

E8 Webinar

8 December 2020



MALARIA IMPORTATION AND THE NEED FOR IMPROVED SURVEILLANCE IN THE E8 REGION



ELIMINATION 8

ANGOLA • BOTSWANA • ESWATINI • MOZAMBIQUE
NAMIBIA • SOUTH AFRICA • ZAMBIA • ZIMBABWE

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ACCESS TO MALARIA PREVENTION, DIAGNOSIS AND TREATMENT IN BORDER AREAS OF E8 COUNTRIES

RESULTS FROM AN EVALUATION OF MALARIA BORDER POSTS IN SECOND LINE COUNTRIES

PRESENTED BY MUKOSHA CHISENGA AND PROF IMMO KLEINSCHMIDT

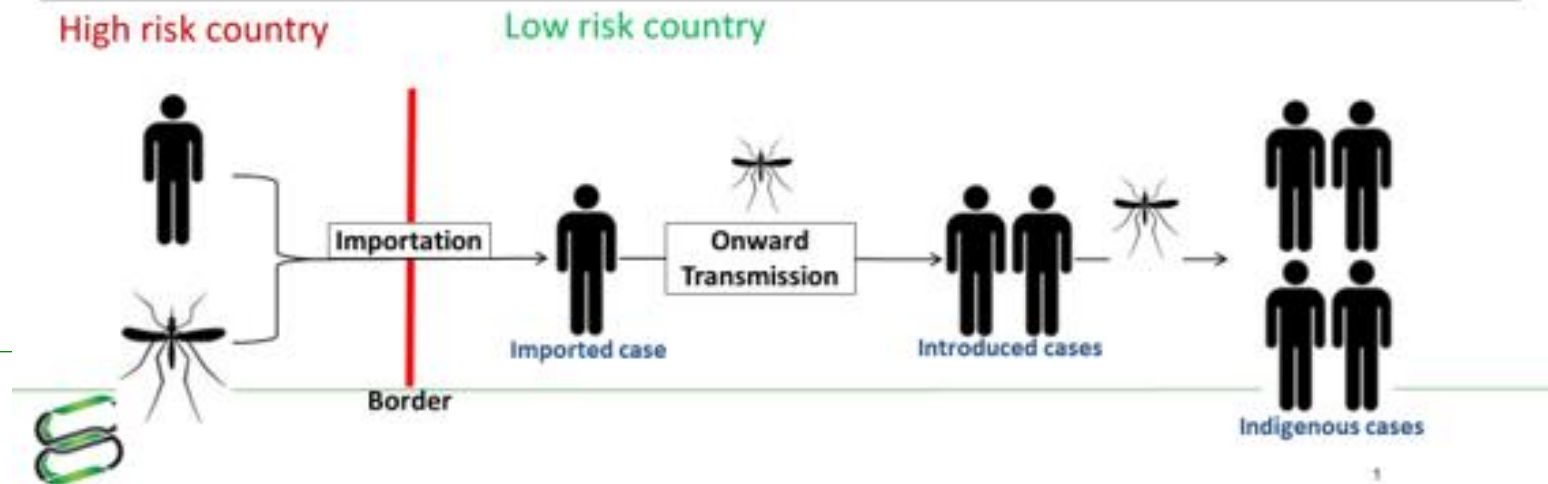
08/12/2020



Border malaria and parasite importation

- In 2013, the Southern African region recorded over 3 million **regular** migrants (IOM) in search for opportunities such as work, education, treatment and safety
- However, Malaria knows no borders
- Conditions surrounding migration and inequalities in health access can make migrants and border resident communities vulnerable
- Lessons from China, the GMS, Sri Lanka, and Yemen suggest that improving access to malaria prevention and treatment through provision of mobile and fixed border malaria clinics can substantially reduce cross-border importation of malaria

1. Travellers from areas of higher malaria risk have significantly higher infection rates
2. In some pre-elimination countries/provinces in the E8 region, the majority of malaria cases are imported
3. Even non-travellers have significantly higher risk of malaria if they are living in neighbourhoods with high proportion of travellers, compared to those living in areas with few travellers



E8 Malaria Border Health Posts



Malaria Plus (21+1)

- RDT, ACT, PHC
- Static
- Nurse(s), CHW, General Hand

Malaria Basic (12)

- RDT, ACT
- Mobile
- Nurse, CHW

Malaria Surveillance units (12)

- RDT, ACT
- Active surveillance (ACD and Proactive screening)
- Nurse, CHW, EHO/Ento Asst.

46 total health posts along 5 priority borders of E8

Year	Total number tested	Total positive (%)
2017	306,051	10,100 (3.3%)
2018	557,020	41,844 (7.5%)
2019	344,582	19,451 (5.6%)
Total	1,207,653	71,395 (5.9%)





E8 Malaria Border Health Post Evaluation

There was a need to evaluate the:

1. Level of access to malaria diagnosis and treatment in border districts
2. Level of access to malaria prevention such as IRS and LLINs in MMPs and residents
3. Origin and destination of migrant travelers and mobile residents
4. Knowledge, attitudes, and practices for malaria prevention, symptoms, and treatment in migrant and border residents

Study Limitations

- Funding was only secured for one round of data collection and was also delayed by lengthy ethical approval processes.
- Findings should be regarded as a single cross-sectional assessment representing a snapshot of the malaria situation in E8 border areas.
- In front line countries comparison between intervention and control sites forms the basis of the evaluation of impact.
- In second line countries no comparison is available (as per protocol), findings are therefore only descriptive in nature

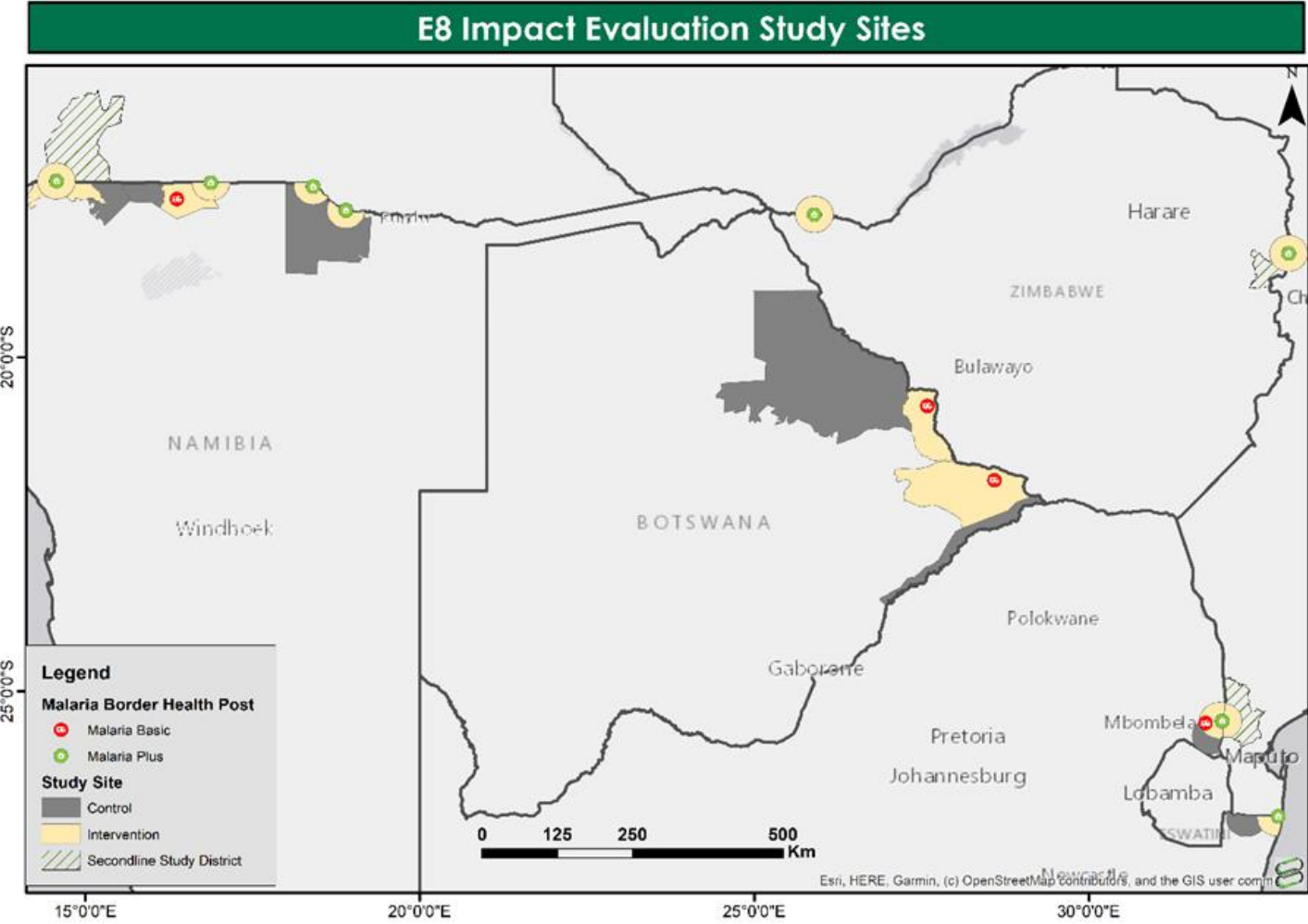


Scope

- 32 Separate surveys of residents and MMPs (> 9600 participants)
- 80 Focus group discussions, 140 Individual in depth interviews, 2-year retrospective data review in frontline countries
- To date:
 - Data collection for the study has been completed in 6/7 of the participating countries
 - Report on border post evaluation studies in second line countries has been completed and is available on the E8 website.
 - Botswana and Namibia are compiling country reports
 - Progress in South Africa was affected by the COVID-19 pandemic, terminating fieldwork. Field work will resume in 2021.
 - Front line regional report will be finalized once SA data is available



E8 Impact Evaluation Study Sites



Country	Implementing partner
ANGOLA	National Malaria Program
MOZAMBIQUE	Centro de investigação de Saúde de Manhiça (CISM)
ZAMBIA	National Malaria Program
ZIMBABWE	National Malaria Program
ESWATINI	N/A
BOTSWANA	University of Botswana
NAMIBIA	University of Namibia
SOUTH AFRICA	South Africa Medical Research Council

In second line countries the study design consisted of four cross-sectional surveys carried out amongst **residents** living within 30km of an E8 border health post



Summary of key results

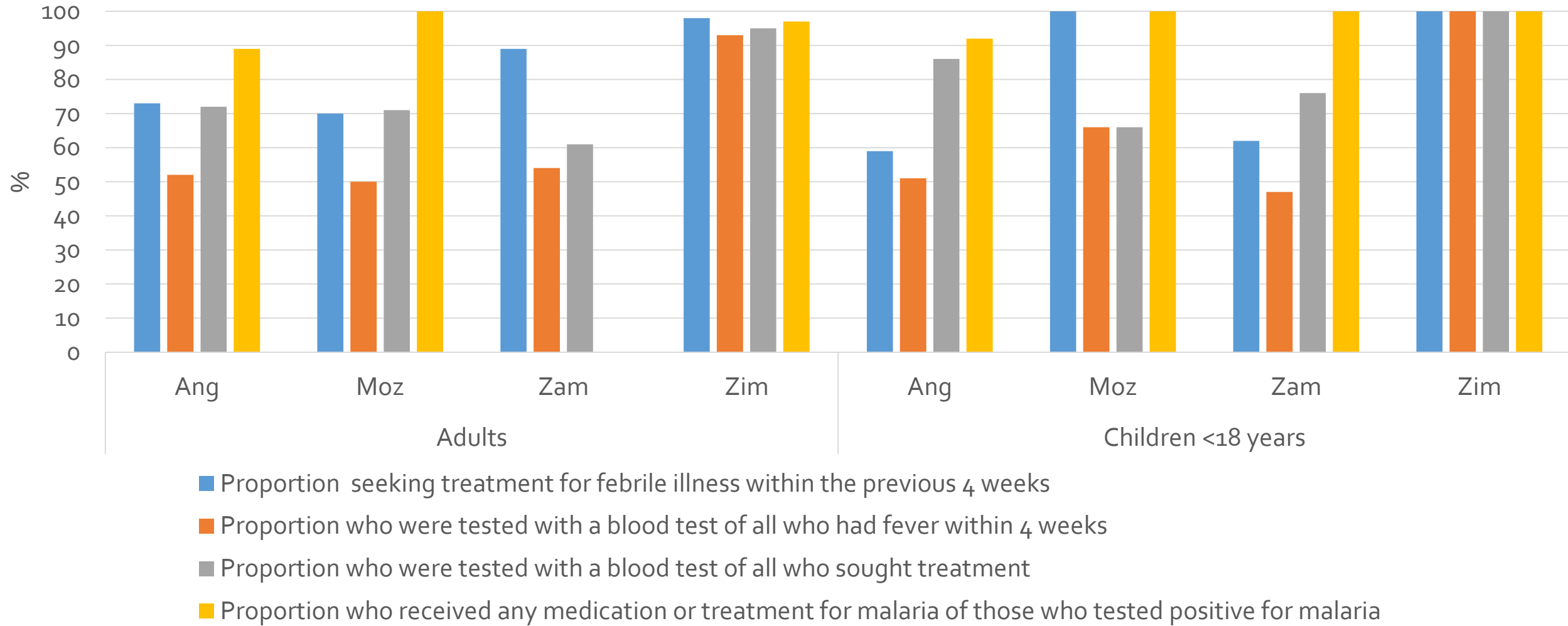
Note:

The results tabulated have been derived from data collected at each of the four study sites.

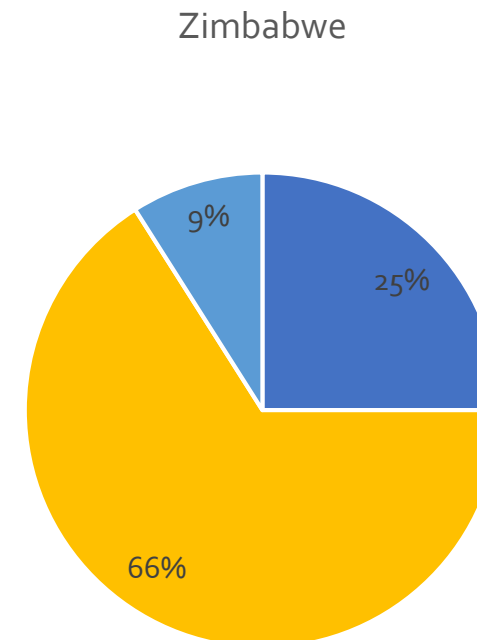
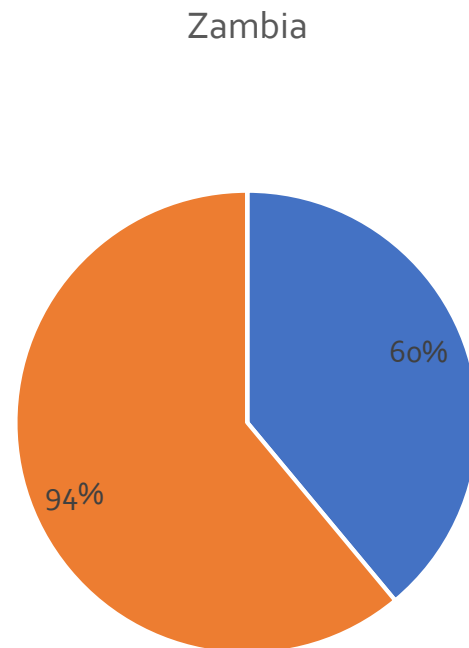
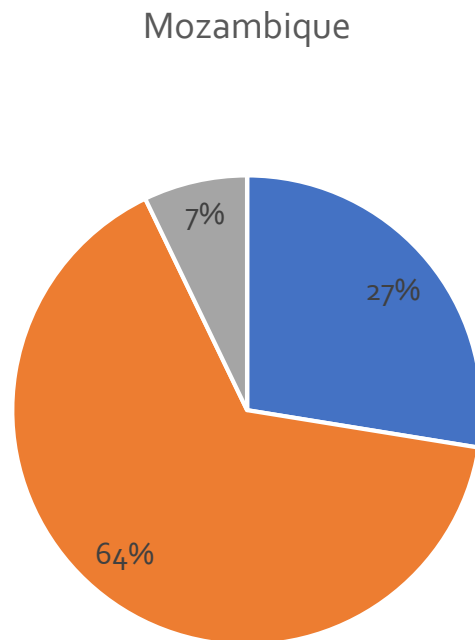
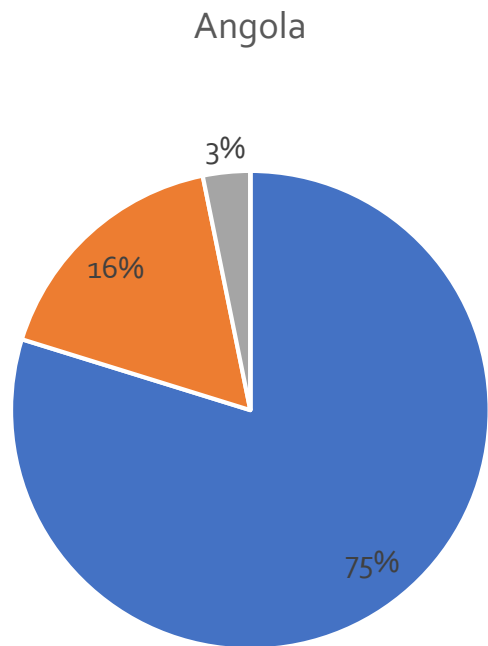
No claim is made that they are nationally representative



Treatment seeking for febrile illness



First choice for diagnosis and treatment



■ Government hospital

■ Govnt. health centre/border post ■ Private hospital / clinic / doctor

■ Community Health Worker

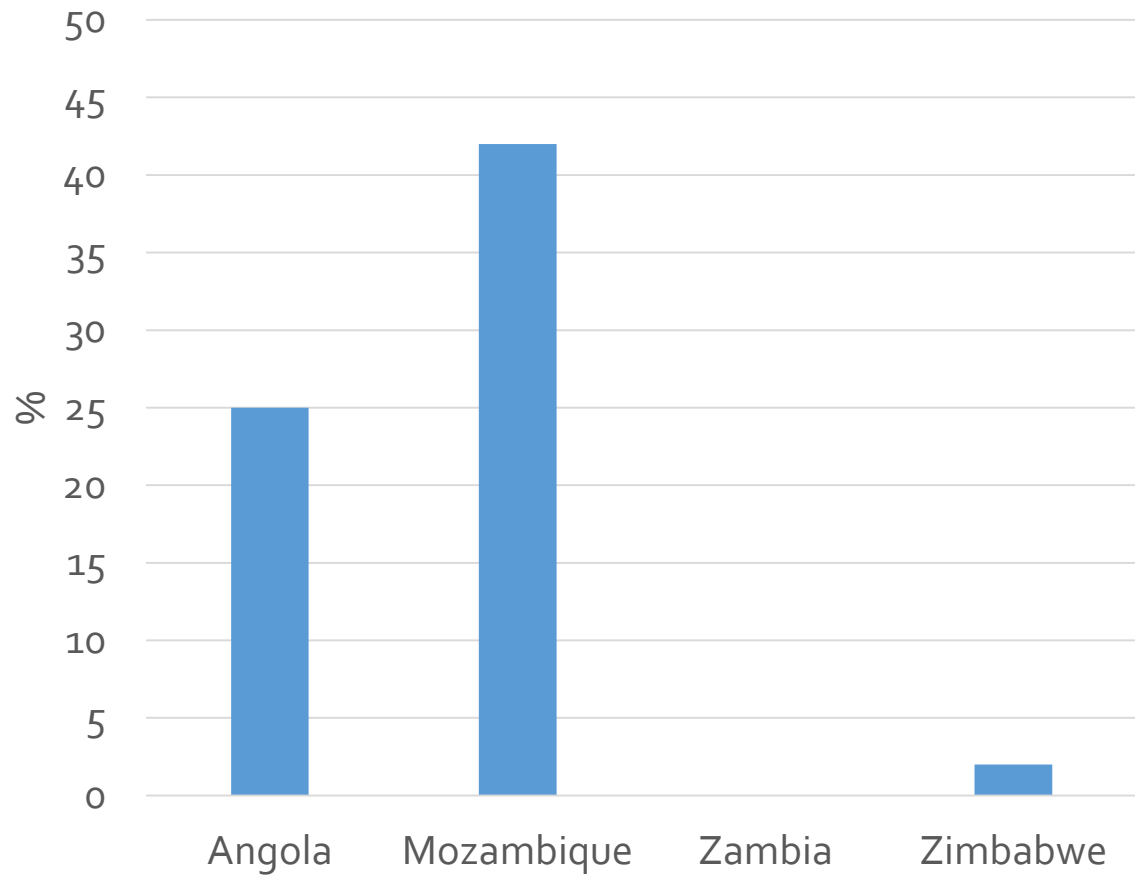
■ Other/don't know



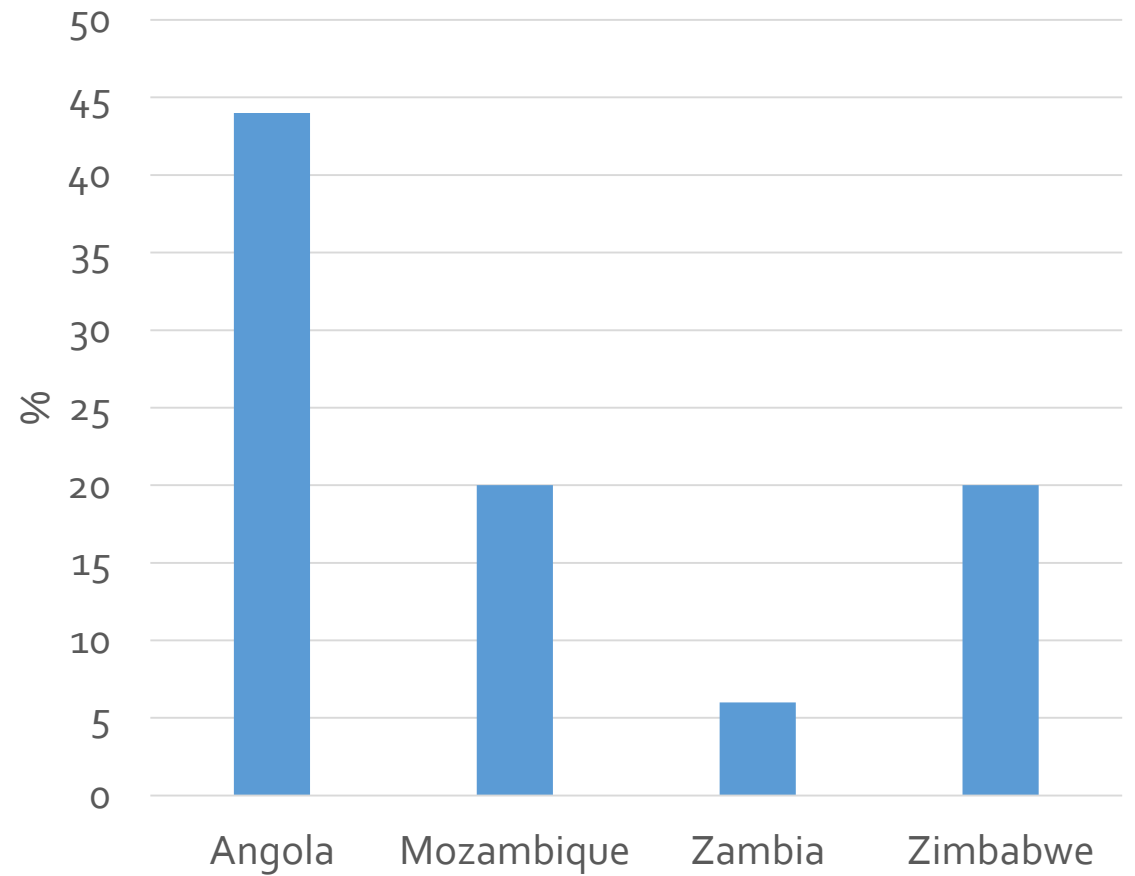
- Majority of respondents noted convenience and closeness as the main reasons for choosing a health facility for treatment
- In some sites local arrangements made it difficult for residents to distinguish between E8 border posts and government health facilities.
- Awareness of E8 border posts was only high in Zimbabwe (70%) and lowest in Mozambique (<1%).

Distance and time travelled for treatment

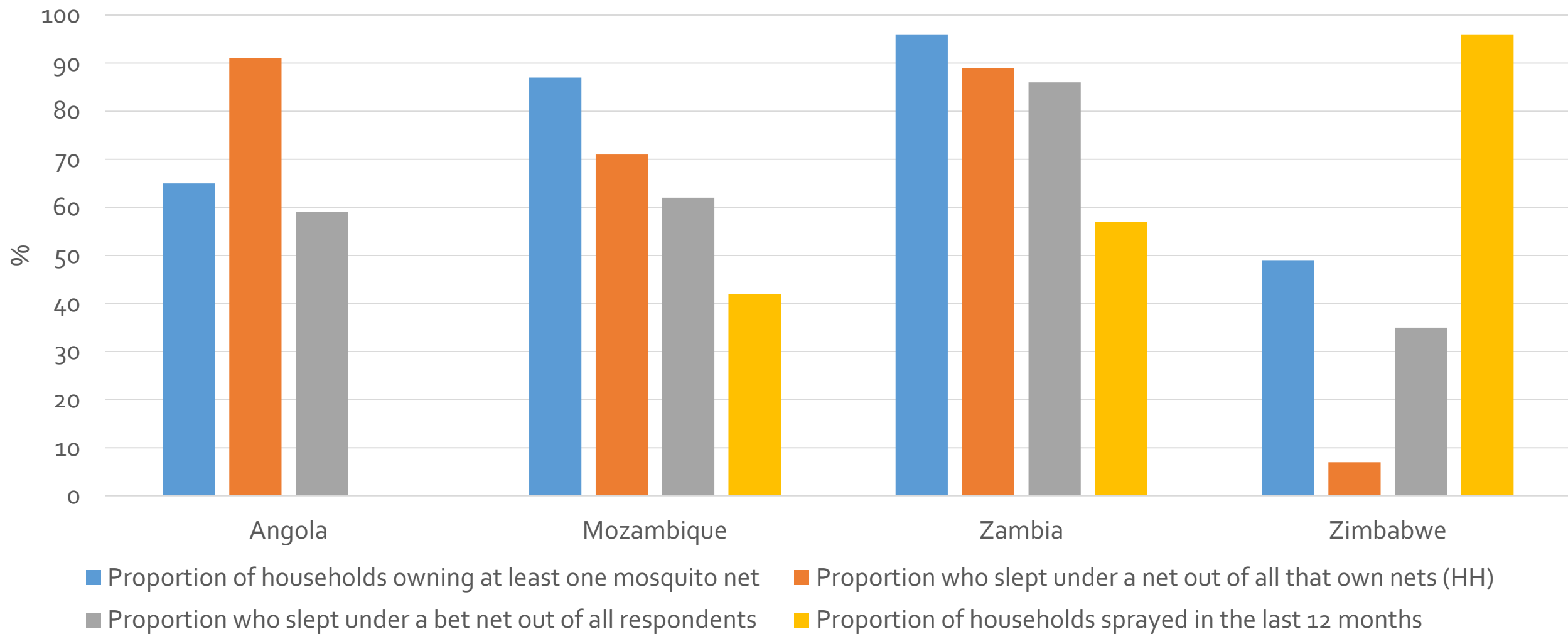
More than 8 Km



More than 45 minutes



Malaria prevention through vector control IRS and LLINs

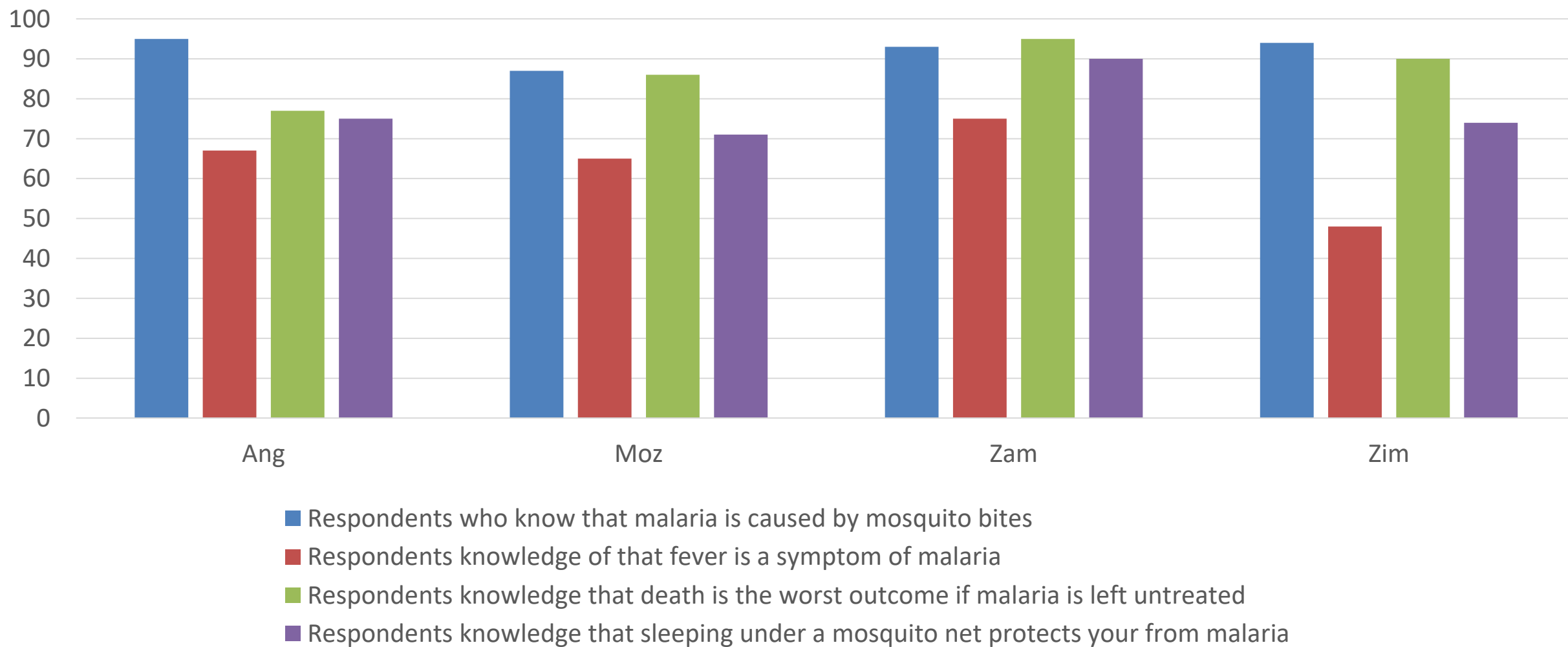


Summary of key results: Local and international travel (recall <3 months)

	Adults				Children <18 years			
	Ang	Moz	Zam	Zim	Ang	Moz	Zam	Zim
Proportion who travelled out of district in last 3 months, %(N)	43(277)	46(352)	8 (229)	16 (331)	9(366)	34(340)	2 (393)	1(72)
Proportion who slept outside at least one night, %(N)	43(120)	43(161)	17 (18)	26 (54)	30(27)	39(114)	0 (6)	0 (1)
Proportion who used protective measures against malaria, %(N)	7(120)	21(152)	22 (18)	39 (54)	4(27)	20(114)	0(6)	100(1)



Knowledge about malaria and its prevention



Key findings

1. Nearly all who reported a **positive blood test** received **medication**
2. **Lack of access** to a health care due to distance or cost or mistrust of the provider **was rare**
3. High levels of **correct knowledge of causes, symptoms and prevention** of malaria were evident
4. Reasonably high levels of **timely treatment seeking and access to diagnosis** when experiencing fever.
5. A minority of border residents **did not receive a blood test when experiencing fever**, either because they did not access health care, or because they were not tested when presenting with fever. **Most providers carried out blood tests** when individuals presented with fever, there were **exceptions that are cause for concern** and remedial action.
6. A majority (but not all) had **access to primary prevention** through either LLINs or IRS. Some households **did not own any nets**, even in sites where this was the main form of vector control.
7. Border residents **travelled frequently**; some cross-border travel was for **seeking healthcare**.
8. **Sleeping outside whilst travelling was common**, mostly **without protection against malaria**; clear **gap in the provision** of malaria prevention for this group.



Recommendations

1. The message about seeking treatment when experiencing fever needs to be re-emphasised in public awareness campaigns.
2. Health post staff need to be reminded that patients presenting with fever should always be tested for malaria parasites.
3. Messaging should include the use of protective measures such as LLINs, malaria chemoprophylaxis and repellents when travelling, particularly if this involves sleeping outside.
4. Provision of health border posts should be extended to those border areas that are currently not served by nearby health facilities, since timely health seeking is dependent on easy access to such facilities
5. Better surveillance is needed to assess the impact of cross-border travel on malaria transmission

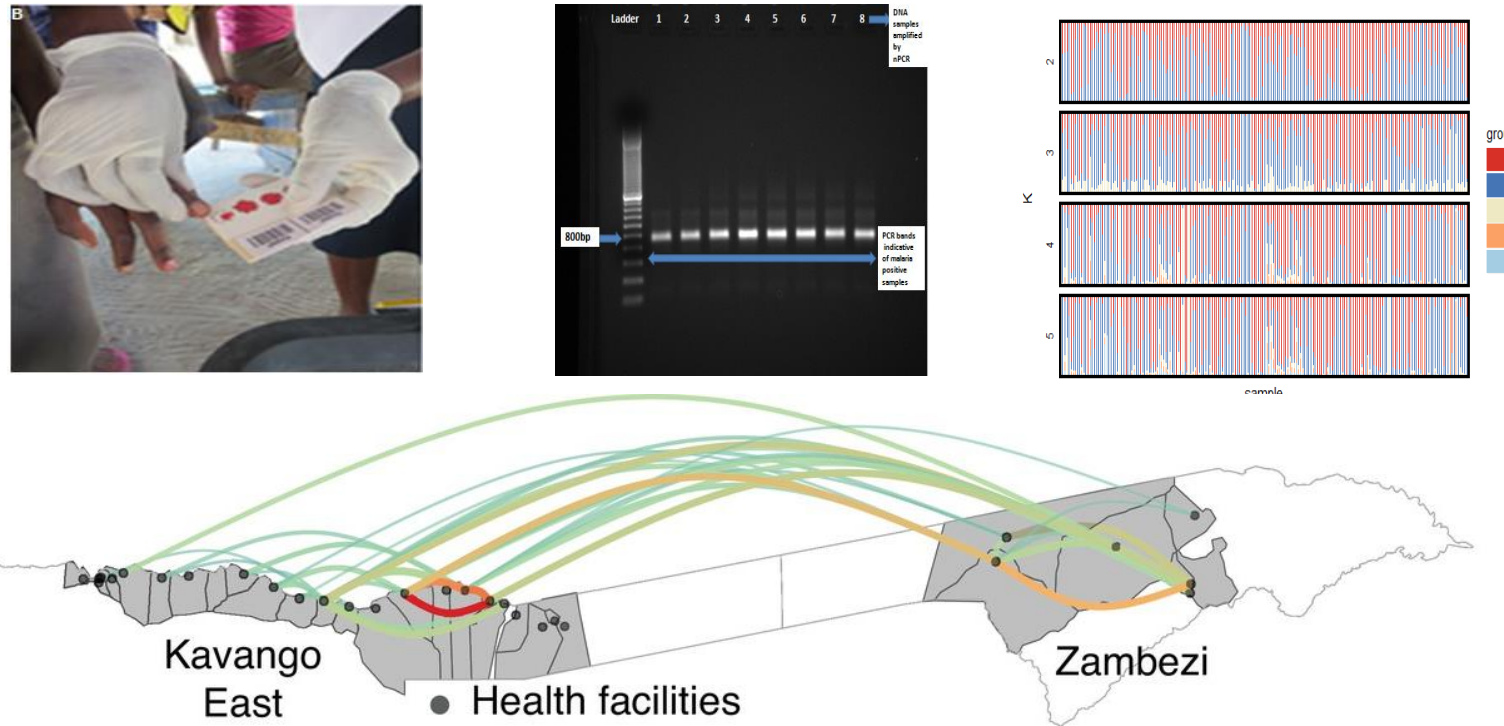


Acknowledgements

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 - National Malaria Control Programme: Maputo, Mozambique
 - National Malaria Elimination Centre: Lusaka, Zambia
 - National Malaria Control Programme: Harare, Zimbabwe
 - Centro de Investigação em Saúde de Manhiça: Manhica, Mozambique
 - UCSF Global Health Group Malaria Elimination Initiative: San Francisco, California, United States of America



Plasmodium genomics as a surveillance tool for monitoring local malaria transmission networks and importation in Northern Namibia

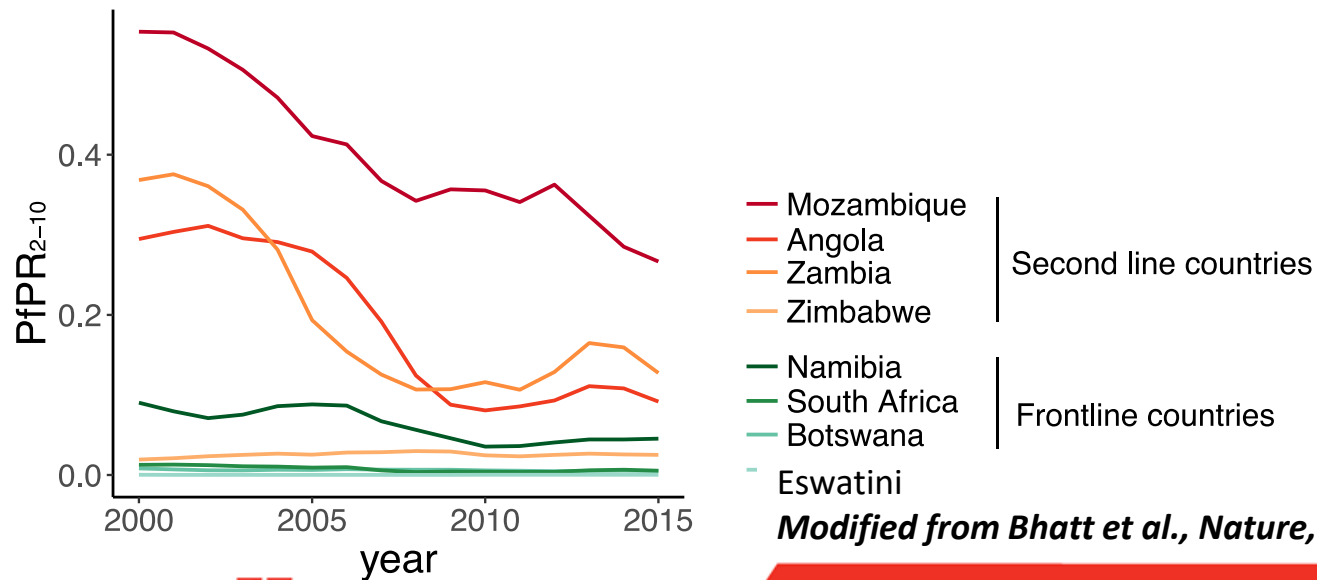


Prof. Davis R. Mumbengegwi
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Multidisciplinary Research Centre

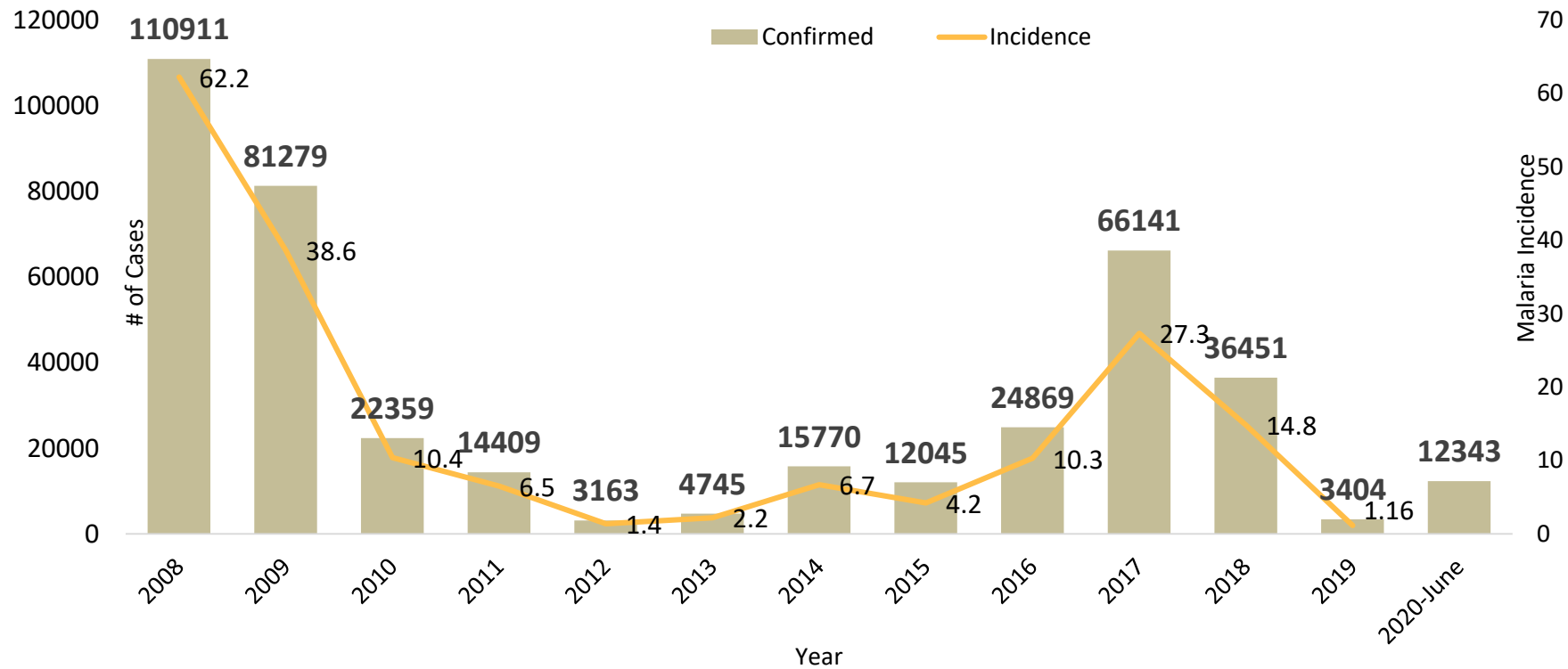
Malaria in SADC



- Malaria knows no boundaries
- Human mobility
- mosquito mobility



Namibia and Malaria

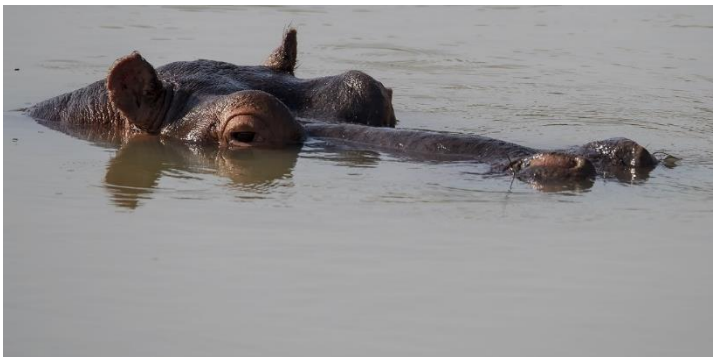


- Namibia is a low transmission country that has experienced a tremendous decline in reported malaria cases
- Targeting malaria elimination by 2022

Challenges of malaria elimination

- Gaps in knowledge about infection risk factors at low malaria transmission,
 - Cross-border importation and domestic spread of malaria, accurate classification of imported infections
 - At low transmission settings, low density asymptomatic infections make up to 70-80% of the total number of reported cases (Okell, 2012)

Symptomatic cases



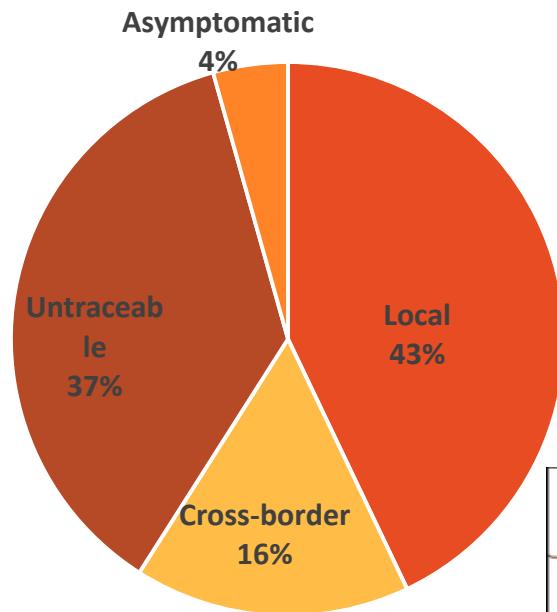
Asymptomatic cases



Challenges of malaria elimination

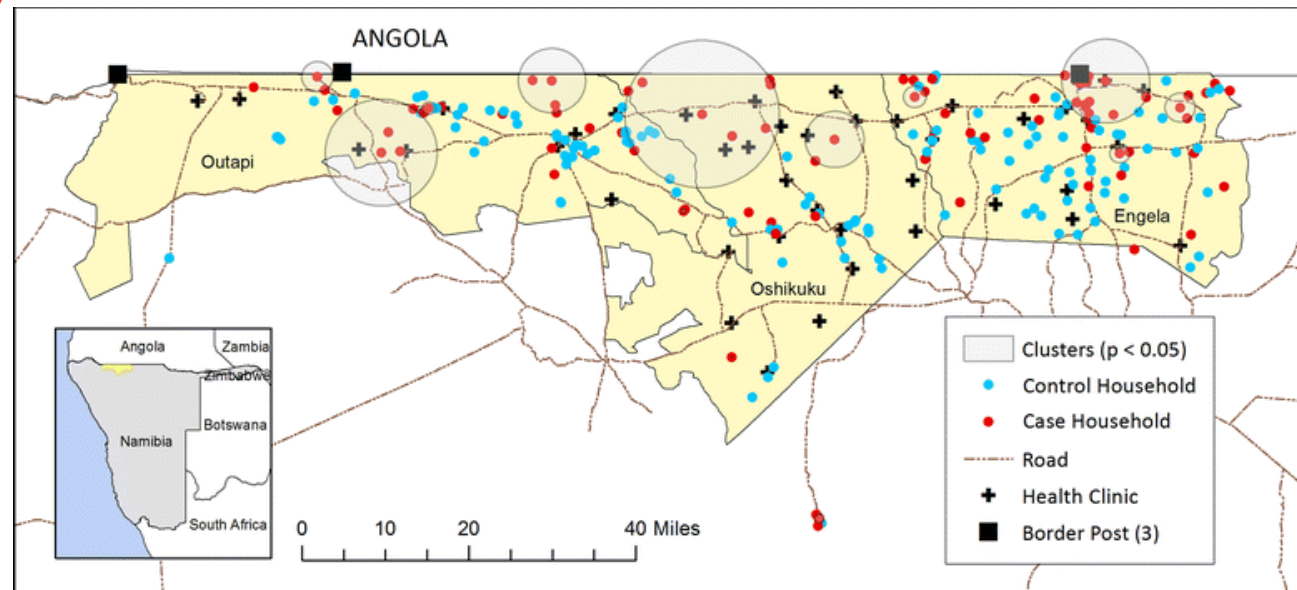
- Need to diagnose and treat all cases, symptomatic and asymptomatic cases to eliminate malaria
 - Classification of cases local vs imported
 - drug resistance
 - Parasite population structure to reveal transmission trends
- This requires new innovative tools to support better surveillance
 - Genomics can address key challenges for elimination

Malaria surveillance using RACD



Reactive case detection made difficult by:

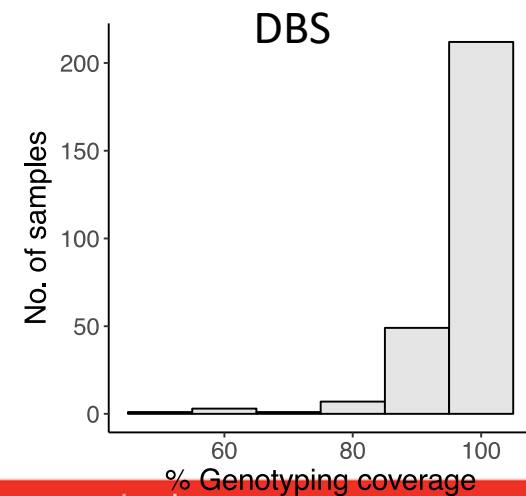
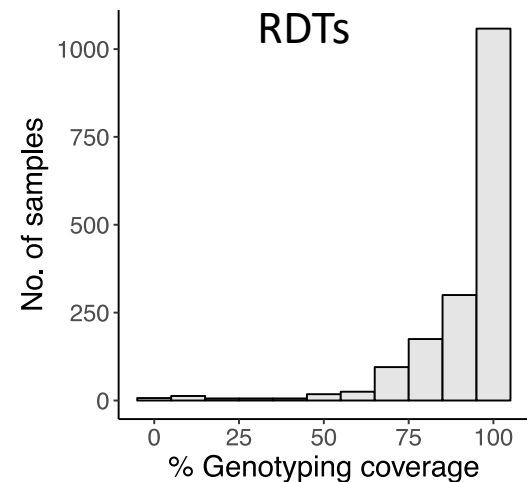
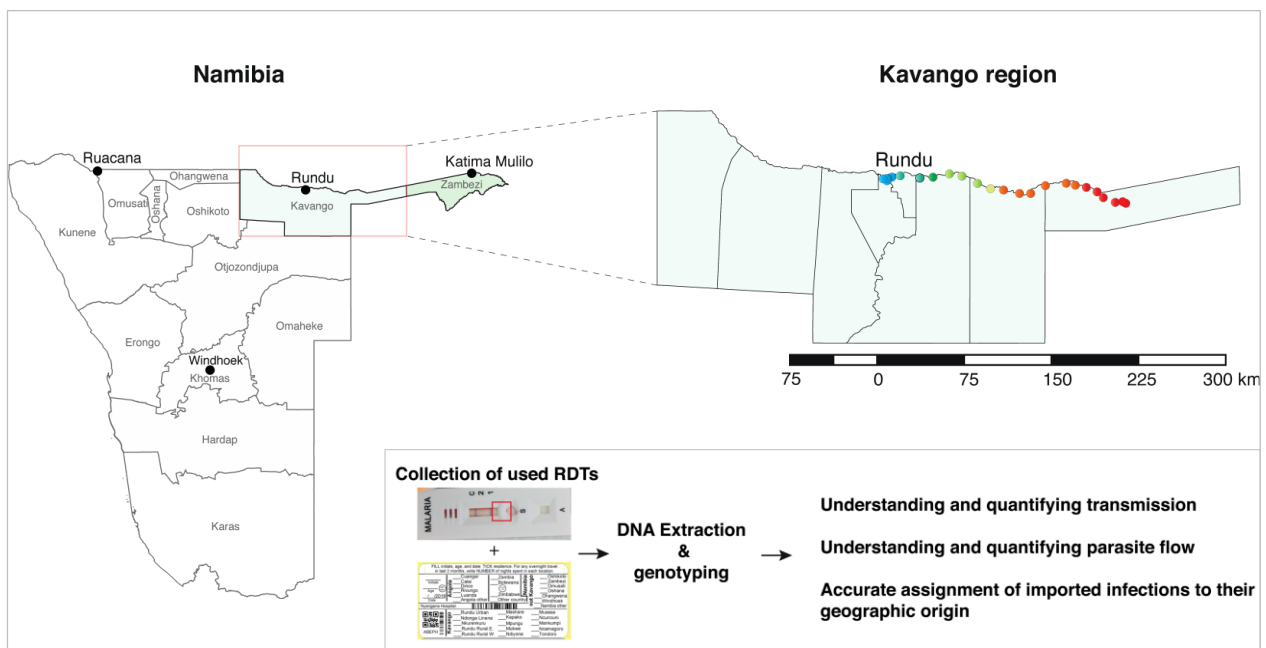
- Cross-border patients
- Patients who gave false residential information
- Cases had distinct travel patterns compared with the general population.
- Travel was the strongest risk factor for malaria in males,
- Highest risk group males ages 15-35
- Malaria cases cluster around index case



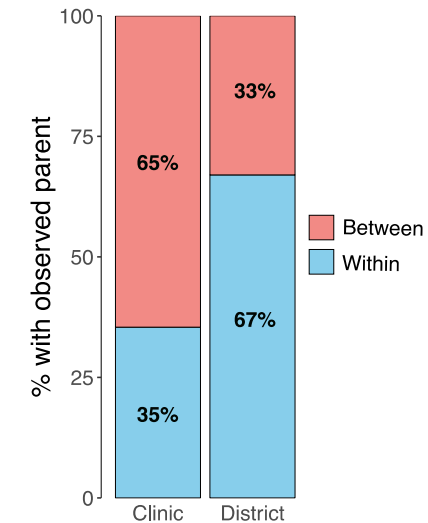
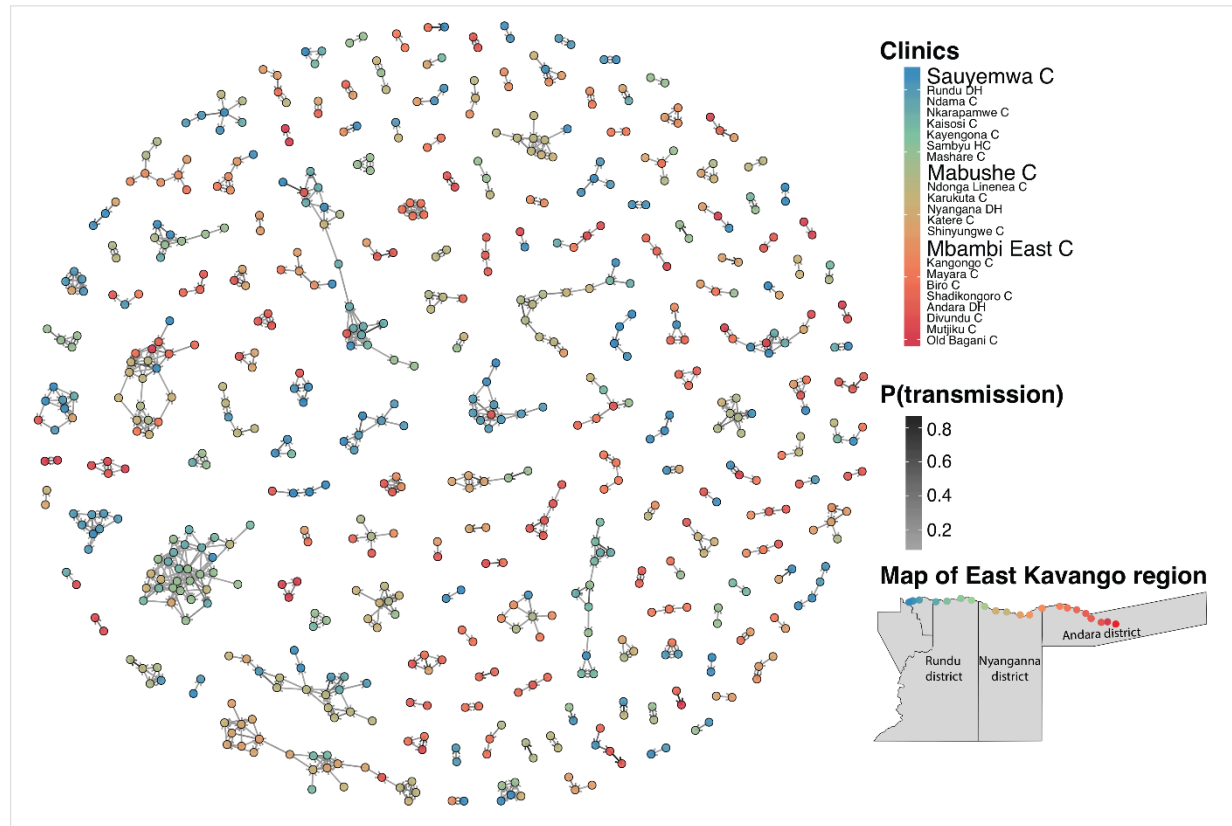
Piloting Plasmodium genomics to monitor malaria transmission

- Determining the usefulness of microsatellites in resolving differences between parasites
 - genetic similarities within and between parasite populations at a regional level
 - classify malaria cases as local or imported in the geographic area where they were detected.
 - quantification of malaria transmission networks
 - Contribution of imported infections to local transmission

RDTs and DBS as a source of DNA for studying Plasmodium genomics

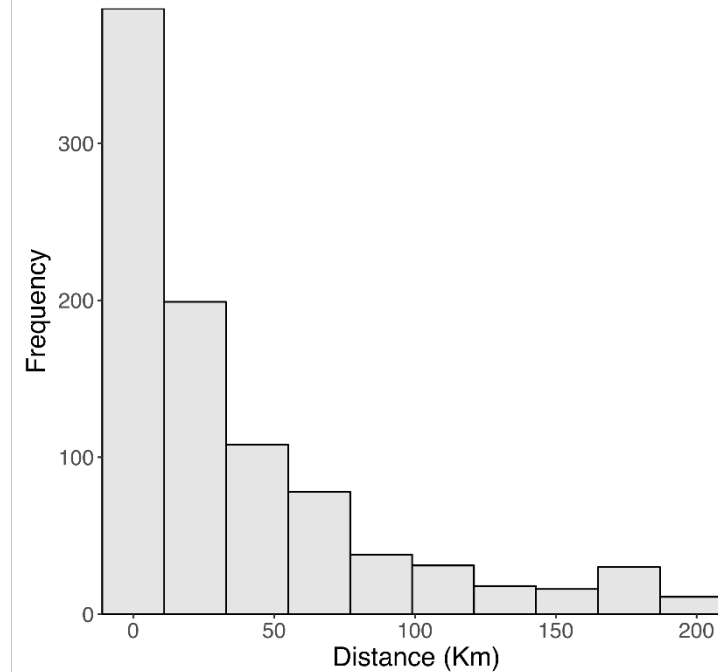
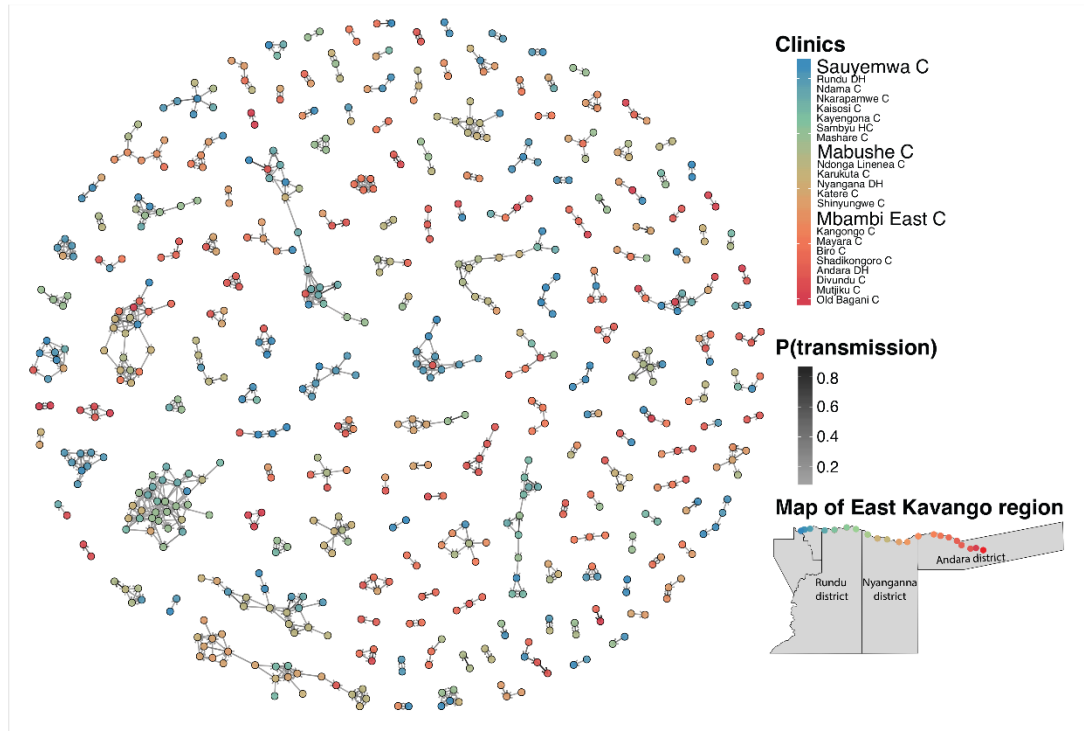


Highly interconnected transmission in Northern Namibia



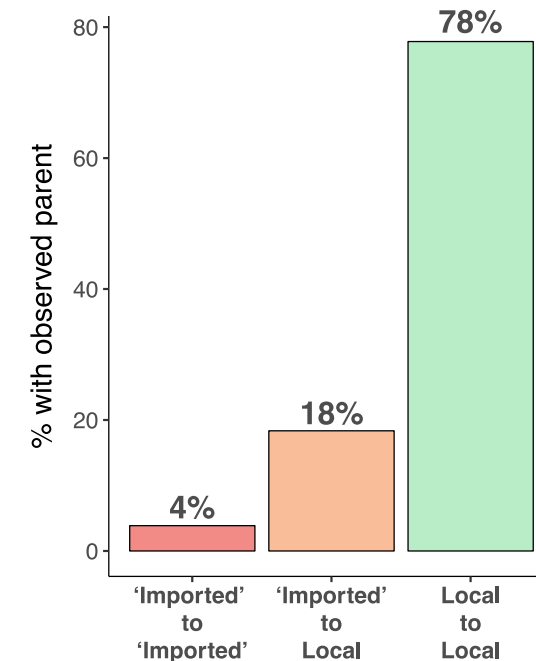
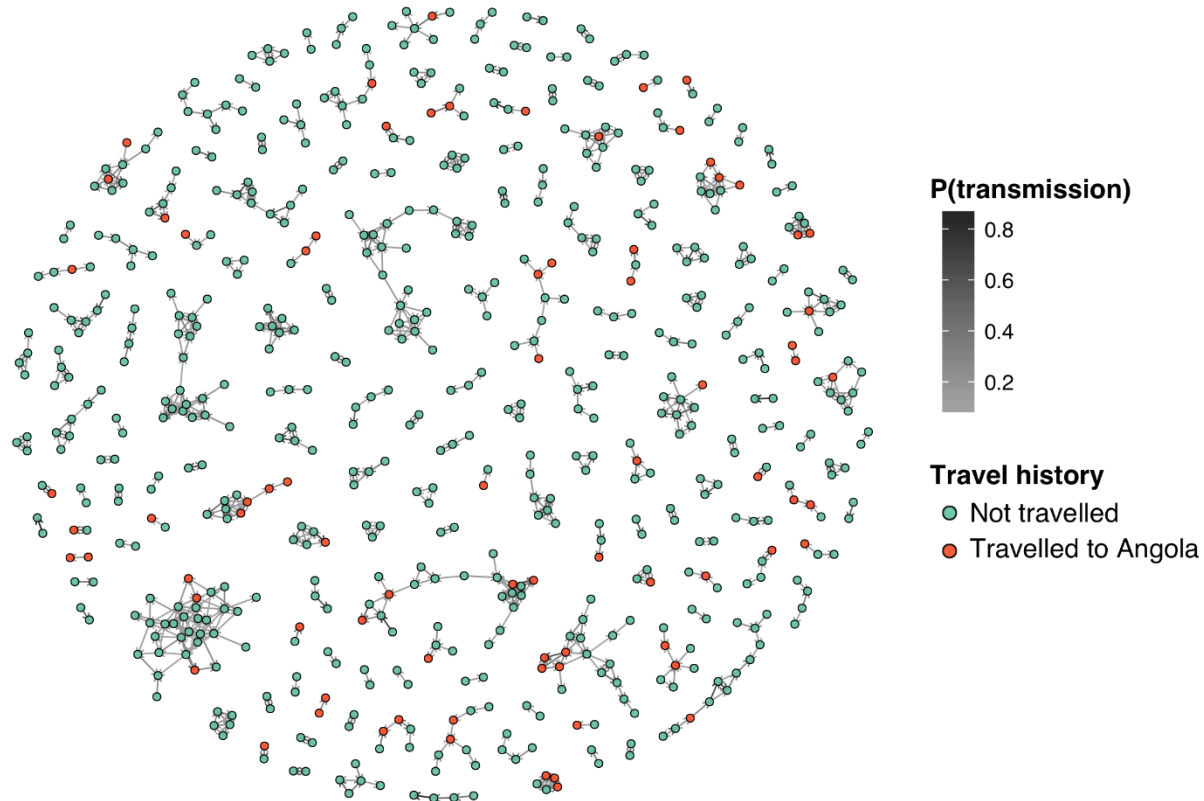
- Genetic similarities within and between parasite populations at a regional level
- Highly interconnected transmission in Northern Namibia
- Majority of transmission occurs within a district with a substantial connectivity between districts

Spatial scale of local transmission



- Links between parasites which are sampled 200km apart

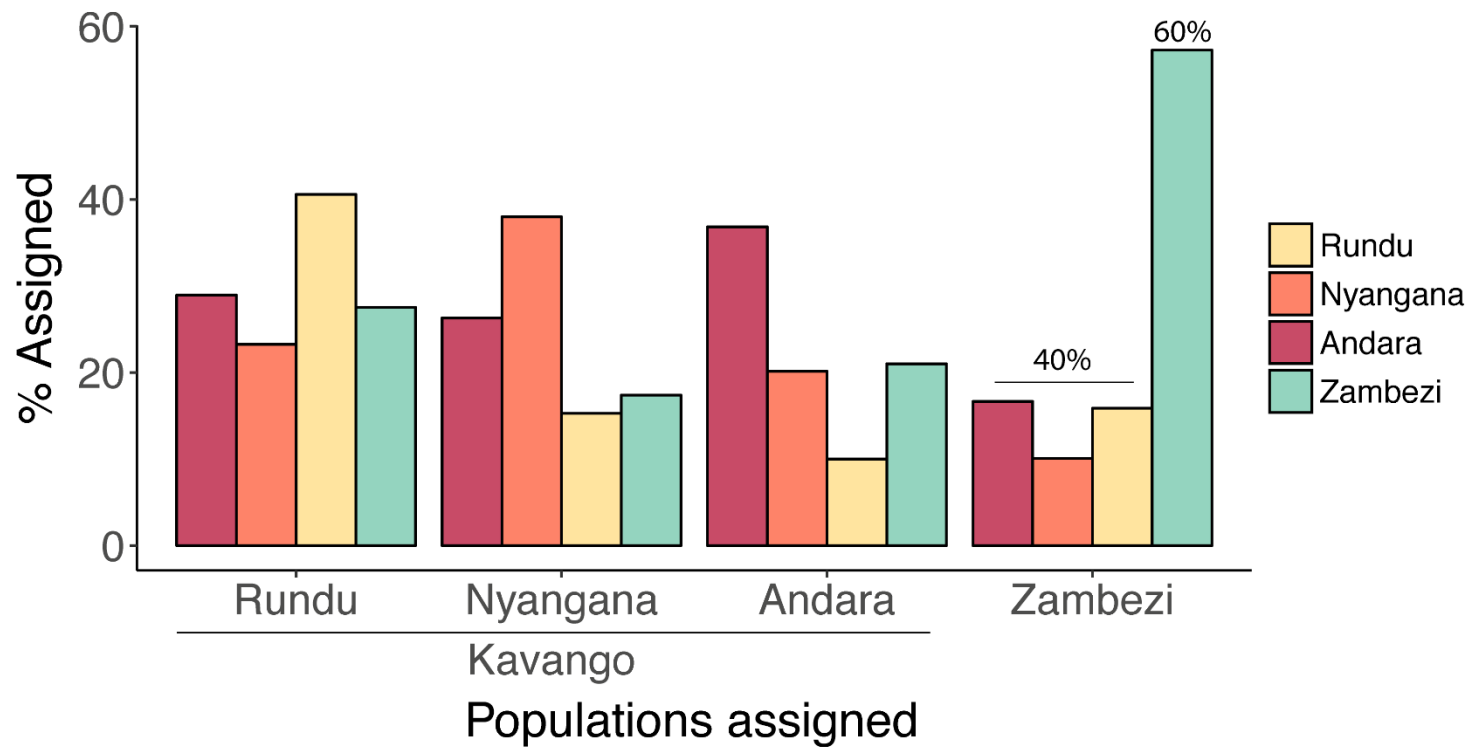
Contribution of imported* infections to local transmission



- Classification of malaria cases as local or imported in the geographic area where they were detected.
- Imported cases seed local transmission

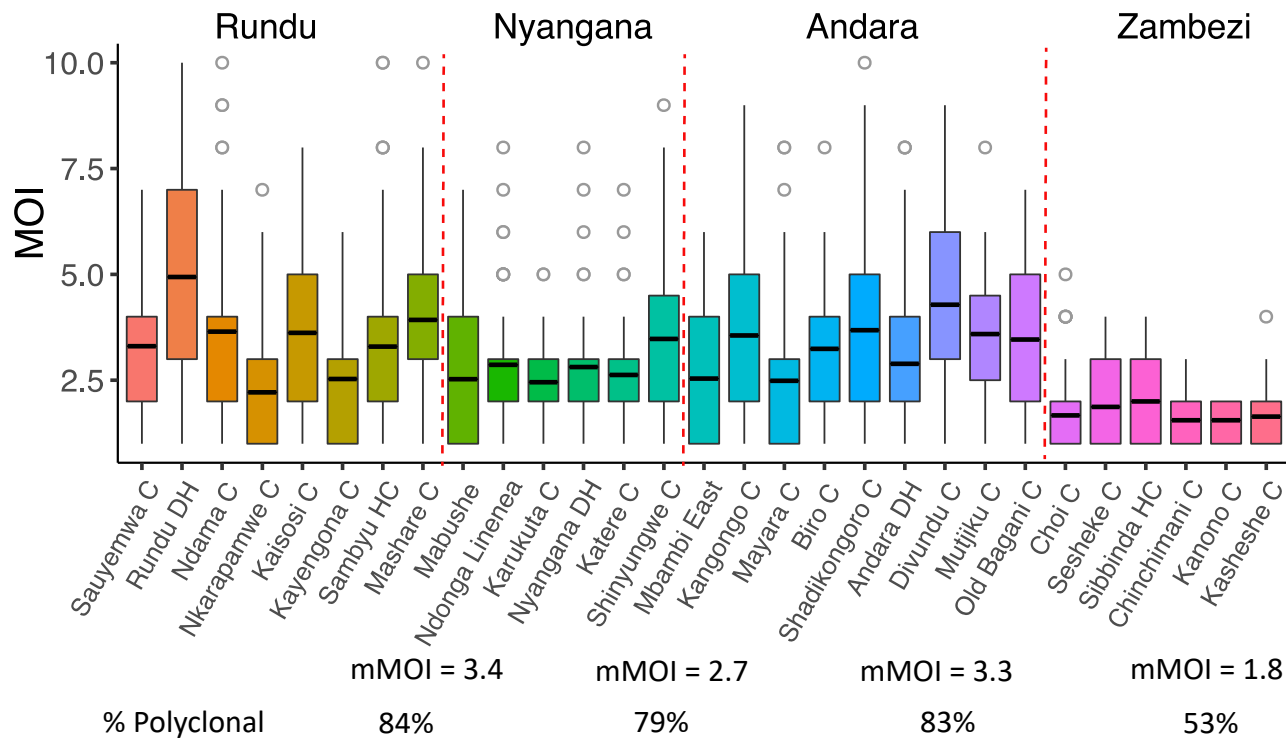
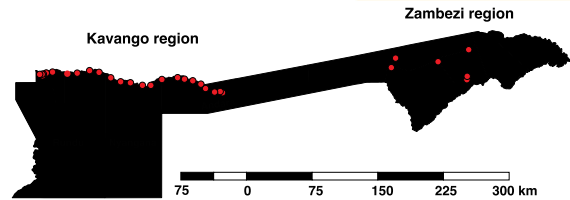
*based on reported travel history

DNA fingerprinting to identify in-country “importation”



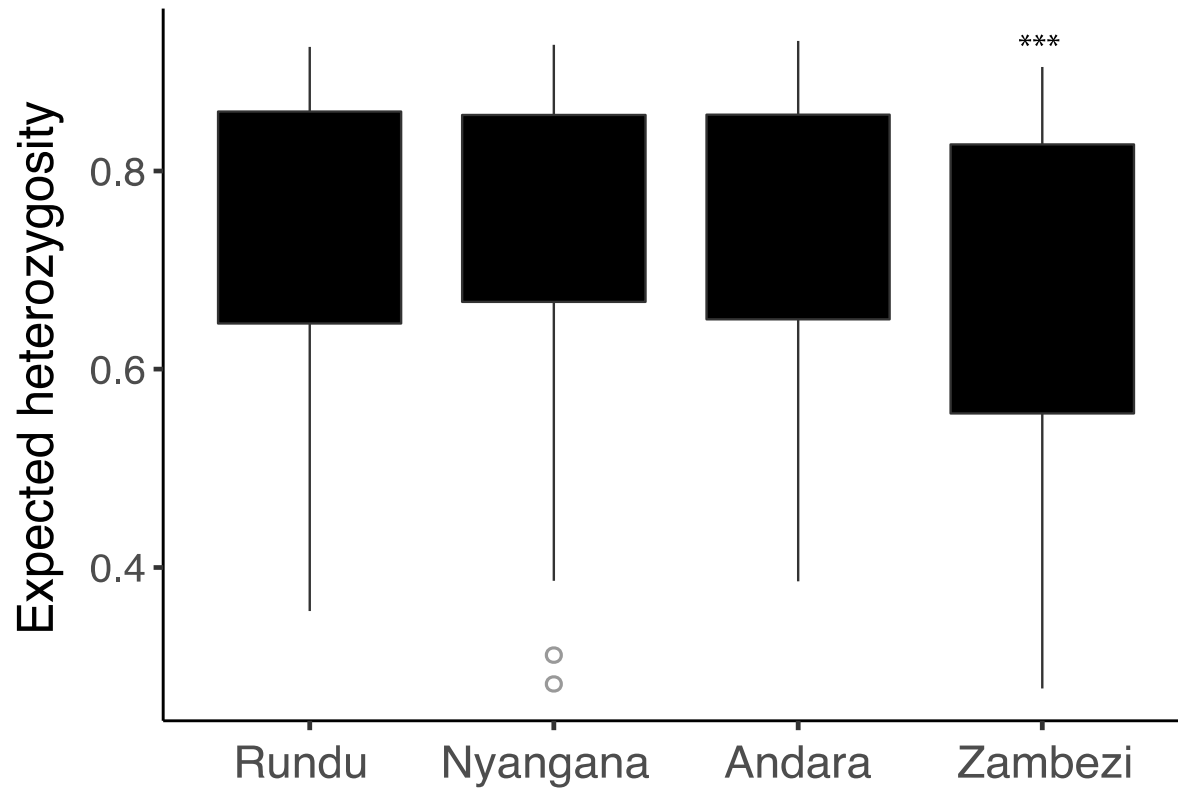
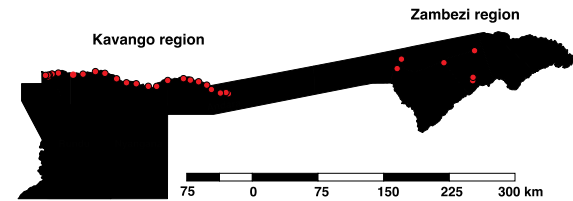
- 40% of parasite in Zambezi related to parasites from Kavango East region
 - Parasites were most likely to be imported from Kavango East region

Moderate to high multiplicity of infection in Northern Namibia



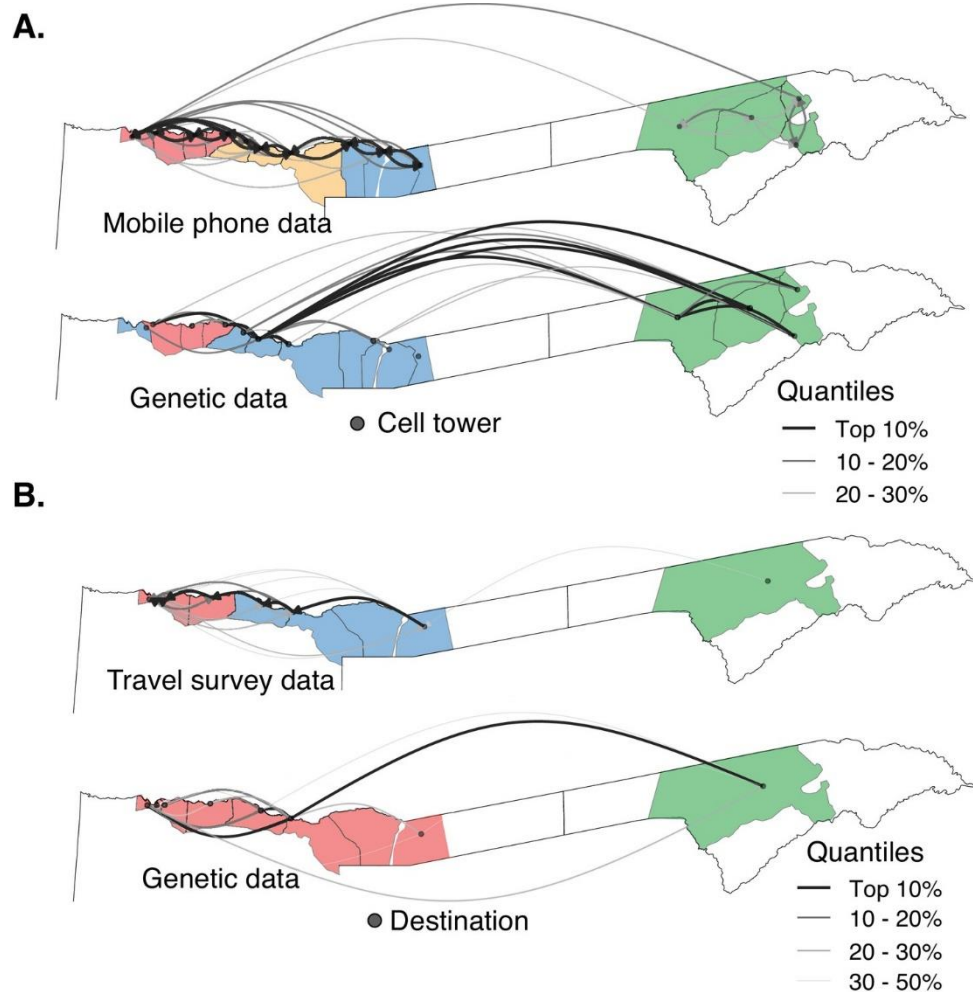
- Higher MOI means parasites in individual not genetically related
 - Polyclonal infections
 - Higher risk of symptomatic malaria,
 - development of drug resistance traits.
- At low transmission expect lower MOI

Moderate expected heterozygosity in Northern Namibia



- Zambezi has lower expected heterozygosity than all districts in Kavango East

Parasite connectivity estimated mobility data and parasite genetic data.



- Parasite genomics gives more detailed data on malaria transmission networks compared to
 - Mobile phone data
 - Travel surveys

Parasite genomics can help to inform malaria elimination in the E8 region

- Routinely collected RDTs and DBS are reliable sources for molecular studies
 - Can be used to understand and quantifying burden of malaria importation
 - Can be used to quantify transmission not just infections
- There is moderate to high multiplicity of infection and parasite heterozygosity not expected in a low transmission setting – probably due to importation
 - Population diversity of *P. falciparum* parasites in the Kavango East and Zambezi regions in Namibia does not fit the current model for pre-elimination settings.
- High levels of parasite genetic diversity need efficient surveillance systems
 - Monitoring for risk of outbreaks and potential resistance to antimalarial drugs

Conclusion

- The *P. falciparum* diversity in Namibia and neighboring Sub-Saharan countries in the E8 regional initiative need to be investigated as the transmission dynamics in this region are not fully understood.
- High resolution genotyping can be used to accurately assign parasites to their origin
- Detectable genetic clusters mean strategically designed genotyping can help address the unique challenges of malaria elimination in the E8 countries
 - Usually requires sophisticated infrastructure with adequate computing and power and highly trained personnel for data analysis
 - Establishment of sub-regional laboratory network
 - Reported use of Nanopore sequencing, MinION (***Runtuwene et al 2018 Nature Research***)
 - Regional genotyping database for identification of origins of imported infections

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MoHSS Zambezi



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Medical Center



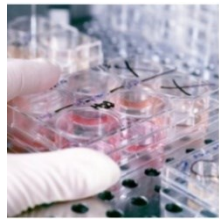
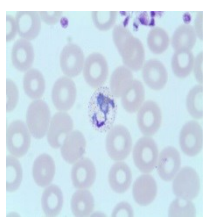
BILL & MELINDA
GATES foundation

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FOUNDATION

UCSF Global Health
Sciences
Global Health Group

Thank you



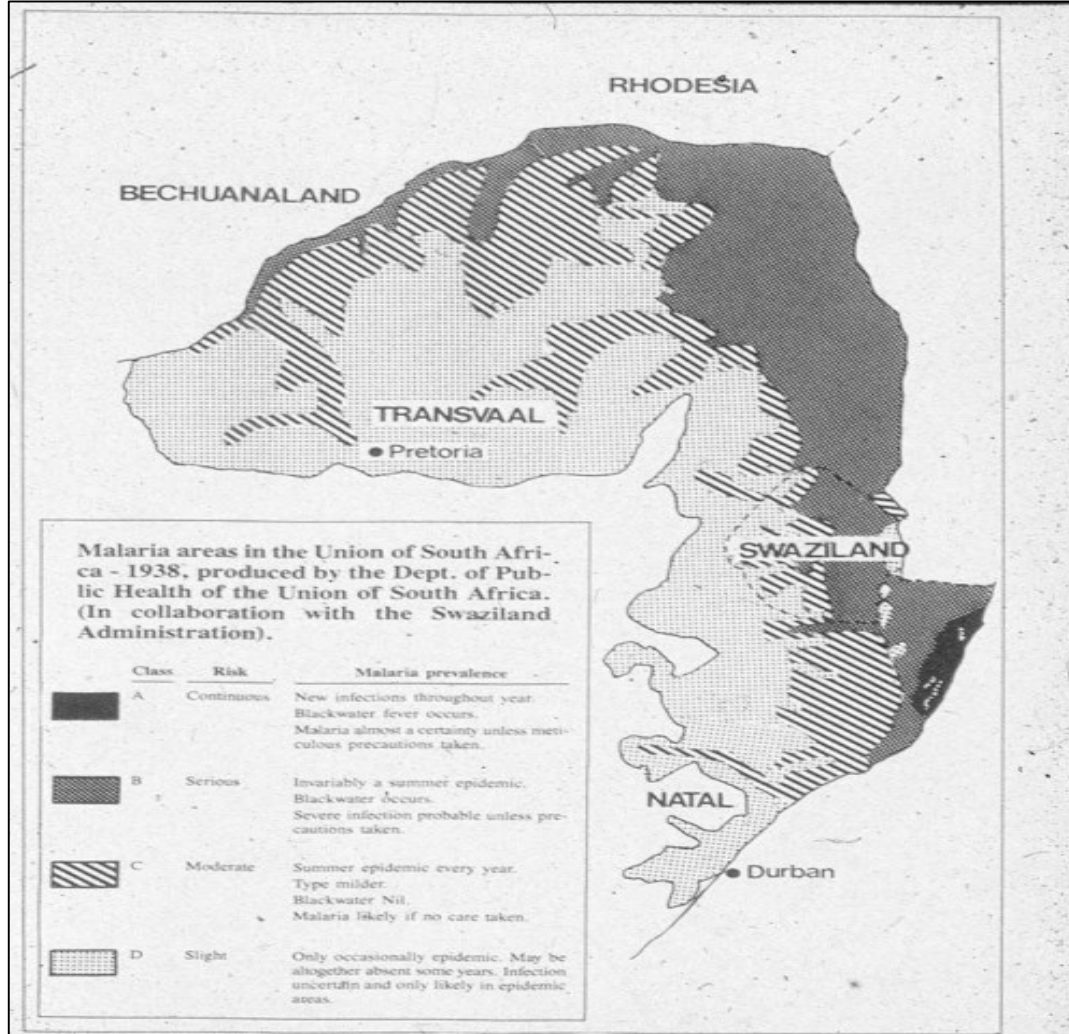
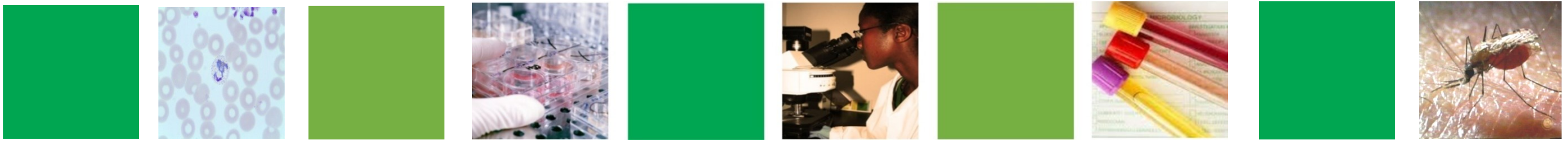


Antimalarial Drug Resistance Surveillance, Primaquine and E8 malaria surveillance units in South Africa

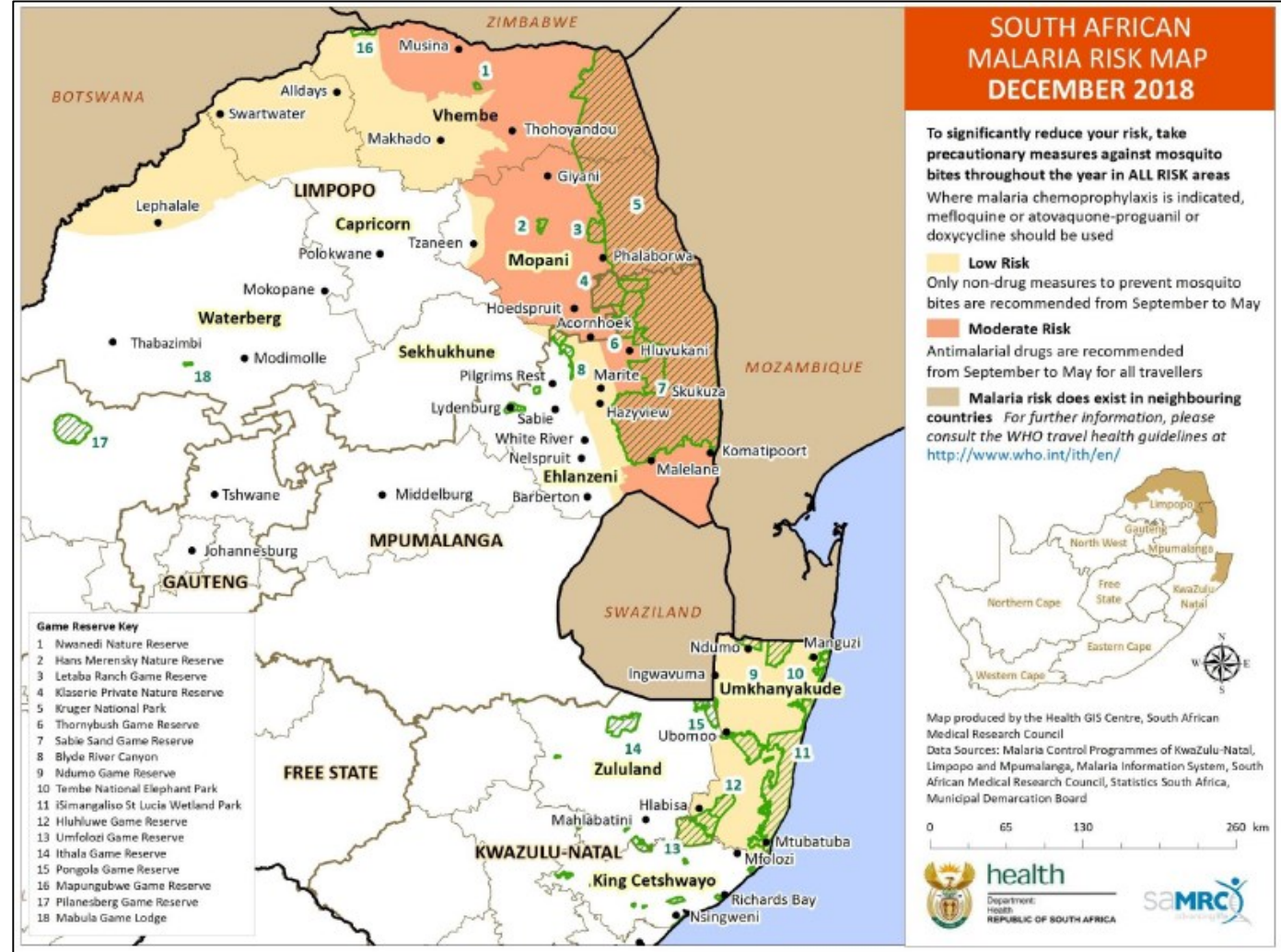
Dr Jaishree Raman

National Institute for Communicable Diseases
WITS Research Institute for Malaria Research
UP Institute for Sustainable Malaria Control
E8 Webinar 8th December 2020

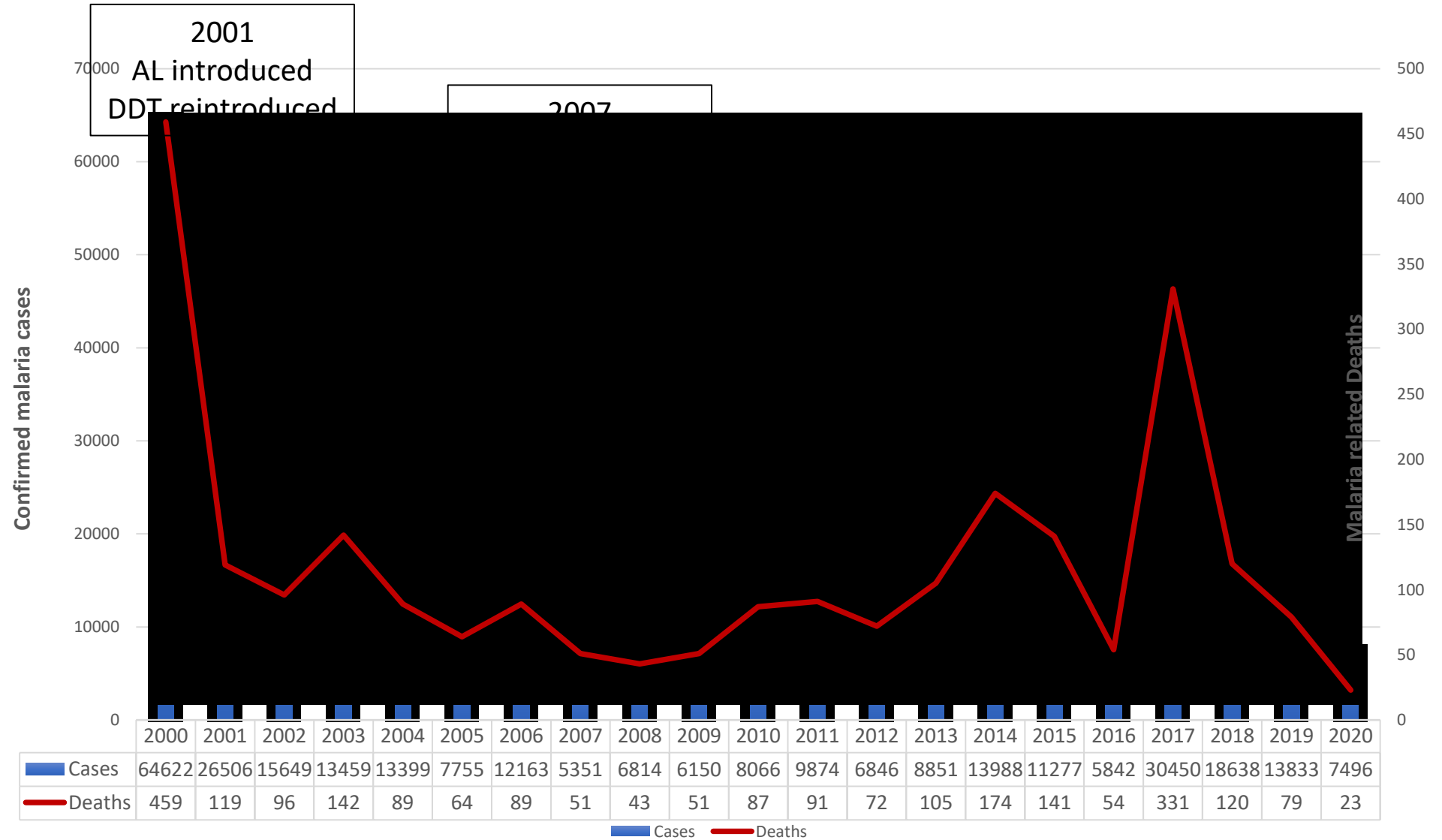


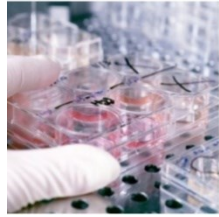
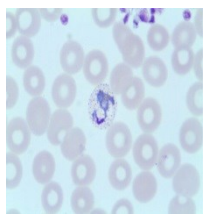
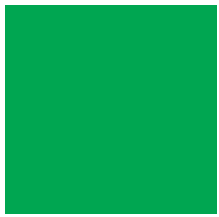


Malaria Risk Map of South Africa, 1938



Malaria Risk Map of South Africa, 2018





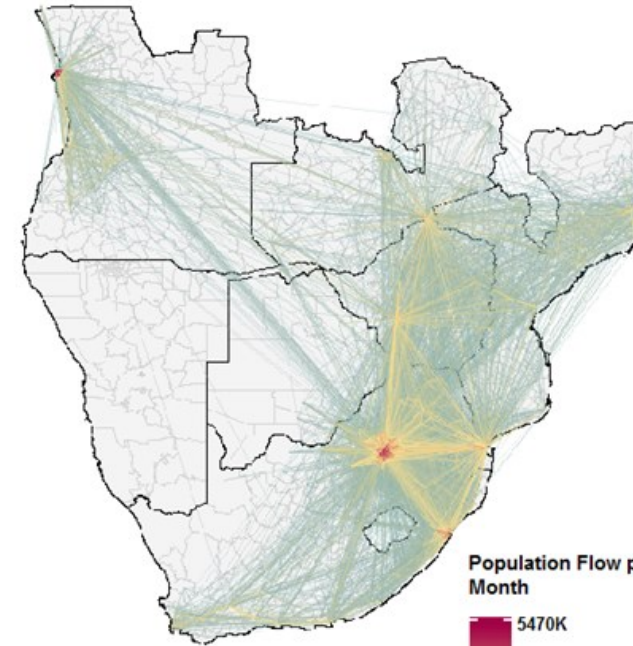
RESEARCH

Open Access



High levels of imported asymptomatic malaria but limited local transmission in KwaZulu-Natal, a South African malaria-endemic province nearing malaria elimination

Jaishree Raman^{1,2,3*}, Laura Gast⁴, Ryleen Balawanth⁴, Sofonias Tesseney Givemore Munhenga^{1,2}, Power Tshikae¹, Vishan Lakan⁶, Tshiamo Mwaru⁷, Moses Mkhabela⁸, Nompumelelo Zondo⁸, Ernest Mohulatsi⁹, Zuziwe Mkhambane¹⁰, Siphon Msimang¹⁰, Nicole Dagata⁴, Bryan Greenhouse⁵, Lyn-Marie Birkhead¹¹, Bhekisizwe Qwabe⁸ and Devanand Moonasar^{3,11}

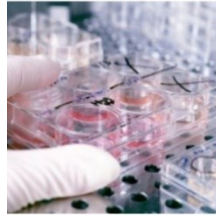
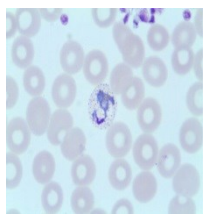


Population Flow per Month
5470K
740K
100K
13K

Ruktanonchai N, University of Southampton 2014

97% of cases were detected by the border unit at one informal border crossing!

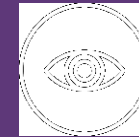




Global technical strategy for malaria 2016–2030

Pillar 1
Ensure universal
access to malaria
prevention,
diagnosis and
treatment

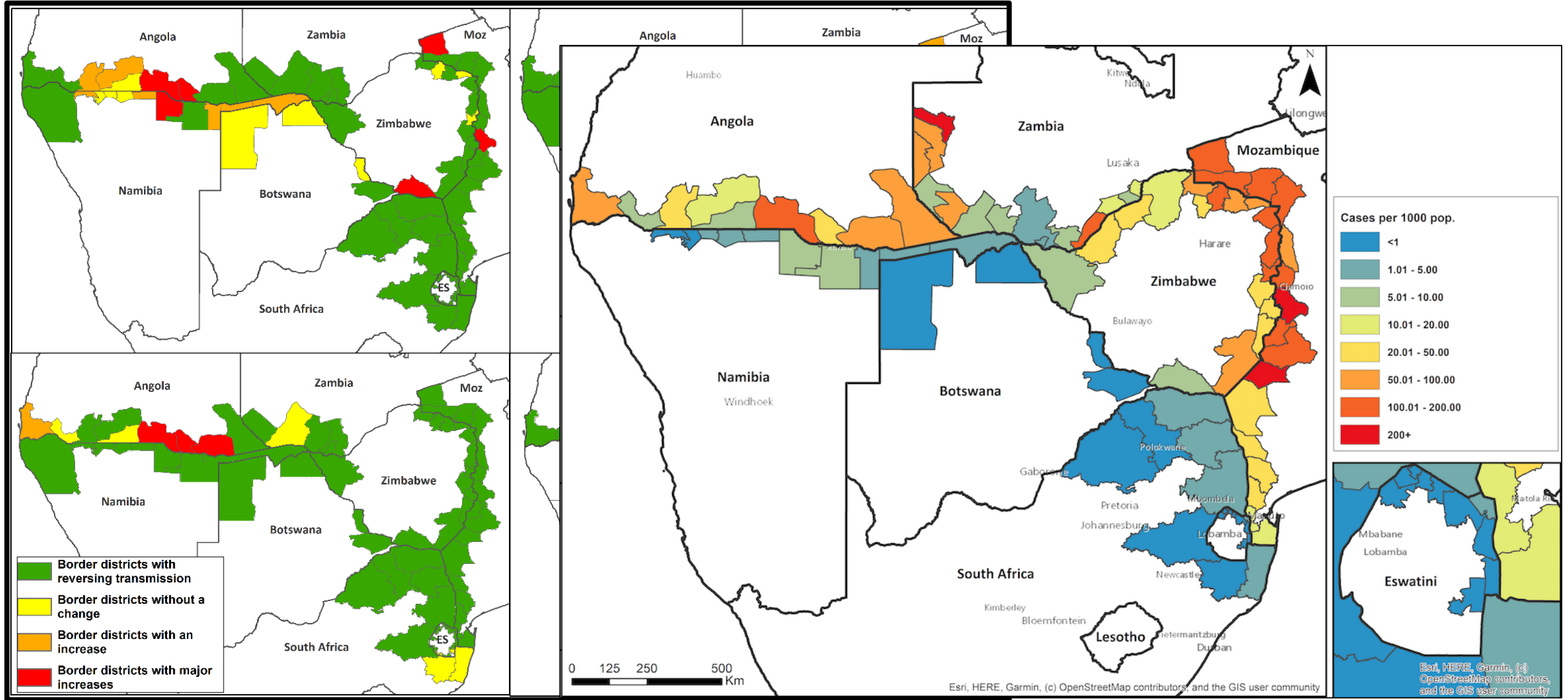
Pillar 2 Accelerate
efforts towards
elimination
and attainment of
malaria-free status



Pillar 3
Transform malaria
surveillance into a
core intervention

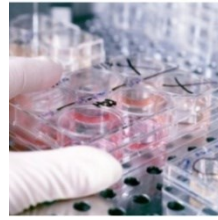
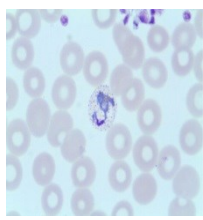
Supporting element 1. Harnessing innovation and expanding research

Supporting element 2. Strengthening the enabling environment



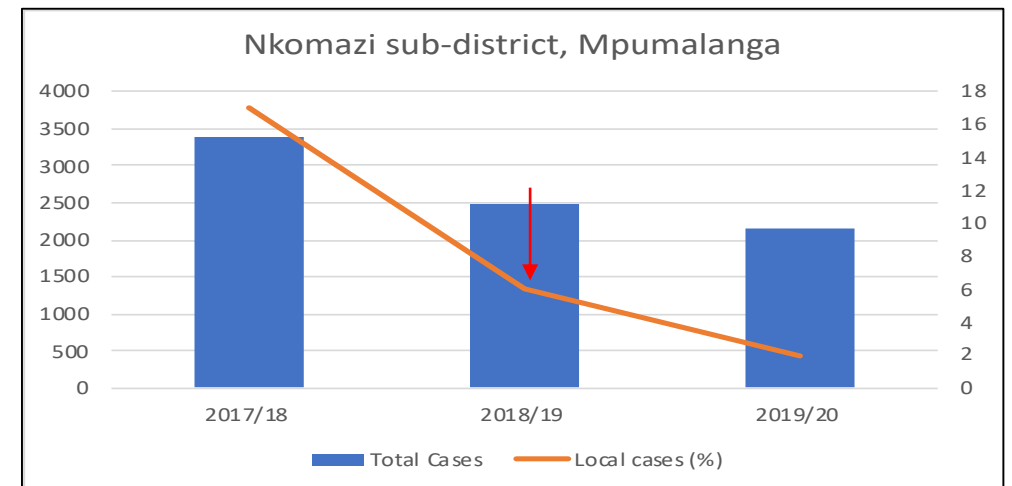
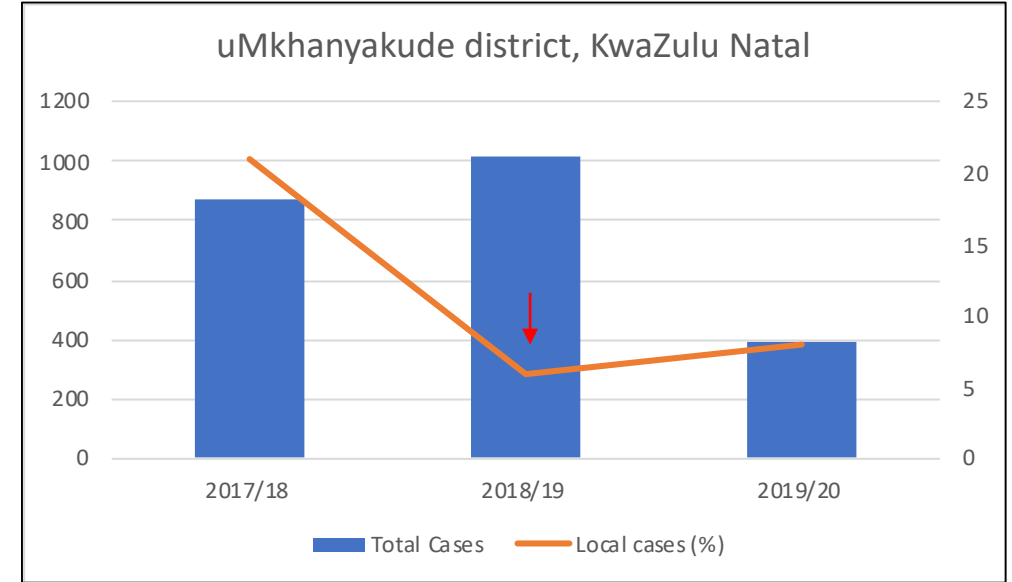
Elimination 8 2020

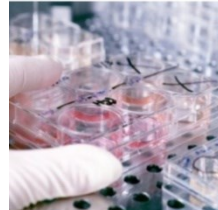
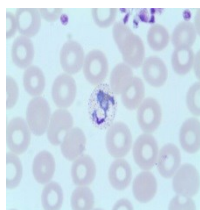
Esri, HERE, Garmin, (c) OpenStreetMap contributors, and the GIS user community



Single Low-dose Primaquine

- 2018/2019 season SLD primaquine deployed in eliminating districts in KwaZulu-Natal and Mpumalanga
- ~80% of doses given by the E8 surveillance teams
- Sustained coverage ~80%
- Marked decrease in local cases in South Africa





RESEARCH

Open Access



False-negative malaria rapid diagnostic tests in Rwanda: impact of *Plasmodium falciparum* isolates lacking *hrp2* and declining malaria transmission

RESEARCH ARTICLE

HRP2 and pLDH-Based Rapid Diagnostic Tests, Expert Microscopy, and PCR for Detection of Malaria Infection during Pregnancy and at Delivery in Areas of Varied Transmission: A Prospective Cohort Study in Burkina Faso and Uganda

Daniel J. Kyabayinze¹*, Issaka Zongo², Jane Cunningham¹, Patrick Angutoko¹, John Ategeka¹, Yves-Daniel Combarros¹, Jerry Mulondo¹, Miriam Nakalembe⁶, Fabrice A. Somgbo¹, Noél Rouamba², Jean-Bosco Ouédraogo², Heidi Hopmann¹

RESEARCH

Open Access



First evidence of the deletion in the *pfhrp2* and *pfhrp3* genes in *Plasmodium falciparum* from Equatorial Guinea

Pedro Berzosa¹*, Vicenta González¹, Laura Taravillo¹, Alfredo Mayor², María Romay-Barja¹, Luz García¹, Policarpo Ncogo^{3,4}, Matilde Riloha^{3,4} and Agustín Benito¹

nature
medicine

LETTERS

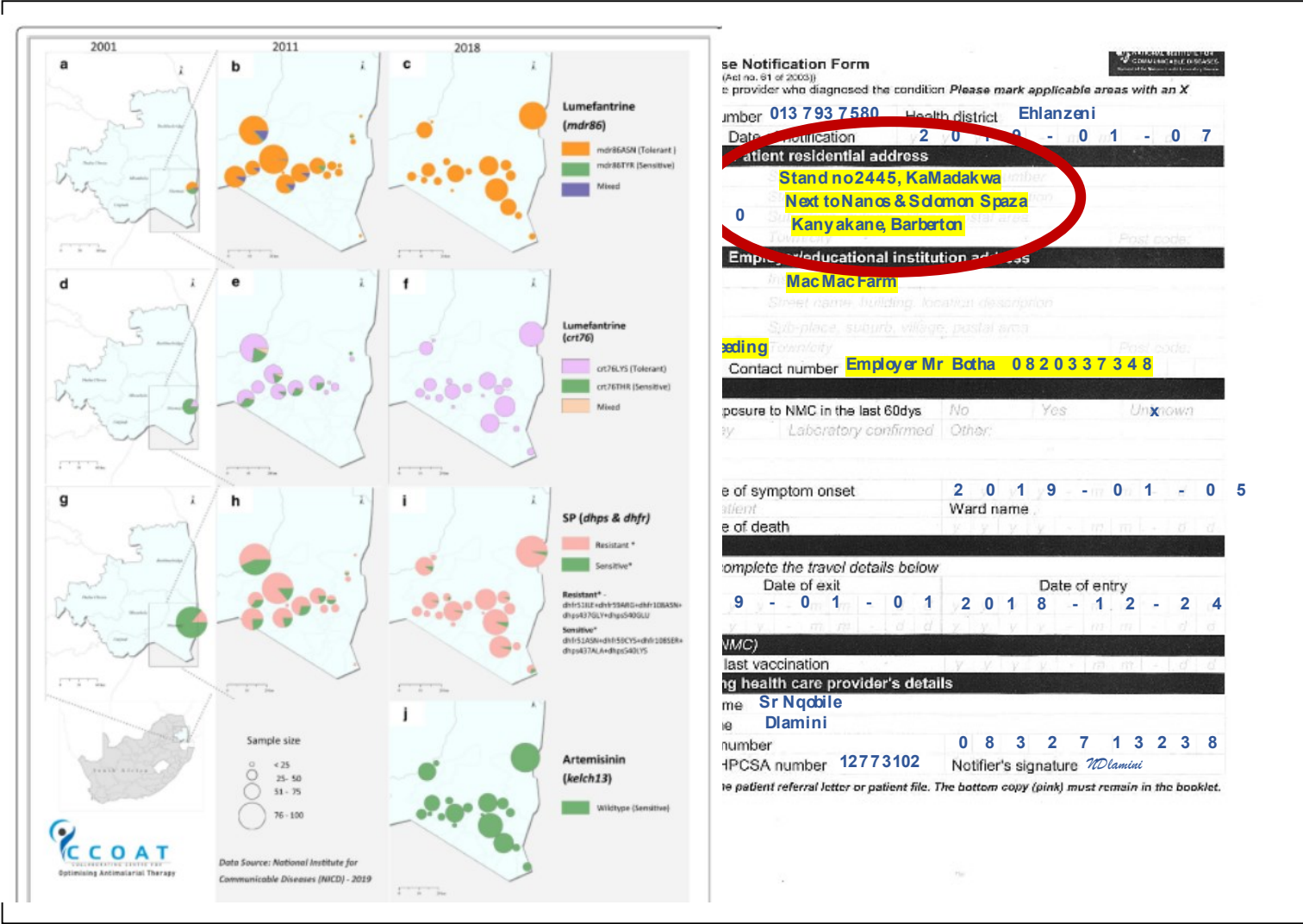
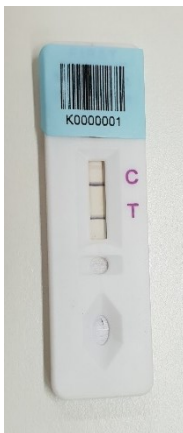
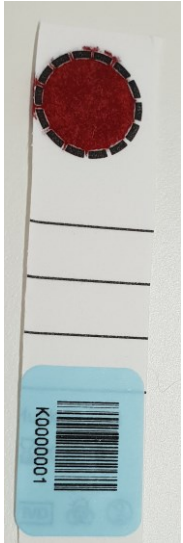
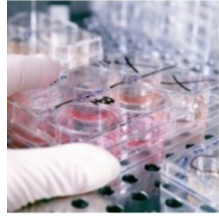
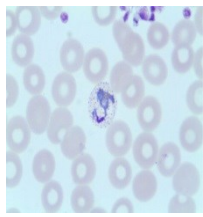
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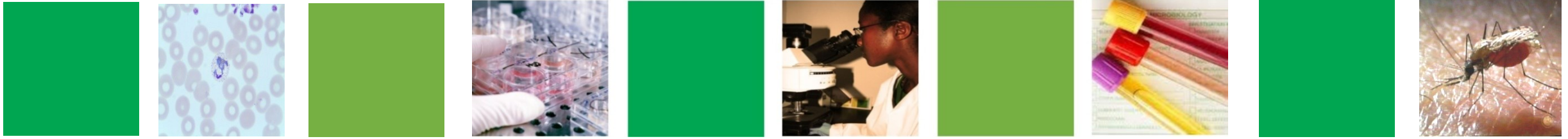
OPEN

Emergence and clonal expansion of in vitro artemisinin-resistant *Plasmodium falciparum* *kelch13* R561H mutant parasites in Rwanda

Aline Uwimana^{1,15}, Eric Legrand^{2,15}, Barbara H. Stokes³, Jean-Louis Mangala Ndikumana¹, Marian Warsame⁴, Noella Umulisa^{5,6}, Daniel Ngamije⁷, Tharcisse Munyaneza⁸, Jean-Baptiste Mazarati⁸, Kaendi Munguti⁹, Pascal Campagne¹⁰, Alexis Criscuolo¹⁰, Frédéric Arieu¹¹, Monique Murindahabi¹², Pascal Ringwald¹³, David A. Fidock^{3,14}, Aimable Mbituyumuremyi¹ and Didier Menard²



- Surveillance of hard to reach populations
- RDTs DNA source
- Antimalarial drug resistance markers
- HRP2/3 deletions
- Residential information allows mapping to facility-level
- Rapid sharing of resistance data across borders



- E8 Surveillance/border units are critical to South Africa's and region's elimination aspirations
- Increase access to malaria testing and treating
- Enable prompt detection and treatment with transmission blocking
- Expand essential routine surveillance activities
- Regional genomic surveillance programme

