Guiding South Africa's Malaria Elimination Interventions using Molecular Epidemiology

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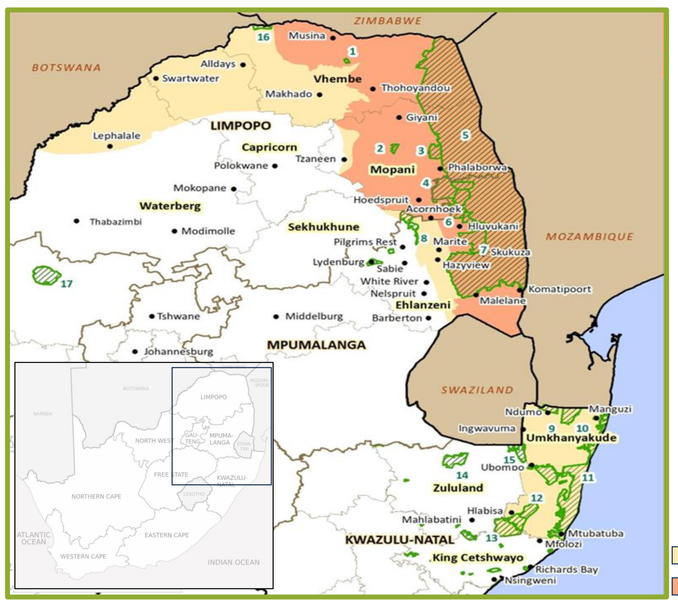
Malaria in South Africa



South Africa is aiming to **eliminate malaria by 2023**

Three endemic provinces:
Limpopo: Moderate transmission, >60% local cases
Mpumalanga (MPN): Low-moderate transmissio>70% imported
KwaZulu-Natal (KZN): Low transmission >85% imported

New interventions needed to reduce residual transmission

- Low risk
- Moderate risk

Methods

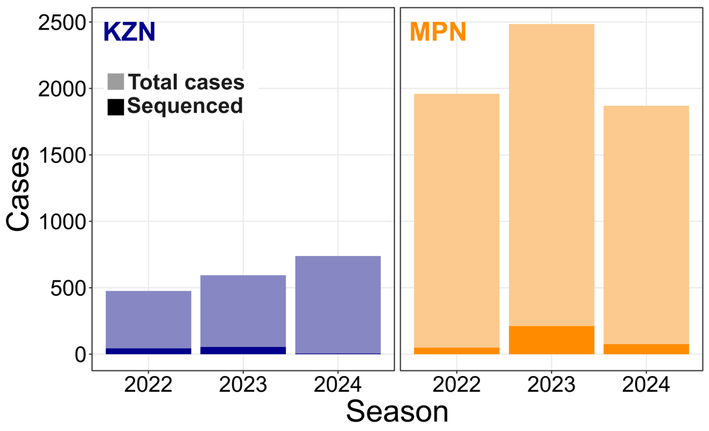
- Dried blood spots and/or rapid diagnostic tests are routinely collected through passive and active case detection surveillance activities.
- Patient metadata are collected for every sample
- Samples from MPN and KZN collected between 2022 and 2024 were sequenced using the targeted amplicon sequencing panel MAD[4]HatTeR[1] at the NICD Sequencing Core Facility

Intra-host and population diversity, including allele frequencies, estimated with MOIRE[2].
Identity-by-descent (IBD) for infection pairs estimated using Dcifer[3].

1: Aranda-Diaz, *et al*. bioRxiv (2024) doi: 10.1101/2024.08.22.609145
2: Murphy and Greenhouse. bioRxiv (2024) doi: 10.1101/2023.10.03.560769
3: Gerlovina et al. Genetics (2022) doi: 10.1093/genetics/iyac126

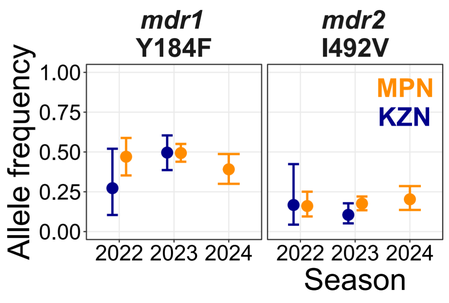
Results

Sequenced samples

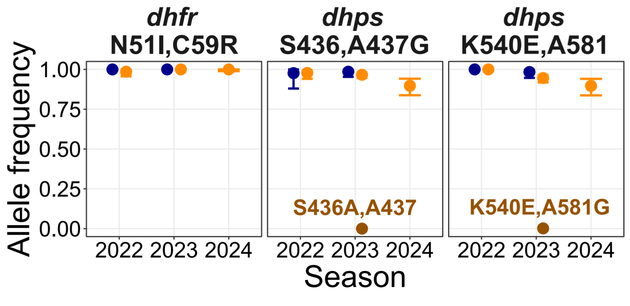


445 samples with parasite concentrations above 100 parasite/µl blood were sequenced

Molecular markers of antimalarial drug resistance

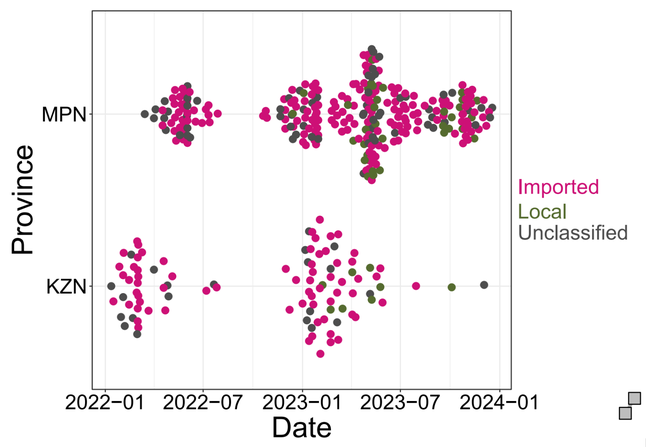


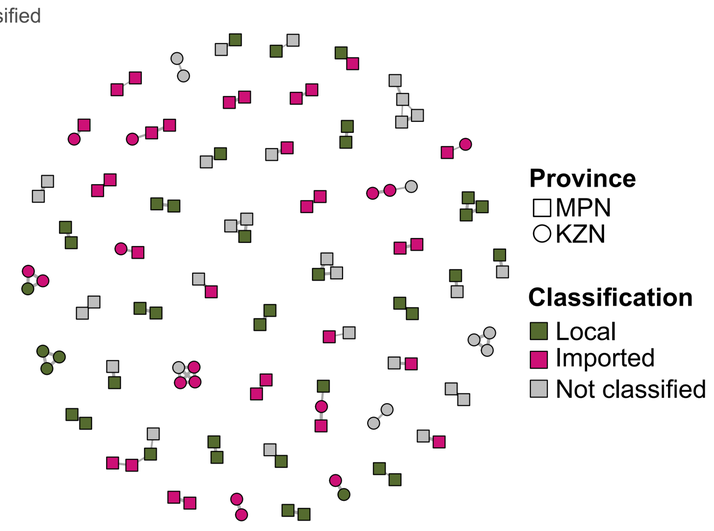
- **No validated or candidate *k13* markers** associated with artemisinin resistance
- **All** parasites carry molecular markers associated with **tolerance to lumefantrine**
- **All** parasites carry molecular markers associated with **susceptibility to chloroquine**



- **All parasites** carry markers associated with **sulfadoxine-pyrimethamine (SP) resistance**

Infection clusters highlight the role of local transmission and co-importation





- **27%** (121/445) of samples belonged in a **cluster of highly related infections** (IBD >0.125).
- Most sequenced **local cases belonged in a cluster**.
- **18% (45/254) of sequenced imported cases belonged in a cluster**. Only 10 of those would be classified as co-imported epidemiologically.

Conclusions

- The lack of mutations associated with artemisinin or lumefantrine resistance suggests South Africa's first-line treatment, **artemether-lumefantrine, is still effective**
- The absence of malaria parasites with *hrp*2/3 deletions (data not shown), suggests ***hrp*2-based falciparum-specific rapid diagnostic tests are still effective** in South Africa
- However, the spread of drug and diagnostic-resistant parasites across East and Central Africa is a **warning sign** and demands **rigorous surveillance**
- Preliminary data suggests **importation** of malaria cases is contributing to **sustained local transmission**. However, more data (coverage of sequenced samples and epidemiological metadata) from South Africa and neighbouring countries is needed to confirm this
- Interventions at the border to **prevent malaria importation** should be prioritized.
- This highlights **the need for regional collaboration and rapid sharing of data** to enable prompt preventative and containment responses.

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