Introducing Intermittent Preventive treatment of malaria for under five children's in Ethiopia: Evidence Brief.

Who is this Evidence brief for?

Policymakers, their support staff, and other stakeholders with an interest in the problem addressed by this Evidence brief.

Why was this Evidence brief prepared?

To inform policy makers by summarizing the best available evidence about the problem and its solution.

What is an evidence brief?

This Evidence briefs brings together global and local evidence to inform policy makers about health policies and programs

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Key Finding

Amodiaquine plus Sulfadoxine-pyrimethamine an effective and safe option for seasonal chemoprevention of Malaria for under-five children.

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Preface

The purpose of this report

The purpose of this evidence brief is to summarize the best available evidence regarding intermittent preventive treatment (IPT) intervention and implementation considerations to be introduced in Ethiopia for prevention of malaria for under-five children. It is not intended to prescribe or proscribe this specific intervention. Rather, its purpose is to allow policymakers and stakeholders to systematically and transparently consider the available evidence about the likely impacts of this intervention with other already available interventions in preventing malaria in pregnancy.

How this report was prepared

This evidence brief brings together global research evidence and local evidence on IPT to prevent malaria for under-five children. We searched for relevant evidence describing the problem in Ethiopian context, the impact of this intervention, barriers to implement, and implementation strategies to address these barriers. Different studies like relevant systematic reviews, RCTs, and other relevant and up to date studies were searched.

Limitations of this report

This evidence brief only focuses on this specific intervention and other viable options are not included. The intention of this evidence brief is not to replace available interventions rather to complement with this specific intervention to maximize the prevention of malaria for under-five children.

Background

Malaria is a life-threatening disease though it is preventable and curable. It remains a leading cause of ill health, causing an estimated 219 million cases of clinical malaria and 465 thousand deaths in 2017. More than 92% of malaria cases and 93% of malaria deaths occur in Africa south of the Sahara, here the vast majority of cases and deaths occur in under five children(Meremikwu *et al.*, 2012; Kafai and Odom John, 2018; Prevention, 2019).

In Ethiopia, malaria is highly seasonal in many communities, but may have nearly constant transmission in some other areas. Peak malaria transmission occurs between September and December in most parts of Ethiopia, after the main rainy season from June to August(PMI Initiative, 2019).

Globally multiple strategies were recommended by the World Health Organization's (WHO's) to control malaria. This combines multiple preventive interventions with case management, Insecticide treated nets (ITNs) and Indoor residual spraying (IRS)(World Health Organisation (WHO), 2010).(4-5) Starting from few years WHO recommends use of seasonal intermittent preventive treatment as additional malaria control strategy(WHO, 2010). In 2017 alone, 15.7 million children in 12 countries in Africa's Sahel subregion were protected through seasonal IPT(WHO, 2018).

In Ethiopia ITN were distributed widely as main strategy to control and eliminate malaria side by side with other strategies, but same with other African countries the coverage and utilization of INTs falls behind which is expected. Among Ethiopian children living in the area of malaria risk INTs use is as low as 45.3%, this indicates the other children are venerable for malaria risk(PMI Initiative, 2019).

The current federal ministry of health of Ethiopia plan does not support IPT because of the relatively low intensity of malaria transmission in most of Ethiopia, but 50% woredas of malaria area still have moderate and high risk for malaria and also malaria in Ethiopia is highly seasonal in many communities(PMI Initiative, 2019). Evidences indicate that IPT can be used

simultaneously with other malaria control strategy which can shorten malaria elimination strategy duration(Meremikwu *et al.*, 2012).

In Ethiopia currently the other two interventions recommended by WHO are in use for malaria for under five children but as many studies suggested these three interventions complement each other and when implemented together effectiveness increases. Therefore, this evidence brief is prepared to inform policy makers and others influential bodies to consider the implementation of this intervention in our country.

Description of Intermittent Preventive treatment with Amodiaquine plus Sulfadoxine-pyrimethamine.

Intermittent treatment, also known as 'intermittent preventive treatment' or 'intermittent presumptive treatment' (IPT), is an alternative strategy and is defined as the administration of a full therapeutic course of an antimalarial or antimalarial combination to a selected, target population at specified times without determining whether or not the subject is infected(Greenwood, 2010). Specifically, IPT for under-five children, defined as a full curative dose of an antimalarial alone or in combination given to children monthly or every two months during the malaria transmission season(Meremikwu *et al.*, 2012).

The recommended dosing schedule by age is:

- For infants up to 11 months old: half of a 153mg tablet of amodiaquine (AQ) base given once daily for three days and a single dose of half a 500/25mg tablet of Sulfadoxine-pyrimethamine (SP); and
- For children 12–59 months: a full tablet of 153mg amodiaquine base given once daily for three days and a single dose of a full tablet of 500/25mg SP. The single dose of SP is given only on the first day, at the same time as the first dose of amodiaquine

The following conditions are contradictions for administration of AQ plus SP:

- A child with an acute febrile illness or to severely ill children unable to take oral medication;
- An HIV-positive child receiving co-trimoxazole prophylaxis;
- A child who has received a dose of either SP or AQ during the past month; and
- A child who is allergic to either SP or AQ.

Effectiveness

We found a systematic review dealing with Intermittent preventive treatment prevents, approximately three quarters of all clinical and severe malaria episodes.

Table 1- Is Amodiaquine plus Sulfadoxine-pyrimethamine an effective and safe option for seasonal chemoprevention?

Is amodiaquine plus Sulfadoxine-pyrimethamine an effective and safe option for seasonal chemoprevention?					
Patient or Population: Children under five **Settings**: Area with seasonal malaria Transmission **Intervention**: seasonal intermittent preventive treatment of malaria **Comparison**: Placebo or No treatment					
Outcome	Comparative risk		Relative Effect (95% CI)	No of participants (studies)	Quality of Evidence
	Placebo	IPT			
Clinical malaria	2.5 episodes per child per year3	0.7 episodes per child per year (0.4 to 1.0)	Rate Ratio 0.26 (0.17 to 0.38)	9321 (6 studies)	⊕⊕⊕⊕ high
Severe Malaria	35 episodes per 1000 children per year4	9 episodes per 1000 children per year (4 to 27)	Rate Ratio 0.27 (0.1 to 0. 76)	5964 (2 studies)	⊕⊕⊕⊕ high

Safety

We found systematic review which showed us Amodiaquine plus Sulfadoxine-pyrimethamine most used combination for IPT and this combination does not have serious side effects but it does cause vomiting in some children(WHO, 2010; Meremikwu *et al.*, 2012).

Applicability

Complementing the use of an ITN, and prompt and effective case management, expanded program for immunization, growth monitoring and outreach services could be applied flexibly, so that the children always receive IPT-AQ plus SP during malaria season.

Expected benefits

Evidence from studies suggests that IPT with SP + AQ administered monthly for up to four months during the malaria transmission season in children aged 3–59 months.

- Prevents approximately 75% of all malaria episodes;
- Prevents approximately 75% of severe malaria episodes;
- May decrease child mortality by about 1 in 1000;
- Probably reduces the incidence of moderately severe anemia;
- Does not result in an increase in clinical malaria cases in the subsequent malaria transmission season after 1 year of IPT, although the consequences of implementing IPT for several years have not yet been evaluated; and
- No serious adverse events have been reported and are probably rare.

Economic consideration

We found systematic deals with effectiveness of IPT which sowed us the median financial cost of protecting one person for one year was $2.20 (range $0.88-$9.54) for ITNs, $6.7 (range $2.22-$12.85) for IRS, $0.60 (range $0.48-$1.08) for IPT in infants, $4.03 (range $1.25-$11.80) for IPT in children. The median financial cost of diagnosing a case of malaria was $4.32 (range $0.34-$9.34)(White *et al.*, 2011).

In terms of prevention of clinical malaria and under five mortality by malaria, IPT was found to be highly cost-effective. The intervention remained cost-effective even with a significant increase in drug and other intervention costs(Conteh *et al.*, 2010; Sicuri *et al.*, 2010; Nonvignon *et al.*, 2016).

Implementation Consideration

The implementation of IPT for under five children were divided in two strategies;

1. Intermittent Preventive Treatment in infancy is the administration of a full therapeutic course of IPT delivered through the Expanded Program on Immunization (EPI) at defined intervals corresponding to routine vaccination schedules usually at 10 weeks, 14 weeks, and ~9 months of age – to infants at risk of malaria.
2. Intermittent Preventive Treatment in children, at school and outreach to reach children's who are completed EPI.

Additionally, the following points are must been considered after implementation consideration of IPT...

- Programs implementing the strategy should regularly monitor and evaluate the impact on immunization services and performance.
- Surveillance of parasite resistance should accompany the implementation of ITP
- Side effects are seen from studies so follow up must been need for the adverse reaction and severe complication form the AQ-SP.

Enablers

- Commitment of the government towards the elimination of Malaria
- Well established primary health care in the country, mainly health extension program
- Commitment from international and local donors and stakeholders towards malaria elimination program
- Easily integration with Expanded Program on Immunization
- It can be administered by low level health care professionals with little training
- Best experience available in many Sub-Saharan African countries which may only need to customize in our context
- Low cost of the intervention

Barriers

Table 2: - Barriers and implementation strategies

Barriers	Descriptions	Implementation strategies
Budget allocation	This intervention may incur additional budget.	Though it might incur additional budget the benefit out way the cost.
Associated side effects	AQ-SP could cause vomiting in some children.	It should be managed accordingly.
Absence of IPT treatment guideline	Absence of national IPT treatment guideline could lead health care professional's misuse of SP for treatment of uncomplicated malaria.	There should be IPT treatment guideline in place to use for preventive treatment rather than for treatment of uncomplicated malaria.
Uncertainty of health professionals to SP administration	Health professionals might not familiar with SP administration could affect the medication adherence	Simplified IPT messages and health worker training should be provided to improve adherence towards AQ- SP

References

Conteh, L. *et al.* (2010) 'The cost-effectiveness of intermittent preventive treatment for malaria in infants in Sub-Saharan Africa', *PLoS ONE*, 5(6). doi: 10.1371/journal.pone.0010313.

Greenwood, B. (2010) 'Anti-malarial drugs and the prevention of malaria in the population of malaria endemic areas', *Malaria Journal*. BioMed Central, p. S2. doi: 10.1186/1475-2875-9-S3-S2.

Kafai, N. M. and Odom John, A. R. (2018) 'Malaria in Children', *Infectious Disease Clinics of North America*. Catholic University in Rome, pp. 189–200. doi: 10.1016/j.idc.2017.10.008.

Meremikwu, M. M. *et al.* (2012) 'Intermittent preventive treatment for malaria in children living in areas with seasonal transmission', *Cochrane Database of Systematic Reviews*. doi: 10.1002/14651858.cd003756.pub4.

Nonvignon, J. *et al.* (2016) 'Cost-effectiveness of seasonal malaria chemoprevention in upper west region of Ghana', *Malaria Journal*, 15(1), p. 367. doi: 10.1186/s12936-016-1418-z.

PMI Initiative, M. (2019) 'PRESIDENT'S MALARIA INITIATIVE ETHIOPIA Malaria Operational Plan FY 2019'. Available at: https://www.pmi.gov/docs/default-source/default-document-library/malaria-operational-plans/fy19/fy-2019-ethiopia-malaria-operational-plan.pdf?sfvrsn=3 (Accessed: 27 June 2019).

Prevention, C.-C. for D. C. and (2019) 'CDC - Malaria - About Malaria - Disease'.

Sicuri, E. *et al.* (2010) 'Cost-effectiveness of intermittent preventive treatment of malaria in pregnancy in Southern Mozambique', *PLoS ONE*, 5(10). doi: 10.1371/journal.pone.0013407.

White, M. T. *et al.* (2011) 'Costs and cost-effectiveness of malaria control interventions - A systematic review', *Malaria Journal*. BioMed Central, p. 337. doi: 10.1186/1475-2875-10-337.

WHO (2010) 'WHO Policy recommendation on Intermittent Preventive Treatment during infancy with sulphadoxine-pyrimthamine (SP-IPTi) for Plasmodium falciparum malaria control in Africa', *Who*. World Health Organization, p. 3. Available at: http://www.who.int/malaria/publications/atoz/policy_recommendation_IPTi_032010/en/ (Accessed: 24 May 2019).

WHO (2018) *Global Malaria Programme; ISBN 978-92-4-156565-3; Malaria; World Health Organization; World malaria report 2018, WHO*. World Health Organization. doi: ISBN 978 92 4 1564403.

World Health Organisation (WHO) (2010) ‘World Health Report 2000: Health Systems: Improving Performance.’, *WHO*. World Health Organization, (2006). Available at: https://www.who.int/whr/2000/en/ (Accessed: 21 May 2019).

Annex 1. How this evidence brief was prepared

The problem that the evidence brief addresses was clarified iteratively through discussion among the authors, review of relevant documents and research. Research describing the problem was identified by reviewing government documents, routinely collected data, searching PubMed and Google Scholar, through contact with key informants, and by reviewing the reference lists of relevant documents that were retrieved.

Strategies used to identify potential options to address the problem included considering interventions described in systematic reviews and other relevant documents, considering ways in which other jurisdictions have addressed the problem, consulting key informants and brainstorming.

We searched electronic databases of systematic reviews, including the Cochrane Library (CENTRAL, Cochrane Database of Systematic Reviews), Health Systems Evidence and supplemented these searches by checking the reference lists of relevant policy documents and with focused searches using PubMed, Google Scholar, and personal contacts to identify systematic reviews for specific topics. The final selection of reviews for inclusion was based on a consensus of the authors.

Potential barriers to implement this intervention were identified by brainstorming using a detailed checklist of potential barriers (SURE guide for identifying and addressing barriers) to implement health policies. Implementation strategies that address identified barriers were identified by brainstorming and reviewing relevant documents