007
Time horizon	Applying shorter time	1 year	4,726	1,166

	horizon.			
UTN relative effectiveness	Varying the relative effective of UTNs compared to LLINs	25%	915	1,954
		75%	915	641
Decreased in effectiveness due to insecticide resistance	Varying the percentage the LLINs effectiveness reduction	33%	855	905
		67%	984	1,042
Number of nets per person	Applying the observed net to person ratio	0.67	672	678
Average time with malaria	Varying the average time an individual has malaria to 1.5 months and 6 months	1.5	1,618	1,713
		6	490	519
Health state costs	Include health state costs	Yes	912	966
ICER – incremental cost-effectiveness ratio; LLIN – long-lasting insecticide net; UTN – untreated net				

3.2.1.3. Adults and children of any age

Table 23 shows the scenario analysis results for adults and children of any age for LLINs versus UTNs. Results are most sensitive to shorter time horizons, varying the average time an individual has malaria and UTN relative effectiveness. Results are also sensitive to the number of nets per person. Results are relatively insensitive to other scenarios.

Table 23: Scenario analyses for children aged between 5 and 18 years old

Parameter	**Scenario**		**ICER vs. NN**	**ICER vs. UTN**
Base case			277	230
Discount rate	Discounting costs and outcomes.	0%	271	221
		6%	282	239
Time horizon	Applying shorter time horizon.	1 year	992	245
UTN relative	Varying the relative	25%	277	477

effectiveness	effective of UTNs compared to LLINs	75%	277	148
Decreased in effectiveness due to insecticide resistance	Varying the percentage the LLINs effectiveness reduction	33%	257	213
		67%	300	250
Number of nets per person	Applying the observed net to person ratio	0.67	199	162
Average time with malaria	Varying the average time an individual has malaria to 1.5 months and 6 months	1.5	533	443
		6	141	117
Health state costs	Include health state costs	Yes	272	226
ICER – incremental cost-effectiveness ratio; LLIN – long-lasting insecticide net; UTN – untreated net				

3.2.2. One-way sensitivity analyses

3.2.2.1. Children aged less than 5 years old

A tornado diagram is presented for LLINs versus UTNs which illustrates the level of uncertainty in results by varying parameters by +/- 20% (Figure 2). Results are most sensitive to the annual probability of malaria with NN. However, all ICERs are below £1,800 per QALY (Table 24).

Figure 2: Tornado diagram (LLINs versus UTNs) for children less than 5 years old

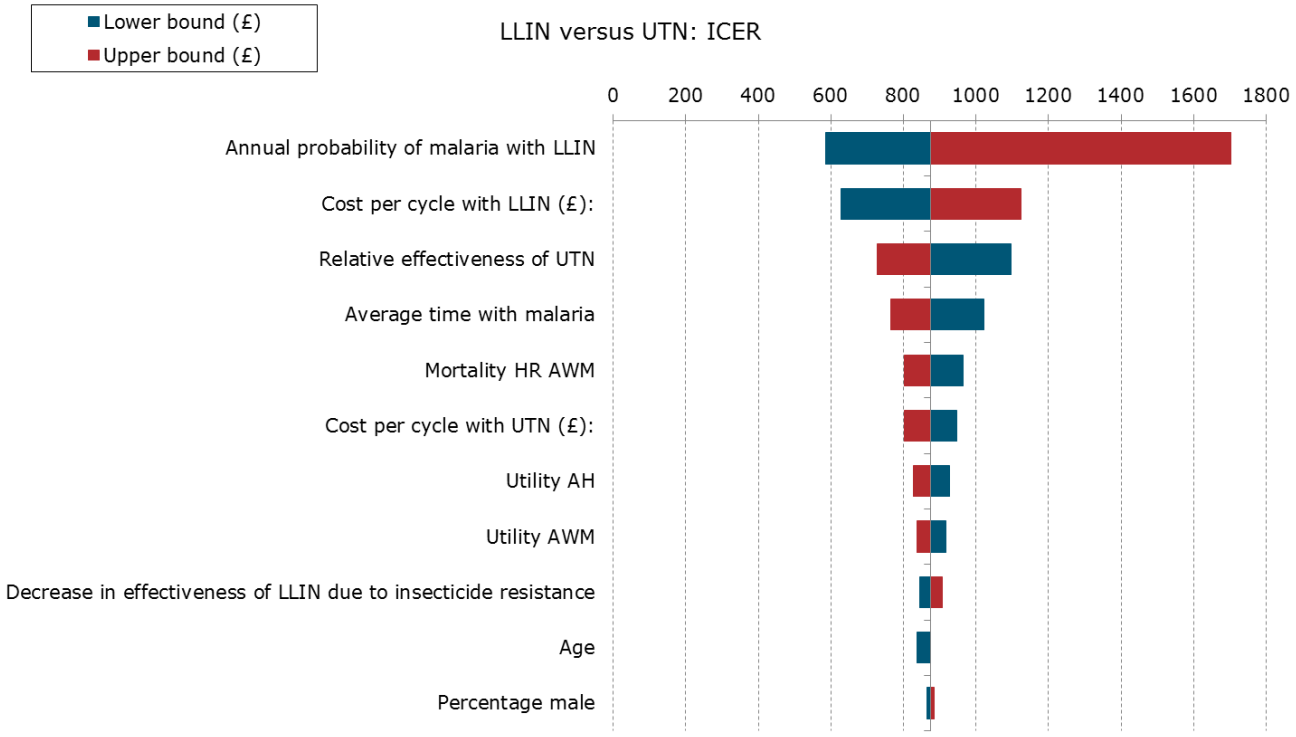


Table 24: OWSA results (LLINs versus UTNs) for children less than 5 years old

Parameter	Lower bound (£)	Upper bound (£)	Difference (£)
Annual probability of malaria with LLIN	586	1703	1117
Cost per cycle with LLIN (£):	627	1123	496
Relative effectiveness of UTN	1097	727	370
Average time with malaria	1021	765	256
Mortality HR AWM	965	802	164
Cost per cycle with UTN (£):	948	802	147
Utility AH	927	828	99
Utility AWM	917	836	81
Decrease in effectiveness of LLIN due to insecticide resistance	845	907	63
Age	837	875	38

Percentage male	864	885	21
Annual probability of malaria with NN	874	876	2
Retreatment cost LLIN	875	875	1
AWM – Alive with malaria; HR – hazard ratio; LLIN – long-lasting insecticide net; NN – no net; UTN – untreated net			

A tornado diagram is presented for LLINs versus NNs which illustrates the level of uncertainty in results by varying parameters by +/- 20% (Figure 3). Results are most sensitive to the annual probability of malaria with NN. However, all ICERs are below £1,500 per QALY (Table 25).

Figure 3: Tornado (LLINs versus NNs) for children aged less than 5 years old

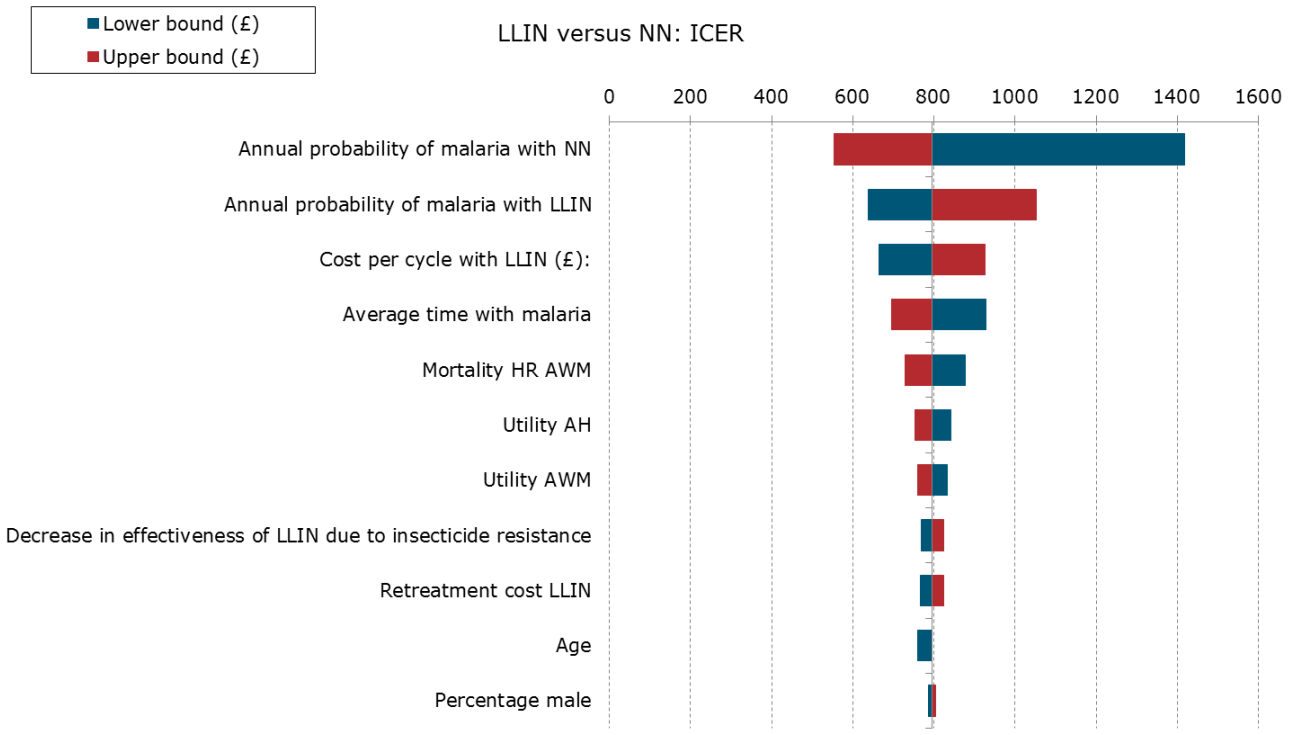


Table 25: OWSA results (LLINs versus NNs) for children aged less than 5 years old

Parameter	Lower bound (£)	Upper bound (£)	Difference (£)
Annual probability of malaria with NN	1417	554	864
Annual probability of malaria with LLIN	638	1052	415

Cost per cycle with LLIN (£):	664	926	262
Average time with malaria	928	695	233
Mortality HR AWM	878	728	150
Utility AH	843	752	90
Utility AWM	834	760	74
Decrease in effectiveness of LLIN due to insecticide resistance	768	824	57
Retreatment cost LLIN	767	823	56
Age	759	795	36
Percentage male	785	805	19
AWM – Alive with malaria; LLIN – long-lasting insecticide net			

3.2.2.2. Children aged between 5 and 18 years old

A tornado diagram is presented for LLINs versus NNs which illustrates the level of uncertainty in results by varying parameters by +/- 20% (Figure 4). Results are most sensitive to the cost per cycle with LLIN. However, all ICERs are below £1,300 per QALY (Table 26).

Figure 4: Tornado diagram (LLINs versus UTNs) - children aged between 5 and 18 years old

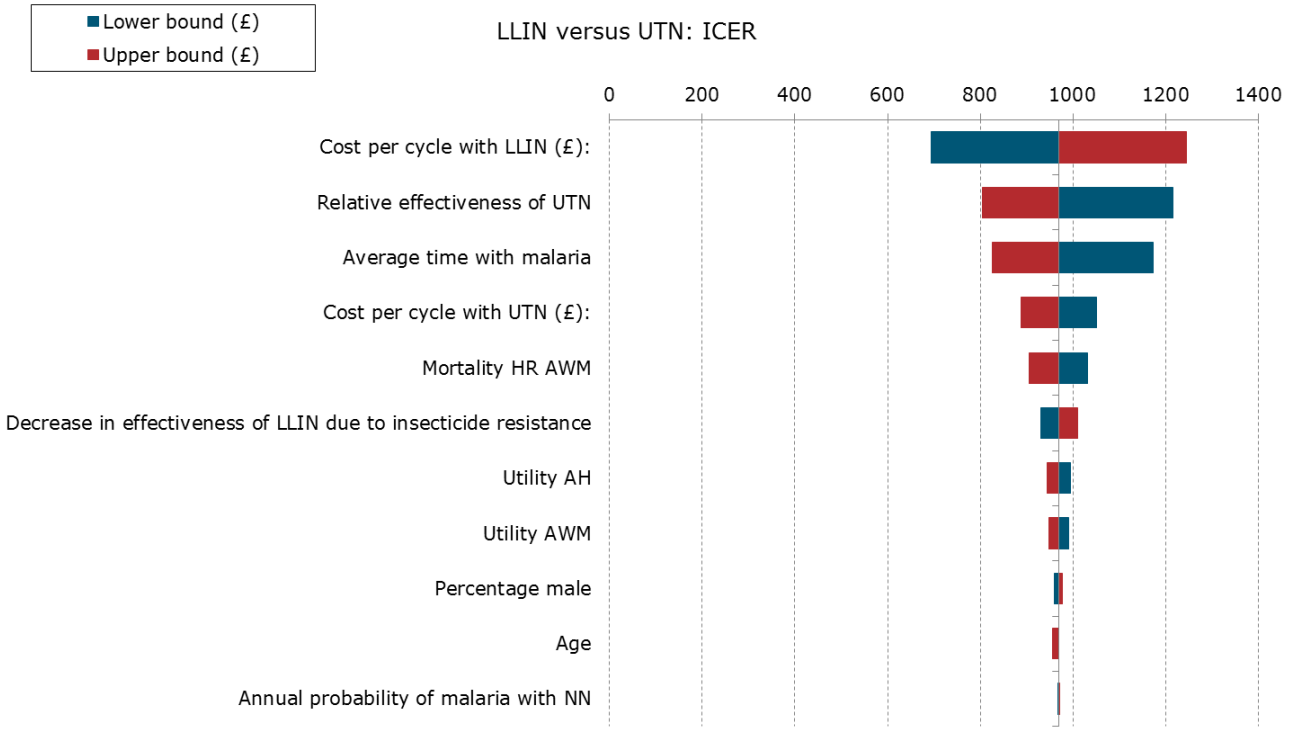


Table 26: OWSA results (LLINs versus UTNs) - children aged between 5 and 18 years olds

Parameter	Lower bound (£)	Upper bound (£)	Difference (£)
Cost per cycle with LLIN (£):	694	1244	550
Relative effectiveness of UTN	1215	805	410
Average time with malaria	1173	826	347
Cost per cycle with UTN (£):	1051	888	163
Mortality HR AWM	1032	905	127
Decrease in effectiveness of LLIN due to insecticide resistance	931	1011	80
Utility AH	995	944	51
Utility AWM	990	949	42
Percentage male	960	978	17

Age	969	956	13
Annual probability of malaria with NN	967	971	4
Retreatment cost LLIN	969	970	1
AWM – Alive with malaria; HR – hazard ratio; LLIN – long-lasting insecticide net; UTN – untreated net			

A tornado diagram is presented for LLINs versus NNs which illustrates the level of uncertainty in results by varying parameters by +/- 20% (Figure 5). Results are most sensitive to the annual probability of malaria with NN. However, all ICERs are below £3,300 per QALY (Table 27).

Figure 5: Tornado (LLINs versus NNs) for children aged between 5 and 18 years old

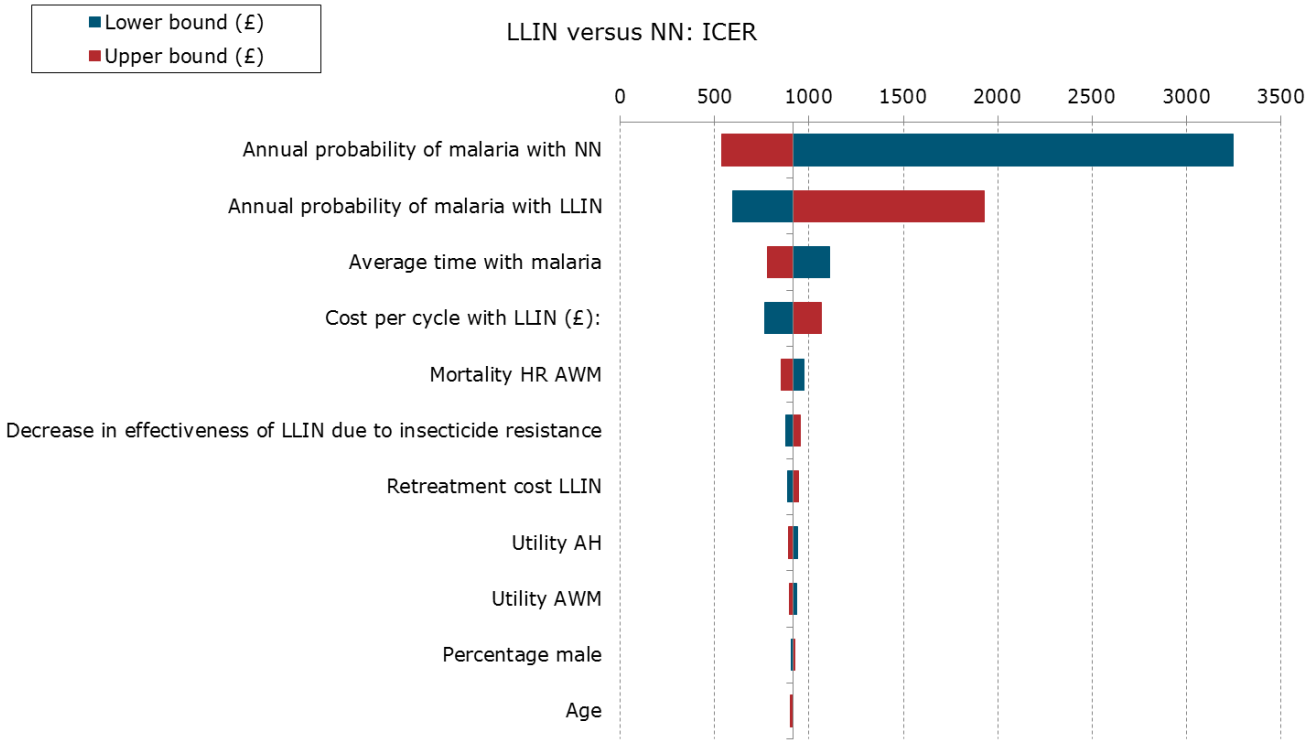


Table 27: OWSA results (LLINs versus NNs) in children aged between 5 and 18 years old

Parameter	Lower bound (£)	Upper bound (£)	Difference (£)
Utility AH	48817	462	48355
Utility AWM	514	4184	3671

Annual probability of malaria with NN	3249	536	2713
Annual probability of malaria with LLIN	596	1927	1332
Average time with malaria	1108	780	328
Cost per cycle with LLIN (£):	763	1068	304
Mortality HR AWM	976	854	123
Decrease in effectiveness of LLIN due to insecticide resistance	879	955	75
Retreatment cost LLIN	884	946	62
Percentage male	907	923	17
Age	915	902	14
AWM – Alive with malaria; HR – hazard ratio; LLIN – long-lasting insecticide net			

3.2.2.3. Adults and children of all ages

A tornado diagram is presented for LLINs versus UTNs which illustrates the level of uncertainty in results by varying parameters by +/- 20% (Figure 6). Results are most sensitive to the annual probability of malaria with LLINs. However, all ICERs are below £4,100 per QALY (Table 28).

Figure 6: Tornado (LLINs versus UTNs) for adults and children of any age

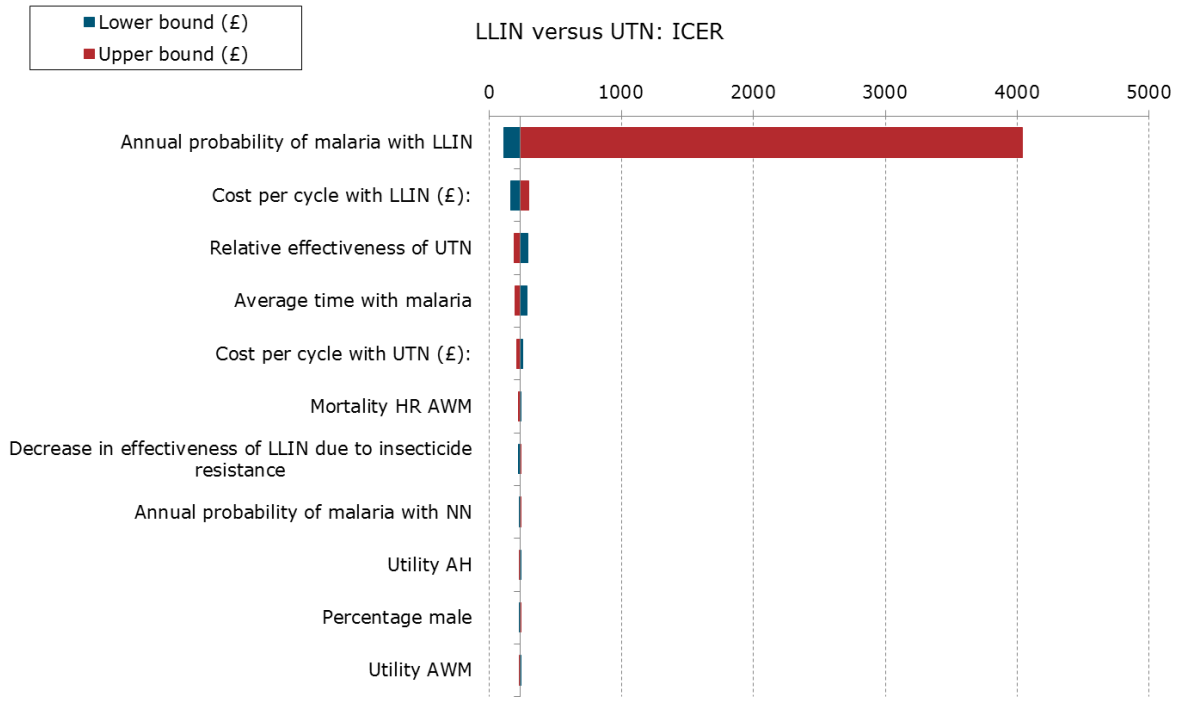


Table 28: OWSA results (LLINs versus UTNs) for adults and children of any age

Parameter	Lower bound (£)	Upper bound (£)	Difference (£)
Annual probability of malaria with LLIN	109	4038	3929
Cost per cycle with LLIN (£):	164	296	132
Relative effectiveness of UTN	292	189	103
Average time with malaria	285	193	92
Cost per cycle with UTN (£):	251	210	41
Mortality HR AWM	240	218	23
Decrease in effectiveness of LLIN due to insecticide resistance	220	241	22
Annual probability of malaria with NN	228	232	5
Utility AH	232	228	3
Percentage male	228	232	3
Utility AWM	231	229	3

Age	230	231	1
AWM – Alive with malaria; HR – hazard ratio; LLIN – long-lasting insecticide treated net ; UTN – untreated net			

A tornado diagram is presented for LLINs versus NNs which illustrates the level of uncertainty of the incremental cost-effectiveness ratio (Figure 7). Results are most sensitive to the annual probability of malaria with NN. However, all ICERs are below £900 per QALY (Table 29).

Figure 7: Tornado (LLINs versus NNs) for adults and children of any age

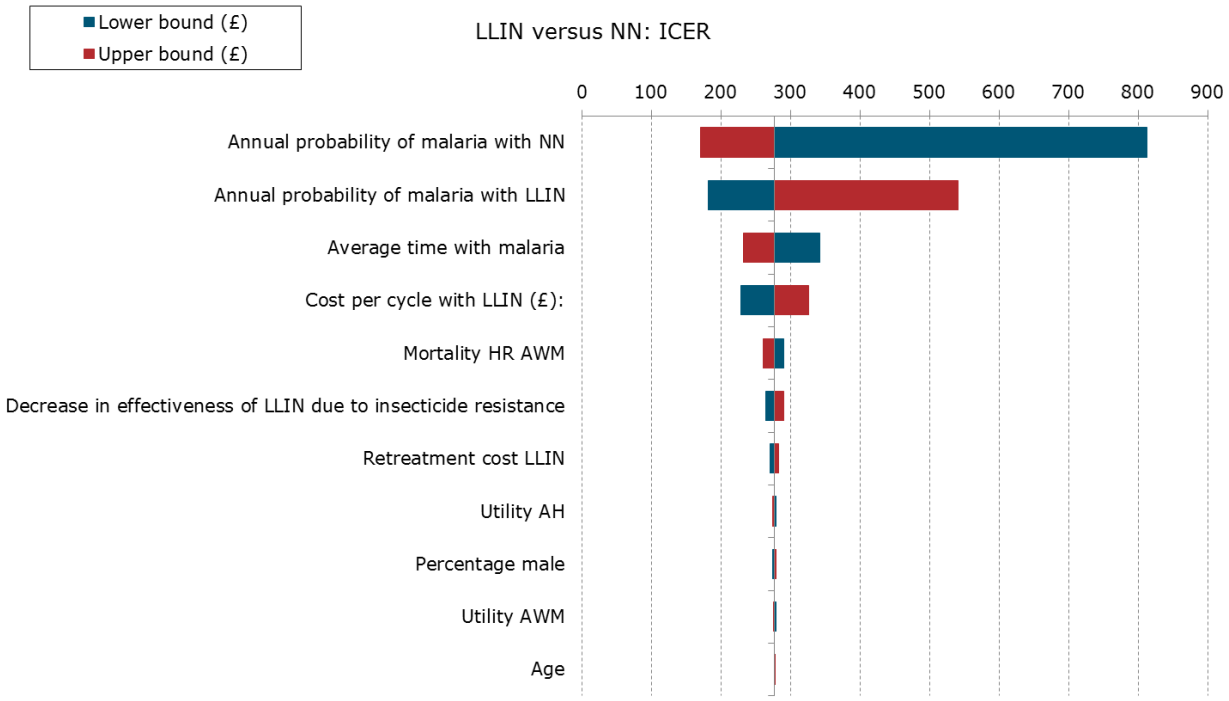


Table 29: OWSA results (LLINs versus NNs) for adults and children of any age

Parameter	Lower bound (£)	Upper bound (£)	Difference (£)
Annual probability of malaria with NN	813	170	643
Annual probability of malaria with LLIN	181	541	360
Average time with malaria	343	232	111
Cost per cycle with LLIN (£):	228	326	98
Mortality HR AWM	290	261	29
Decrease in effectiveness of LLIN due to	265	290	25

insecticide resistance			
Retreatment cost LLIN	270	283	13
Utility AH	279	275	4
Percentage male	275	279	4
Utility AWM	278	275	3
AWM – Alive with malaria; HR – hazard ratio; LLIN – long-lasting insecticide net; UTN – untreated net			

3.2.3. Probabilistic sensitivity analyses

3.2.3.1. Children aged less than 5 years old

Table 30 shows the mean results for PSA for children aged less than 5 years old. Results are very similar to that of the base case. For LLINs versus UTNs the ICEP (Figure 8) shows that the majority of simulations (75%) are where LLINs is more costly and more effective. LLINs are shown to be more costly but less effective than UTNs in 25% of simulations. For LLINs versus NNs, LLINs are more costly and more effective in 82% of the simulations, and less effective but more costly in 18% of the simulation. LLINs are never less costly and less effective or less costly and more effective. The CEAC (Figure 9) shows than LLINs have a higher probability of being cost-effectiveness compared to NNs at a willingness to pay (WTP) of approximately £1000 or higher. As the WTP is increased, the probability of LLINs being cost-effective does not increase past approximately 72%. Similar results are observed for LLINs versus UTNs. The CEAF (Figure 10) shows that between WTP of £0 and approximately £1000 LLINs are not expected to achieve a greater mean net monetary benefit. However, from approximately a WTP of £1000 and beyond, LLINs are expected to achieve a greater mean net monetary benefit than UTNs or NNs.

Table 30: Mean PSA results for children aged less than years old

	Total Costs (£)	Total QALYs	Incremental Costs (£)	Incremental QALYs	ICER (£) versus baseline (QALYs)	ICER (£) incremental (QALYs)
NN	0.00	2.050	-	-	-	-
UTN	2.13	2.054	2.13	0.003	697	697

LLIN	4.77	2.057	2.64	0.003	779	860
ICER – incremental cost-effectiveness ratio; LLIN – long-lasting insecticide net; NN – no net; UTN – untreated net; QALYs- quality adjusted life year						

Figure 8: Incremental cost-effectiveness plane for children aged less than 5 years old

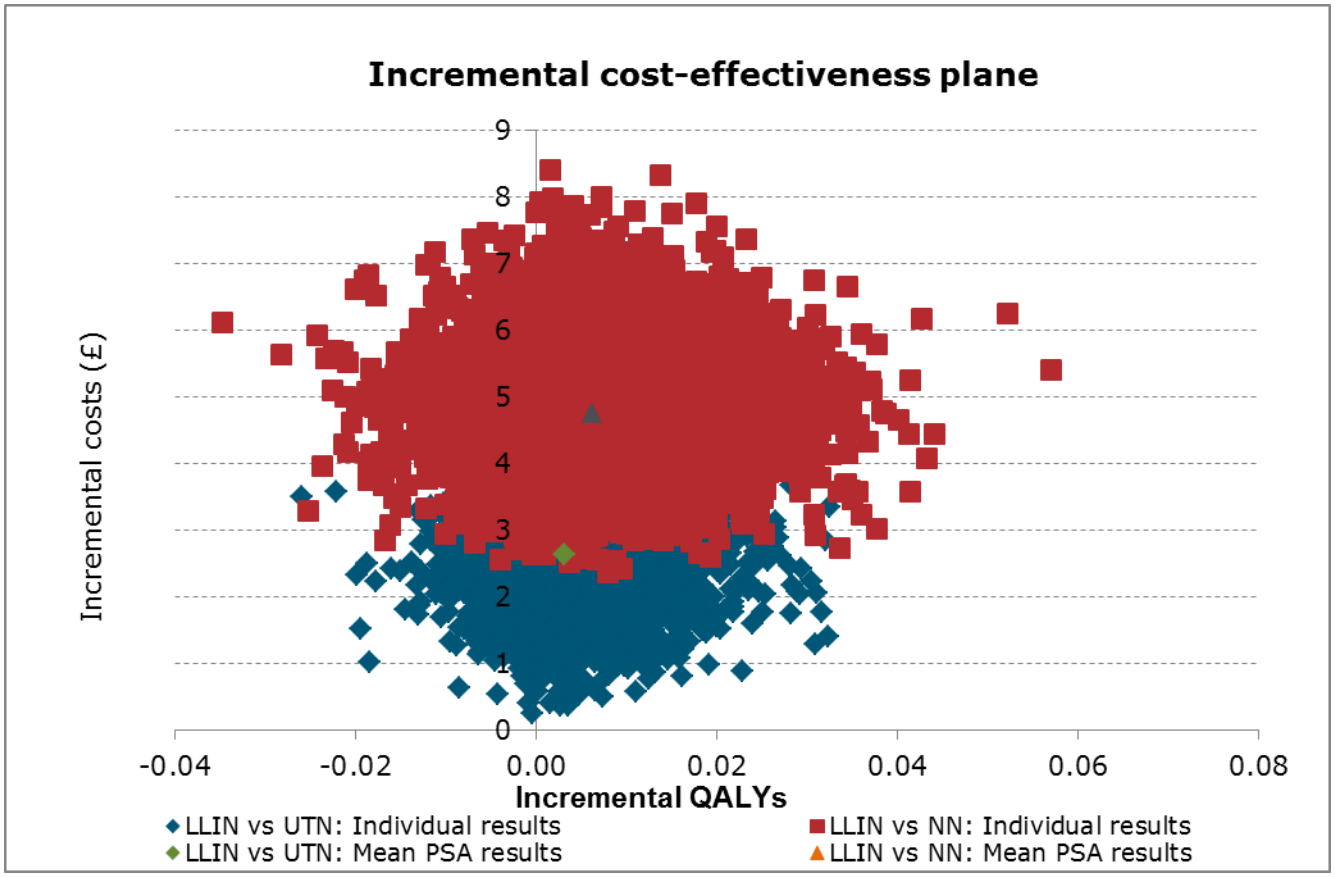


Figure 9: Cost-effectiveness acceptability curve for children aged less than 5 years old

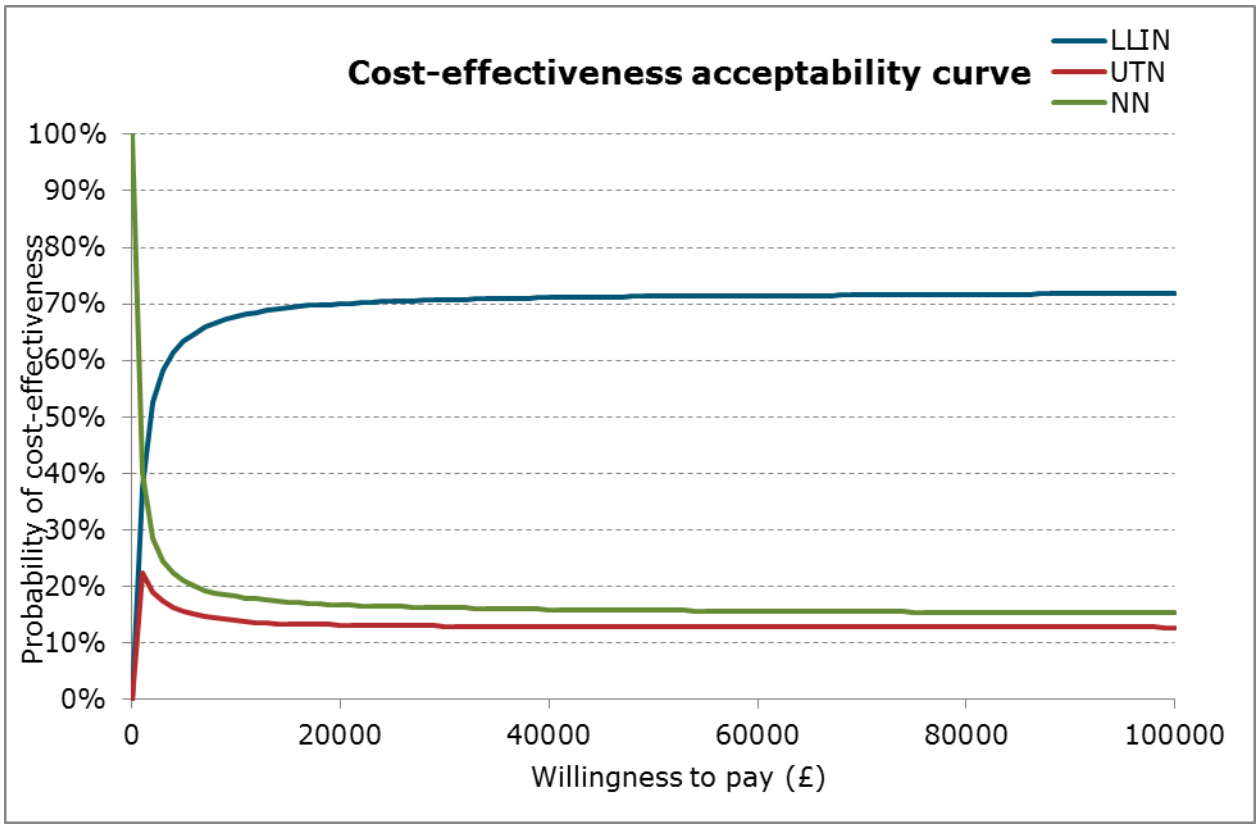
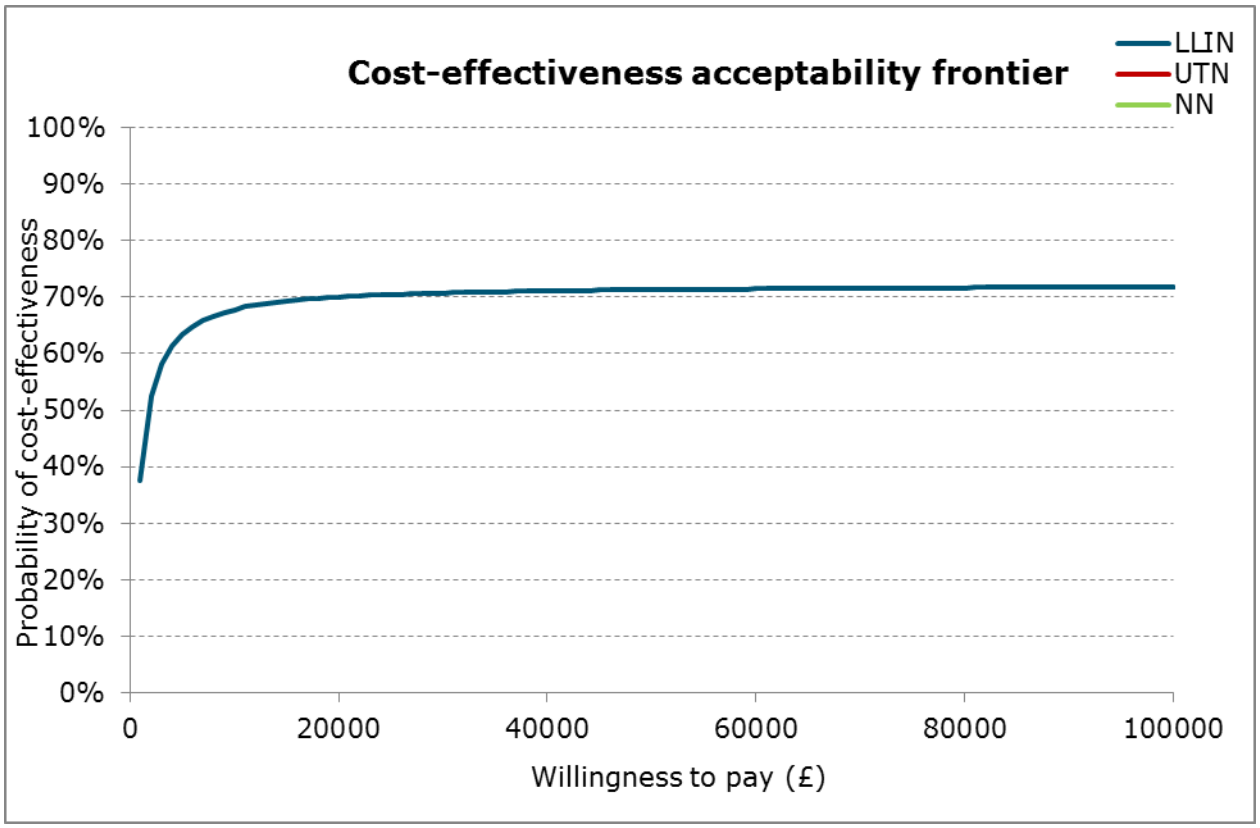


Figure 10: Cost-effectiveness acceptability frontier for children aged less than 5 years old



3.2.3.2. Children aged between 5 and 18 years old

Table 31 shows the mean results for PSA for children aged between 5 and 18 years old. Results are very similar to that of the base case. For LLINs versus UTNs the ICEP (Figure 11) shows that the majority of simulations (63%) are where LLINs is more costly and more effective. LLINs are shown to be more costly but less effective than UTNs in 37% of simulations. For LLINs versus NNs, LLINs are more costly and more effective in 72% of the simulations, and less effective but more costly in 28% of the simulation. LLINs are never less costly and less effective or less costly and more effective. The CEAC (Figure 12) shows than LLINs have a higher probability of being cost-effectiveness compared to NNs at a WTP of approximately £1,000 or higher. As the WTP is increased, the probability of LLINs being cost-effective does not increase past approximately 54%. Similar results are observed for LLINs versus UTNs. The CEAF (Figure 13) shows that between WTP of £0 and approximately £1,000, LLINs are

not expected to achieve a greater mean net monetary benefit. However, from approximately a WTP of £1,000 and beyond, LLINs are expected to achieve a greater mean net monetary benefit than UTNs or NNs.

Table 31: Mean PSA results for children aged between 5 and 18 years old

	Total Costs (£)	Total QALYs	Incremental Costs (£)	Incremental QALYs	ICER (£) versus baseline (QALYs)	ICER (£) incremental (QALYs)
NN	0.00	2.077	-	-	-	-
UTN	2.32	2.080	2.32	0.003	833	833
LLIN	4.94	2.083	2.62	0.003	891	950
ICER – incremental cost-effectiveness ratio; LLIN – long-lasting insecticide net; NN – no net; UTN – untreated net; QALYs- quality adjusted life year						

Figure 11: Incremental cost-effectiveness plane for children aged between 5 and 18 years old

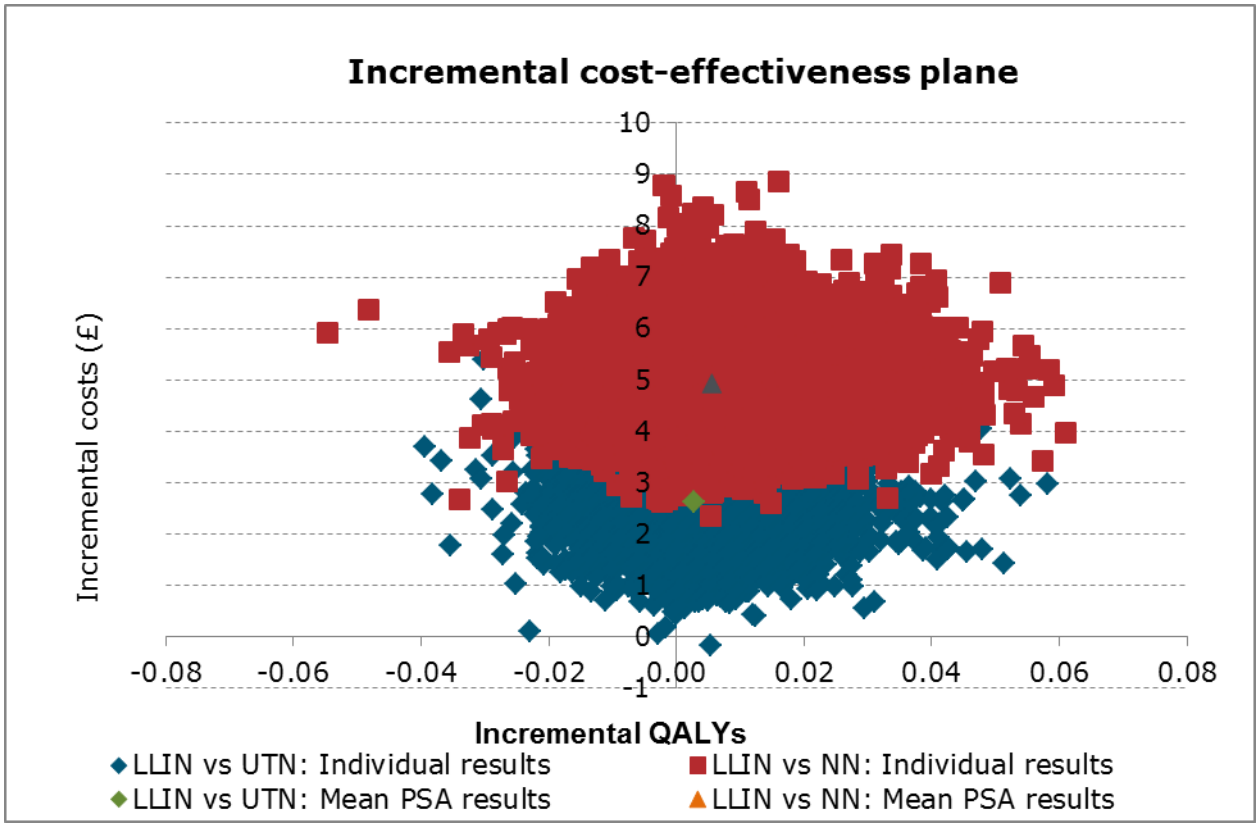


Figure 12: Cost-effectiveness acceptability curve for children aged between 5 and 18 years old

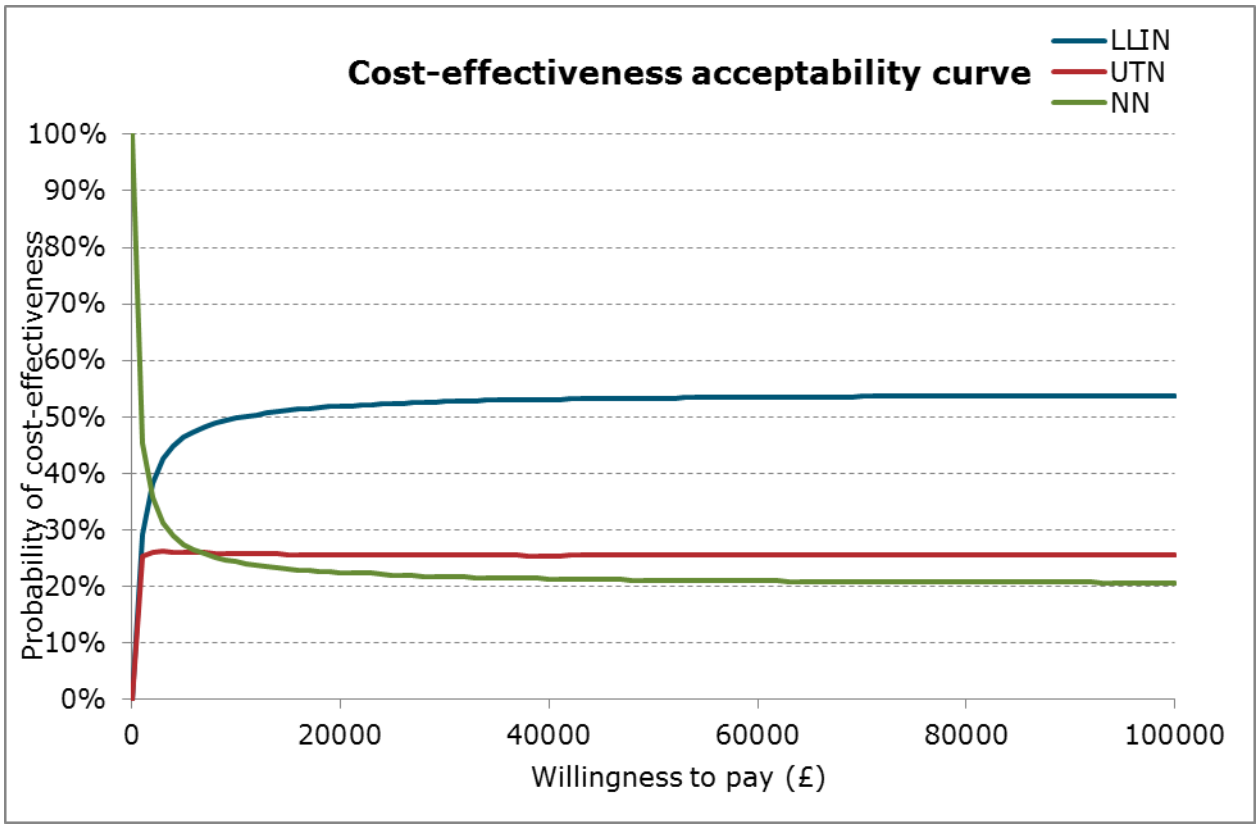
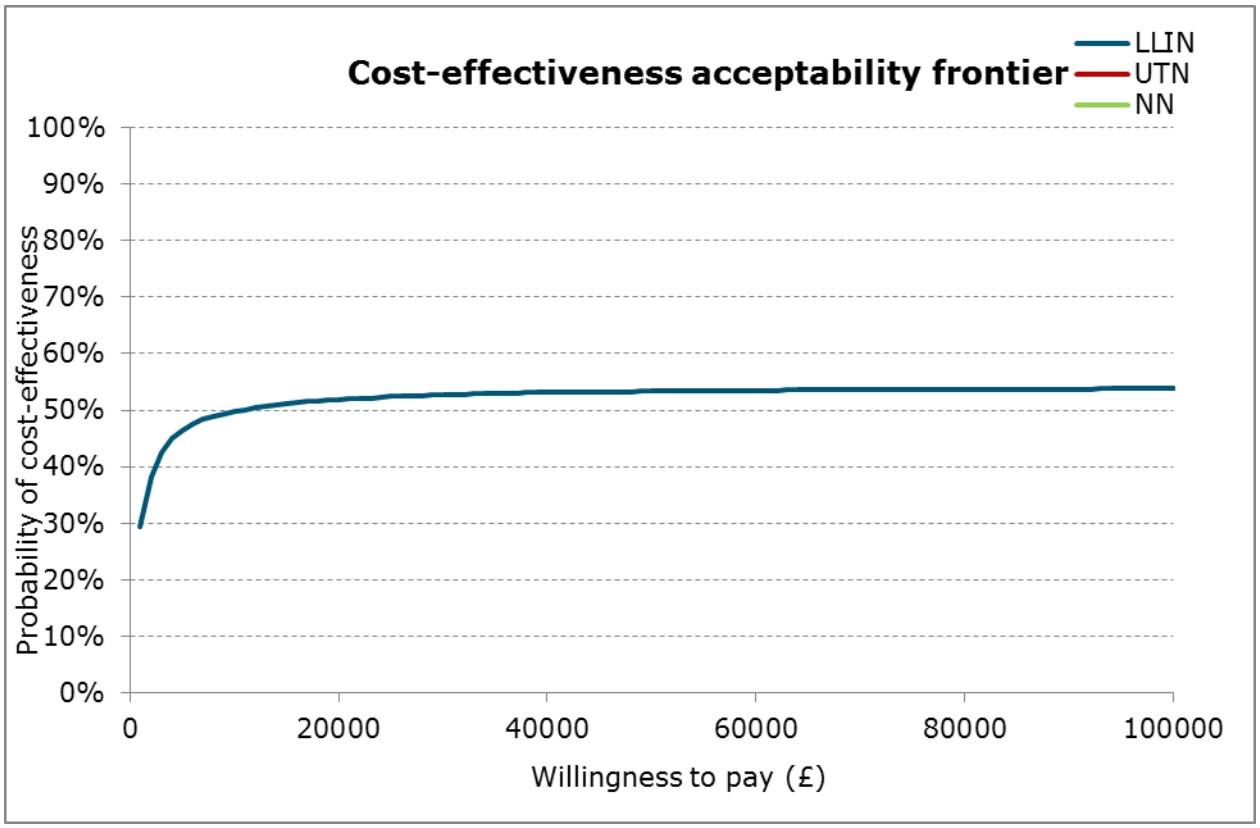


Figure 13: Cost-effectiveness acceptability frontier for children aged between 5 and 18 years old



3.2.3.3. Adults and children of any age

Table 32 shows the mean results for PSA for adults and children of any age, Results are very similar to that of the base case. For LLINs versus UTNs the ICEP (Figure 14) shows that the majority of simulations (63%) are where LLINs is more costly and more effective. LLINs are shown to be more costly but less effective than UTNs in 37% of simulations. For LLINs versus NNs, LLINs are more costly and more effective in 72% of the simulations, and less effective but more costly in 28% of the simulation. LLINs are never less costly and less effective or less costly and more effective. The CEAC (Figure 15) shows than LLINs have a higher probability of being cost-effectiveness compared to NNs at a WTP of approximately £900 or higher. As the WTP is increased, the probability of LLINs being cost-effective does not increase past approximately 59%. Similar results are observed for LLINs versus UTNs. The CEAF (Figure 16) shows that between WTP of £0 and approximately £900 LLINs are not expected to achieve a greater mean net monetary benefit. However, from

approximately a WTP of £900 and beyond, LLINs are expected to achieve a greater mean net monetary benefit than UTNs or NNs.

Table 32: Mean PSA results for adults and children of any age

	Total Costs (£)	Total QALYs	Incremental Costs (£)	Incremental QALYs	ICER (£) versus baseline (QALYs)	ICER (£) incremental (QALYs)
NN	0.00	1.983	-	-	-	-
UTN	3.42	1.994	3.42	0.011	306	306
LLIN	5.88	2.005	2.46	0.011	268	230

ICER – incremental cost-effectiveness ratio; LLIN – long-lasting insecticide net; NN – no net; UTN – untreated net; QALYs- quality adjusted life year

Figure 14: Incremental cost-effectiveness plane for adults and children of any age

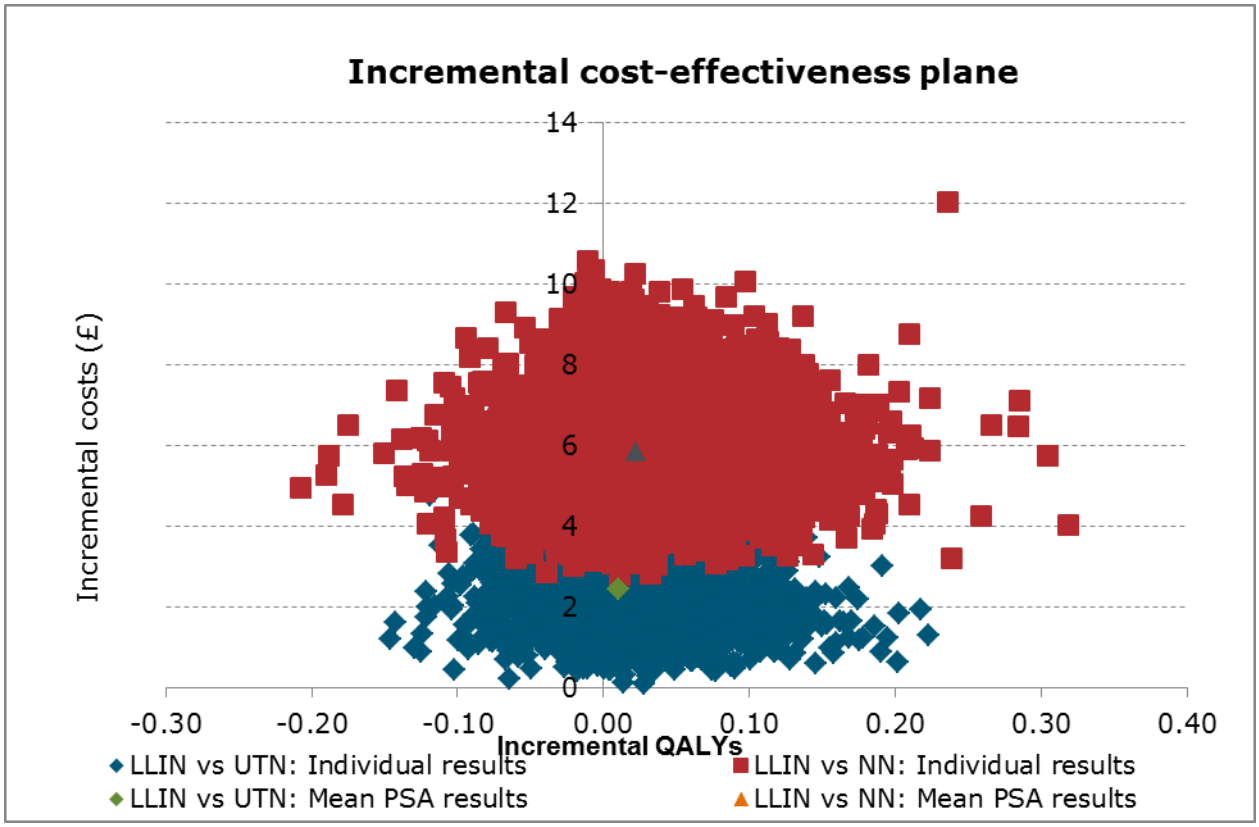


Figure 15: Cost-effectiveness acceptability curve for adults and children of any age

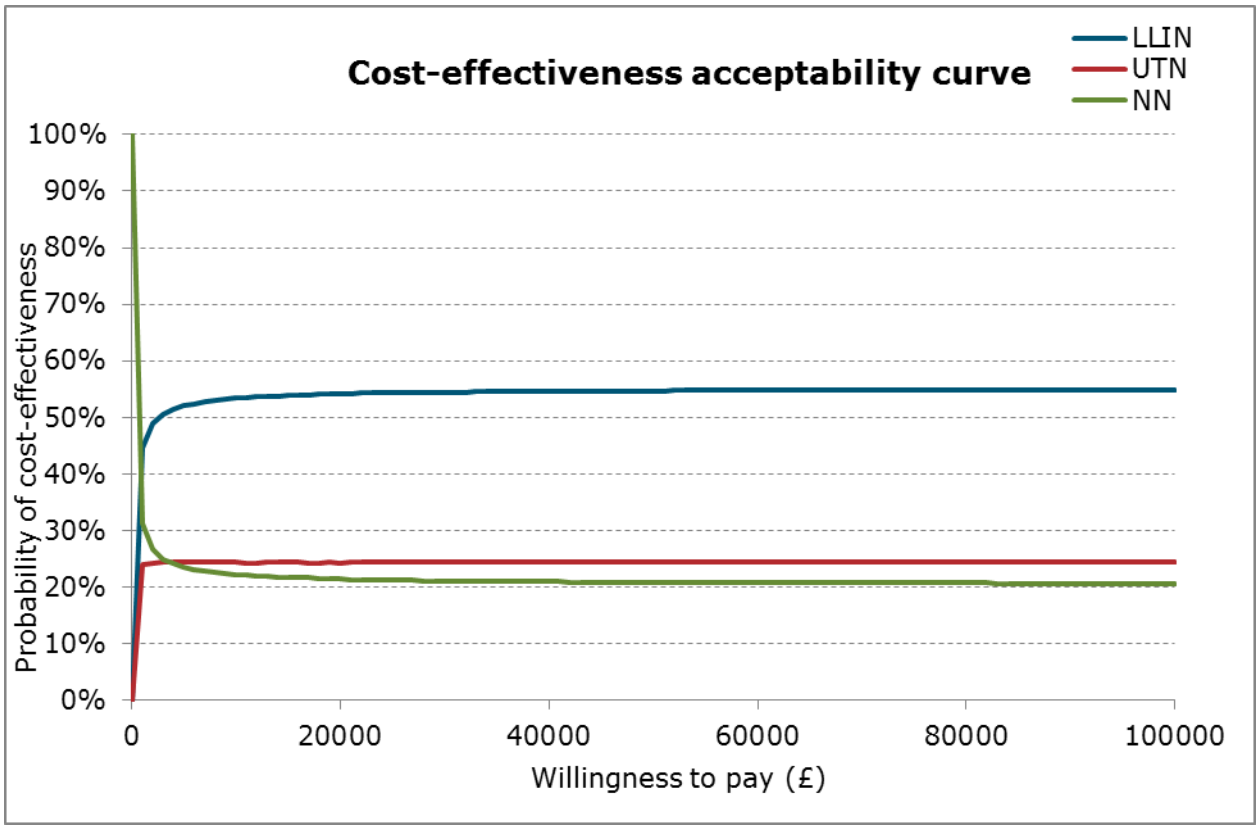
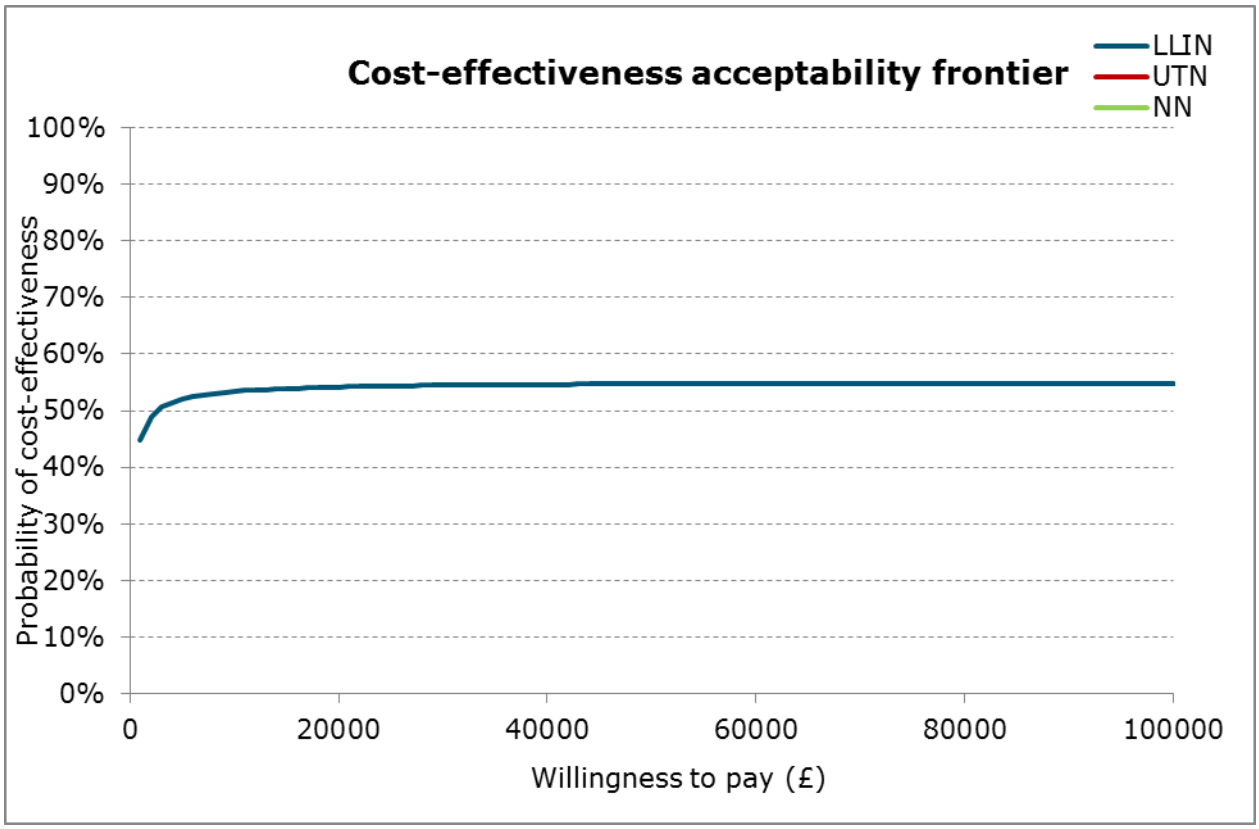


Figure 16: Cost-effectiveness acceptability frontier for adults and children of any age



4. Discussion

The base case results found that LLINs are cost-effective in comparison to UTNs and NNs with an incremental cost-effectiveness ratio (ICER) below £1,000 per QALY in all populations. In England and Wales, NICE are willing to pay £20,000 to £30,000 per QALY; as such LLINs can be considered extremely cost-effective. In addition, all sensitivity analyses performed resulted in ICERs less than £5,000 per QALY in all cases. Finally, it would appear that the use of LLINs is more cost-effective in mixed age populations as opposed to infants, which is likely due to the excess mortality risk due to other causes in children less than 5 years.

The current estimates by GiveWell suggest that the cost per death averted is approximately $2,000 in children aged less than 5 years whilst the cost per death averted in this analysis is slightly higher at $2,952. However, if one were to consider net sharing at 0.67 nets per person the cost per death averted is almost identical.

Despite the fact that the analysis uses an entirely different model structure compared to GiveWell, a variety of different sources to derive clinical effectiveness, and a broader scope to include older populations than children aged less than 5 years, it is reassuring to observe that the cost-effectiveness results calculated by GiveWell are similar to those calculated in this analysis. It should also be noted that focusing on deaths averted does not account for the quality of life benefits achieved by preventing malaria; as such the cost per QALY is a far better representation of the overall value of LLINs.

Limitations of the analysis include assumptions in relation to the effectiveness of UTNs relative to LLINs and insecticide resistance. However, both were tested extensively in scenario analyses and surprisingly large variations in these estimates did not dramatically impact the cost-effectiveness of LLINs. In addition, in some instances limited data were available for children between 5-18 years and adults and children of any age, and as such results for these populations should be considered with more caution. With these limitations aside, it can be confidently concluded that LLINs for the prevention of malaria are a cost-effective intervention in all populations where malaria is at high risk. We hope this will encourage donors to give to this great cause.

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6. Appendix 1

Objective

The objective of the systematic literature review (SLR) was to determine the magnitude of clinical benefit and risk of residence with insecticide-treated bed nets to inform the cost-effectiveness model of the use of LLINs for the prevention or malaria.

Methods

The SLR specified two review questions which sought to identify existing clinical studies conducted in malaria:

- What is the magnitude of the impact of long lasting insecticide-treated bed nets or curtains on mortality and malarial risk?
- What is the clinical evidence base for insecticide resistance risk with insecticide-treated bed nets or curtains?

For the review, eligibility criteria were specified with no limits on language or date of publication. Database searching using pre-defined search strategies was conducted in EMBASE, the Cochrane Library and LILACS. In addition, grey literature searching was performed searching conference proceedings and Google Scholar. Studies were selected by one independent reviewers based on title and abstract (first pass) and then full text articles (second pass). Relevant studies were then extracted by one reviewer.

Results

The SLR retrieved 88 references of which met the eligibility criteria for clinical studies. Of these, 10 references were extracted: 9 references were extracted as they reported all-cause mortality related outcomes; and 1 reference was extracted as it reported insecticide resistance related outcomes. All of the 10 extracted references were randomised controlled trials; 9 of which were cluster RCTs. Of these 10 extracted references, 6 references examined the impact of permethrin insecticide-treated-nets versus a control of no bednets; 1 reference examined the impact of permethrin long-lasting-insecticide-nets versus a control of no bednets; 1 reference examined the impact of permethrin insecticide-treated-nets versus a control of untreated nets; and 2 references examined the impact of insecticide-treated-curtains versus a control of no curtains.

Conclusions

The SLR identified 9 references to infer the magnitude of benefit with insecticide-treated bednets and 1 reference which considered the risk of resistance with insecticide-treated bednets. For further detail on the SLR please contact mark.fisher@fiecon.com or lydia.walder@fiecon.com.

7. Appendix 2

7.1. Children aged less than 5 years old

LLIN transition matrices

Year 1

	AH	AWM	*Total*
AH	99%	1%	*TRUE*
AWM	0%	100%	*TRUE*

Year 2

	AH	AWM	*Total*
AH	98%	2%	*TRUE*
AWM	0%	100%	*TRUE*

Year 3

	AH	AWM	*Total*
AH	98%	2%	*TRUE*
AWM	0%	100%	*TRUE*

UTN transition matrices

Year 1

	AH	AWM	*Total*
AH	98%	2%	*TRUE*
AWM	0%	100%	*TRUE*

Year 2

	AH	AWM	*Total*
AH	98%	2%	*TRUE*
AWM	0%	100%	*TRUE*

Year 3

	AH	AWM	*Total*
AH	98%	2%	*TRUE*
AWM	0%	100%	*TRUE*

NN transition matrices

Year 1+

	AH	AWM	*Total*
AH	97%	3%	*TRUE*
AWM	0%	100%	*TRUE*

7.2. Children aged between 5 and 18 years old

LLIN transition matrices

Year 1

	AH	AWM	*Total*
AH	97%	3%	*TRUE*
AWM	0%	100%	*TRUE*

Year 2

	AH	AWM	*Total*
AH	96%	4%	*TRUE*
AWM	0%	100%	*TRUE*

Year 3

	AH	AWM	*Total*
AH	96%	4%	*TRUE*
AWM	0%	100%	*TRUE*

UTN transition matrices

Year 1

	AH	AWM	*Total*
AH	96%	4%	*TRUE*
AWM	0%	100%	*TRUE*

Year 2

	AH	AWM	*Total*
AH	96%	4%	*TRUE*
AWM	0%	100%	*TRUE*

Year 3

	AH	AWM	*Total*
AH	96%	4%	*TRUE*
AWM	0%	100%	*TRUE*

NN transition matrices

Year 1+

	AH	AWM	*Total*
AH	96%	4%	*TRUE*
AWM	0%	100%	*TRUE*

7.3. Adults and children of any age

LLIN transition matrices

Year 1

	AH	AWM	*Total*
AH	86%	14%	*TRUE*
AWM	0%	100%	*TRUE*

Year 2

	AH	AWM	*Total*
AH	83%	17%	*TRUE*
AWM	0%	100%	*TRUE*

Year 3

	AH	AWM	*Total*
AH	81%	19%	*TRUE*
AWM	0%	100%	*TRUE*

UTN transition matrices

Year 1

	AH	AWM	*Total*
AH	83%	17%	*TRUE*
AWM	0%	100%	*TRUE*

Year 2

	AH	AWM	*Total*
AH	82%	18%	*TRUE*
AWM	0%	100%	*TRUE*

Year 3

	AH	AWM	*Total*
AH	81%	19%	*TRUE*
AWM	0%	100%	*TRUE*

NN transition matrices

Year 1+

	AH	AWM	*Total*
AH	81%	19%	*TRUE*
AWM	0%	100%	*TRUE*

8. Appendix 3

Table 33: Base case results in USD - children aged less than 5 years old

	Total Costs ($)	Total LYG	Total QALYs	Incremental Costs ($)	Incremental LYG	Incremental QALYs	ICER ($) versus baseline (QALYs)	ICER ($) incremental (QALYs)
NN	0.00	2.831	2.055	-	-	-	-	-
UTN	3.08	2.832	2.058	3.08	0.001	0.003	1,030	1,030
LLIN	6.86	2.834	2.061	3.78	0.001	0.003	1,146	1,261
ICER – incremental cost-effectiveness ratio; LLIN – long-lasting insecticide net; NN – no net; UTN – untreated net; QALYs- quality adjusted life year								

Table 34: Base case results in USD - children aged between 5 and 18 years old

	Total Costs ($)	Total LYG	Total QALYs	Incremental Costs ($)	Incremental LYG	Incremental QALYs	ICER ($) versus baseline (QALYs)	ICER ($) incremental (QALYs)
NN	0.00	2.876	2.078	-	-	-	-	-
UTN	3.35	2.876	2.081	3.35	0.000	0.003	1,241	1,241
LLIN	7.12	2.877	2.084	3.77	0.000	0.003	1,319	1,397
ICER – incremental cost-effectiveness ratio; LLIN – long-lasting insecticide net; NN – no net; UTN – untreated net; QALYs- quality adjusted life year								

Table 35: Base case results in USD - adults and children of any age

	Total Costs ($)	Total LYG	Total QALYs	Incremental Costs ($)	Incremental LYG	Incremental QALYs	ICER ($) versus baseline (QALYs)	ICER ($) incremental (QALYs)
NN	0.00	2.835	1.981	-	-	-	-	-
UTN	4.93	2.835	1.991	4.93	0.001	0.011	467	467
LLIN	8.48	2.836	2.002	3.55	0.001	0.011	399	331
ICER – incremental cost-effectiveness ratio; LLIN – long-lasting insecticide net; NN – no net; UTN – untreated net; QALYs- quality adjusted life year								