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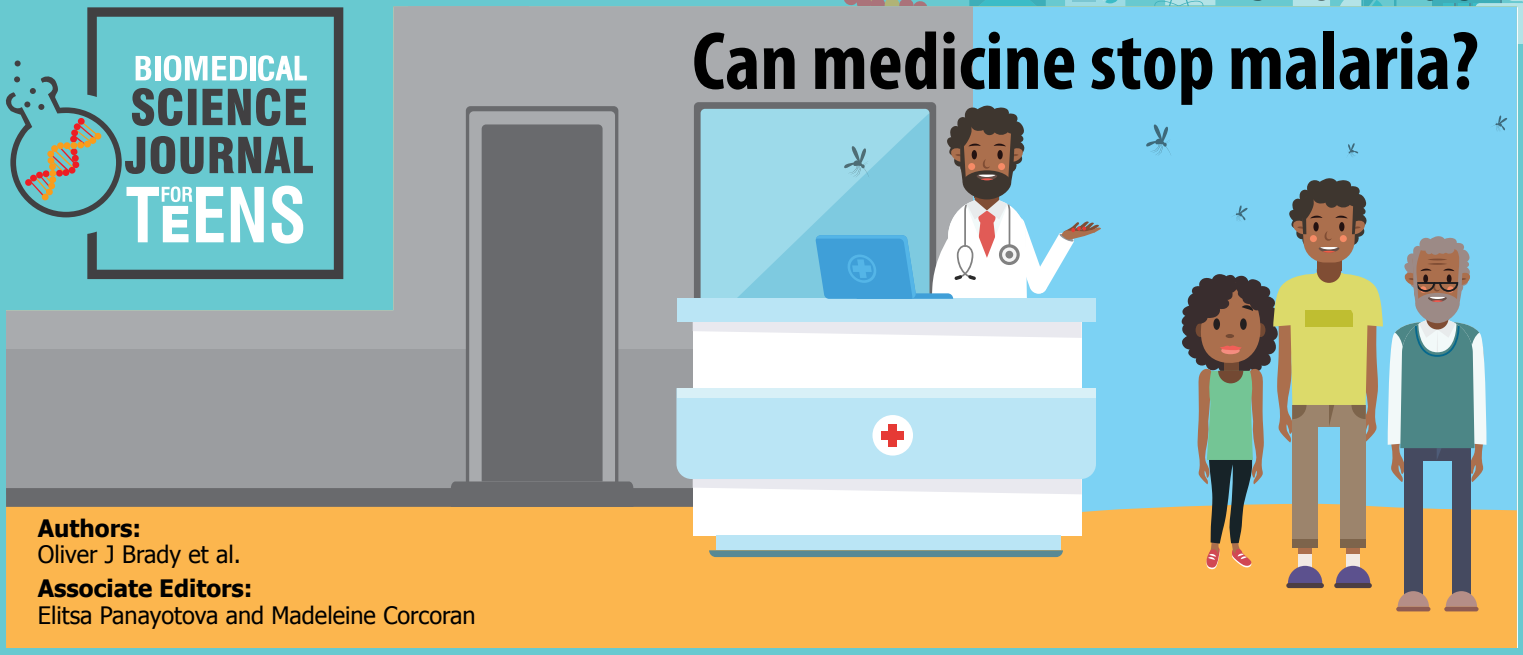
Can medicine stop malaria?



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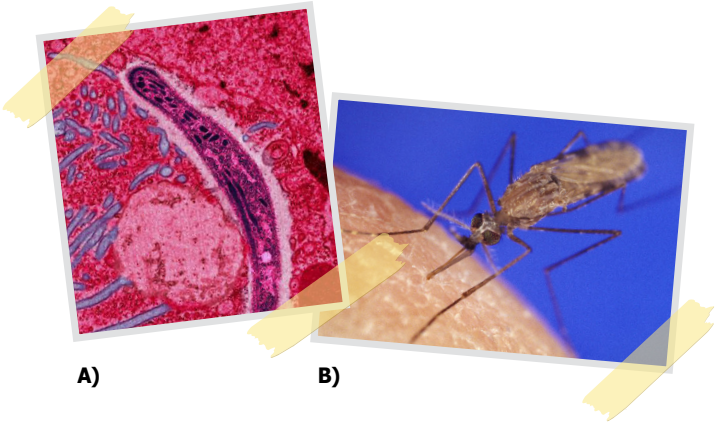
Abstract

What comes to mind when you think of the most dangerous animals? Sharks? Tigers? ...How about mosquitoes? Mosquito bites are responsible for the deaths of around 400,000 people every year. The largest single cause of these deaths is malaria – which can be a severe disease, caused by a tiny *parasite* carried by some mosquitoes. The current *vaccine* against malaria is only partially effective and not yet widely used so prevention mainly comes down to *mosquito control* (getting rid of mosquitoes from populated areas or preventing them from biting people). Another method for prevention being tried out in some places is to give drugs that kill the malaria parasite to large numbers of people. This technique is known as *mass drug administration*, shortened to 'MDA'. Using mathematical models we wanted to find out when and where MDA works well. Our four models each predicted different levels of effectiveness for MDA, but overall we discovered the important factors that made MDA work better. Although MDA can be useful in malaria control programmes it still needs to be combined with good mosquito control.

Introduction

Malaria is one of the deadliest diseases in the world. Every year it kills 400 000 people and makes another 200 million sick – all of this because of mosquito bites. Malaria is caused by a tiny parasite called *Plasmodium*. It enters the body through a mosquito bite and makes the person sick with fever, vomiting and headaches. In more severe cases it can cause coma and death. If a second mosquito bites a sick person, the parasite can enter the insect and through further bites, can infect other people.

Many countries (mostly in tropical and *sub-tropical* regions) are struggling to get rid of malaria. Vaccines for the disease are not very effective and not yet widely used, so preventing it from spreading in the first place is key. *Mosquito control* is the main approach to malaria prevention – the fewer mosquitoes there are, the fewer bites people receive, making malaria infection less likely. In recent years the World Health Organization has recommended another method in some situations: *mass drug administration* (MDA). Basically, a group of the population (both sick and healthy people) receive medication against malaria for a period of time.This reduces malaria spread or *transmission* in three ways: 1) it cures people who have the disease, 2) it cures people who don't even know they have malaria but are carrying the parasite and 3) it prevents at-risk people from becoming infected over the coming malaria season.



A) **B)**

Figure 1:
A) *Plasmodium* - the parasite which causes malaria.
B) An Anopheles gambiae mosquito, one of the varieties of mosquito which commonly carries a species of the Plasmodium parasite.
Source:
A) Ute Frevert, Wikimedia Commons
B) James D. Gathany, The Public Health Image Library.

Governments have used MDA before but there are not many studies which explore how and whether it helps to stop the spread of malaria. Moreover, it's important to understand in what circumstances MDA can be useful and effective. So, does MDA work? And when does it work best? This is what we wanted to find out. Computer simulation models can be a useful way to explore how well MDA works. We cannot be sure how realistic any one model is, so by using four different models, we can check whether they predict the same outcomes and if so, feel more confident about the results.

Methods

We collaborated with researchers doing MDA *field trials* to better understand the status of the disease and how it is spreading (known as *epidemiological* factors) in different countries where malaria is present. We asked these researchers how many times the drugs were given and when they were given.

From this, we defined a 'standard' scenario that we could compare to possible different scenarios:

1. Two rounds of treatment with an anti-malaria drug per year
2. Five weeks gap between rounds
3. 70% of the population received the drug
4. The treatment program lasted two years
5. No malaria infections were brought in by people from outside the area
6. There would be one rainy season per year (this is the period of the year in the tropics when there is heavy rainfall)
7. In the given area 5% of people are infected with detectable malaria before the MDA begins.

We then put the above conditions into four previously established mathematical models. We varied all of the conditions within the models (Table 1) in order to find out the best course of action for using MDA. Essentially, we asked if each one of the conditions above increased or decreased, how much better or worse is MDA at stopping malaria?

Figure 2:
Table 1. The conditions we put into the models to compare different drug programs and settings with our standard scenario.

	Standard scenario	How we varied it in the models
Number of times the drugs are given per year	2	3
Proportion of the population that receive the drugs	70%	30%; 50%; 90%
Amount of time between rounds of drugs	5 weeks	4 weeks; 6 weeks
Duration of the drug giving programme	2 years	1 year
Time of the year when the drugs are given	Dry season (fewer mosquitoes are around)	Every month of the year
Is there mosquito control? (E.g. the government sprays areas with insecticides to kill mosquitoes.)	Yes	No
Is malaria brought in by people from other areas?	No	Yes
Human population size	10,000	1000
Are the malaria pathogens resistant to the drugs (i.e. the drugs will not work very well to eliminate them)?	No	Some of them are

Results

In all four models MDA showed good results immediately after the treatment started (Fig. 3). If malaria is not fully eliminated in the region though, the models predicted that the *prevalence* of the infection would eventually return to how it was before the drug was given, meaning the effect is only temporary.

Taken together, the simulations we conducted showed us how the different conditions affected the spread of the disease and how useful MDA was:

- It is important that nearly everyone receives the treatment in order for there to be a reduction in malaria.
- The duration of the programme was also important. Longer (two years) was better than shorter (one year).
- The number of rounds of MDA per year was not that important
- The dry season is the best time for using MDA
- When two rainy seasons occur in the treatment period MDA is slightly less effective (there are more mosquitoes around in the rainy season).
- MDA alone is not good enough to totally replace mosquito control
- If the prevalence of malaria in a population is high (i.e. 10% of the people carry the parasite), MDA is less effective.

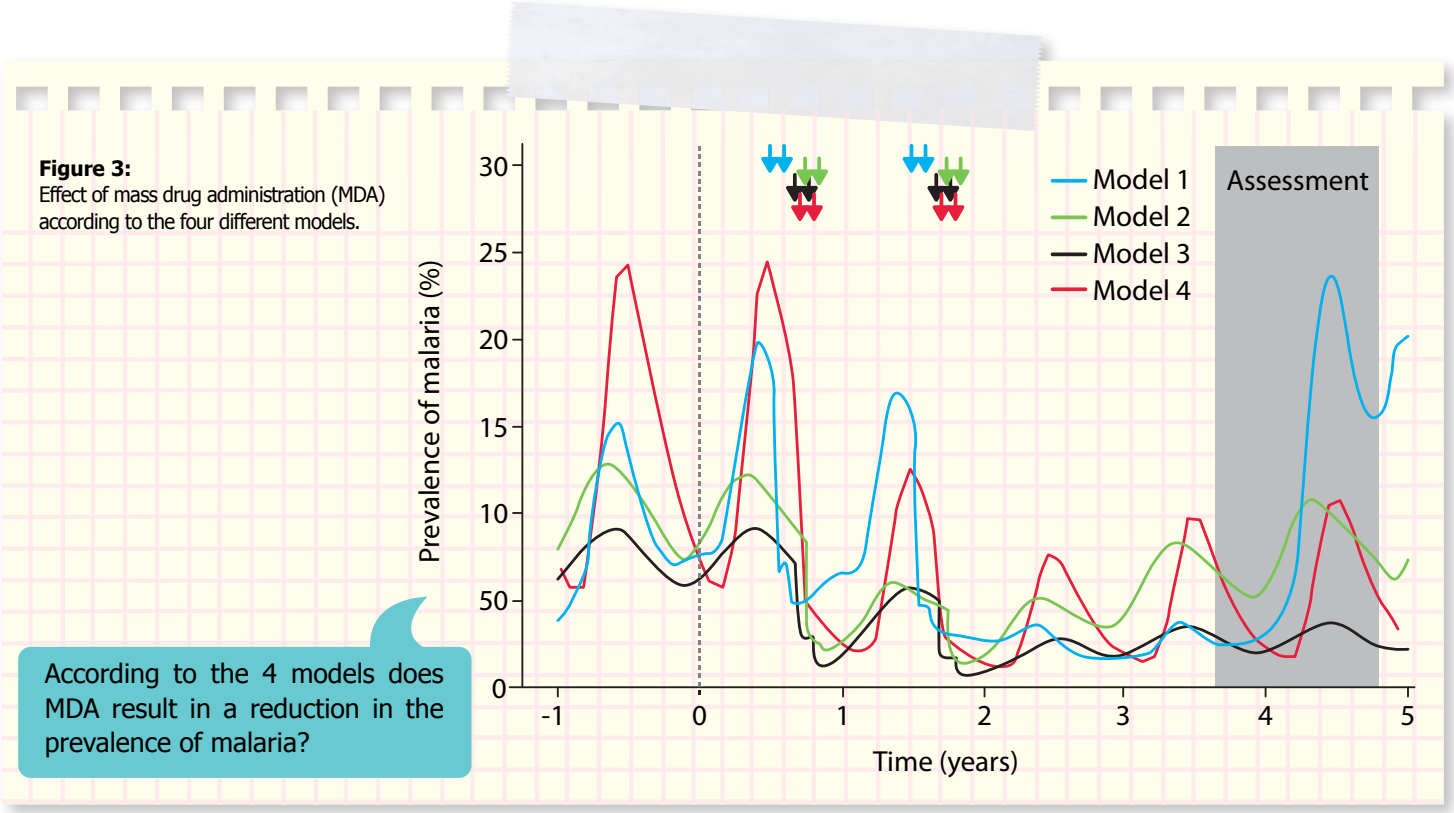


Figure 3:
Effect of mass drug administration (MDA) according to the four different models.

Discussion

The models show different results for how effectively MDA reduces malaria but they all show that the same factors have the greatest influence on whether MDA works well. The effectiveness of MDA was best when there was a low transmission rate, a longer MDA programme and the proportion of people who received the drug was higher. This information is useful to people starting to do MDA, and the fact that all the models agreed on these key factors increases people's confidence in their findings.

We are not certain why the four models predicted different levels of effectiveness for MDA. There are many differences in the details entered into the models, regarding, for example,

people's immunity to malaria, among other things, which change their predictions.

We think these models could be useful not only to assess where and when MDA will be effective but also to help us find out if MDA is capable of stopping new malaria outbreaks after it has been wiped out in a certain area. The models could also show us if MDA could lead to drug *resistance*, which could have dangerous consequences.

Conclusion

Our results show that MDA can be useful in controlling malaria in certain circumstances. However, all four models showed that MDA is not powerful enough to be able to replace mosquito control as our main method of fighting malaria. Rather than relying only on mass drug treatment, we should make sure to prevent the spread of malaria (and other diseases spread by mosquitoes).
So what should you do if there is no malaria where you live, but you plan to visit a place where it occurs? First of all, you should get advice from a travel physician who may prescribe medicine to keep you safe during your visit.

Whether you live in a place where malaria occurs, or you are just visiting, you should avoid getting mosquito bites:

- Sleep under an insecticide-treated mosquito net (certain insecticides kill mosquitoes)
- Use mosquito and insect repellents
- Wear long sleeves and long pants
- Get rid of any standing water around your house and neighbourhood (mosquitoes need standing water to reproduce)

Glossary of Key Terms

Drug resistance – This is when a medicine becomes less effective at fighting a disease because the pathogen that it targets has evolved to be able to survive attacks from the drug.

Epidemiology – part of medicine which studies the spread of a disease – how does someone get infected, how many people are at risk, where people are at risk and so on. For example, there is no risk for you to get Ebola unless you have been to Africa or you had contact with someone who's had it.

Mass drug administration: whole populations – both sick and healthy people receive drugs (e.g. against malaria), aiming to reduce the presence of the parasite.

Mosquito control – the management of mosquito populations to reduce their damage to human health as many mosquitoes carry diseases. Most commonly authorities kill the mosquitoes with insecticides.

Parasite – an organism that lives in or on other organisms (the host), or draws its food from that organism, and benefits at the expense of the host.

Plasmodium – a parasite which causes malaria. Five different species of *Plasmodium* cause malaria, mostly *P. falciparum* and *P. vivax*.

Prevalence – the percentage of people in a population at a given time who have an infection (or other condition).

Transmission – the passing of a disease from one individual to another.

Tropical (regions) – the area in the middle of the Earth furthest away from the poles, and closest to the equator. For example, most of Brazil is tropical.

Subtropical (regions) – areas next to the tropics, but closer to the poles. Usually less warm than the tropics. For example, South Africa is mostly subtropical.

Vaccine – an injection of a killed or weakened pathogen, in order to stimulate the immune system against that pathogen (a pathogen is something that makes you sick). This means that the immune system can recognize those pathogens if they ever come back, and destroy or disable them, preventing disease.

Vector-borne diseases – diseases that are transmitted through the bite of blood sucking arthropods such as mosquitoes, ticks, fleas, sandflies and others. Examples for vector-borne diseases other than malaria are Yellow fever, dengue, Zika, West Nile Fever, Lyme disease, and Tick-borne encephalitis.

Check your understanding

1. How can you get malaria?

2. What is the best way to avoid malaria and other vector-borne diseases?

3. Should we use MDA instead of mosquito control to fight malaria?

4. Herpes simplex virus is very common among people. Does this mean its overall prevalence is high or low?

5. What is the advantage of using four different mathematical models to look at the effect of MDA, instead of just one?

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