E8 Webinar
8 December 2020

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

Moderator
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Director South African Medical Research Council

Speakers
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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
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.
E8 Malaria Border Health Posts

46 total health posts along 5 priority borders of E8

<table>
<thead>
<tr>
<th>Year</th>
<th>Total number tested</th>
<th>Total positive (%)</th>
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<tbody>
<tr>
<td>2017</td>
<td>306,051</td>
<td>10,100 (3.3%)</td>
</tr>
<tr>
<td>2018</td>
<td>557,020</td>
<td>41,844 (7.5%)</td>
</tr>
<tr>
<td>2019</td>
<td>344,582</td>
<td>19,451 (5.6%)</td>
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<tr>
<td>Total</td>
<td>1,207,653</td>
<td>71,395 (5.9%)</td>
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</table>

**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.
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
• 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.
• 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
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

- Proportion seeking treatment for febrile illness within the previous 4 weeks
- Proportion who were tested with a blood test of all who had fever within 4 weeks
- Proportion who were tested with a blood test of all who sought treatment
- Proportion who received any medication or treatment for malaria of those who tested positive for malaria
First choice for diagnosis and treatment

- 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

Proportion of households owning at least one mosquito net
Proportion who slept under a net out of all that own nets (HH)
Proportion who slept under a bed net out of all respondents
Proportion of households sprayed in the last 12 months

Angola
Mozambique
Zambia
Zimbabwe
## Summary of key results: Local and international travel (recall <3 months)

<table>
<thead>
<tr>
<th></th>
<th>Adults</th>
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<td>Zim</td>
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<td>Moz</td>
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<tr>
<td>Proportion who travelled</td>
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<tr>
<td>out of district in last 3 months, % (N)</td>
<td>43(277)</td>
<td>46(352)</td>
<td>8 (229)</td>
<td>16 (331)</td>
<td>9(366)</td>
<td>34(340)</td>
<td>2 (393)</td>
<td>1(72)</td>
</tr>
<tr>
<td>Proportion who slept outside at least one night, % (N)</td>
<td>43(120)</td>
<td>43(161)</td>
<td>17 (18)</td>
<td>26 (54)</td>
<td>30(27)</td>
<td>39(114)</td>
<td>0 (6)</td>
<td>0 (1)</td>
</tr>
<tr>
<td>Proportion who used protective measures against malaria, % (N)</td>
<td>7(120)</td>
<td>21(152)</td>
<td>22 (18)</td>
<td>39 (54)</td>
<td>4(27)</td>
<td>20(114)</td>
<td>0(6)</td>
<td>100(1)</td>
</tr>
</tbody>
</table>
Knowledge about malaria and its prevention

- Respondents who know that malaria is caused by mosquito bites
- Respondents knowledge of that fever is a symptom of malaria
- Respondents knowledge that death is the worst outcome if malaria is left untreated
- Respondents knowledge that sleeping under a mosquito net protects your from malaria
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.

The full report is available on the E8 website, https://malariaelimination8.org/
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
Malaria Operational Research Program
Multidisciplinary Research Centre
Malaria in SADC

- Malaria knows no boundaries
- Human mobility
- Mosquito mobility

Modified from Bhatt et al., Nature, 2015
Namibia and Malaria

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

- Malaria is heterogeneous with highest incidence in North Eastern Namibia

- 90%> of national cases from Kavango East, Kavango West, Zambezi region bordering Angola

- Character of malaria similar in border areas between Namibia and Angola

Modified from Bhatt et al., Nature, 2015
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
Acknowledgments

Namibia Malaria Elimination Partnership (NAMEP)

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MoHSS
Petrina Uusiku
Astrid Augusto
MoHSS Kavango East
MoHSS Zambezi

UCSF – MEI
Michelle Hsiang
Jenny Smith
Roly Gosling

UCSF Global Health Sciences
Global Health Group

Open your mind
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

To significantly reduce your risk, take precautionary measures against mosquito bites throughout the year in ALL RISK areas where malaria transmission exists. In areas where chloroquine-resistant malaria is indicated, mefloquine or atovaquone/proguanil or doxycycline should be used.

Low Risk

Antimalarial drugs are recommended from September to May for all travellers.

Malaria risk does exist in neighbouring countries. For further information, please consult the WHO travel health guidelines at http://www.who.int/tdr/dg
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<td>2020</td>
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**Key Events:**
- 2001: AL introduced
- 2007: DDT reintroduced
- 2007: Discussion on elimination began
- 2012: Elimination agenda adopted

**Notes:**
- Malaria related Deaths
- Confirmed malaria cases
High levels of imported asymptomatic malaria but limited local transmission in KwaZulu-Natal, a South African malaria-endemic province nearing malaria elimination

Jaishree Raman1,2,3*, Laura Gast4, Ryleen Baiawanth5, Sofonias Tesse6, Givemore Munhenga1,2, Power Tshikae1, Vishan Lakan6, Tshiamo Mwab6, Moses Mkhabela6, Nompumelelo Zondo6, Ernest Mohulatsi7, Zuziwe Sipho Msimang4, Nicole Dagata4, Bryan Greenhouse3, Lyn-Marie Birk8, Bheki Qwabe8 and Devanand Moonasar3,11

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

WHO GTS for Malaria 2015
Since implementation in 2015 tested ~ 1.8 million individuals

- 750,000 RDT-malaria positives treated on-site

- Reductions of 30% in incidence and 46% in mortality in border regions and E8 countries in general

Elimination 2020
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
First evidence of the deletion in the pfhrp2 and pfhrp3 genes in Plasmodium falciparum from Equatorial Guinea

Pedro Berzosa, Vicenta González, Laura Taravillo, Alfredo Mayor, Maria Romay-Barja, Luz García, Policarpo Ncogo, Matilde Riloña and Agustín Benito
<table>
<thead>
<tr>
<th>Date of infection</th>
<th>Date of death</th>
<th>Wards name</th>
<th>Complete the travel details below</th>
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<table>
<thead>
<tr>
<th>Name of patient</th>
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<tr>
<td>Mr. Mphela</td>
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<tr>
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<tr>
<td>Seraphin &amp; Solomon Spaza</td>
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<th>Surveillance of hard to reach populations</th>
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<tr>
<td>RDTs DNA source</td>
</tr>
<tr>
<td>Antimalarial drug resistance markers</td>
</tr>
<tr>
<td>HRP2/3 deletions</td>
</tr>
<tr>
<td>Residential information allows mapping to facility-level</td>
</tr>
<tr>
<td>Rapid sharing of resistance data across borders</td>
</tr>
</tbody>
</table>
• 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