**MODELLING COST-EFFECTIVENESS OF MALARIA DIAGNOSTIC METHODS IN SUB-SAHARAN AFRICA**

**AIMS AND OBJECTIVES**

The aim of this project was to carry out the economic evaluation methods to a real world example. The objective was to build a decision analytic model for two different methods of the diagnosis of malaria in Sub-Saharan Africa. The context of this study is based on information from WHO publications and online materials[[1]](#footnote-1).

**CONTEXT OF THE STUDY[[2]](#footnote-2):**

The introduction of high-cost antimalarial drugs such as artemisinin-based combination therapy (ACT) is encouraging malaria-endemic countries in sub-Saharan Africa to reassess diagnostic practices. Traditional practice for outpatients has been to treat presumptively for malaria based on a history of fever, but a significant proportion of those treated may not have parasites (over 50% in many settings) and hence waste a considerable amount of drugs. Widespread prescription of *chloroquine* to patients not having malaria has been tolerated, partly because *chloroquine* is relatively cheap. However, ACT costs at least 10 times more per treatment. Additionally, over-diagnosis of malaria implies under-diagnosis and inappropriate treatment of *non-malarial febrile illness (NMFI)*: while a high proportion of such illnesses are self-limiting *viral diseases*, a significant minority, such as acute respiratory infections or bacterial meningitis, are *bacterial diseases* and potentially fatal.

WHO currently makes the tentative recommendation that parasite-based diagnosis should be used in all cases of suspected malaria with the possible exception of children in high-prevalence areas. Parasite-based diagnosis can be done in two main ways; microscopy and rapid diagnostic tests (RDTs). As microscopy is generally limited to larger clinics, rapid diagnostic tests (RDTs) for malaria could be considered for most patients in endemic regions. However, there is very little evidence to guide decision-makers on the relative cost-effectiveness of presumptive treatment (PT) versus RDTs.

**The objective** of this project was to *use a* ***decision tree model*** *to estimate the* ***relative cost-effectiveness*** *of RDTs versus presumptive treatment (PT)* in Kenya[[3]](#footnote-3) and fill this information gap.

**DECISION RULE (ALTERNATIVE TREATMENTS):**

The process starts with ambulatory patients presenting with fever to health facilities in rural Kenya and then proceeds through diagnosis and treatment to disease outcomes accordingly to the diagnostic. Once the test is done the patient will either receives ACT if the test is positive or antibiotics if the test is negative. However, given the possibility of the tests provide misleading results (false negative of false positive – *see section with probabilities*) patients may receive a treatment that is not advised (ACT for NFMI, e.g.).

A patient with malaria can either have s*evere* or *uncomplicated* malaria, and a patient with NMFI can have either a Viral Infection (VI) or a Bacterial Infection (BI) – in the latter case the condition can be *severe* or *uncomplicated*. The available treatments for malaria are *inpatient care* (severe cases), *outpatient care* (uncomplicated) or *no care* (for both types of malaria). The available treatments for BI are *inpatient care* (severe cases), *outpatient care* (uncomplicated) or *no care* (for both types of BI). For all cases of malaria and bacterial infection the possible outcomes are *fully recovers, recovers with neurological sequel*, or *death*.All cases of viral infection result in fully recovers.

**PROBABILITIES:**

It is assumed that all patients admitted with fever health facilities in Kenya have either malaria or NMFI, the probability of having malaria is ***0.48*** (C.I. 040 – 0.56). The best estimates for drug efficacy are set at 85% for ACT in cases of malaria and 75% for antibiotics in bacterial disease. For simplicity we may assume that antibiotics and ACT have a lower efficacy when used wrongly (NMFI treated with ACT, e.g.). However, all cases treated wrongly will develop the severe condition for both malaria and bacterial infection (The probabilities you need to consider are in page 5.).

Table 1: Test outcomes

|  |  |  |
| --- | --- | --- |
| **Test** | **Values** | |
| Rapid Diagnostic Test (RDT) | *Sensitivity* | 0.96 |
| *Specificity* | 0.95 |
| Presumptive Treatment (PT) | *Sensitivity* | 1 |
| *Specificity* | 0 |

SOURCE: Shillcutt, S. et al. (2008).

Other parameters are:

* The probability that a *non-malarial Febrile* case is due to a bacterial infection is 30%;
* The probability that a bacterial infection become severe is:
* *0.20 if diagnosed as non-malarial at the time of the test;*
* *0.95 if diagnosed after incorrect treatment with ACTs.*
* 70% of the severe cases of bacterial infections will be treated by inpatient care while 25% of the uncomplicated cases will be treated by outpatient care (the probability of recover and other outcomes are given below);
* The probability that a malaria case become severe is:
* *0.05 if corrected diagnosed at the time of the test;*
* *0.87 if diagnosed after incorrect treatment with antibiotics.*
* 90% of the severe cases of malaria will be treated by inpatient care while 40% of the uncomplicated cases will be treated by outpatient care (the probability of recover and other outcomes are given below);

Table 2: Probabilities associated with the different treatments are:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Description** | **Treated with ACT** | | **Treated with Antibiotics** | |
| **Malaria (severe)** | **Probability** | **C.I.** | **Probability** | **C.I.** |
| *Fully recover* | 0.92 | 0.89 – 0.95 | 0.35 | 0.30 - 0.40 |
| *Recover with neurological sequels* | 0.05 | 0.03 – 0.07 | 0.4 | 0.38 - 0.42 |
| *Death* | 0.03 | 0.01– 0.05 | 0.25 | 0.20 - 0.30 |
| **Malaria (uncomplicated)** |  | | | |
| *Fully recover* | 0.97 | 0.95 - 0.99 | 0.4 | 0.35 - 0.45 |
| *Recover with neurological sequels* | 0.027 | 0.02 - 0.3 | 0.45 | 0.40 - 0.50 |
| *Death* | 0.003 | 0.001 - 0.004 | 0.15 | 0.10 - 0.20 |
| **Non-malarial Febrile Illness** |  | | | |
| Bacterial infection (severe) |  | | | |
| *Fully recover* | 0.8 | 0.78 - 0.83 | 0.95 | 0.93 - 0.98 |
| *Recover with neurological sequels* | 0.15 | 0.12 - 0.16 | 0.04 | 0.02 - 0.06 |
| *Death* | 0.05 | 0.03 - 0.07 | 0.01 | 0.005 - 0.012 |
| Bacterial infection (uncomplicated) |  | | | |
| *Fully recover* | 0.98 | 0.95 - 0.99 | 0.98 | 0.96 - 0.99 |
| *Recover with neurological sequels* | 0.015 | 0.012 - 0.018 | 0.02 | 0.01 - 0.03 |
| *Death* | 0.005 | 0.003 - 0.007 | 0 | N/A |
| Viral infection |  | | | |
| *Fully recover* | 1 | N/A | 1 | N/A |

SOURCE: hypothetical parameters.

**OUTCOMES/CONSEQUENCES:**

The health outcomes are measured in terms of disability-adjusted life years (DALYs) averted and life years saved (LY), both given in present values (i.e., a discount rate has been applied for the effects occurring in the future). The table 3 below presents the DALY’s averted and life years saved for each treatment strategy, these numbers are hypothetical.

Table 3: Health outcomes (in DALY’s)

|  |  |  |
| --- | --- | --- |
| **Description** | **DALYS averted** | **LY** |
| **Malaria (severe)** |
| *Fully recover* | 28 | 45 |
| *Recover with neurological sequels* | 13 | 35 |
| *Death* | 0 | 0 |
| *No care* | 0 | 0 |
| **Malaria (uncomplicated)** | | |
| *Fully recover* | 18 | 30 |
| *Recover with neurological sequels* | 9 | 22 |
| *Death* | 0 | 0 |
| *No care* | 13 | 35 |
| **Non-malarial Febrile Illness** | | |
| Bacterial infection (severe) | | |
| *Fully recover* | 16 | 20 |
| *Recover with neurological sequels* | 8 | 12 |
| *Death* | 0 | 0 |
| *No care* | 0 | 0 |
| Bacterial infection (uncomplicated) |  |  |
| *Fully recover* | 10 | 15 |
| *Recover with neurological sequels* | 6 | 9 |
| *Death* | 0 | 0 |
| *No care* | 2 | 4 |
| Viral infection | | |
| *All cases* | 8 | 10 |
| **Malaria (treated with ACT)- treatment effective** | 33 | 50 |
| **Non-malarial Febrile Illness (treated with antibiotics)- treatment effective** | 21 | 25 |

SOURCE: hypothetical parameters.

**COSTS:**

The cost are calculated GBP (2018 prices) and it includes the perspective of providers and patients. RDT diagnosis includes the unit cost of the test, each kit is assumed to cost £3.50; diagnosis according to presumptive treatment is assumed to cost nothing. The cost of ACT is £2.40 (C.I. £1 - £3.00) per adult and the cost of antibiotics is £0.90 (C.I. £0.72 - £1.20). The average length of stay as an inpatient is 4.5 for a case of severe malaria and fully recovered and 6 for those recovered with sequels. For severe case of bacterial infection the average length of stay is 4.5 and 3 respectively. For all illnesses the Average length of stay for inpatients who died is 2. The number of outpatients visits for malaria is 3 for all malaria outcomes and 2 for bacterial infection (e.g., someone fully recovered, recovered with sequels or those who died from malaria will visit the outpatient services 3 times during the treatment).

Table 4: direct costs of treatment (2018 £)\*

|  |  |  |
| --- | --- | --- |
| **Description** | **Providers** | **Patients** |
| Inpatient (cost per day) |  |  |
| *Malaria* | 19 | 3.84 |
| *Bacterial Infection* | 7.0 | 2.40 |
| Outpatient (cost per visit) |  |  |
| *Malaria* | 4.62 | 0.74 |
| *Bacterial Infection* | 1.2 | 0.80 |
| Drug costs (Adult Doses) |  |  |
| *ACT's* | 2.4 | - |
| *Antibiotics* | 0.90 | - |

SOURCE: Shullcutt et al., 2007; the numbers for BI are hypothetical.

**METHODS:**

I have developed a decision tree model to estimate the relative cost-effectiveness of RDTs versus presumptive treatment (PT). I have estimated the costs from health providers perspective and expressed benefits as disability-adjusted life years (DALYs) averted. Some of the parameters were obtained from Shillcutt, S. et al. (2008) study and some of them were hypothetical. I performed deterministic and probabilistic sensitivity analyses to assess the impact of uncertainty in the model’s parameter values on the cost-effectiveness results. I used Monte Carlo simulations to estimate uncertainty and presented this using cost-effectiveness acceptability curve (CEAC).

**RESULTS:**

Average costs per person receiving RDT were £6.74 and receiving PT were £4.86. Mean DALYs averted were 19.77 per person for RDT and 18.96 for PT. Thus, the average incremental cost per person receiving RDT was £1.88 compared to PT, while the average DALY averted gain was 0.8. This resulted in an ICER of £2.34 per DALY averted. CEAC show that the probability of RDT being cost-effective compared to PT is 0.56 and 0.60 at the thresholds of £3 and £5 respectively per DALY averted. This probability increases to 0.65 at the threshold of £10 per DALY averted.

I conclude that RDT is more expensive but have higher benefits than PT. Considering GDP-based thresholds, RDT is highly cost-effective. If price of RDT decrease by £2 RDT even become cost saving.

**REFERENCE**

Shillcutt S. et al. (2008).*Cost-effectiveness of malaria diagnostic methods in sub-Saharan Africa in an era of combination therapy*. Bulletin of the World Health Organization, Vol. 86(2): 101-10.

1. See: <http://www.wpro.who.int/sites/rdt> [↑](#footnote-ref-1)
2. Adapted from Shillcutt, S. et al. (2008). [↑](#footnote-ref-2)
3. For the purposes of this exercise we are ignoring potential differences in endemcity in the epidemiological settings of sub-Saharan Africa where *Plasmodium falciparum* predominates. [↑](#footnote-ref-3)