

Malaria Elimination: How Are We Actually Going to Do It?

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Americas: Relapsing Malaria in Amazon

- Malaria largely restricted to marginal communities in Amazon River valley
- Vast majority of cases due to relapsing (vivax) malaria; falciparum likely gone soon
- Biggest problem is civil disruption of Venezuela



Africa: Wide Range of Epidemiology

- Elimination at the edges of malaria transmission
- Heart land of malaria still has very efficient vectors and very few health services
- Near term progress most likely in highly seasonal malaria areas (Sahel)



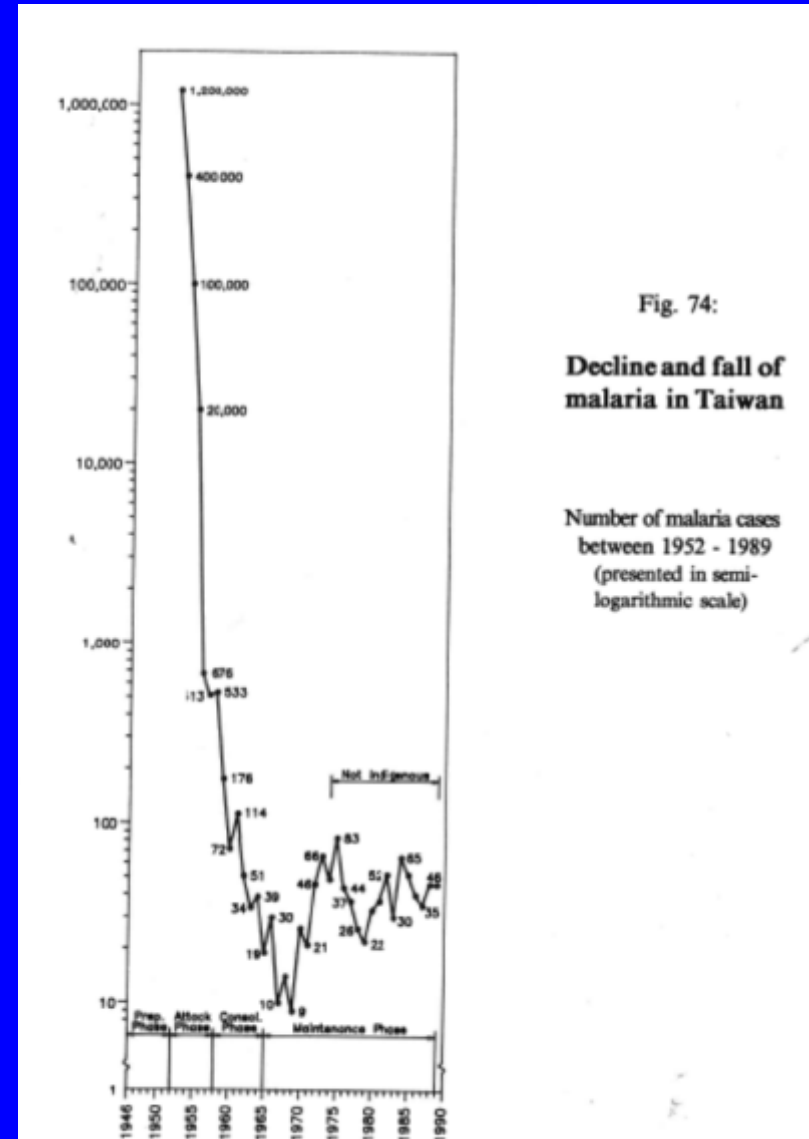
Asia: Drug Resistant Malaria

- Highly drug resistant falciparum in ever decreasing amounts as in Cambodia
- India with huge numbers of relapsing malaria will be the longest lasting problem
- Malaria elimination in China has been outstanding success story along with Sri Lanka



Taiwan Eliminated Malaria in 1965

- Malaria problem was as great as PNG in 1940s
- Chinese Civil War came to Taiwan with the evacuation of Nationalist Army
- DDT spray and obsessive blood smears ended malaria transmission



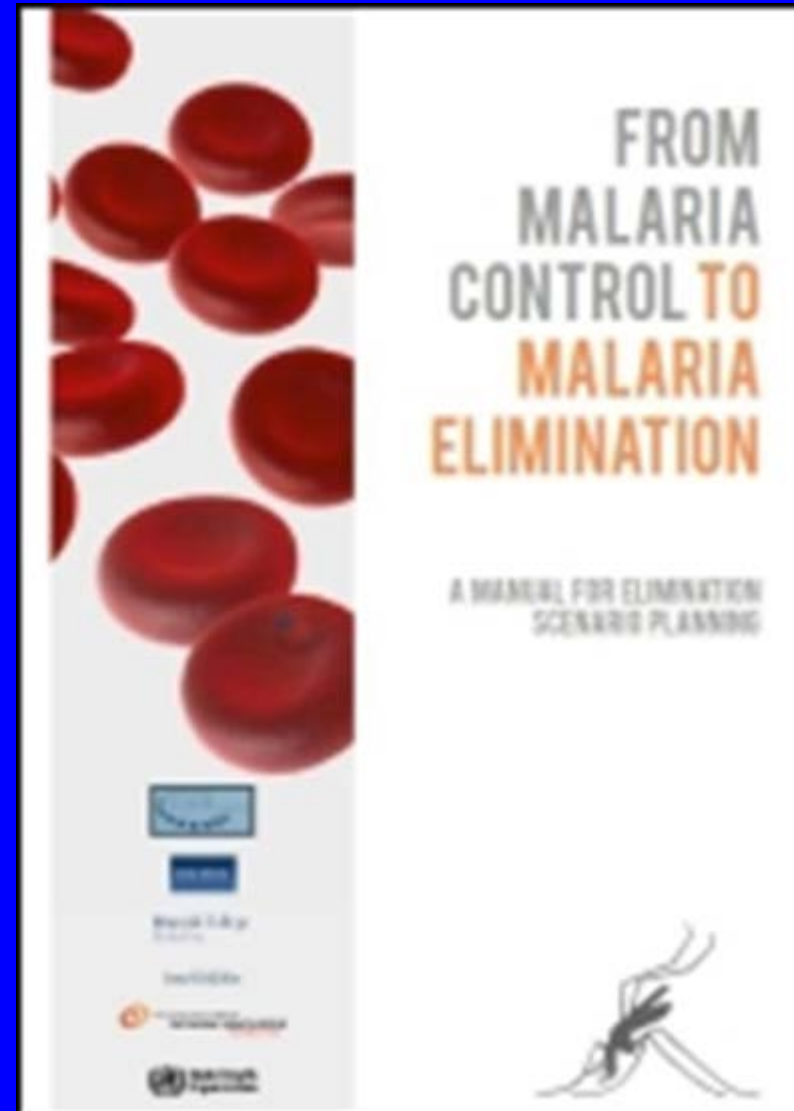
China: No Recent Malaria Transmission

- Relapsing malaria now gone from Central China; in 1980s > 1M cases / yr
- Used mass drug administration of huge amounts of primaquine
- Workers returning from African construction projects with falciparum



Malaria Elimination in Phases

- Reduce death and illness with drugs
- Control transmission with bet nets / spray
- Eliminate residual parasites in human reservoir



Reduce Death and Disease

- **Diagnosis with RDTs**
- **Artemisinin drug combinations given to all malaria cases**
- **Health service penetration / logistics is usually the critical gap**



Control Transmission of Malaria

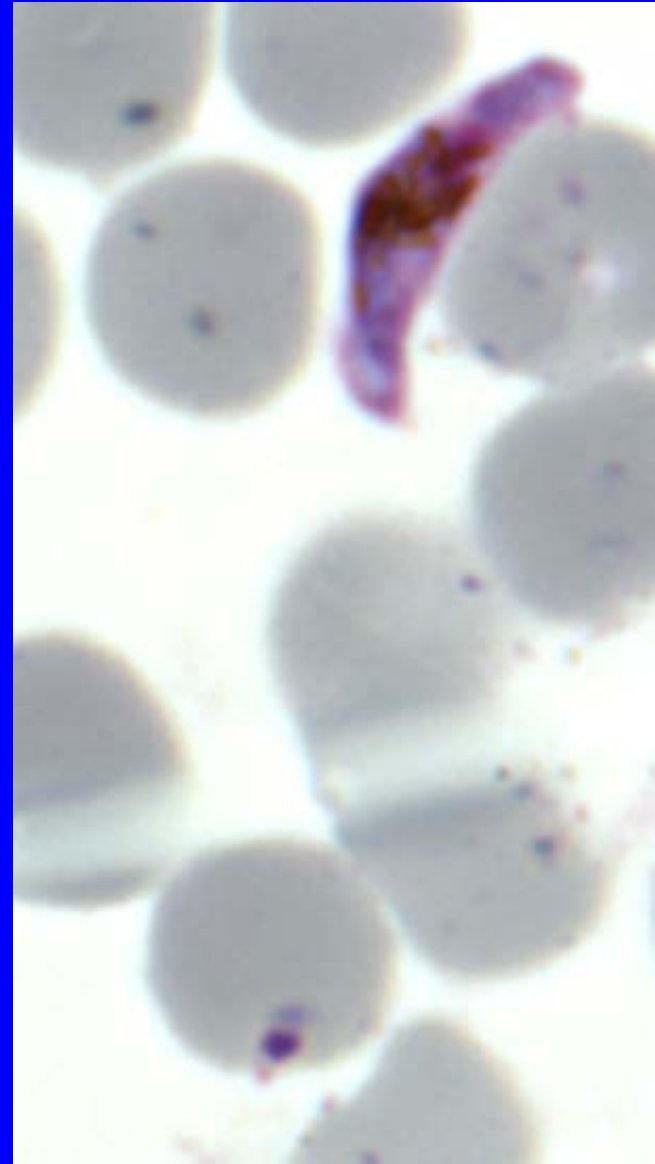
- Permethrin treated bed nets for wide distribution
- Residual house spraying of insecticides often also using permethrin
- Insecticide resistant mosquitoes of uncertain significance to programs



PAOC

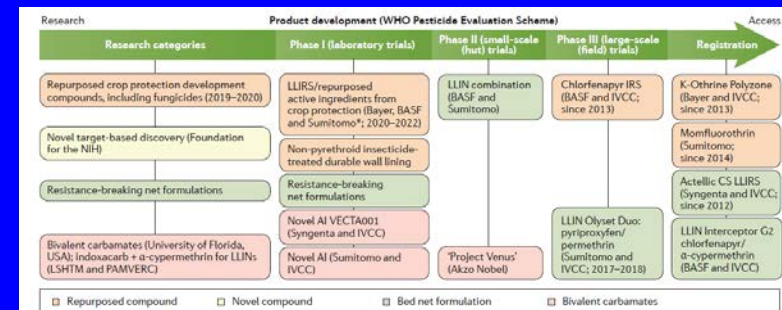
Eliminate Residual Parasites in Humans

- Destruction of residual parasites is difficult, time consuming and expensive
- Vivax: latent liver parasites called hypnozoites can wait months to years to emerge
- Falciparum: dormant stages in blood and gametocytes resist treatment with ordinary drugs



New Insecticides for Mosquitoes

- Agriculture market drives introduction of insecticides
- Public health use is a tiny market of little commercial significance
- New compounds in advanced testing (Sumimoto, BASF, Syngenta, Bayer, others)



Nature Reviews

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New Anti-Insect Modalities

- Attractive sugar baits to kill *Anopheles* while sparing other insects through selective membrane biting poisoning only mosquitoes
- Spatial repellents designed to fill living area over days to weeks that can be placed by the household members without help



Genetically Modified Mosquitoes

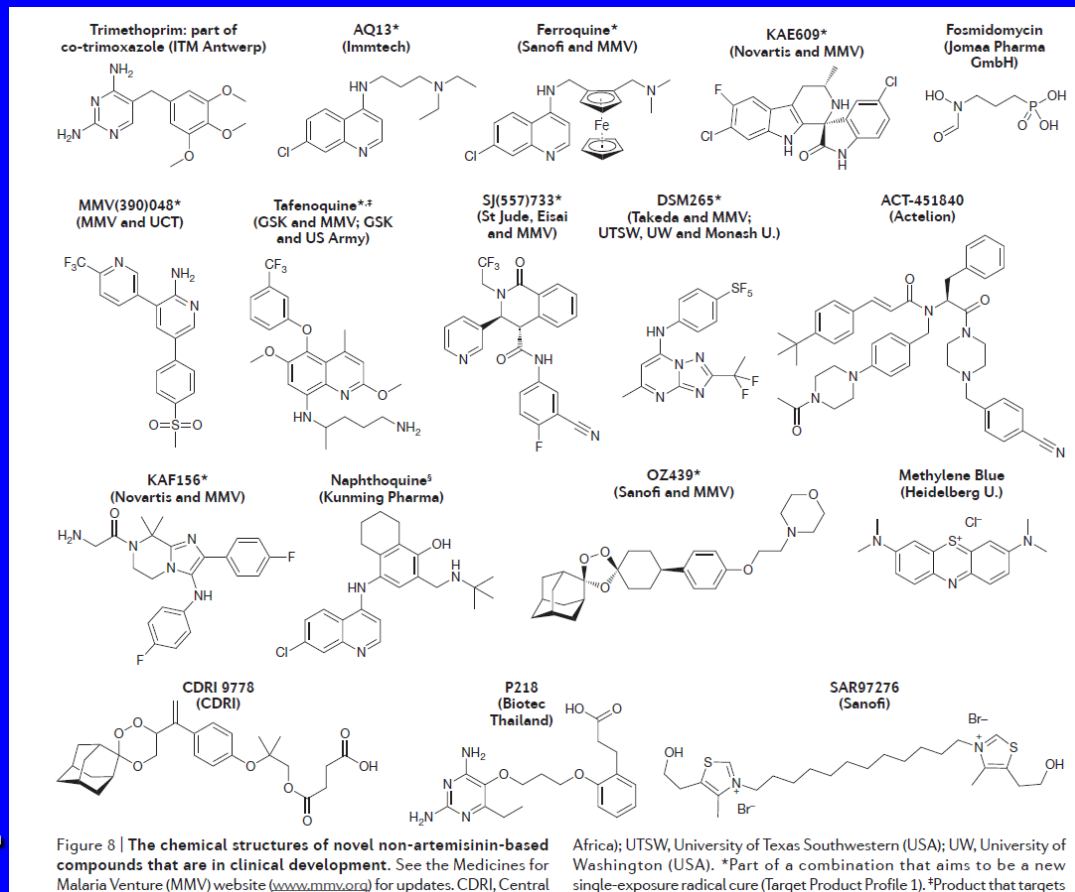
- Only a few species of *Anopheles* transmit malaria which is also a parasite of mosquitoes
- Making a vector incompetent to parasite growth in GI tract
- Gene drive required to move through population



US CDC

New Drugs in Advanced Clinical Testing

- **Tafenoquine: long-acting primaquine analogue, GSK**
- **Ferroquine: redox active chloroquine, Sanofi Aventis**
- **Cipargamin: PfATP4 inhibitor, Novartis**



Africa; UTSW, University of Texas Southwestern (USA); UW, University of Washington (USA). *Part of a combination that aims to be a new single-exposure radical cure (Target Product Profile 1). ²Product that targets

Drugs Against Mosquito Vector?

- Ivermectin used in filarial elimination projects given safely to > 1B people in tropics
- Mosquito biting someone with ivermectin in their blood has a shortened life-span
- Likely have to use longer acting drug to make an impact on malaria transmission



Malaria Vaccines Still in the Future

- **Anti-disease:** minimize impact on vulnerable populations (children)
- **Anti-parasite:** immune system to kill parasites in blood
- **Anti-transmission:** blocking ability of parasite to infect mosquitoes

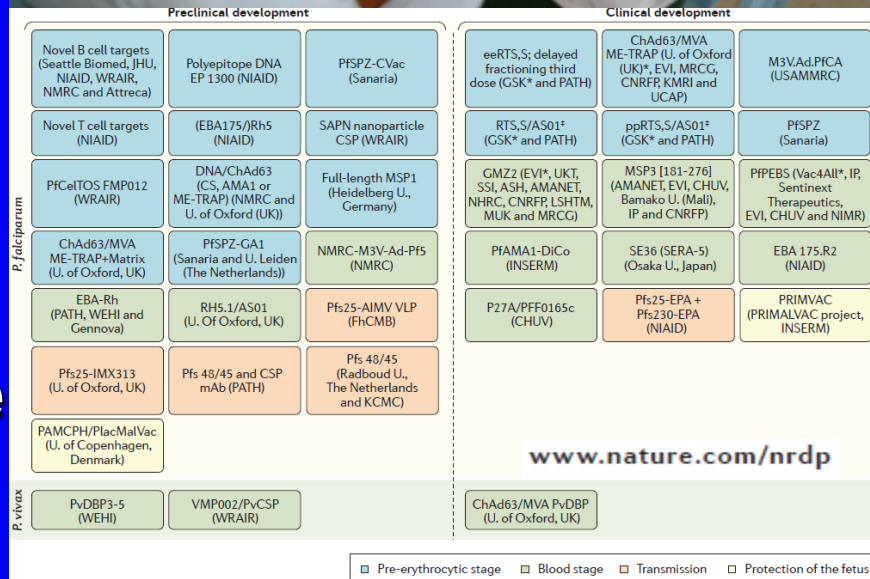


Figure 6 | The global pipeline for malaria vaccines. The main data source NIAID, National Institute of Allergy and Infectious Diseases (USA); NIMR

RTSS: Why It Has No Role in Elimination

- Registered after 30y and > \$2B by GSK, US Army
- Able to protect infants for 6 months but does not show long-term protection
- Four dose schedule does not match well with childhood vaccinations



Is It Too Late for Malaria Vaccines?

- 26y ago we were waiting for the vaccine
- Only vaccines passed by a stringent regulatory authority can be used
- Any vaccine not currently in advanced human trials will not be available in time



What Does Failure Look Like?

- Some countries will certainly eliminate malaria leaving others behind (Africa, PNG)
- Global consensus to eliminate disease is weak especially given experience with polio
- Must show great progress to continue resource priority



War / Civil Unrest: Real Limitations

- Malaria parasite resurges during human conflict / disaster breakdown of health system (Solomons)
- Venezuela cannot import drugs or insecticides
- Wars in Sub-Saharan Africa threaten malaria progress (Mali, Chad)



Malaria Contained Within Limits?

- Once malaria is eliminated, it is not easily re-established unlike polio
- Motivation to finish malaria program in other countries has low priority to national leaders
- Another gap in malaria elimination will leave PNG with endemic malaria



Malaria Elimination: 2030 Deadline

- **Have to maintain sense of progress and success in order to continue**
- **Competition for resources with non-communicable diseases (diabetes)**
- **New tools are needed for high transmission areas, but a great deal can be done with what we have now**

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From evidence to action

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