EVIDENCE BRIEF

Treat fever with ACT
no testing, high malaria setting
(DCP4 ID: MALR03-01,02,03)
Cluster: Malaria

FairChoices
DCP Analytic Tool

Malaria treatment in high endemic settings

Authors: Fekadu L, Ellertsen C, Kaur G, Ahmed S, Watkins D, Hirpesa GM, Coates MM, Økland JM, Haaland ØA, Johansson KA

Date for updating: 2020-07-14, 2021-11-26, 2021-12-01

Description of condition and intervention

In high malaria transmission settings where rapid tests and microscopy are unavailable, presumptive treatment of febrile illness with ACTs (non-severe cases) or ACTs plus antibiotics (severe cases). The primaquine therapy is the only accessible and effective treatment to avoiding relapse of malaria. World Health Organization (WHO) recommended single dose of 15 mg to 30 mg for 14 days to treat plasmodium falciparum malaria infection in high endemic areas to reduce the risk of the infection. Chloroquine is remained as highly effective first-line therapy in most of high endemic countries to treat vivax malaria infection. If diagnostics are available, use intervention malaria treatment with ACT preceded by rapid diagnostic testing. In this evidence brief, we present the effects and costs of the following interventions being analysed in FairChoices-DCP Analytical tool:

Treat fever with ACT (no testing), to target malaria in high malaria settings

Add primaquine to malaria treatment

P. vivax and chloroquine

Treat fever with ACT
no testing, high malaria setting
(DCP4 ID: MALR03-01,02,03)
Cluster: Malaria

FairChoices
DCP Analytic Tool

International guidelines

Organization	Indications/recommendations	Applicability in LIC & Lower MIC settings
World Health Organization 2021	WHO guidelines for the treatment of malaria	Yes

Intervention attributes

Type of interventions
Curative

Delivery platform
This intervention may be delivered through the community platform.

Equity
In addition to considerations like cost-effectiveness and health systems factors, dimensions of equity can be relevant for priority setting. The opportunity for a long and healthy life varies according to the severity of a health condition that individuals might have, so there are inequities in individuals' opportunities for long and healthy lives based on the health conditions they face. Metrics used to estimate the severity of illness at an individual level can be used to help prioritize those with less opportunity for lifetime health. FairChoices: DCP Analytics Tool uses Health adjusted age of death (HAAD), which is a metric that estimates the number of years lived from birth to death, discounting years lived with disability. A high HAAD thus represents a disease less severe in terms of lifetime health loss, while a low HAAD represents a disease that is severe on average, causing early death or a long period of severe disability. It is also possible to estimate the distribution of HAAD across individuals with a health condition. FairChoices shows for each intervention an average HAAD value of the conditions that are affected by respective interventions that have health effects. Additionally, a plot shows HAAD values for around 290 conditions (Johansson KA et al 2020).

Time dependence

High level of urgency. Treatment outcomes may be highly affected by some days of delay in high malaria settings.

Population in need of interventions

Treated population: All incident cases of fever/malaria irrespective of the age (0 to 99 years) and gender receive the treatment with ACT in high malaria settings. The treated fraction is assumed to be 0.285.

Affected population: The affected population is same as the above-mentioned treated population. The affected fraction is same as treated fraction.

Table 1: Population in need of interventions

Intervention	**Treated population**		**Affected population**		**Disease state addressed**
	Treated age	Treated fraction	Affected age	Affected fraction	
Treat fever with ACT	0 to 99 years both genders; incidence based	0.285	0 to 99 years both genders; incidence based	1	Malaria
Add primaquine to malaria treatment	0 to 99 years both genders; all	Malaria elimination indicator	In absence of malaria transmission mode, no effects assumed in this version of model.		Malaria
P. vivax and chloroquine	0 to 99 years both genders; incidence based	0.8	0 to 99 years of those with the condition	0.7*	Malaria

*Affected fraction adjusted for proportion who had recurrence=1-0.324=0.676~0.7

Intervention effect and safety

Table 2: Effect and safety of treatment for malaria

Effect of intervention		Certainty of evidence
Prevalence Treat fever with ACT	A meta-analysis by Gebreyohannes EA et al 2017 reported treatment success of 98.1% (97.0-99.2) for Plasmodium falciparum malaria patients, treated with artemether-lumefantrine in Ethiopia. Pooled event rate of treatment failure with P. falciparum patients was 7.8% (95% CI: 2.1-13.6), but with AL treatment, failure was noted in 21/1497 patients (n/N). These outcomes were assessed at 28 days.	See appendix
Add primaquine to malaria treatment P. vivax and chloroquine	In absence of malaria transmission mode, no effects assumed in this version of model. Prevalence reduction of 0.947 (0.926 to 0.962) Commons et al 2018)	

Model assumptions

Table 2: Summary of model parameters and values used in FairChoices – DCP Analytical Tool

Category	Model parameter	Notes
Interventions	Treat fever with ACT (no testing), to target malaria in high malaria settings Add primaquine to malaria treatment P. vivax and chloroquine	
Cost parameters		
Treated population	Incidence of Malaria	Global Burden of Disease study 2019
Gender	See table 1	

Age		
Treated fraction		
Effect parameters		
Affected Population	With condition	
Affected gender	See table 1	
Affected fraction age		
Affected fraction		
Comparison	No intervention	
Mortality Reduction Treat fever with ACT	0.98	Gebreyohannes EA et al 2017
Prevalence Reduction P. vivax and chloroquine	0.95	

Intervention Cost

The total unit cost for treating fever with ACT to target malaria in high-malaria settings is estimated to be USD 3.05 (Year: 2011).

Unit cost of adding primaquine to malaria treatment to target malaria in high-malaria settings is estimated to be USD 0.02 (Year: 2016) (Source Watkins 2020).

Unit cost of treating P.vivax malaria with chloroquine is estimated to be USD 0.92 (Year: 2016) (Source Watkins 2020).

References

WHO 2021: WHO Guidelines for malaria, 13 July 2021. Geneva: World Health Organization; 2021 (WHO/UCN/GMP/2021.01Rev. 1)

Johansson KA et al 2020: Johansson KA, Coates MM, Økland JM, Tsuchiya A, Bukhman G, Norheim OF, Haaland Ø. Health by disease categories. Distributional Cost-Effectiveness Analysis: Quantifying Health Equity Impacts and Trade-Offs. 2020 Sep 30:105.

Gebreyohannes EA et al 2017: Gebreyohannes EA, Bhagavathula AS, Seid MA, Tegegn HG. Anti-malarial treatment outcomes in Ethiopia: a systematic review and meta-analysis. Malar J. 2017 Jul 3;16(1):269. doi: 10.1186/s12936-017-1922-9. PMID: 28673348; PMCID: PMC5496337.

Commons RJ, Simpson JA, Thriemer K, Humphreys GS, Abreha T, Alemu SG, Añez A, Anstey NM, Awab GR, Baird JK, Barber BE, Borghini-Fuhrer I, Chu CS, D'Alessandro U, Dahal P, Daher A, de Vries PJ, Erhart A, Gomes MSM, Gonzalez-Ceron L, Grigg MJ, Heidari A, Hwang J, Kager PA, Ketema T, Khan WA, Lacerda MVG, Leslie T, Ley B, Lidia K, Monteiro WM, Nosten F, Pereira DB, Phan GT, Phyo AP, Rowland M, Saravu K, Sibley CH, Siqueira AM, Stepniewska K, Sutanto I, Taylor WRJ, Thwaites G, Tran BQ, Tran HT, Valecha N, Vieira JLF, Wangchuk S, William T, Woodrow CJ, Zuluaga-Idarraga L, Guerin PJ, White NJ, Price RN. The effect of chloroquine dose and primaquine on Plasmodium vivax recurrence: a WorldWide Antimalarial Resistance Network systematic review and individual patient pooled meta-analysis. Lancet Infect Dis. 2018 Sep;18(9):1025-1034. doi: 10.1016/S1473-3099(18)30348-7. Epub 2018 Jul 20. PMID: 30033231; PMCID: PMC6105624.

Watkins DA, Qi J, Kawakatsu Y, Pickersgill SJ, Horton SE, Jamison DT. Resource requirements for essential universal health coverage: a modelling study based on findings from Disease Control Priorities, 3rd edition. Lancet Glob Health. 2020 Jun;8(6):e829-e839. doi: 10.1016/S2214-109X(20)30121-2. PMID: 32446348; PMCID: PMC7248571.

Appendix

Literature Review for effectiveness & safety

This literature search is an example of a structured, focused review of literature and guidelines. You can choose to do one of the following literature reviews for your Evidence Brief:

Level 1: intervention inputs taken from DCP3 or generated in an ad hoc manner (e.g., quick google search found one study of cervical cancer screening cost-effectiveness that was used to create an effectiveness parameter for that intervention).

Level of evidence of efficacy studies:

1. low (expert opinions, case series, reports, low-quality case control studies)
2. moderate (high quality case control studies, low quality cohort studies)
3. high (high quality cohort studies, individual RCTs)
4. very high (multiple RCTs, meta-analysis, systematic review, clinical practice guidelines).

Supplementary details for P. Vivax and chloroquine (Commons 2018)

Prevalence reduction

0.947 (0.926 to 0.962)

Treat fever with ACT

no testing, high malaria setting
(DCP4 ID: MALR03-01,02,03)
Cluster: Malaria

Prevalence (Reduction of recurrence)

Risk of recurrence = 0.324

Proportion who stayed healthy = 0.676

Risk recurrence with treatment = 0.82 * 0.324 = 0.266 overall

Prevalence reduction = 1-0.266 = 0.734

Risk recurrence with treatment = 0.59 * 0.324 = 0.191 for children (<5yo)

Prevalence reduction = 1-0.191 = 0.809