

Science AMA Series: This is Teun Bousema, PhD. I do research in malaria epidemiology, with a specific focus on malaria transmission and parasite biology, and I'm here today to talk about it. AMA!

eLife_{AMA}¹ and *ScienceAMAs*¹

¹Affiliation not available

April 17, 2023

Abstract

Hi Reddit! I'm Teun Bousema and I'm an epidemiologist in the Department of Medical Microbiology at Radboud University Medical Center in Nijmegen, the Netherlands. My research focuses on understanding the transmission of the malaria parasite *Plasmodium falciparum* (*P. falciparum*) – that is, how malaria-infected humans are able to infect mosquitoes. I lived and worked for many years in Kenya, Tanzania and the United Kingdom before moving to Radboud University Medical Center. One of the unique achievements of my department is the development of a safe controlled human infection model for malaria. In our current publication in eLife, we utilized this model to study the biology and transmission potential of controlled *P. falciparum* infections in Dutch volunteers who were exposed to malaria-infected mosquitoes. Our volunteers received treatment that controlled the pathogenic forms of malaria (and thus kept them safe) but stimulated the production of non-pathogenic transmissible stages of malaria parasites – the so-called gametocytes. We successfully induced gametocytes in all volunteers in sex ratios that resemble those observed in natural infections, and found that parasites start producing gametocytes immediately upon appearing in the bloodstream. Our model provides a new way to investigate malaria infection, and could help to test the impact of drugs and vaccines on gametocytes in the future. I look forward to talking more about our findings and anything related to my area of expertise more broadly. Together with Isaie Reuling, a clinician researcher and first author on the eLife manuscript, I'll start answering questions at 2pm EDT. You can read the full eLife paper, and use the annotation tool to make notes and discuss the findings further. A plain-language summary is also available here. AMA!

[REDDIT](#)

Science AMA Series: This is Teun Bousema, PhD. I do research in malaria epidemiology, with a specific focus on malaria transmission and parasite biology, and I'm here today to talk about it. AMA!

ELIFE_AMA [R/SCIENCE](#)

[Hi Reddit!](#)

I'm Teun Bousema and I'm an epidemiologist in the Department of Medical Microbiology at Radboud University Medical Center in Nijmegen, the Netherlands. My research focuses on understanding the transmission of the malaria parasite *Plasmodium falciparum* (*P. falciparum*) – that is, how malaria-infected humans are able to infect mosquitoes. I lived and worked for many years in Kenya, Tanzania and the United Kingdom before moving to Radboud University Medical Center. One of the unique achievements of my department is the development of a safe controlled human infection model for malaria. In our current publication in eLife, we utilized this model to study the biology and transmission potential of controlled *P. falciparum* infections in Dutch volunteers who were exposed to malaria-infected mosquitoes. Our volunteers received treatment that controlled the pathogenic forms of malaria (and thus kept them safe) but stimulated the production of non-pathogenic transmissible stages of malaria parasites – the so-called gametocytes. We successfully induced gametocytes in all volunteers in sex ratios that resemble those observed in natural infections, and found that parasites start producing gametocytes immediately upon appearing in the bloodstream. Our model provides a new way to investigate malaria infection, and could help to test the impact of drugs and vaccines on gametocytes in the future. I look forward to talking more about our findings and anything related to my area of expertise more broadly. Together with Isaie Reuling, a clinician researcher and first author on the eLife manuscript, I'll start answering questions at 2pm EDT. You can read the full eLife paper, and use [the annotation tool to make notes and discuss the findings further](#). A plain-language summary is also available [here](#). AMA!

[READ REVIEWS](#)

[WRITE A REVIEW](#)

CORRESPONDENCE:

DATE RECEIVED:
March 15, 2018

DOI:
10.15200/winn.152103.31852

ARCHIVED:
March 14, 2018

CITATION:
eLife_AMA , r/Science ,
Science AMA Series: This is
Teun Bousema, PhD. I do
research in malaria
epidemiology, with a specific
focus on malaria transmission
and parasite biology, and I'm

How does the transmission rate today compare with a decade ago?

[questionable2](#)

The burden of malaria has approximately halved compared to one decade ago. Still, more than 200 million clinical malaria cases occur worldwide annually and approximately 0.5 million individuals die of malaria.

Hi Teun and Isaie! Thanks for doing this AMA!

My question is: Can malaria be eliminated after one or two generations of immunized humans? Or can mosquitos carry the virus across their own generations, even without access to human carriers?

[n3ovice](#)

here today to talk about it.
AMA!, *The Winnower*
5:e152103.31852 , 2018 , DOI:
[10.15200/winn.152103.31852](https://doi.org/10.15200/winn.152103.31852)

© et al. This article is distributed under the terms of the [Creative Commons Attribution 4.0 International License](https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and redistribution in any medium, provided that the original author and source are credited.



Malaria, unlike some other pathogens, cannot be transmitted vertically (from mosquito to offspring). So every mosquito starts without an infection and then needs to get infected. For the human malaras, this can only happen by biting an infected human. A completely efficacious vaccine could theoretically whipe out malaria. Of course this does depend on vaccine effectiveness and coverage. Since many individuals in a population can infect mosquitoes, one would need to vaccinate a very large fraction of the total population. In some settings >99% to achieve elimination.

Hi Teun and Isaie! Thanks for doing this AMA.

My question is regarding the promise of targetting different points of infection for prevention and therapy. What I mean is, is there a particular point within the parasite's life-cycle (i.e. its sporogonic cycle (while it's developing in the mosquito), exo-erythrocytic cycle (the human life cycle) or erythrocytic cycle (where matured and awaiting further re-vectorisation by the mosquito)) during which there is the most promise in treating or even eradicating the disease?

Also, you mention the development of gametocytes in Dutch volunteers. Now, I have seen a fair number of flyers for Malaria clinical trials around my university and have always been curious if there was any potential danger of infection in such a trial if the control of the pathogenic development fails?

[Big_Fil_Preetza](#)

Great question. The best point to break the cycle by vaccination is determined by i) where parasite burden is lowest and, ii) where genetic diversity is lowest. The sexual stage is a promising stage in this respect since many tens of millions of asexual parasites circulate in the bloodstream of an infected host whilst at most several hundreds of sexual stage parasites are ingested by blood feeding mosquitoes. In addition, there is very limited genetic variation in gametocyte proteins, making it a very promising target to develop vaccines or neutralizing antibodies against.

Do bioinformatics play a role in your research or the analysis of the gathered data? I'd really like to know if you have interacted with bioinformatics and maby you can tell me how it comes handy in your research.

Thanks

[Swagmatic1](#)

bioinformatics becomes increasingly important in our work. We recently published a purely bioinformatics paper that aimed to understand what proteins and what transcripts are specific for gametocytes (<http://www.nature.com/articles/s41598-017-18840-7>), the parasite stage that we induced in our recent eLife paper. This information is essential to understand biology, develop diagnostics and potentially new interventions. Bioinformatics is becoming crucial in all biology research, malaria is no exception!

Thank you very much for doing this AMA, I have two questions for you as a non-specialist.

(1) I would like to know whether you have any thoughts on why it has taken this long for research on malaria to finally pick up some steam, especially considering the fact that it has been a problem for such a great number of people for such a long time (e.g. Europeans in their expeditions to, and conquests of, the 'non-Western' world, as well as those who were 'discovered' to be living in that world; or soldiers fighting on tropical fronts in the two world wars).

(2) In the eLife paper you very briefly mention that malaria is a contributor to ongoing poverty in affected countries. It is an interesting point to raise, and I realize that this particular paper was not the right place to discuss it at length. I was therefore wondering if you could elaborate a little bit more on it here. Also, do you have any rough ideas on how the complete (or virtual) elimination of malaria may affect developing economies in the future?

[JimTonic](#)

Regarding the second question, malaria is estimated to 'cost' Africa approximately 30 billion USD annually. This is the total cost, including deaths, loss of working days, treatment costs etc. In this way reducing the burden of diseases like malaria (and tb and hiv and neglected tropical diseases) is a great way of contributing to economic development.

regarding 1). malaria is a tricky pathogen. Highly complex and in this sense it is not surprising that it is hard to find a solution for it. It is also rather unlikely that there will be a magic bullet that solves the malaria problem on its own. In recent years, there has been great momentum for malaria control and research. This is not due to one factor but the involvement of the Bill & Melinda Gates Foundation is certainly a very positive contributor here. Not only because of financial investments but also in the sense that highly ambitious targets are set.

How do you see malaria control and prevention changing in the next ten years? What's the most dramatic/innovative/important change that's happened in the last ten years? How do national policies and international/ngo groups like PAHO/WHO affect outcomes for individuals and communities? How could they be more effective?

[FauxmingAtTheMouth](#)

The last decade has been a great success for control. Not due to particularly novel interventions but because of widescale deployment of effective drugs and vector (=mosquito) control. The challenge for the coming years will be to move beyond what we achieved so far (reducing burden by half since 2000!) and maintain the gains that are threatened by the development and spread of resistance against both drugs and insecticides.

New drugs and new insecticides are highly needed. One difficult to predict new intervention is the use of malaria-resistant mosquitoes. That holds great promise but also great challenges ahead. The deployment of the first partially efficacious vaccine (mosquirix) in the coming years is also something to look out for. The efficacy is modest at present but it could save many lives.

Hi Teun, thanks for taking time to do this AMA! Do you think your safe controlled human infection model can be applied to other infectious diseases?

[edwinksl](#)

Yes, definitely. Recently a great model was developed for schistosomiasis by colleagues in Leiden (<http://www.sciencemag.org/news/2018/02/seventeen-volunteers-let-worm-live-inside-them-help-defeat-dangerous-disease>). There are many models under development.

Thanks Teun and Isaie!

Really interesting research! My question is fairly practical: how did you go about finding people who would *volunteer* to be bitten by malaria-infected mosquitos? (As someone who can't stand the itching

of insect bites, I can't quite imagine doing it myself.)

[StuartRFKing](#)

It is reasonably easy to find people that want to participate in our malaria studies. Many participants are interested in contributing to malaria research for the best possible reasons: Wanting to contribute to the fight against malaria or improve vaccines and drugs. So far, more than 500 people have participated in these studies in our institute.

What is the most challenging aspect of controlling malaria, especially in high-burden low and middle income countries? Funding? Man-power? Human/cultural elements? Thank you!

[anyvways](#)

This is an excellent question. It is a combination of all.

Many tools that we have are actually not properly deployed. This article <https://doi.org/10.7554/eLife.09672> is a great example of just how difficult it is to reach very high coverage with the highly efficacious nets that form a cornerstone of the recent gains in malaria control.

Funding is definitely a major issue. To sustain gains an investment of 5 billion USD/year may be required. Even if we were to eradicate malaria, this amount is needed for several years to ensure malaria is truly gone and there is no resurgence.

At the same time, malaria is a tremendously impressive parasite. Flexible in its appearance in humans in mosquitoes, ingenious in escaping human immunity and utilizing the mosquito to maximize its spread. It is no surprise that human malaria parasites have been on the planet pretty much as long as humans exist. The rapid development of parasite resistance against many antimalarial drugs also demonstrates the challenge we are up against. A PhD candidate of mine compared it to the Red Queen from Alice in Wonderland. We need to run to keep up with the parasite and move twice as fast to really gain ground!

Hi and thanks for joining us today!

1. What are your thoughts about the claim of health risks in India regarding the release of mosquitoes bearing the "alien bacteria", Wolbachia?
2. Any word on the RTS,S pilot? Anything on the horizon as a potential replacement?
3. Has the situation with the [C580Y mutant](#) worsened?
4. Thoughts on the Naled spraying controversy in Florida?

[PHealthy](#)

1) I would need to know more about these claims. 2) RTS,S is the only current vaccine that is piloted for implementation. Some other vaccines are under development and may soon enter larger trials. A great overview of timelines is given on <http://www.malariavaccine.org/malaria-and-vaccines/malaria-vaccine-roadmap> (download at the right side of the screen) 3) great question. This is a real fear. For many years it was hard to see the impact of artemisinin resistance but now it is considered by some to be a global concern. I tend to agree. True failure rates of antimalarial drugs are rising. So far, it seems largely contained to the SE Asia Greater Mekong Subregion but if it spreads to the highly endemic regions in Africa, a disaster is looming.

4) no. But I do know and have experienced myself in Uganda that spraying with efficacious insecticides can have a tremendous positive impact on the malaria situation.

Thank you. That's an enormous amount of fatalities

[questionable2](#)

It is still enormous. With continued interest from world leaders and donors, there are reasons to be optimistic that the burden can be further reduced. >1 million deaths in the year 2000, roughly 0.5 million in 2015.

On the other hand, the last World Malaria Report of the World Health Organization indicated that the positive trend is currently not continuing. There appears to be a flattening of the curve and perhaps even an increase in disease and deaths again in most recent years. Perhaps the low hanging fruits in malaria control have been picked and an increased investment is needed in maximizing the impact of currently available tools (nets, antimalarials, diagnostics, insecticides); and on top of that novel tools are needed to move forward. Our presented controlled human infection - transmission model may prove to be a highly relevant model to test such novel interventions.