Malaria and Lymphatic filariasis research updates

Moses Laman

PNG Institute of Medical Research

Current priorities

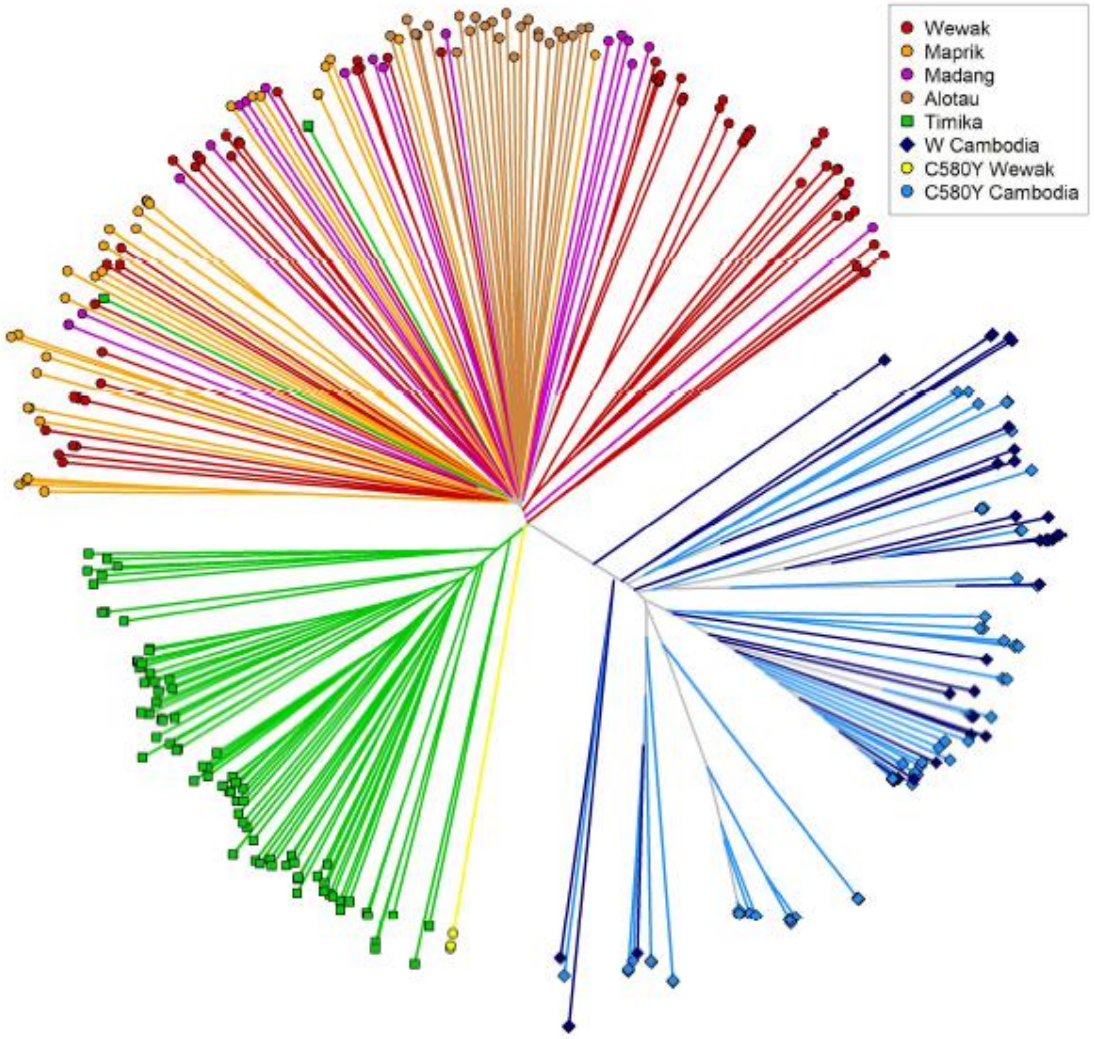
Malaria

- Artemisinin resistance
- Trends in malaria burden
- Insecticide resistance monitoring
- Vector Control tools
- Vivax malaria

Lymphatic filariasis

- Policy change - elimination efforts
- Treatment of adult worm
- MDA stopping criteria
- Integrated approach (NTD)

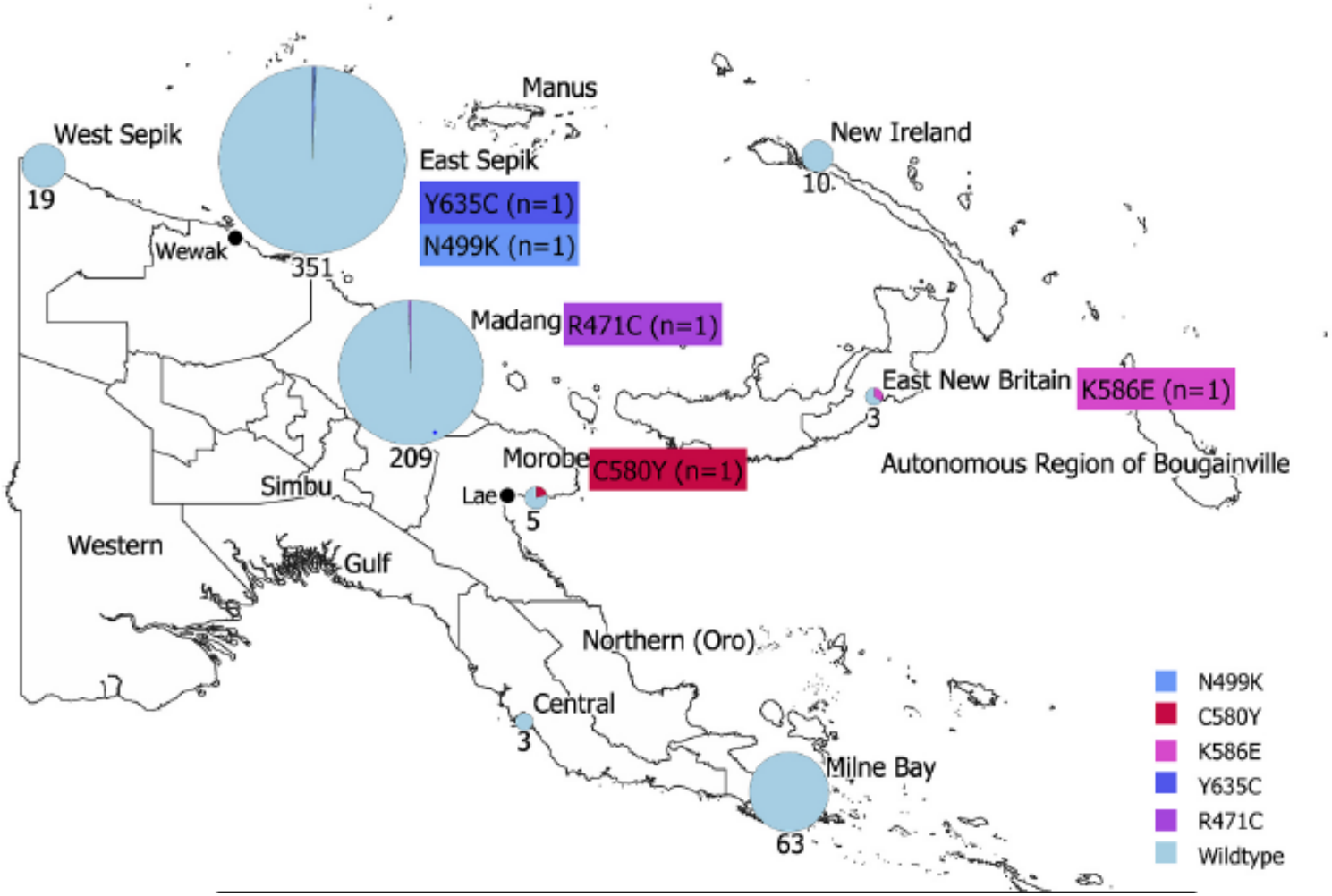
Artemisinin resistance (C580Y)



Miotto et al, 2020

Artemisinin resistance

International Journal for Parasitology: Drugs and Drug Resistance 16 (2021) 188–193



Therapeutic efficacy studies

Tavul *et al. Malar J (2018) 17:350*
https://doi.org/10.1186/s12936-018-2494-z

Malaria Journal

RESEARCH Open Access

Efficacy of artemether–lumefantrine and dihydroartemisinin–piperaquine for the treatment of uncomplicated malaria in Papua New Guinea

Livingstone Tavul[1*†], Manuel W. Hetzel[2,3†], Albina Teliki[1], Dorish Walsh[1], Benson Kiniboro[1], Lawrence Rare[1], Justin Pulford[1,4], Peter M. Siba[1], Stephan Karl[1,5,6], Leo Makita[7], Leanne Robinson[1,5,6], Johanna H. Kattenberg[1,10], Moses Laman[1], Gilchrist Oswyn[8] and Ivo Mueller[5,6,9]

Conclusions: AL and DHA-PPQ were efficacious as first- and second-line treatments for uncomplicated malaria in PNG. Continued in vivo efficacy monitoring is warranted considering the threat of resistance to artemisinin and partner drugs in the region and scale-up of artemisinin-based combination therapy in PNG.

TES (current data) n=13/139 (9.4%)

	Day 0	Day 3	Day 7
Patient 1	+	-	-
Patient 2	+	-	-
Patient 3	+	-	-
Patient 4	+	-	-
Patient 5	+	-	-
Patient 6	+	+	-
Patient 7	+	-	-
Patient 8	+	-	-
Patient 9	+	+	+
Patient 10	+	+	-
Patient 11	+	-	-
Patient 12	+	-	-
Patient 13	+	-	-

The bed-net story

nature COMMUNICATIONS

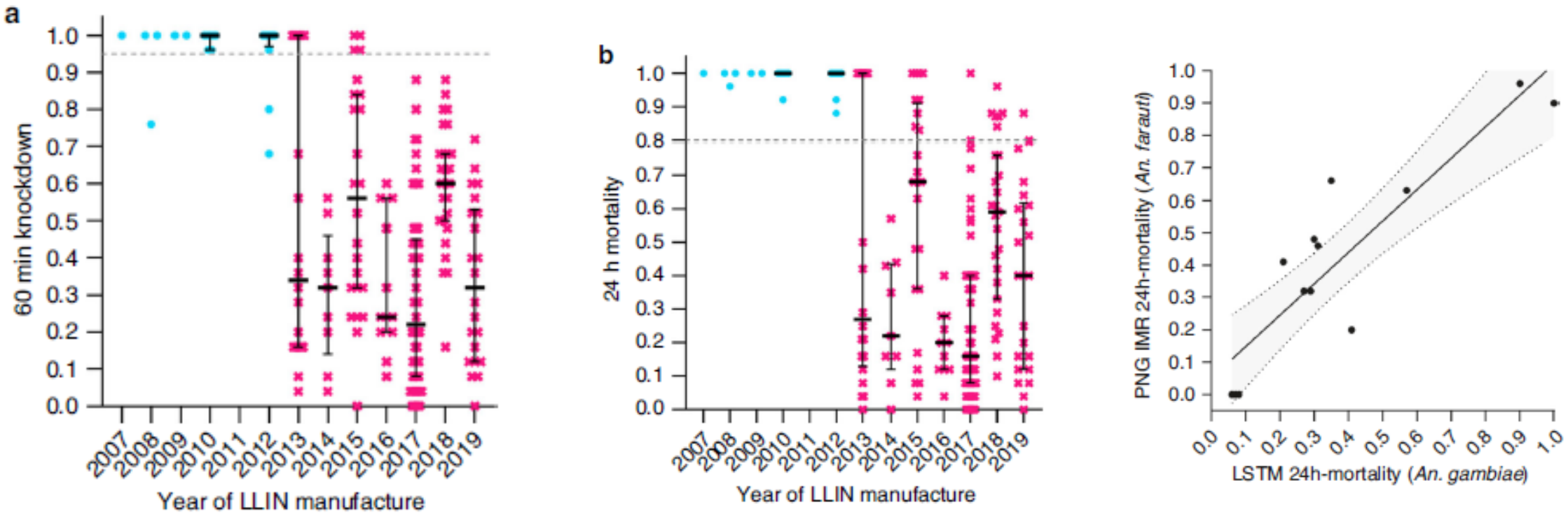
ARTICLE

https://doi.org/10.1038/s41467-020-17456-2 OPEN

Decreased bioefficacy of long-lasting insecticidal nets and the resurgence of malaria in Papua New Guinea

Rebecca Vinit[1,8], Lincoln Timinao[1,2,8], Nakei Bubun[1,8], Michelle Katusele[1,8], Leanne J. Robinson[1,3], Peter Kaman[1], Muker Sakur[1], Leo Makita[4], Lisa Reimer[5], Louis Schofield[2], William Pomat[1], Ivo Mueller[6], Moses Laman[1], Tim Freeman[7] & Stephan Karl[1,2]✉

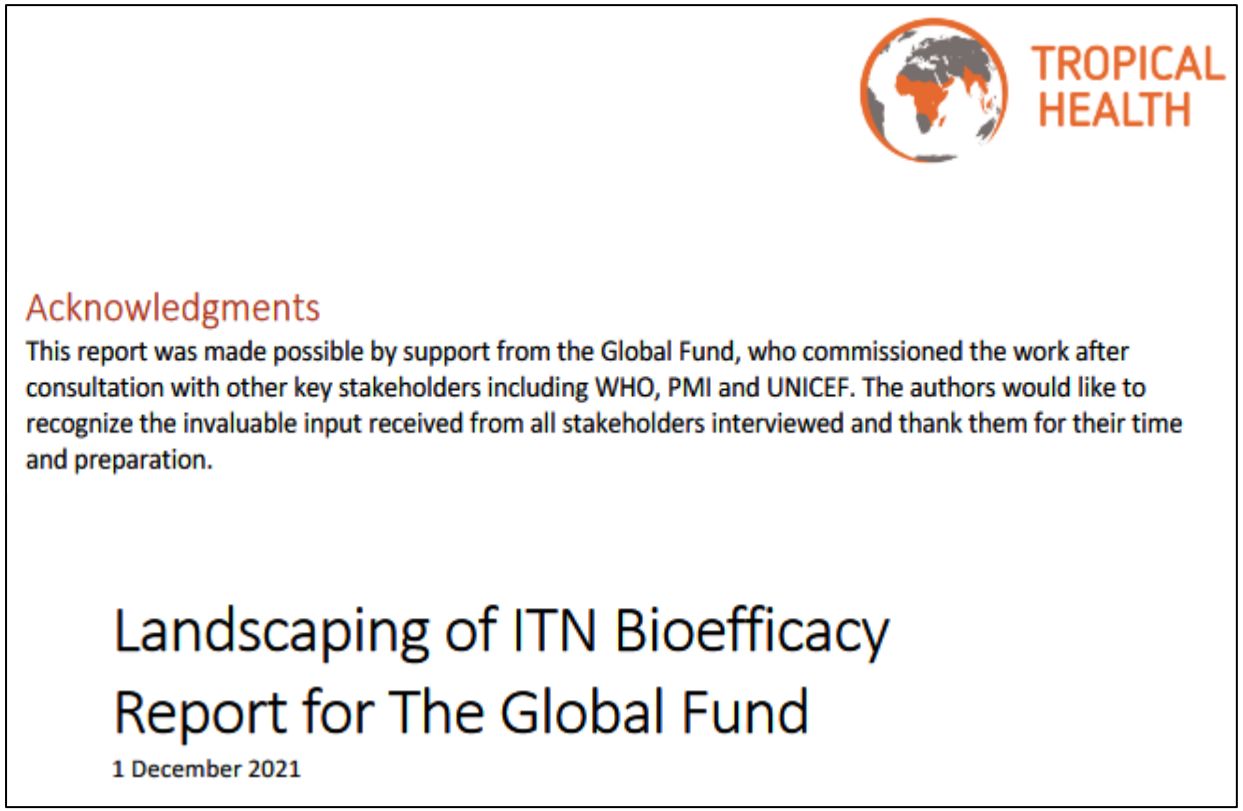
Reduced LLIN bioefficacy after 2012



Vinit R, Nature Communications 2020

Immediate local and global impact

- WHO Global Director – Malaria
- Global Fund
- Other countries followed
- Change in LLIN brand locally
- Monitoring continues
- Relevance of PNGIMR



TROPICAL HEALTH

Acknowledgments

This report was made possible by support from the Global Fund, who commissioned the work after consultation with other key stakeholders including WHO, PMI and UNICEF. The authors would like to recognize the invaluable input received from all stakeholders interviewed and thank them for their time and preparation.

Landscaping of ITN Bioefficacy Report for The Global Fund

1 December 2021

NATNAT CORE OBJECTIVES

1. Strengthen laboratory, semi-field and field capacity to test new VCTs in PNG

2. Conduct rigorous field evaluations of new VCTs

3. Investigate the community and health system acceptability and cost analysis of new VCTs

4. Support a NMCP-led formal network for vector control tools and interventions in PNG

1. Strengthen laboratory, semi-field and field capacity to test new VCTs in PNG

- Build capacity for testing of residual spraying products, larvicides and spatial emanators
- Plan to extend the existing PNGIMR Entomology facilities
- Establish a semi-field testing site

1. Strengthen laboratory, semi-field and field capacity to test new VCTs in PNG

New Insectary Laboratory

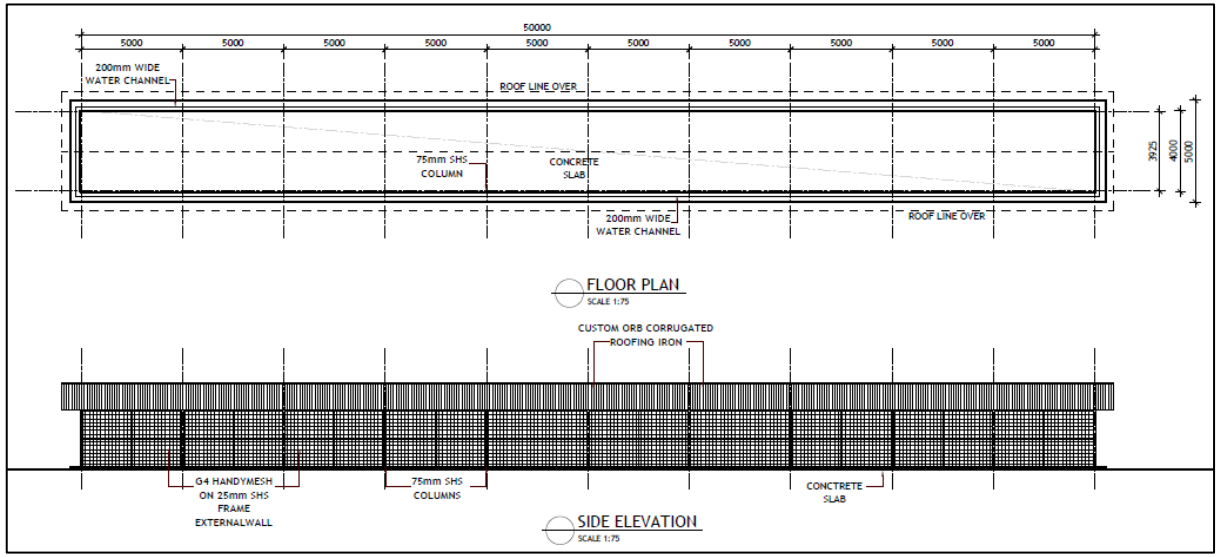
Gum site insectary lab taking shape

1. Strengthen laboratory, semi-field and field capacity to test new VCTs in PNG

Mosquito Tunnel

- Mosquito tunnel will be used to study various VCT products, in particular spatial emanators and LLINs

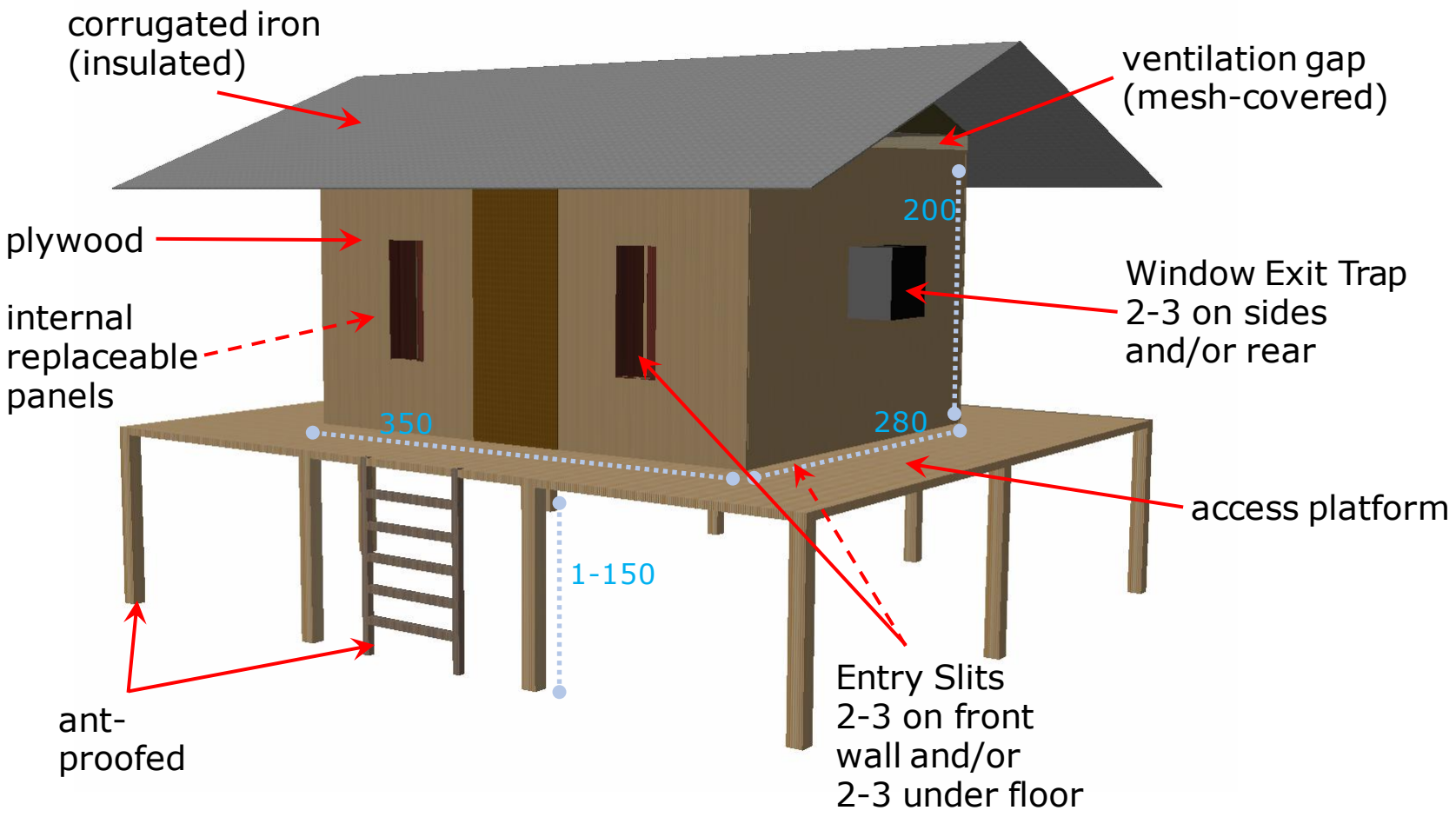
Mosquito Tunnel (I-ACT) in Tanzania (Massue et al., 2019)



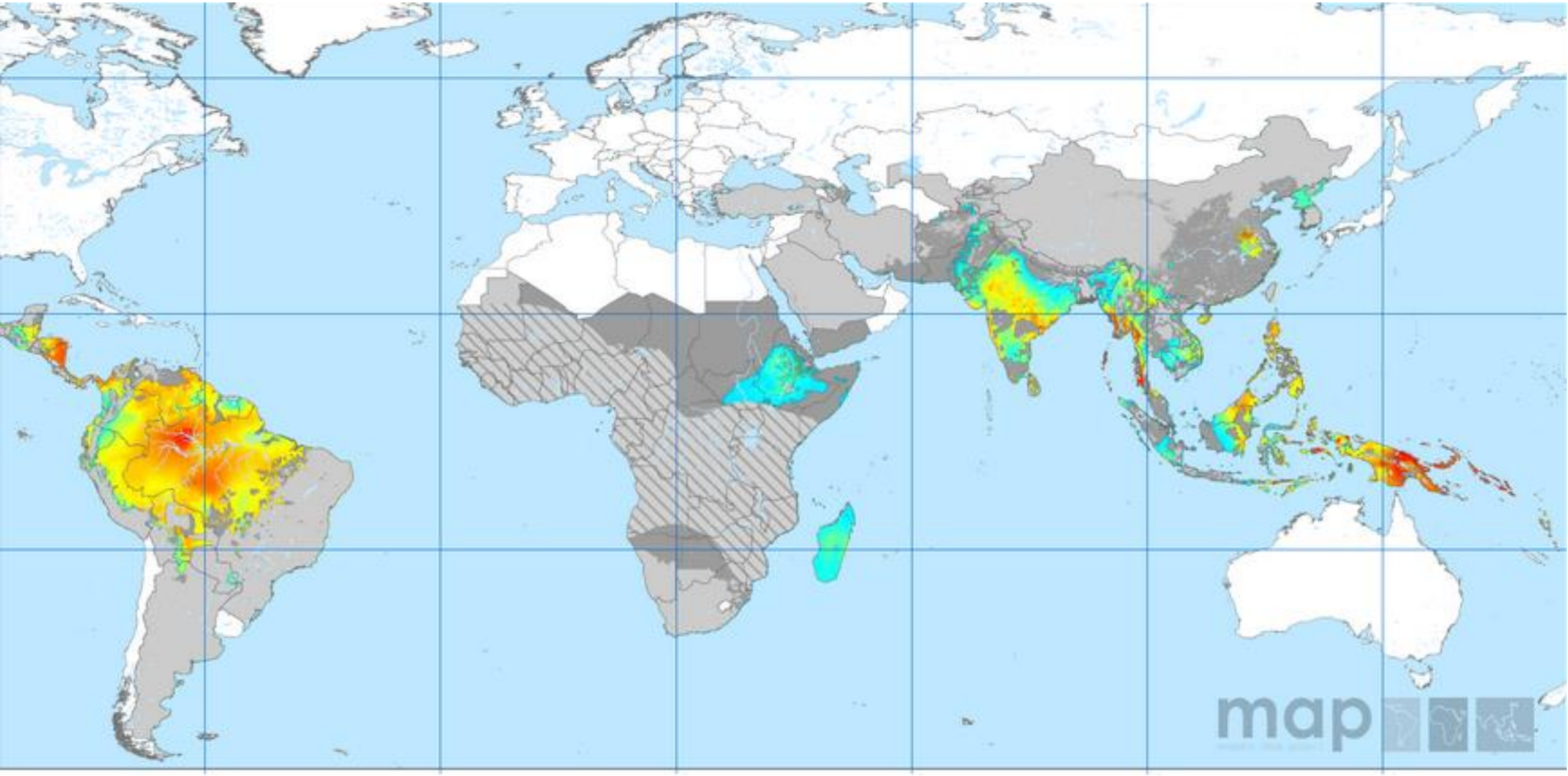
Mosquito tunnel at Gum site taking shape

1. Strengthen laboratory, semi-field and field capacity to test new VCTs in PNG

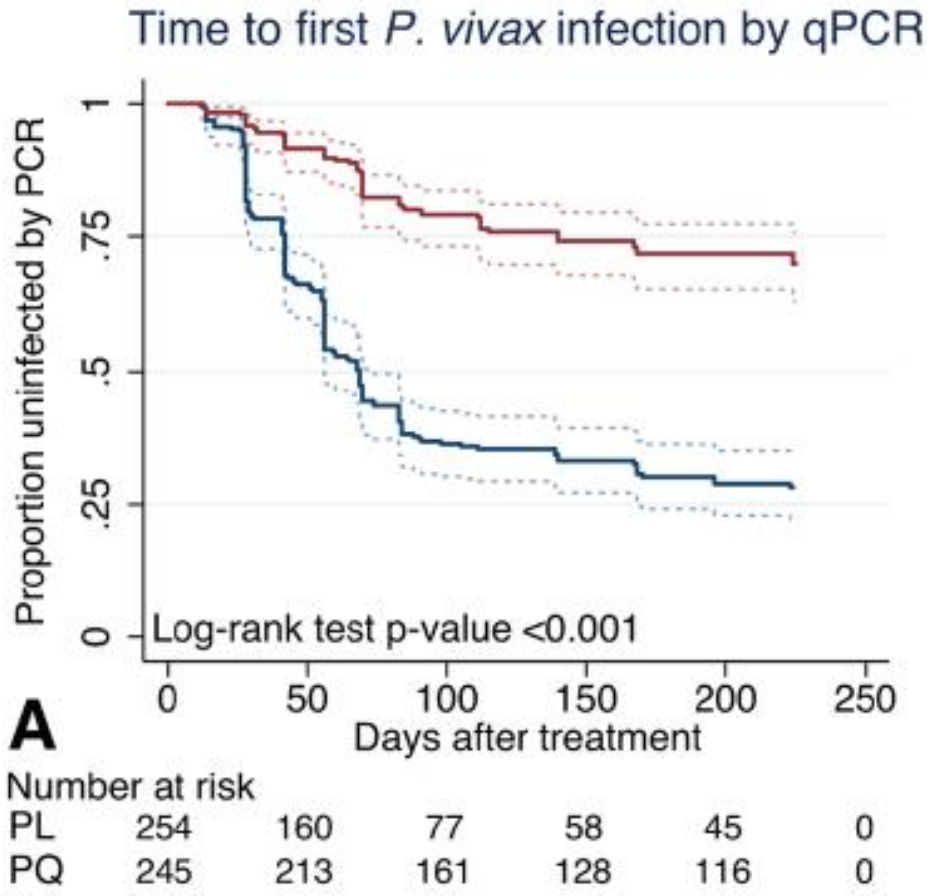
Experimental Hut Design



Global Burden of Vivax Malaria



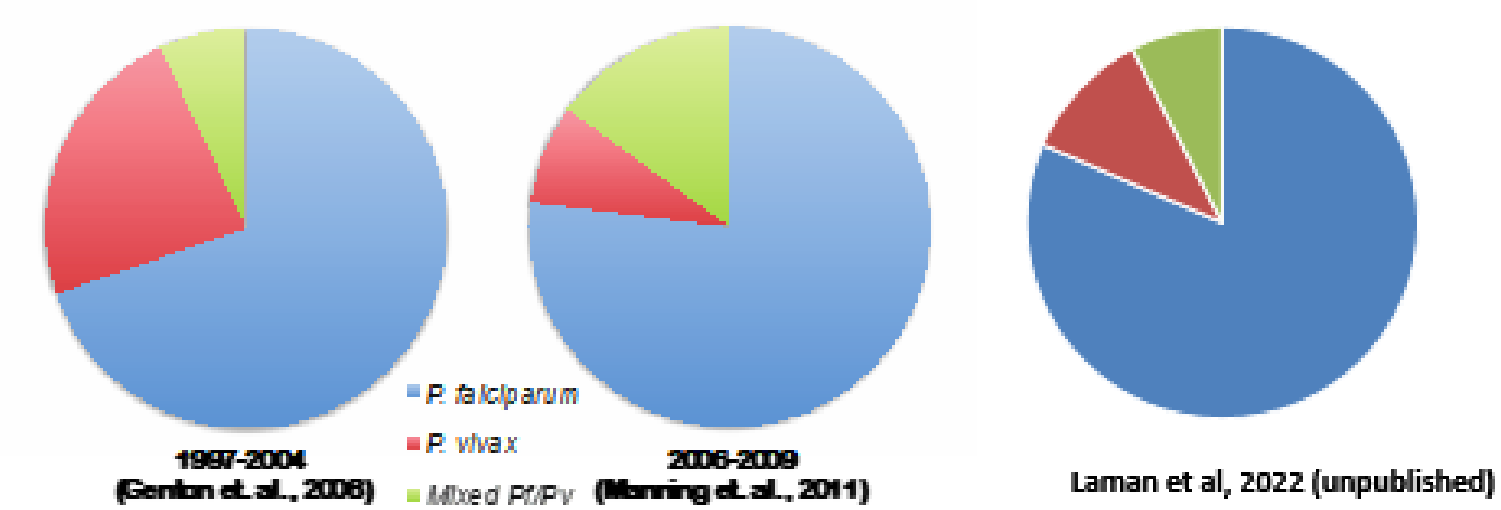
Relapses account for 80% Pv infections



Robinson et al, Plos Med 2015

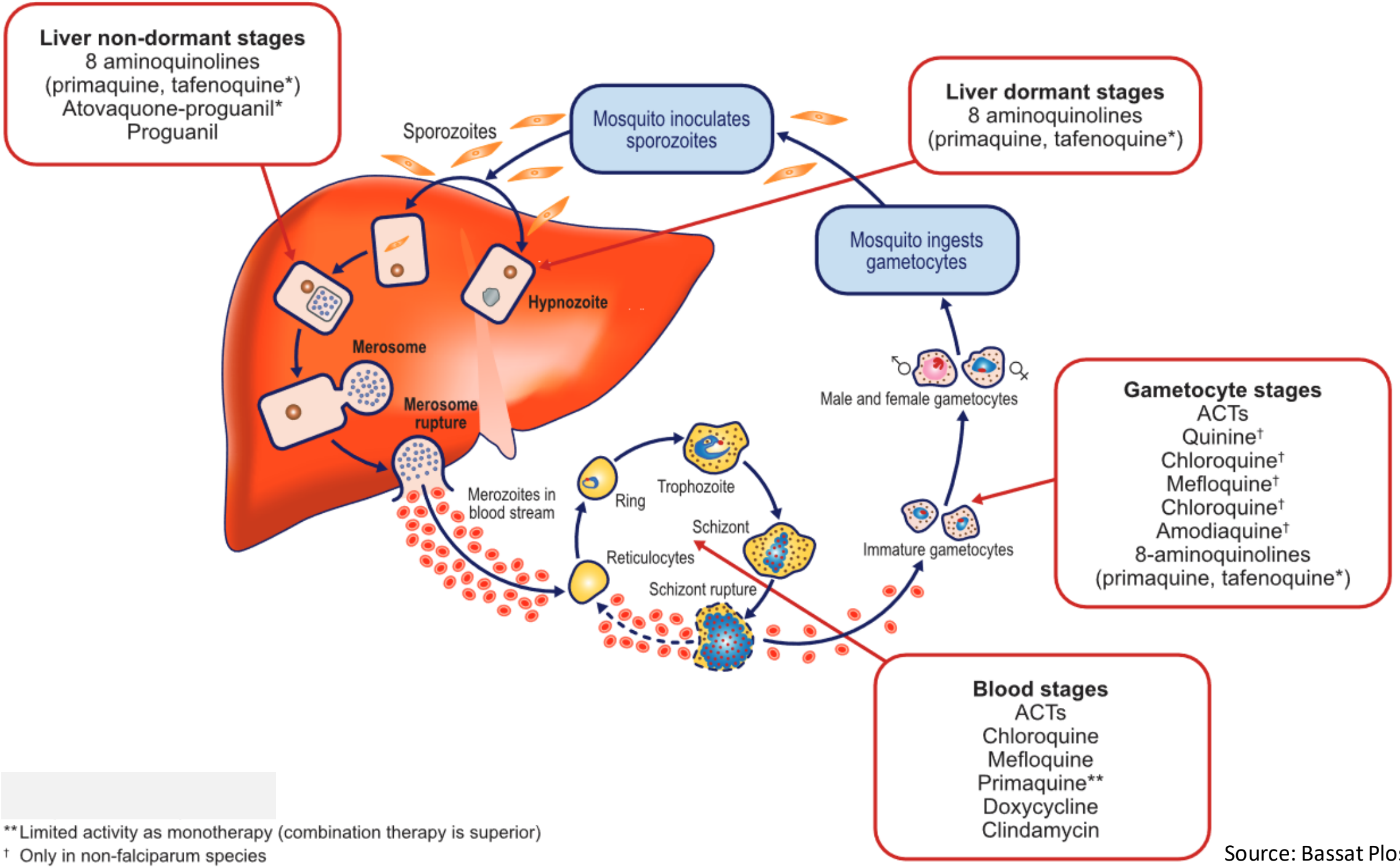
Hospital surveillance of P vivax admissions

1997-2004 **2006-2009** **2015-2019**



Laman et al, 2022 (unpublished)

- 8-23% of severe malaria cases due to *Pv* alone
- 7-15% of mixed *Pf/Pv* infections



**Limited activity as monotherapy (combination therapy is superior)

† Only in non-falciparum species

Source: Bassat Plos NTD

Current practice in PNG

- Primaquine 0.25mg/kg daily for 14 days after 3 days of artemether-lumefantrine
- Routine pre-treatment G6PD testing is not available
- No treatment supervision during treatment with PQ
- Drug supply challenges in facilities that need primaquine the most
- No formal pharmacovigilance system of monitoring for primaquine use

Short **CO**urse **P**rimaquin**E** for the radical cure of *P. vivax* (SCOPE)

PAPUA NEW GUINEA INSTITUTE OF MEDICAL RESEARCH

Burnet Institute
Medical Research. Practical Action.

PATH

Collaboration & Partnership

Local project lead team

Mr Leo Makita (NMCP)
- Project PI

Dr Maria Ome-Kaius (PNGIMR)
- Project PI

Miss Annie Dori (PATH)
- Project Manager

Dr Mary Malai (PNGIMR)
- Project Clinician/Coordinator

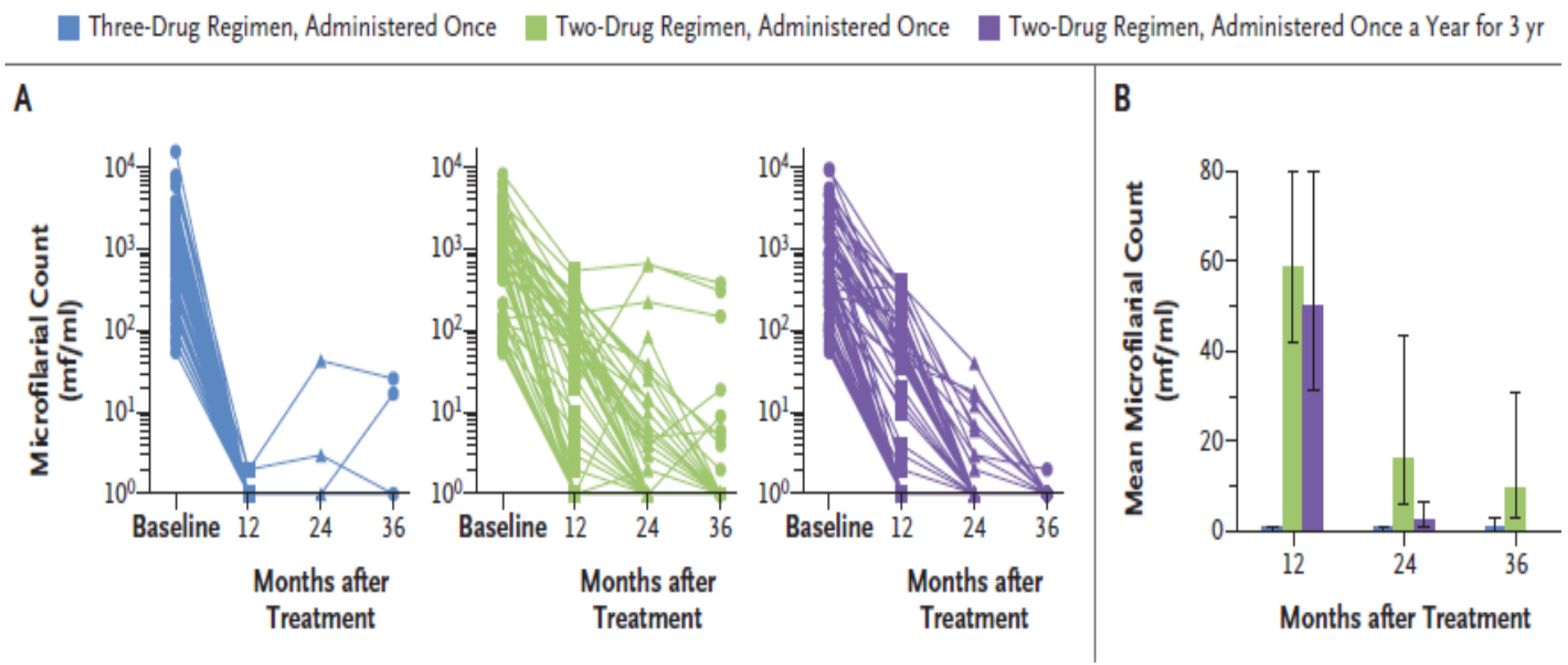
East New Britain: Dr Ako Yap, East New Britain Health Authority, Catholic Mission, Napapar health centre staff and community

West Sepik: Dr Trevor Kelebi, West Sepik Provincial Health Authority, Baro clinic staff and community members

East Sepik: Dr Jimmy Kambo, East Sepik Provincial Health Authority, Wiriu clinic staff and community members

Madang: Dr Martin Daimen, Madang Provincial Health Authority, Catholic Mission, Mugil health centre staff and community members

LF studies – IMR Sepik



King C, NEJM 2018

PLOS MEDICINE

RESEARCH ARTICLE

The safety of double- and triple-drug community mass drug administration for lymphatic filariasis: A multicenter, open-label, cluster-randomized study

Gary J. Weil[1]*, Joshua Bogus[1], Michael Christian[2], Christine Dubray[3], Yenny Djuardi[2], Peter U. Fischer[1], Charles W. Goss[1], Myra Hardy[4], Purushothaman Jambulingam[5], Christopher L. King[6], Vijesh Sridhar Kuttiat[5], Kaliannagounder Krishnamoorthy[5], Moses Laman[7], Jean Frantz Lemoine[8], Katiuscia K. O'Brian[1], Leanne J. Robinson[7,9], Josaia Samuela[10], Kenneth B. Schechtman[1], Anita Sircar[3], Adinarayanan Srividya[5], Andrew C. Steer[4], Taniawati Supali[2], Swaminathan Subramanian[5], the DOLF IDA Safety Study Group[¶]

1 Washington University, St. Louis, Missouri, United States of America, **2** Universitas Indonesia, Jakarta, Indonesia, **3** Centers of Disease Control and Prevention, Atlanta, Georgia, United States of America, **4** Murdoch Children's Research Institute, Melbourne, Australia, **5** ICMR-Vector Control Research Centre, Puducherry, India, **6** Case Western Reserve University, Cleveland, Ohio, United States of America, **7** Papua New Guinea Institute of Medical Research, Madang, Papua New Guinea, **8** Ministère de la Santé Publique et de la Population (MSPP), Port-au-Prince, Haïti, **9** Burnet Institute, Melbourne, Australia, **10** Fiji Ministry of Health and Medical Services, Suva, Fiji

Check for updates

OPEN ACCESS

Triple drug was safe and efficacious (n=26,836)

Table 1. Filarial infection prevalence in the study sites.

Site	District	Mf Prevalence[a]
Fiji	Gau	33/1,957 (1.7%)
	Rotuma	106/1,454 (7.3%)
Haiti	Northern Dept	114/5,987 (1.9%)
India	Yadgir	591/8,825 (6.7%)
Indonesia	Flores	20/1,254 (1.6%)
	Sumba	94/2,667 (3.5%)
PNG	Bogia	199/4,518 (4.4%)

GUIDELINE

ALTERNATIVE MASS DRUG ADMINISTRATION REGIMENS TO ELIMINATE LYMPHATIC FILARIASIS

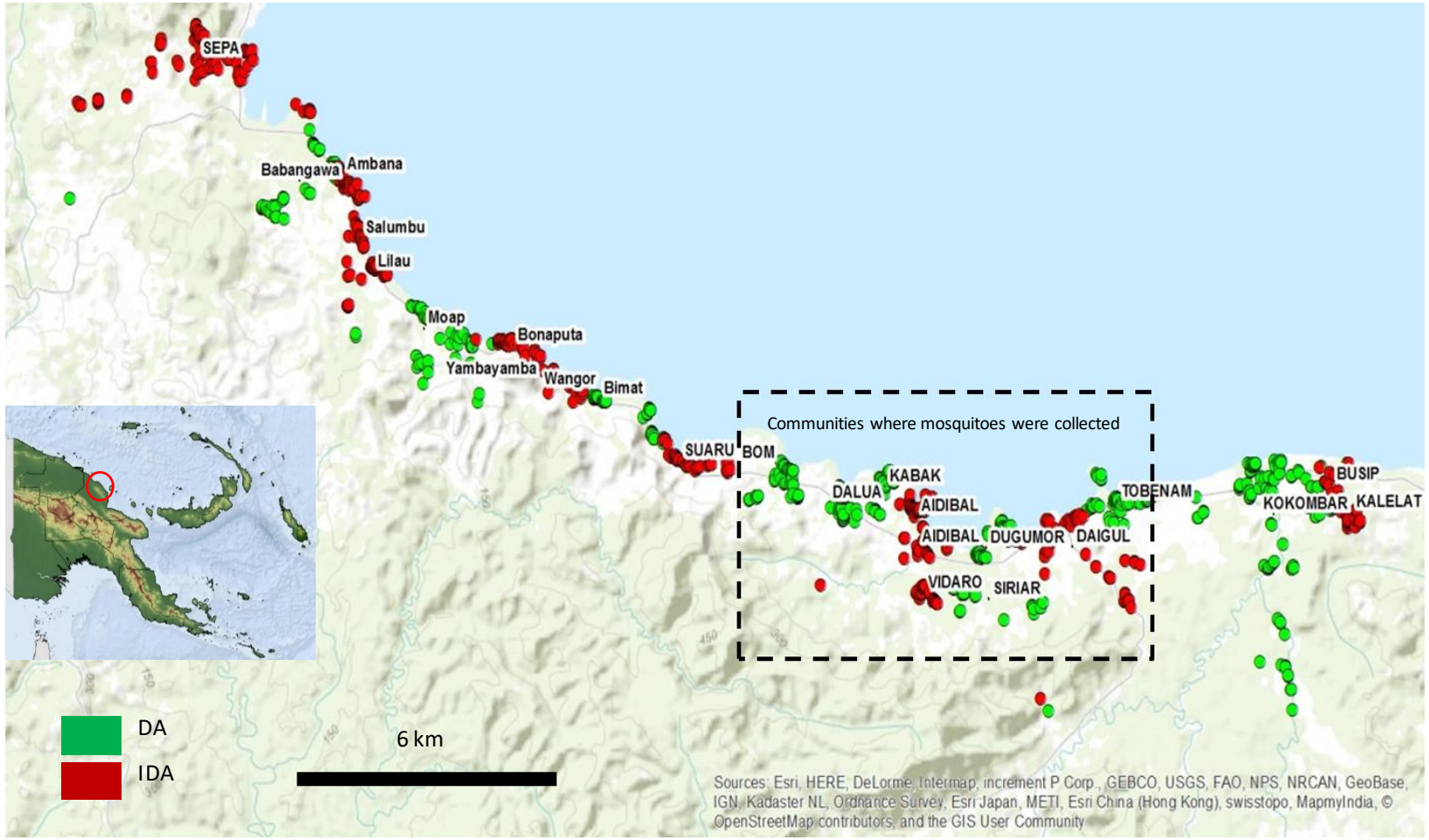
Mectizan Donation Program - Merck.com

https://www.merck.com › about › featured-stories › mectizan

In November 2017, in support of new WHO guidelines, **Merck** announced an expansion of the MECTIZAN® **Donation** Program (MDP) to reach up to an additional 100 million people per year through 2025 as part of the global effort to **eliminate lymphatic filariasis** (**LF**).

World Health Organization

Trial site – 24 villages in Bogia District



Lancet Infect Dis. 2022 May

Mass drug administration of ivermectin, diethylcarbamazine, plus albendazole compared with diethylcarbamazine plus albendazole for reduction of lymphatic filariasis endemicity in Papua New Guinea: a cluster-randomised trial

Moses Laman, Livingstone Tavul, Stephan Karl, Bethuel Kotty, Zebede Kerry, Stephen Kumai, Anna Samuel, Lina Lorry, Lincoln Timinao,

Interpretation Mass administration of the triple-drug regimen was more effective than the two-drug regimen in reducing microfilariae prevalence in communities to less than the target level of 1%, but did not reduce circulating filarial antigen prevalence to less than 2%. These results support the use of mass drug administration with the triple-drug regimen to accelerate elimination of lymphatic filariasis.

effectiveness of mass drug administration with the triple-drug and two-drug regimens for reducing microfilariae prevalence to less than 1% and circulating filarial antigen prevalence to less than 2%, levels that are unlikely to sustain transmission of lymphatic filariasis, in Papua New Guinea.

See Online/Comment
https://doi.org/10.1016/S1473-3099(22)00063-9

Conclusion

- Artemether-lumefantrine as first-line treatment is still effective
- Early signs of delayed parasite clearance but there has been no treatment failures to date
- Additional studies on primaquine short course for radical cure with G6PD testing are underway
- Recent surges in malaria are likely to have been due to reduced bioefficacy of LLINs (the only vector control tool in PNG)
- IDA triple drug regimen is an effective tool that can be used for LF elimination in endemic settings