

World Malaria Day, April 24th2023

Malaria is a potentially fatal disease that occurs mainly in tropical countries. It is a preventable and curable disease. However, without prompt diagnosis and effective treatment, an uncomplicated case of malaria can progress to a severe form of the disease, which is often fatal if left untreated. Malaria is not contagious and cannot be transmitted from person to person; it is transmitted by the bites of female Anopheles mosquitoes. Five species of parasites are responsible for malaria in humans and two of these species – Plasmodium falciparum and Plasmodium vivax – are particularly dangerous. There are more than 400 different species of Anopheles mosquitoes and about 40 of them, called vector species, can transmit the disease. The risk of infection is higher in some areas than in others due to different factors, such as the mosquito species present locally. In addition, the risk of infection may vary depending on the season, knowing that it is during the rainy season in tropical countries that it is highest (WHO, 2022).

Malaria is the main cause of morbidity and mortality in Cameroon, in Sub-Saharan Africa and in the world. This makes this pathology an important public health problem. Indeed, in 2018; Malaria represents in health facilities, 25.8% of consultations including 31.5% among children under 5 years old and 14.3% of deaths including 28.4% among children under 5 years old. These data are a clear increase compared to those of the years 2016, 2017 and 2018, (annual reports PNLP 2016-). There are three main epidemiological facies linked to geo-climatic variations: the Sudano-Sahelian facies (Far North and North Regions), the great interior plateau savannah (Adamawa Region), the great equatorial forest (every 7 southern regions). Existing climatic conditions are favorable for the development of vectors and parasites. As part of this celebration, the Center for the Development of Best Practice in Health, propose these summaries of Cochrane systematic reviews aiming to inform the patients, medical staff and others stakeholders in the prevention and the treatment of Malaria.

Journée mondiale du Paludisme, 24 AVRIL 2023

Le paludisme est une maladie potentiellement mortelle qui sévit principalement dans les pays tropicaux. Il s'agit d'une maladie évitable et dont on peut guérir. Cependant, en l'absence de diagnostic rapide et de traitement efficace, un cas de paludisme non compliqué peut évoluer vers une forme grave de la maladie, souvent mortelle si elle n'est pas traitée.

*Le paludisme n'est pas contagieux et ne peut pas se transmettre d'une personne à une autre ; il est transmis par les piqûres d'anophèles femelles. Cinq espèces de parasites sont responsables du paludisme chez les êtres humains et deux de ces espèces – *Plasmodium falciparum* et *Plasmodium vivax* – sont particulièrement dangereuses. On recense plus de 400 espèces différentes de moustiques anophèles et environ 40 d'entre elles, appelées espèces vectrices, peuvent transmettre la maladie. Le risque d'infection est plus élevé dans certaines régions que dans d'autres en raison de différents facteurs, comme les espèces de moustiques présentes localement. En outre, le risque d'infection peut varier selon la saison, en sachant que c'est durant la saison des pluies dans les pays tropicaux qu'il est le plus élevé (OMS, 2022).*

Le paludisme est la principale cause de morbidité et de mortalité au Cameroun, en Afrique Sub-Saharienne et dans le monde. Ceci fait de cette pathologie un important problème de santé publique. En effet, en 2018 ; le paludisme représente dans les formations sanitaire, 25,8% de consultation dont 31,5% chez les moins de 5 ans et 14,3% des décès dont 28,4% chez les moins de 5 ans. Ces données sont en nette augmentation en comparaison de celle des années 2016, 2017 et 2018, (rapports annuels PNLP 2016-). On distingue trois principaux faciès épidémiologiques liés aux variations géo climatiques : faciès soudano-sahélien (Régions de l'Extrême Nord et du Nord), la grande savane de plateau intérieur (Région de l'Adamaoua), la grande forêt équatoriale (toutes les 7 régions du Sud). Les conditions climatiques existantes sont favorables au développement des vecteurs et des parasites (PNLP, 2019). Dans le cadre de cette célébration, le Centre pour le développement des Bonnes pratiques en santé, propose ces résumés de revues systématiques Cochrane visant à informer les patients, le personnel médical et les autres parties prenantes sur les moyens de prévention et la prise en charge du Paludisme.

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1. Adding rapid diagnostic tests to community-based programmes for treating malaria

Key messages

- In regions where malaria is a serious problem (malaria-endemic areas), many people cannot access the treatment they need.
- Rapid diagnostic tests for diagnosing malaria (mRDTs) are simple to use: they involve dropping a finger prick of blood onto a small cassette.
- In the context of community-based programmes in malaria-endemic areas, when people without professional healthcare qualifications use mRDTs rather than providing a diagnosis based on physical signs and symptoms (clinical diagnosis), the treatment of malaria improves.
- Further research is needed to understand the impact of mRDTs on how often antibiotics are prescribed.

How is malaria diagnosed and treated in community-based programmes?

There are effective and safe treatments for malaria (antimalarial medicines, also known as antimalarials), but many people still cannot access the medicines they need, especially if they live far from health facilities. To improve this situation, local people without formal healthcare qualifications have been trained to diagnose and treat malaria either by recognising malaria signs and symptoms or using an mRDT. These people can be community health workers or vendors in non-pharmacy medicine shops.

What did we want to find out?

We aimed to compare the effect of two different techniques for diagnosing malaria (mRDTs and clinical diagnosis) used by local people without formal healthcare qualifications, on the treatment given. We also wanted to compare the community use of mRDTs with the routine care provided in health facilities, such as hospitals, to find out which approach resulted in better treatment for people with suspected malaria.

What did we do?

This is an update of a published Cochrane Review. We searched online databases for studies that compared mRDT diagnosis to clinical diagnosis in the community, or mRDT diagnosis and treatment in the community to health facility care. We extracted information about the study designs, the people being treated, the type of non-medically qualified health worker, their training, the mRDTs and treatments used, and the results (including deaths, number of people with or without malaria treated with an antimalarial, and use of antibiotics). Where possible, we combined results using statistical software.

What did we find?

We found six studies from Africa, one from Myanmar, and one from Afghanistan. Five studies compared community use of mRDT to community clinical diagnosis of malaria, and three compared community use of mRDT to health facility care. Five studies used laboratory tests to double-check the community diagnosis of malaria (whether mRDT or clinical). All studies except one offered less than one week's training to the staff. The antimalarials used were mostly for taking by mouth, although two studies also trained staff to give medicine to very ill children by inserting it into their bottoms. Most studies also trained staff to send people who had a negative mRDT result, people who were very ill, young babies, and pregnant women to a health facility. The medicines were sometimes free to patients or customers. Customers who had to pay in medicine shops often paid a reduced price. The mRDTs were usually free.

When mRDTs were used in the community, far fewer people who did not actually have malaria received antimalarials (about 71 fewer per 100 people). Community health workers may be less likely than medicine shop vendors to give antimalarials to people without malaria.

Similarly, more people diagnosed by mRDT (about 45 more per 100) got the right treatment: an antimalarial if they definitely had malaria (proven by laboratory tests), no antimalarial if they did not. Some studies found that a few people with a negative mRDT result (as read by the community health worker or medicine shop vendor) received antimalarial anyway. One small study found that some people with a negative clinical diagnosis received an antimalarial. Conversely, other studies found that a few people with a positive mRDT result did not get an antimalarial.

We also found some increased antibiotic use in the mRDT group in people with a negative laboratory test result compared to the clinical diagnosis group (about 13 more uses of antibiotic per 100 people). We were unable to draw any conclusion about people's health or use of treatments when comparing use of mRDTs in the community with the usual health facility care.

There were very few deaths in the study population.

What are the limitations of the evidence?

We are moderately confident that fewer people without malaria receive antimalarials after an mRDT, and that more people diagnosed by mRDT get the right treatment, because the studies that provided these results included a large number of people, even if there were some differences in study methods.

How up to date is this evidence?

This evidence is up-to-date to 14 September 2021.

Authors' conclusions

Implications for practice

The results of this review update suggest that training community health workers (CHWs) and drug sellers to use malaria rapid diagnostic tests (mRDTs) and dispense or sell antimalarials for the diagnosis and treatment of malaria has important benefits. These strategies improve targeting of antimalarials, in that people who are malaria-positive have access to a drug, while those who are malaria-negative generally do not. These programmes seem to reduce the provision of antimalarials to uninfected people, which is to be expected, although a small proportion of customers testing negative by mRDT may receive an antimalarial, and some who test positive by mRDT may not receive an antimalarial. Indirect comparisons suggest programmes with mRDTs work better with CHWs than with drug sellers.

Implications for research

These programmes appear to improve targeting of antimalaria treatment. Future research could examine how such programmes can be sustained, particularly in drug shops, or even among people testing themselves at home. One possible area of research is antibiotic use in mRDT-negative and mRDT-positive people, as the staff responsible for managing people with malaria symptoms need support in the challenging area of non-malarial fevers or coinfections

Citation: Allen EN, Wiyeh ABeriliy, McCaul M. Adding rapid diagnostic tests to community-based programmes for treating malaria. Cochrane Database of Systematic Reviews 2022, Issue 9. Art. No.: CD009527. DOI: 10.1002/14651858.CD009527.pub3.

<https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD009527.pub3/full#CD009527-abs-0002>

2. Indoor residual spraying for preventing malaria in communities using insecticide-treated nets

What was the aim of this review?

Indoor residual spraying (IRS) is the regular application of chemical insecticides to household walls. The insecticide lasts for several months, killing mosquitoes that land on them. Insecticide-treated nets (ITNs) are bed nets treated with insecticides,

preventing mosquitoes from biting people and reducing the mosquito population. Both interventions help to control malaria by reducing the number of people being bitten by mosquitoes infected with malaria. Implementing IRS in communities that are using ITNs may be better for malaria control than using ITNs alone simply because two interventions may be better than one; but also because it may improve malaria control where mosquitoes have become resistant to the pyrethroid insecticides used in ITNs. Pyrethroids were the only class of insecticides approved for use in ITNs until 2018, but growing resistance of mosquitoes to pyrethroids impairs their effectiveness. The addition of IRS could counteract this reduction in ITN effectiveness and may help to slow the emergence of pyrethroid resistance. We could expect that IRS insecticides that have a different way of working to pyrethroids ('non-pyrethroid-like') could restore effectiveness better than those that have the same way of working ('pyrethroid-like'). The aim of this review was to summarize the impact of pyrethroid-like or non-pyrethroid-like IRS on malaria, when implemented in communities that are using ITNs.

Key messages

The addition of IRS using a non-pyrethroid-like insecticide was associated with reduced malaria prevalence. Malaria incidence may also be reduced on average, but this effect was absent in two studies, and consequently there remains some uncertainty over whether the intervention will be effective in all settings.

When a pyrethroid-like insecticide was used for IRS, data were limited but there was no additional effect demonstrated.

What was studied in the review?

We searched for studies that evaluated the impact on malaria transmission when IRS, using a World Health Organization (WHO)-recommended dosage, was implemented in communities that were using either ready-treated ITN products or standard nets treated with insecticide at a WHO-recommended dose. We considered effects on both human health outcomes and on mosquito populations.

What were the main results of the review?

In total, we identified 10 studies matching our inclusion criteria, from which we made 12 comparisons. Seven studies (providing eight comparisons) used a non-pyrethroid-like IRS throughout the study. Each of these were conducted in areas where the vectors were described as resistant or highly resistant to pyrethroids. Two studies (providing two comparisons) used a pyrethroid-like IRS throughout. One further study used a pyrethroid-like IRS in the first study year and switched to a

non-pyrethroid-like IRS in the subsequent years, therefore providing two different comparisons. All studies were conducted in sub-Saharan Africa.

Adding non-pyrethroid-like IRS in communities using ITNs appeared to improve malaria outcomes in most settings. Overall, the results from the eight included studies found lower malaria parasite prevalence, while there may be a reduction in malaria incidence and anaemia prevalence. We do not know if there is an impact on the number of infected bites received per person per year.

When adding pyrethroid-like IRS in communities using ITNs, the data from three studies indicate there is probably no effect on malaria incidence or parasite prevalence, and there may be little or no effect on the prevalence of anaemia. Data on the number of infected bites received per person per year were too limited to draw a conclusion.

How up to date is the review?

We searched for relevant studies up to 8 November 2021.

Authors' conclusions

Implications for practice

With the evidence to date, in communities using ITNs, IRS with a non-pyrethroid insecticide appears to reduce malaria parasite prevalence and may also reduce malaria incidence on average, but this effect was not always present. These benefits have not been observed when using a pyrethroid-like insecticide. The evidence from these studies was insufficient to evaluate whether adding IRS in communities using ITNs would be an effective strategy to prevent pyrethroid resistance emerging.

Implications for research

There was unexplained qualitative heterogeneity between studies examining IRS using non-pyrethroid-like IRS. Consequently, there is uncertainty over whether this intervention will be effective in all settings, and other factors may influence its impact on malaria transmission. Researchers and policymakers may wish to consider pragmatic approaches to generate further evidence, such as programme implementation using stepped wedge designs and other quasi-experimental methods during programme implementation. Other sources of evidence such as modelling and entomological indices from experimental hut study designs may also help unpick where IRS is most likely to be effective. Standardization of measuring and reporting both entomological outcomes and insecticide resistance in efficacy studies would also help strengthen the evidence base and allow for better comparisons between studies.

Citation :Pryce J, Medley N, Choi L. Indoor residual spraying for preventing malaria in communities using insecticide-treated nets. Cochrane Database of Systematic Reviews 2022, Issue 1. Art. No.: CD012688. DOI: 10.1002/14651858.CD012688.pub3.

<https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD012688.pub3/full#CD012688-abs-0002>

3. House modifications for preventing malaria

What is the aim of this review?

House modifications, such as screening (covering or closing potential house entry points for mosquitoes with mesh or other materials) or the use of specific house materials or designs, such as metals roofs instead of thatched roofs, or elevated rooms, may contribute to reducing the burden of malaria. They work by preventing mosquitoes from entering houses, and reducing the number of bites householders receive indoors. Some house modifications under consideration additionally aim to kill any mosquitoes that attempt to enter houses by incorporating insecticide into the modification.

Key messages

Modifying houses to prevent mosquitoes entering the home was associated with a reduction in the proportion of people with malaria parasites in their blood and reduced anaemia, based on evidence from seven studies conducted in Africa. The effect of house modifications on the number of cases of malaria identified during specific time periods was mixed, and the effect on indoor mosquito density was less clear due to differences between study results. Six trials awaiting publication are likely to enrich the current evidence base.

What was studied in the review?

This review summarized studies investigating the effects of house modifications on human malaria outcomes. If studies additionally reported the effect of the house modifications on mosquitoes (those with potential to carry the parasites that cause malaria), or householders' views, we also summarized this data. After searching for relevant studies, we included seven published trials and six ongoing trials. All complete trials assessed screening (of windows, doors, eaves, ceilings, or any combination of these), either alone or in combination with roof modification or eave tube installation (a "lure and kill" device positioned in eave gaps to attract and kill mosquitoes). One trial incorporated insecticide into their house screening.

What are the main results of the review?

The seven included trials all assessed either the number of cases of malaria identified during specific time periods in people living in the house, the proportion of

people with malaria parasites in their blood, or both. Overall, the studies showed that people living in modified houses were around 32% less likely to have malaria parasites in their blood, and were 30% less likely to experience moderate or severe anaemia. Our confidence in these results was moderate to high. The studies demonstrated 37% reduction in the number of mosquitoes trapped indoors at night in modified houses, although this result varied between trials. The trials showed mixed results for the likelihood of experiencing an episode of clinical malaria (caused by *Plasmodium falciparum* parasites), ranging from a 62% lower rate to a 68% higher rate of malaria for people living in modified houses. Due to the high inconsistency between these results, we have very low confidence in this evidence.

How up to date is this review?

The review authors searched for studies available up to 25 May 2022.

Authors' conclusions

Implications for practice

The trials published to date show in these studies that house modifications protect against anaemia and may reduce parasite prevalence for children and adults, and this is consistent with previous research. The evidence from studies to evaluate whether house modifications reduce clinical malaria incidence was mixed, and although pooled evidence suggested a reduction in indoor mosquito density, this was not always present.

Implications for research

House modifications may provide an important, long-term, sustainable option to reduce malaria. Further research will help delineate the best implementation approaches to assure the effect. It will also identify co-interventions that may enhance the effect, and those factors which may mitigate the effects, including epidemiological, structural, and social influences. The success of implementation of modifications will likely be affected by perceived benefits by users, the cost of implementation, and the ability of home-owners to introduce modifications themselves. How best to optimize roll-out and facilitate communities to take charge of modifying their own houses would be useful operational research to maximise the potential of this strategy in malaria.

Citation : Fox T, Furnival-Adams J, Chaplin M, Napier M, Olanga EA. House modifications for preventing malaria. Cochrane Database of Systematic Reviews 2022, Issue 10. Art. No.: CD013398. DOI: 10.1002/14651858.CD013398.pub4.

<https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013398.pub4/full#CD013398-abs-0002>

4. Mass drug administration for malaria

What is mass drug administration (MDA) for malaria?

MDA for malaria consists of giving a full treatment course of antimalarial medicine (even to persons with no symptoms of malaria and regardless of whether malaria is present) to every member of a defined population or every person living in a defined geographical area (except to those for whom the medicine could be harmful) at approximately the same time and often at repeated intervals.

How can MDA reduce malaria transmission in a population?

The life cycle of the malaria parasite consists of human liver, human blood, and mosquito stages. Malaria infection begins with the bite of an *Anopheles* species mosquito carrying the malaria parasite. During the bite, the infective mosquito injects the malaria parasite into the human host. After initially replicating in the liver, the parasites are released into the bloodstream. During the blood stage, parasites multiply in red blood cells, sometimes causing fever and other symptoms characteristic of malaria. Some of these parasites become a form which is infectious to mosquitoes. When the infected person is bitten again, the mosquito ingests blood containing the parasites, which then restarts the transmission cycle.

MDA with antimalarial drugs temporarily prevents new and clears existing malaria infections in the population. Depending on the characteristics of the antimalarial drug used, MDA targets parasites at different stages, which can lead to reduced disease burden and transmission in the population. Whether MDA can successfully reduce or interrupt malaria transmission may depend on how much malaria there is in the area; the use of other tools to control malaria, including preventing mosquito bites; the proportion of the population who receive at least one round of MDA; population movement; and when MDA rounds occur in relation to the peak malaria transmission season.

What was the aim of the review?

To guide policy-making and future research for malaria control and elimination, the aim of this review was to update the evidence evaluating the effect of MDA compared to no MDA on malaria outcomes in moderate- to high-transmission

settings and very low- to low-transmission settings. Our search of relevant published and unpublished literature identified 13 studies that met our inclusion criteria.

What are the main findings of the review?

Malaria burden was compared in people receiving MDA and those who did not receive MDA, at different time points. The findings differed by malaria transmission setting. In areas with malaria prevalence of 10% or higher (moderate- to high-transmission areas), based on one trial, MDA did not reduce malaria in the population (low-certainty evidence). In areas with malaria prevalence under 10% (very low- to low-endemicity areas), evidence from seven trials indicates that MDA reduced malaria in the population immediately after MDA has stopped (low-certainty evidence), but we are uncertain if the decline continues long-term because the number of malaria cases in both intervention and control groups were low (very low-certainty evidence).

In all settings of malaria transmission, the type of antimalarial drug used for MDA, co-interventions such as mosquito control, coverage of MDA, and risk of re-introduction may have an impact on the effect of MDA compared to no MDA. However, we were unable to explore these factors due to the limited number of studies.

How up to date is the review?

We included studies available up to 11 February 2021.

Authors' conclusions

Implications for practice

In moderate- to high-transmission settings, only two studies contributed data to assess the effect of MDA on outcomes. Based on results from a single trial, MDA probably reduces parasitaemia incidence, but does not reduce parasitaemia prevalence at one to three months after MDA. However, it is worth noting that there was a large overall reduction in parasitaemia prevalence in both the intervention and control arms from baseline to post-MDA. The second trial showed no effect of a single round of MDA at four to six months after MDA. Given the absence of data in moderate- to high-transmission settings at time points after six months, we were unable to determine the longer-term effects of MDA on malaria transmission.

In very low- to low-transmission settings, MDA probably reduces *P falciparum* parasitaemia incidence at under one month, and *P falciparum* and *P vivax* prevalence at one to three months after MDA. The short- and long-term effects of MDA on *P falciparum* and *P vivax* parasitaemia prevalence at time periods after four months is uncertain due to very low-certainty evidence, but the immediate large

reduction in parasitaemia prevalence is not sustained over time. Based on data provided in studies conducted in very low- to low-transmission settings, we did not find evidence in any study of interruption of transmission as measured by a reduction to zero indigenous cases following MDA.

Other variables, such as type of antimalarial drug, MDA coverage, number of rounds, and co-interventions, may affect the impact of MDA on malaria outcomes and should be considered when conducting MDA. Additionally, the degree of population mobility and potential for importation of parasites also plays an important role in the effect of MDA. These considerations should be weighed carefully in recommendations surrounding MDA.

Our findings in very low- to low-transmission settings support the existing WHO Malaria Policy Advisory Committee's (MPAC) 2015 recommendations on the use of MDA in areas approaching elimination with high coverage of vector control and surveillance, good access to treatment, and limited risk of re-introduction of infection ([WHO 2015a](#)). These recommendations are currently being updated through a revised guideline development process at WHO ([WHO 2020b](#)).

Implications for research

Given the addition of several cRCTs since the publication of the previous review on this topic ([Poirot 2013](#)), this updated review provides additional information about MDA in the context of a renewed interest in MDA as a strategy to accelerate progress towards malaria elimination. Although several studies, conducted more recently in very low- to low-endemicity settings, attempted to collect data on outcomes at longer time points following MDA, the certainty of the evidence on the sustained effect of MDA was very low due to high risk of bias and large imprecision. Although of higher certainty evidence compared to trials conducted in very low- to low-endemicity settings, none of the included studies in moderate- to high-endemicity settings measured the effect of MDA after four to six months. Future studies should measure the longer-term effect of MDA and ensure that outcomes from a sufficient number and representative sample of participants are collected to obtain more precise estimates of effect. In relation to study design, cRCTs should be designed with a sufficient number of clusters to help to ensure that measured and unmeasured confounders are balanced across randomized arms, studies designed for interrupted time series analysis should include sufficient pre- and post-intervention data to adequately capture seasonal malaria trends, and co-interventions should be balanced across study arms.

Citation: Shah MP, Hwang J, Choi L, Lindblade KA, Kachur SP, Desai M. Mass drug administration for malaria. Cochrane Database of Systematic Reviews 2021, Issue 9. Art. No.: CD008846. DOI: 10.1002/14651858.CD008846.pub3.

<https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD008846.pub3/full#CD008846-abs-0002>

5. Intermittent preventive treatment for malaria in infants

What is the aim of the review?

This Cochrane Review aimed to find out if administering repeated doses of antimalarial treatment to infants living in sub-Saharan Africa can prevent malaria. We found and analysed results from 12 relevant studies conducted between 1999 and 2013 that addressed this question in infants (defined as young children aged between 1 to 12 months).

Key messages

Intermittent preventive treatment with sulfadoxine-pyrimethamine (SP)

Giving SP as preventive antimalarial treatment to infants probably reduced the risk of clinical malaria, anaemia, and hospital admissions in the African countries it was evaluated. However, this effect was attenuated in more recent studies.

Intermittent preventive treatment with artemisinin-based combination therapy (ACT)

Giving ACT as preventive antimalarial treatment to infants may reduce the risk of clinical malaria. It may also reduce the proportion of infants with malaria parasites in their blood.

What was studied in the review?

In areas where malaria is common, infants often suffer repeated episodes of malarial illness. In areas where malaria transmission occurs all-year, some authorities recommend intermittent preventive treatment, which requires giving drugs at regular intervals (at child vaccination visits) regardless of whether the child has malaria symptoms or not to prevent malarial illness.

We studied the effects of IPTi with SP and other medicines (including ACTs) on malaria-related outcomes. Review outcomes included clinical malaria, severe malaria, death, hospital admission, parasitaemia, anaemia, change in haemoglobin level, and side effects.

What are the main results of the review?

We included 12 studies that enrolled 19,098 infants. All studies were done in sub-Saharan Africa (Gabon, Ghana, Kenya, Mali, Mozambique, Tanzania, and Uganda). These studies compared infants who received IPTi to those who received

placebo pills or nothing. The infants in the IPTi group were given different medicines, in different doses, and for different lengths of time.

Ten studies evaluated IPTi with SP from 1999 to 2013. The effect of SP appear to wane over time, with trials conducted after 2009 showing little or no effect of the intervention. The studies show that IPTi with SP probably resulted in fewer episodes of clinical malaria, anaemia, hospital admission, and blood parasites without symptoms (moderate-certainty evidence). IPTi with SP probably made little or no difference to the risk of death (moderate-certainty evidence).

Since 2009, IPTi some small studies have evaluated artemisinin-based combination medicines and indicate impact on clinical malaria and blood parasites. A small study of IPTi with dihydroartemisinin-piperazine in 2013 showed up to 58% reduction in episodes of clinical malaria (moderate-certainty evidence) and reductions in proportion of infants with blood parasites (moderate-certainty evidence).

How up-to-date is this review?

The review authors searched for studies published up to 3 December 2018.

Authors' conclusions

Implications for practice

On the basis of the more recently conducted trials that showed no effect of IPTi with SP, the prospects for the continued use of SP as IPTi are limited. This is likely due to widespread resistance to SP. Several antimalarial drug combination options have been evaluated and show high levels of effectiveness. IPTi with other antimalarial drug combination options may reduce the risk of clinical malaria and asymptomatic parasitaemia. However, as long as SP remains the drug of choice for IPTi, resistance monitoring should be integrated into relevant epidemiological studies and surveillance programmes within national malaria control programmes in sub-Saharan Africa.

Implications for research

The evidence for the benefit of IPTi with SP is mainly from trials conducted up to 10 years ago. Questions remain regarding the efficacy of SP in the prevention of malaria in the face of widespread parasite resistance especially with the emergence of mutant *P falciparum* isolates carrying sulfadoxine resistance associated A437G and K540E mutations in the *Pfdhps* gene across West Africa. Concerns also remain about the potential for IPTi to increase the carriage and spread of drug-resistant *P falciparum* parasites.

There are a few trials that evaluated other drug combination options for use as IPTi with some evidence of effectiveness ([Bigira 2014 UGA](#); [Gosling 2009 TZA](#); [Massaga](#)

[2003 TZA](#); [Odhiambo 2010 KEN](#)). However, larger adequately powered trials are needed to provide more robust evidence for or against IPTi. Additional trials would most likely improve our confidence in the effect estimates for the effectiveness of IPTi. Also, as more trials evaluate alternative drug options for IPTi, subgroup analyses based on the type of antimalarial drug would become more robust and informative.

Future studies should investigate the efficacy, safety, operational feasibility, and cost-effectiveness of IPTi with multi-day antimalarial drugs in a programmatic setting.

Citation :Esu EB, Oringanje C, Meremikwu MM. Intermittent preventive treatment for malaria in infants. Cochrane Database of Systematic Reviews 2021, Issue 7. Art. No.: CD011525. DOI: 10.1002/14651858.CD011525.pub3.

<https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD011525.pub3/full#CD011525-abs-0002>

6. Ivermectin treatment in humans for reducing malaria transmission

What is the aim of this review?

The aim of this Cochrane Review was to find out if giving the drug ivermectin to entire communities could reduce malaria transmission. We examined all relevant studies to answer this question, and found one relevant study.

Key messages

It is not possible to say at this point if treating an entire community with ivermectin reduces malaria. Several research studies are in progress; we anticipate they will provide more answers in the future.

What was studied in the review?

Malaria is a disease transmitted to humans through the bite of mosquitoes infected with *Plasmodium* parasites. It results in nearly half a million deaths every year. Ivermectin is a drug that is given to whole communities to control the parasites that are responsible for elephantiasis and river blindness. It has been observed that ivermectin can kill mosquitoes when they feed on the blood of people who have taken this medication. Therefore, it is believed that by giving this drug to whole communities, it will kill many mosquitoes, and could reduce malaria transmission.

In this review, we assessed whether treating entire communities with ivermectin would reduce malaria transmission. We looked for studies from different sources, and only included studies that took place in communities with malaria, and that randomly assigned groups of people to ivermectin or a control, which could be

a placebo or standard community drug treatments. We wanted to know if the treatment influenced the occurrence of malaria in the community.

What are the main results of the review?

One study met the inclusion criteria. This study included eight villages in Burkina Faso, which were randomly assigned to receive ivermectin or a control. All villages received ivermectin, as part of the scheduled control of lymphatic filariasis. In addition, the treatment villages received five more doses of ivermectin, once every three weeks. The effect of ivermectin on malaria was measured in children younger than five years of age. In these children, the treatment did not show a notable difference in the presence of malaria between the treatment and control groups (very low-certainty evidence).

Therefore, it is not possible to say at this point if the treatment of entire communities with ivermectin has an effect on reducing malaria. Several studies are currently ongoing; we anticipate they will provide more answers in the future.

How up-to-date is this review?

We searched for studies published up to 14 January 2021.

Authors' conclusions

Implications for practice

Although ivermectin has been demonstrated to reduce the lifespan of *Anopheles* mosquitoes ([Appendix 1](#)), we do not know if community administration of ivermectin has an effect on malaria transmission.

The available evidence on the effect of ivermectin on malaria transmission comes from one published trial ([Foy 2019](#)). The intervention did not show an effect in reducing the cumulative incidence of uncomplicated malaria. Therefore, we are uncertain whether community administration of ivermectin reduces malaria transmission.

Implications for research

The results of this trial, published in the *Lancet*, were contested based on differences in the analytical protocol used in presenting the primary outcome results ([Bradley 2019](#); [Foy 2019](#) ([Foy 2019](#) Authors' reply)). It is important that ongoing trials consider and adopt a consistent protocol for analysis in cRCTs to improve our confidence in the effectiveness of ivermectin in malaria transmission.

While children under five years of age are considered most vulnerable to disease, transmission is more likely to be sustained via the older population, who are typically asymptomatic carriers ([Bousema 2014](#); [Lindblade 2013](#)). Other trials reporting on the

incidence and prevalence of infection would be useful in addressing the question of possible herd effect in the community.

There are a number of trials in progress addressing the question of whether community administration of ivermectin reduces malaria transmission; the results will be included in updates of this review when available ([Rabinovich ongoing](#); [NCT04844905 \(MATAMAL\)](#); [NCT03074435 \(REACT\)](#); [NCT03576313 \(MASSIV\)](#); [NCT03967054 \(RIMDAMAL II\)](#); [PR150881](#)). See details in [Characteristics of ongoing studies](#).

There is some uncertainty about what entomological outcomes are critical for making public health decisions and; recommendations, and how these should be measured. Comparative data from ongoing trials could help address this.

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