



Université
Cheikh Anta Diop



Malaria: Innovations, Strategies Challenges in endemic countries, example of Senegal

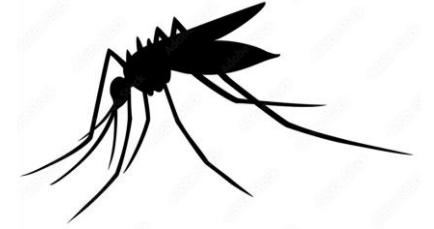
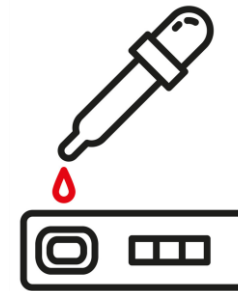
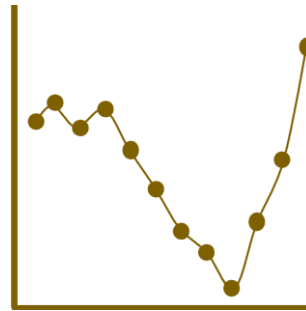
Professor Daouda Ndiaye, PharmD, PhD, FASTMH

CIGASS & UCAD

EMERGING THREATS OF DRUG, DIAGNOSTIC AND INSECTICIDE RESISTANCE THROUGH GENOMIC SURVEILLANCE

- *Monitor key genetic indicators of risk and identify emerging threats to malaria elimination strategies including:*

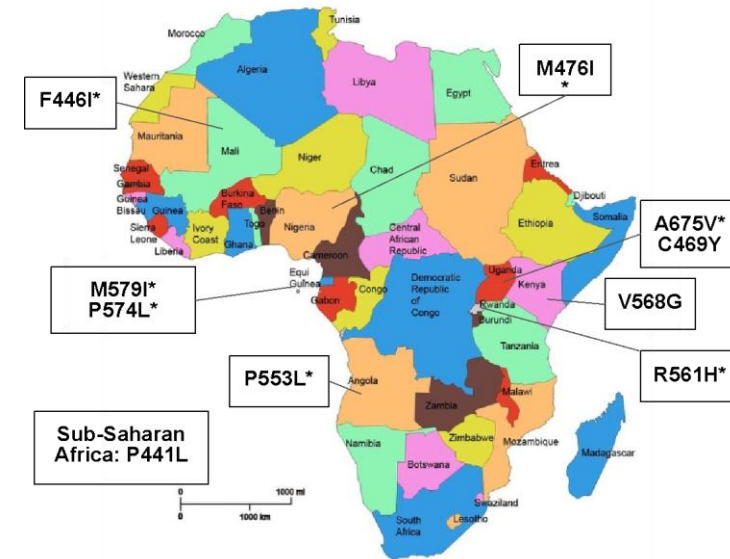
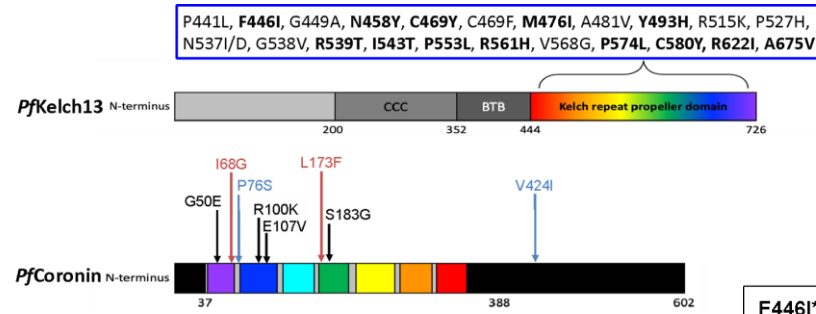
- *drug resistance*
- *hrp2/3 gene deletion*
- *insecticide resistance*



- *Evaluate the consequences of resistance-implicated genetic variants on parasite phenotypes and validate with gene editing*

PARTIAL ARTEMISININ RESISTANCE AND PARTNER DRUG RESISTANCE REMAIN MAJOR THREATS TO EFFECTIVE ANTIMALARIAL DRUG THERAPY.

- *Rwanda and Uganda have rapid increases in novel, Africa-specific Pfk_{elch}13 mutations.*
- *Emerging Pfc_{oronin} mutations implicated in drug resistance in Uganda now in Senegal.*
- *Shown to confer ART resistance in vitro.*
- *Ongoing threat surveillance to provide an early warning strategy for ART resistance.*



- **This risk can be mitigated in Senegal by providing the NMCP with agile, real-time molecular surveillance of the *Pfk_{elch}13* locus.**
- **Analysis of entire *Pfk_{elch}13* locus both from whole genome and amplicon sequencing.**

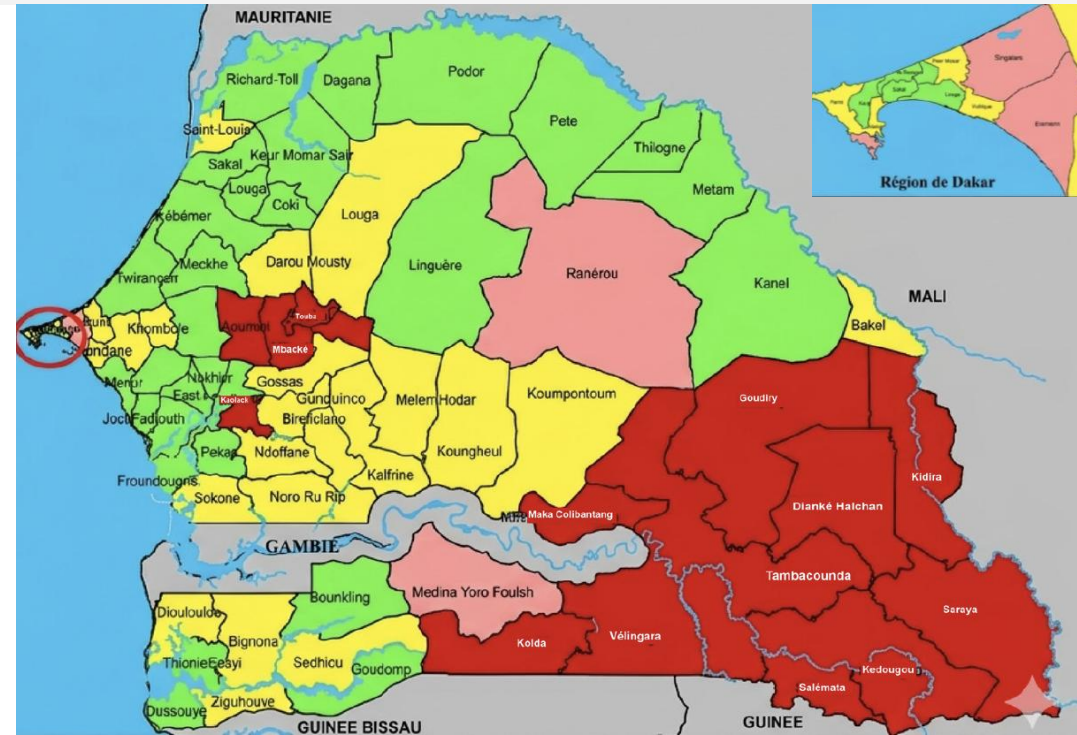
Senegal MMS Project Overview

- Senegal has distinct ecological zones with range of malaria annual incidence from $<1 \text{ ‰}$ to $> 1000 \text{ ‰}$.
- National Malaria Elimination Agenda 2030.



- *NMCP uses MMS data for planning & decision making*
- *Routine Coordination: NMCP + CIGASS*
- *NMCP uses co-developed Data Dashboard*

CIGASS is the Research Reference Center for new Senegal Malaria Elimination Plan



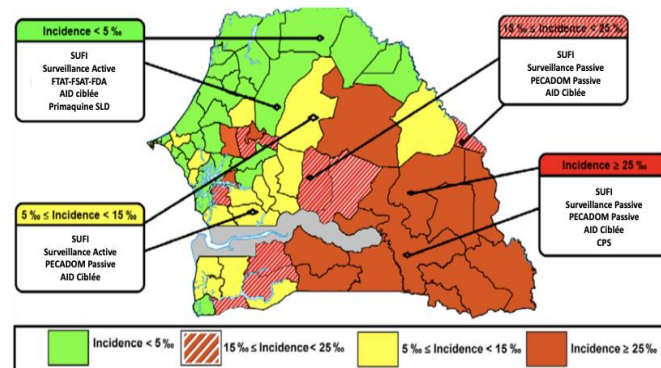
Political Will

+

Strategic Use of Interventions

+

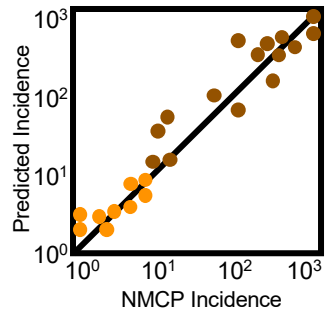
Research and Data



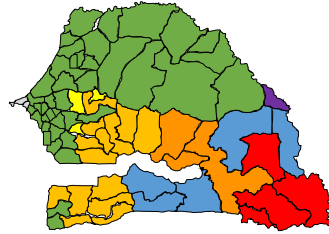
Innovations: Genomics for Public Health Decision-Making

Generate, analyze, and interpret MMS data in direct support of NMCP operational priorities

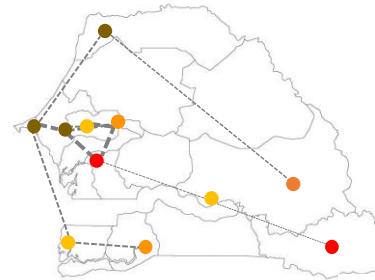
Routine Surveillance & Trend Detection



Intervention Guidance & Evaluation



Human mobility & transmission connectivity



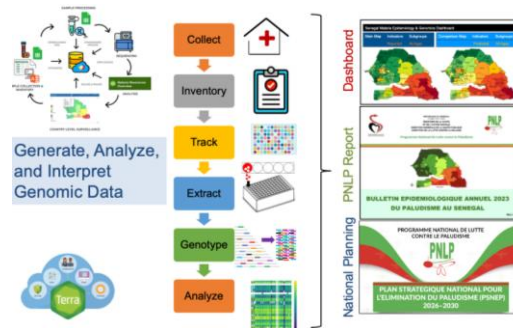
Data integration & Decision support tools



Regional Capacity & Sustainability

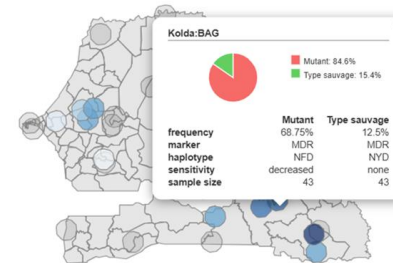


Sustainable MMS Platform



Integrate and Apply Genomic Data for Decision-Making

Routine MMS Use for Decision Making

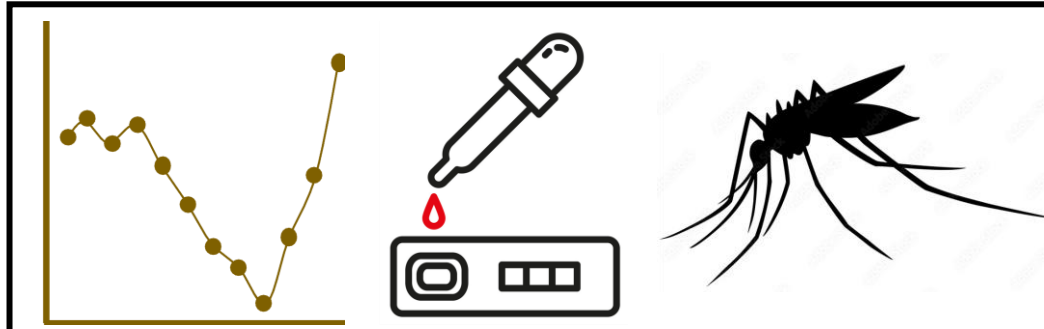


Share Knowledge Beyond Senegal



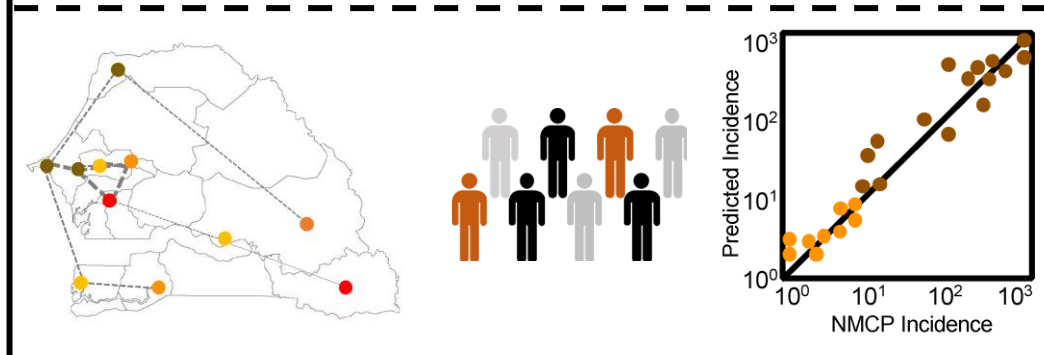
Pathogen Genomics for Public Health Decision-Making

Threat Detection & Response



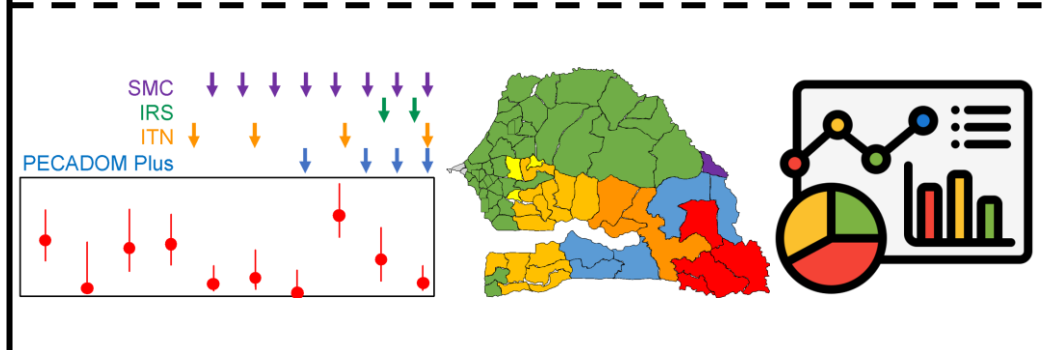
- *Resistance Surveillance*
- *Emerging Threats*
- *Drug Efficacy*
- ***New Vaccination***

Transmission Surveillance



- *Transmission Surveillance*
- *Imported vs. Local*
- *Incidence Estimation*

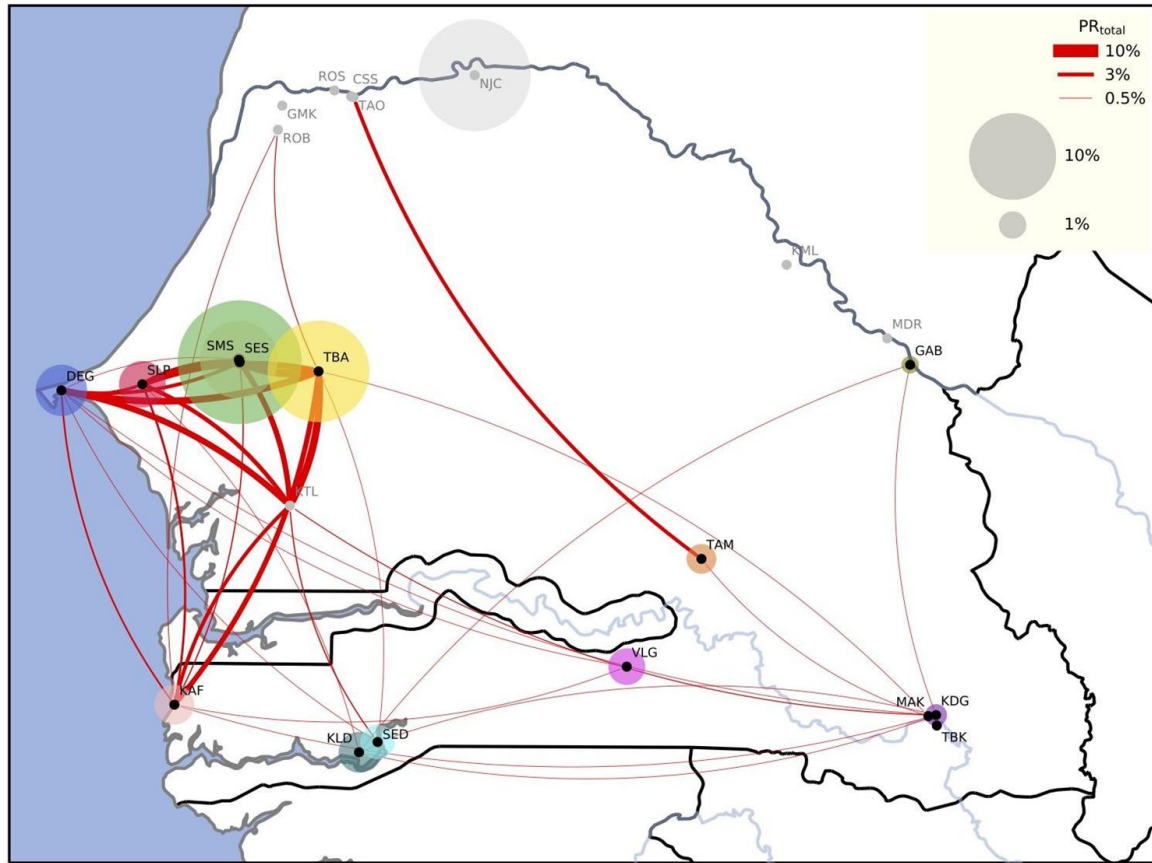
Modeling for Decision-Making



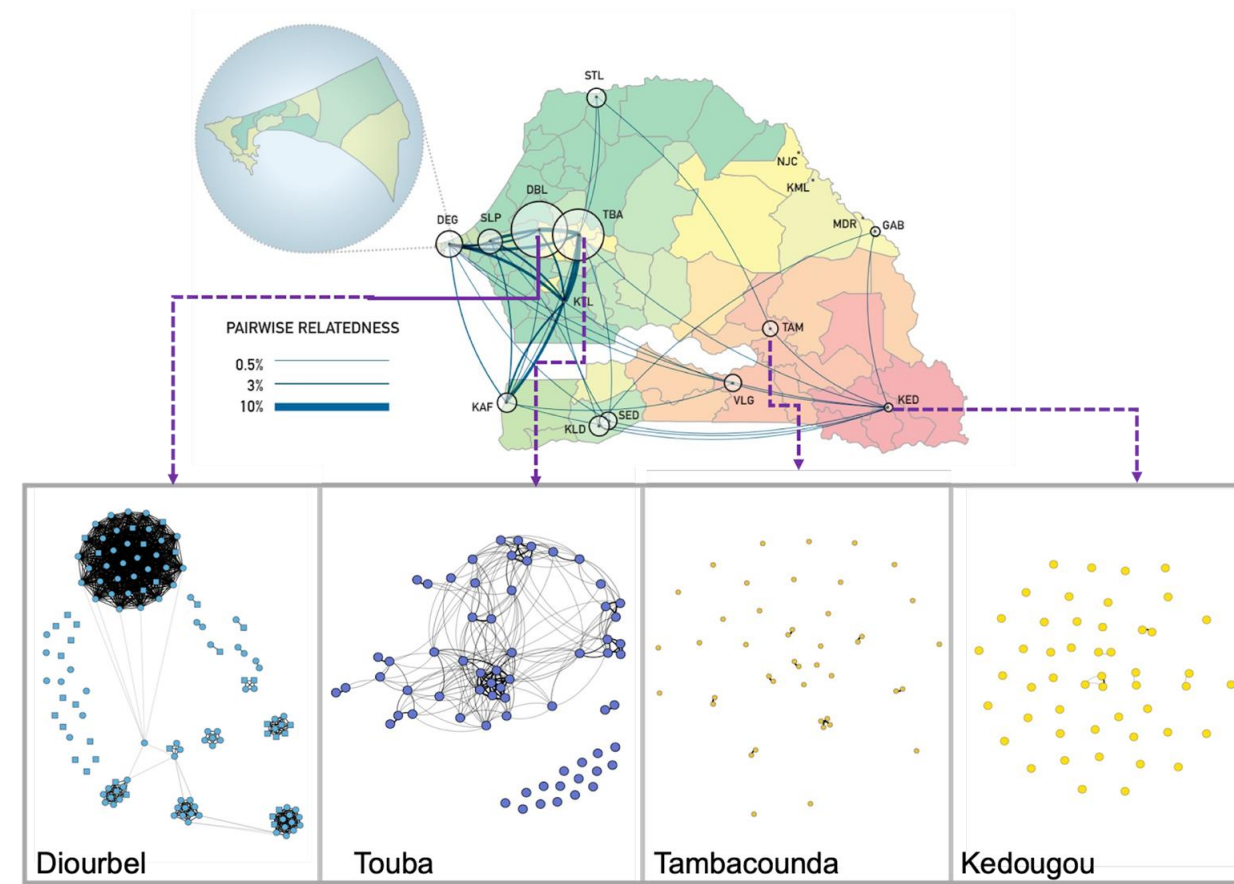
- *Model Calibration*
- *Genomic-Guided Intervention Targeting*
- *Dashboard Development*

Transmission Surveillance: Patterns and Dynamics

Highly Related Parasites Across Senegal (Identical By Descent)

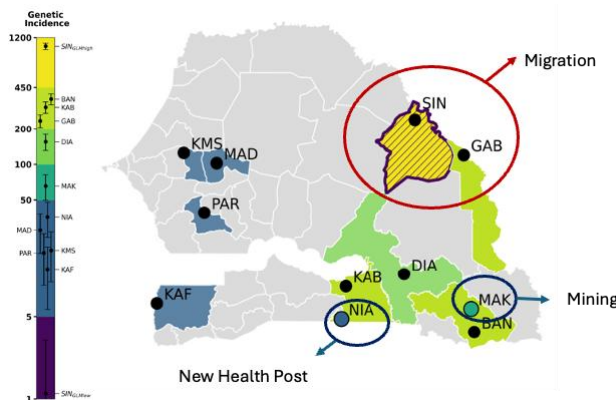
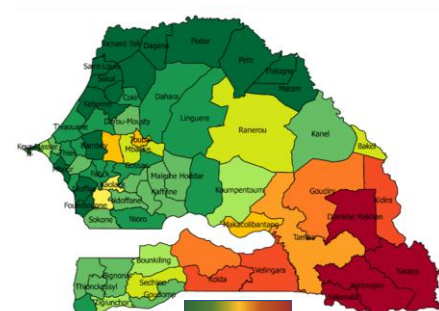
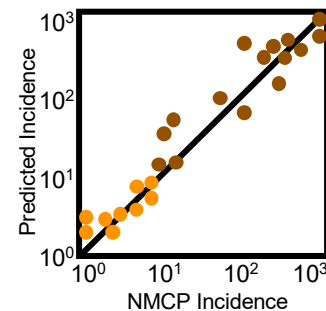
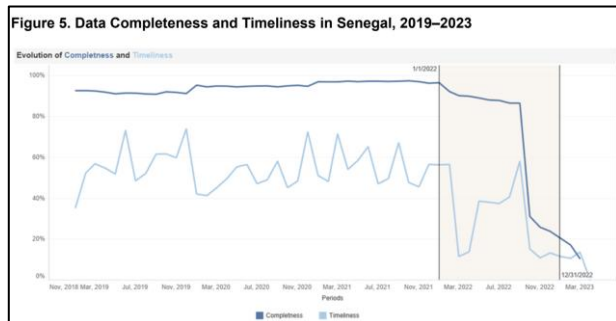


Distinct patterns of parasite relatedness detected across transmission strata



Strategies

- Estimated malaria incidence
- Targeted mobile populations and investigating migration corridors
- Guided Interventions deployment
- Motivated targeted intervention use in at-risk urban populations.
- Guided optimal drug choice in SMC areas.
- Safeguarded pre-elimination areas.
- Confirmed diagnostic and treatment policies.



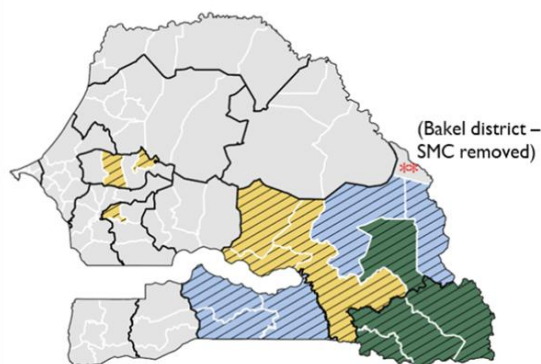
Health Post



Household

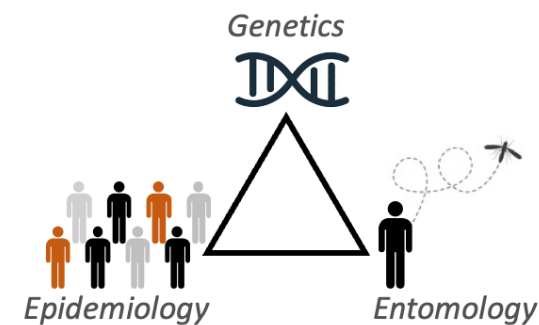
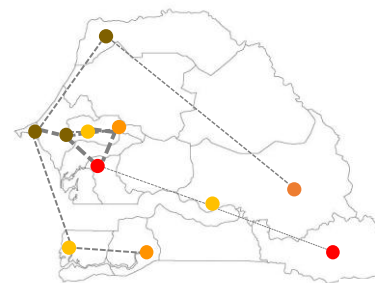


Community



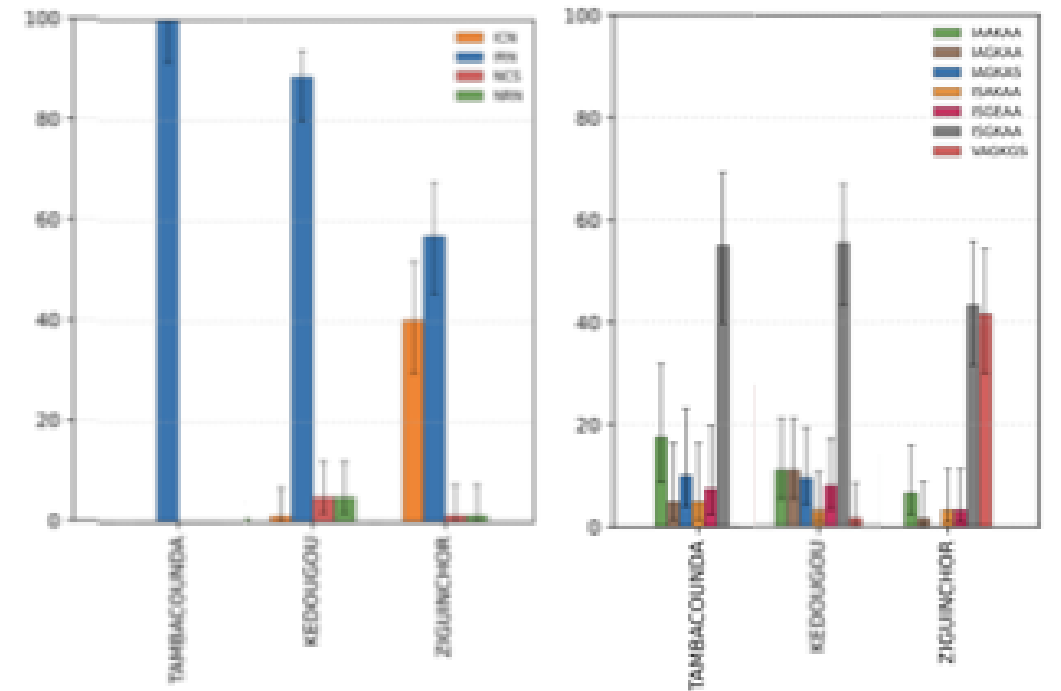
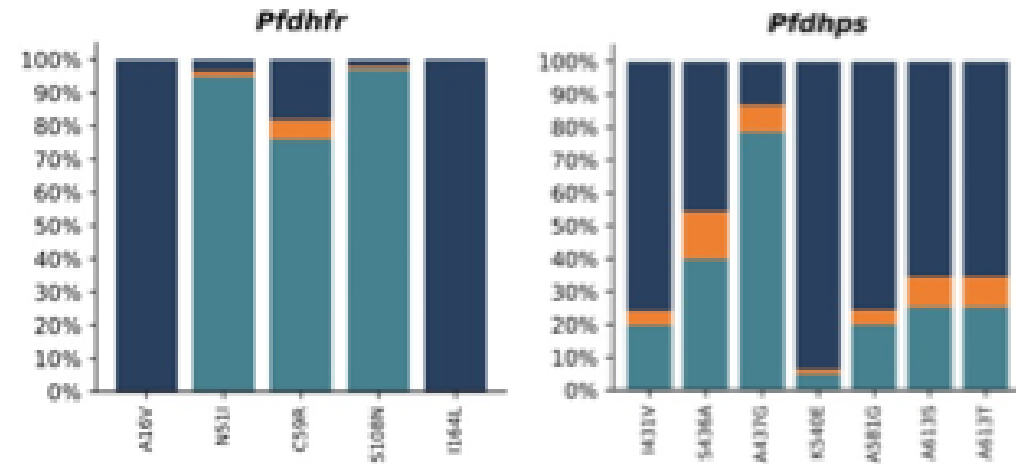
SMC Funde
PMI

SMC Cycles
3
4
5



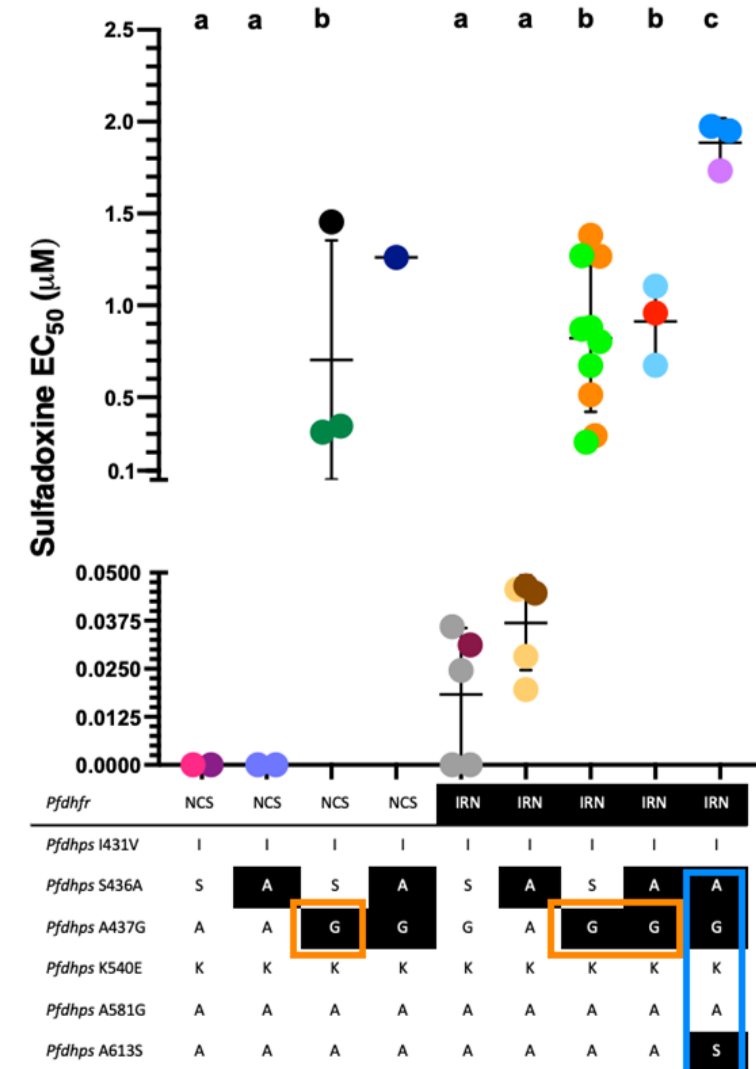
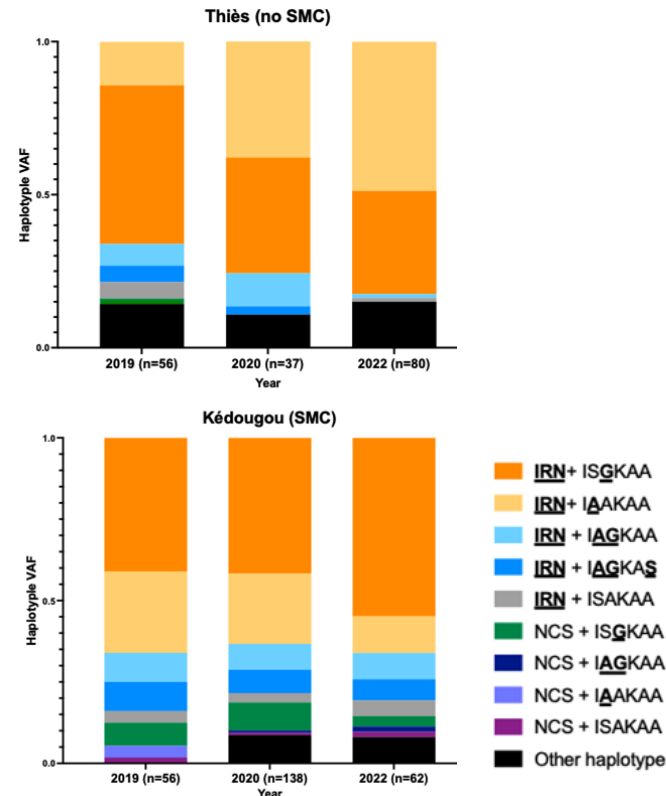
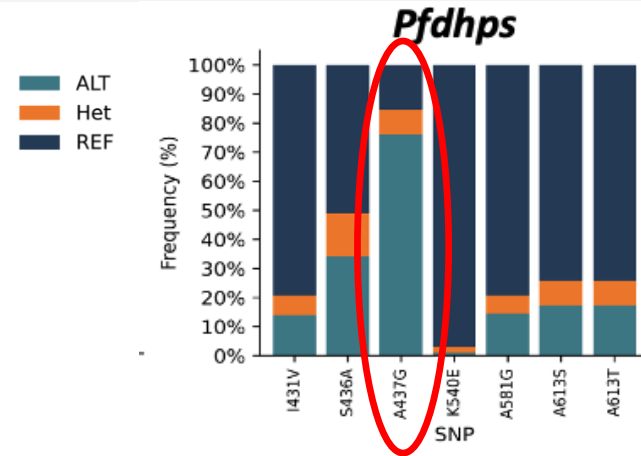
Drug Resistance Surveillance: SMC + *Pfdhfr* & *Pfdhps*

- *Pfcr* and *Pfmdr1* mutations stable
- SMC driving *Pfdhfr* and *Pfdhps* haplotypes
 - Near fixation of *Pfdhfr* **IRN** increased with SMC intensity (OR = 1.77, P<0.001); **ICN** haplotype in some regions
 - Detect *Pfdhps* K540E and increased **ISGEAA** haplotype
 - Negative association of *Pfdhps* **VAGKGS** with SMC rounds (OR=0.15, p<0.001)
 - Positive association of **ICN** + **VAGKGS** (OR = 1.37, p<0.001)
- Preliminary finding of K13 C469Y (mixed infection Kafountine)
- Data directly used by Senegal NMCP
 - Positive association of SMC use and *Pfdhfr* and *Pfdhps* mutations motivated enhanced surveillance with SMC use.
 - Preliminary finding of K13 C469Y mutation confirmed by allele-specific qPCR that detected both mutant and wildtype alleles in mixed infection.
 - Ongoing investigation for parasite genetic background (local/imported) and enhanced surveillance in local and transit corridors ongoing.



Genotype-To-Phenotype: Increased SDX Resistance *Pfdhps* A437G & A613S

- Surveillance reveals potential threats to SMC and IPTp use in Senegal.
- Increased frequency of *Pfdhps* **A437G** among SMC areas (~55% of parasites).
- Validate through “genotype-to-phenotype” investigations.
- Parasites with *Pfdhps* **A437G** show SDX resistance; adding *Pfdhps* **A613S** further increases SDX resistance.
- *Pfdhfr* IRN + *Pfdhps* A437G haplotypes dominate in SMC areas.
- Data directly used by Senegal NMCP

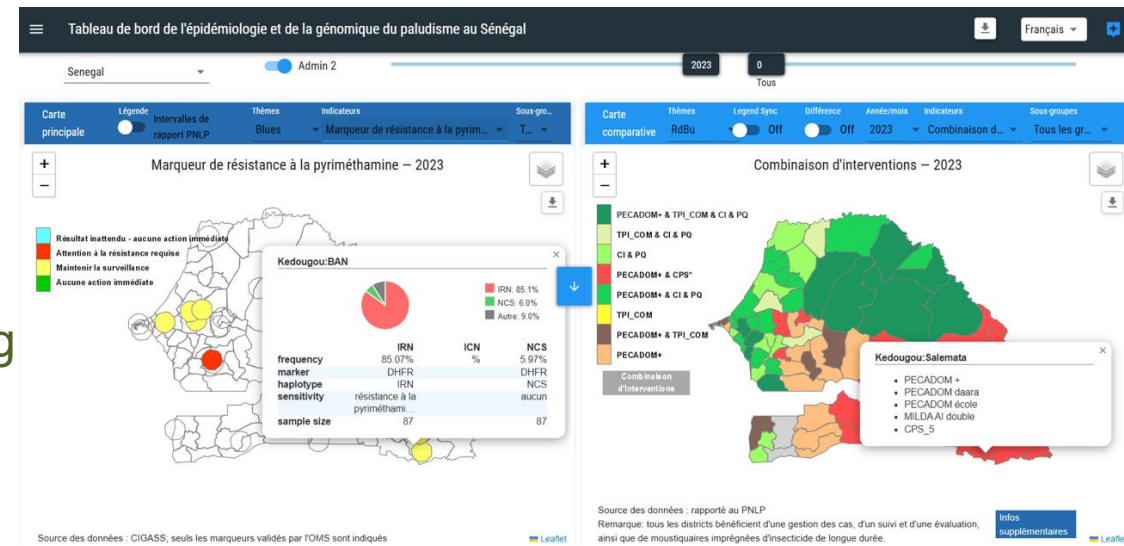
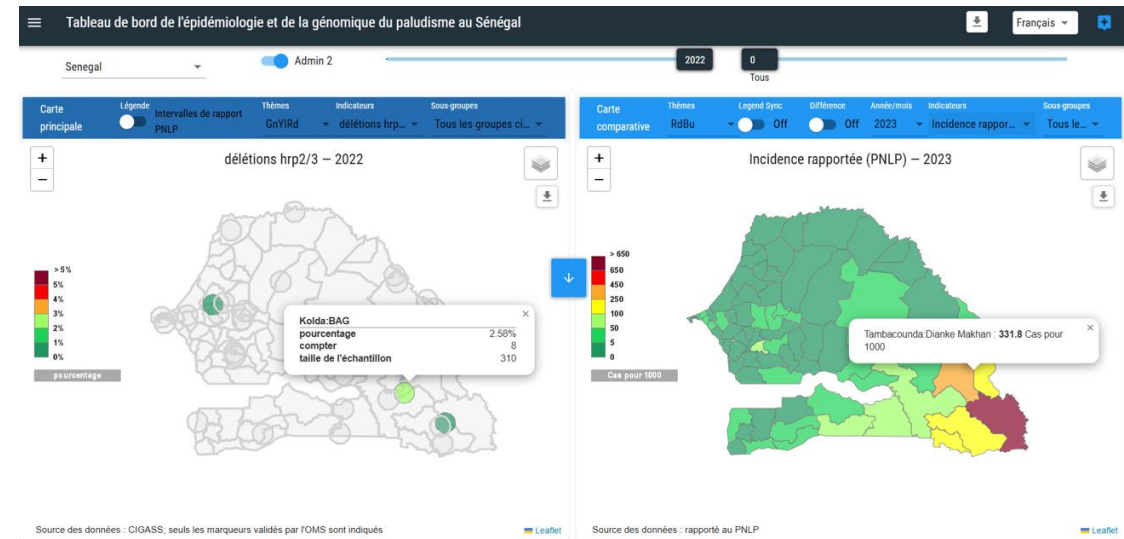


- Increased SDX resistance associated with A437G and A613S motivated surveillance for these *Pfdhps* mutations.
- Evidence for increased SP resistant haplotypes in *Pfdhfr* and *Pfdhps* motivated enhanced surveillance with SMC use.

Pfdhfr mutations increasing in Senegal contribute to SDX resistance. SMC and IPTp risk.

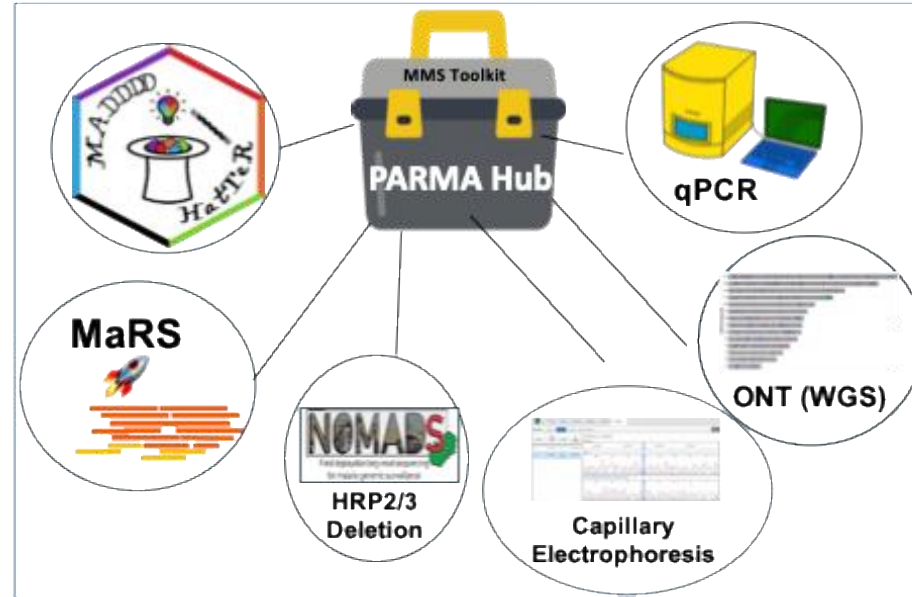
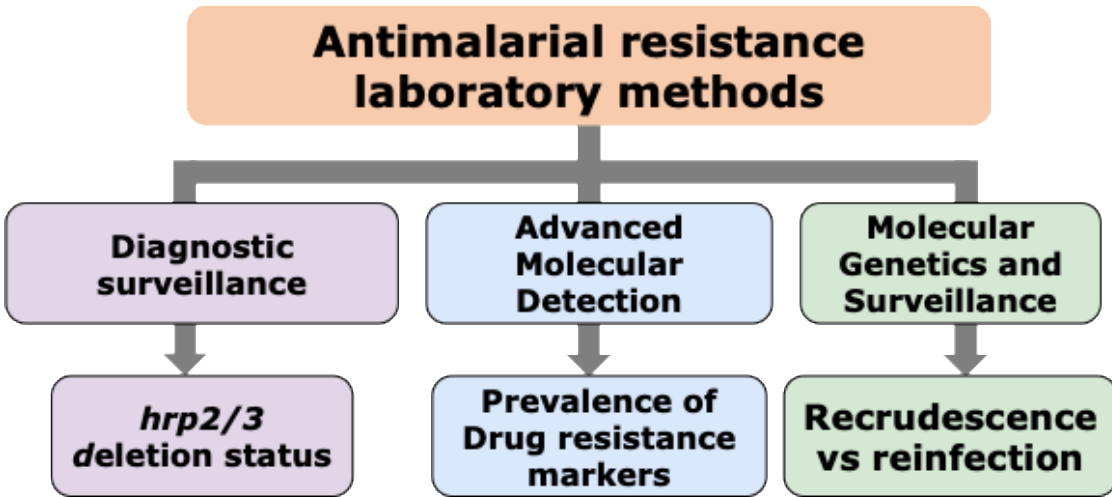
Data Dashboard 4 Decision Making

- Integrates NMCP epidemiological, entomological, intervention data with MMS data (Admin 2), climatic, demographic, and modeled (MAP) data.
- Visual display of threats and impact:
 - *Hrp2/3* deletion
 - Incidence dynamics
 - Pyrimethamine Resistance
 - Intervention Combinations Deployed
- Data directly used by NMCP for faster and targeted decision-making:
 - Resistance-informed strategy adjustments
 - Diagnostic policy readiness
 - SMC and intervention optimization
 - Institutionalized genetic surveillance in elimination planning
 - Track core indicators for routine dashboard reviews
 - Interpretation capacity for clear operational actions (foci investigations, intervention mixes, resistance response).



PARMA Hub: The African Solution

- **Vision:** Diagnose and treat every malaria case with effective diagnostic tools and antimalarial drugs
- **Mission:** Support African countries to conduct quality surveillance to inform malaria diagnostic and treatment policies



TRAINING!

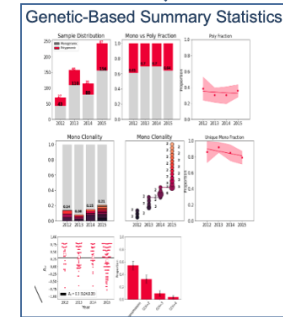
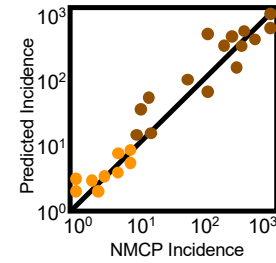


Year	Country	# TES Samples
2022	Guinea	800
2023	Cameroon	433
2023	Niger	438
2023	DRC	1339
2023	Benin	315
2025	Burkina Faso	1800
2025	Niger	436
2025	Benin	336

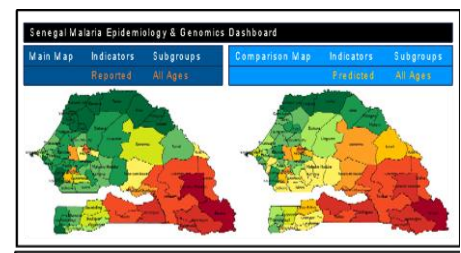
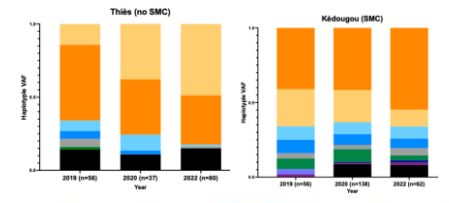
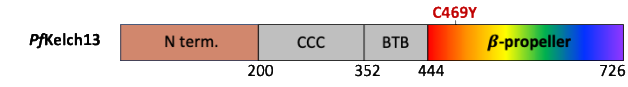
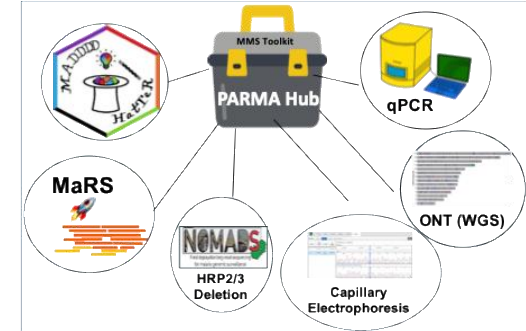
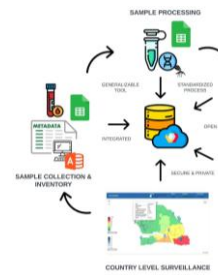
- **TES overview report:** top-level phenotypic results, day 3 parasitemia, Kaplan-Meier treatment efficacy rates
- **Molecular markers report:** variant allelic frequencies of molecular resistance markers.
- **Hrp2/3 deletion report:** genotypic results of the *hrp2* gene deletion.
- **TES complete scientific report:** all results, study methodology, conclusions, and recommendations

Challenges & Perspectives

- Threat Surveillance:
 - SMC Risk: AQR + SDXR
 - K13 C469Y
- Transmission Tracking:
 - Improve incidence prediction
 - Use genetic relatedness to track infection sources
- Intervention Guidance
 - Tracking intervention impact and consequences
 - Subnational tailoring
- Data integration and decision-making
 - STEWARD → Terra → Dashboard
 - Use of MMS in Elimination Agenda by NMCP
- Regional and continental support and tool sharing
 - PARMA Hub
 - Training & Capacity Building
 - Tool Sharing



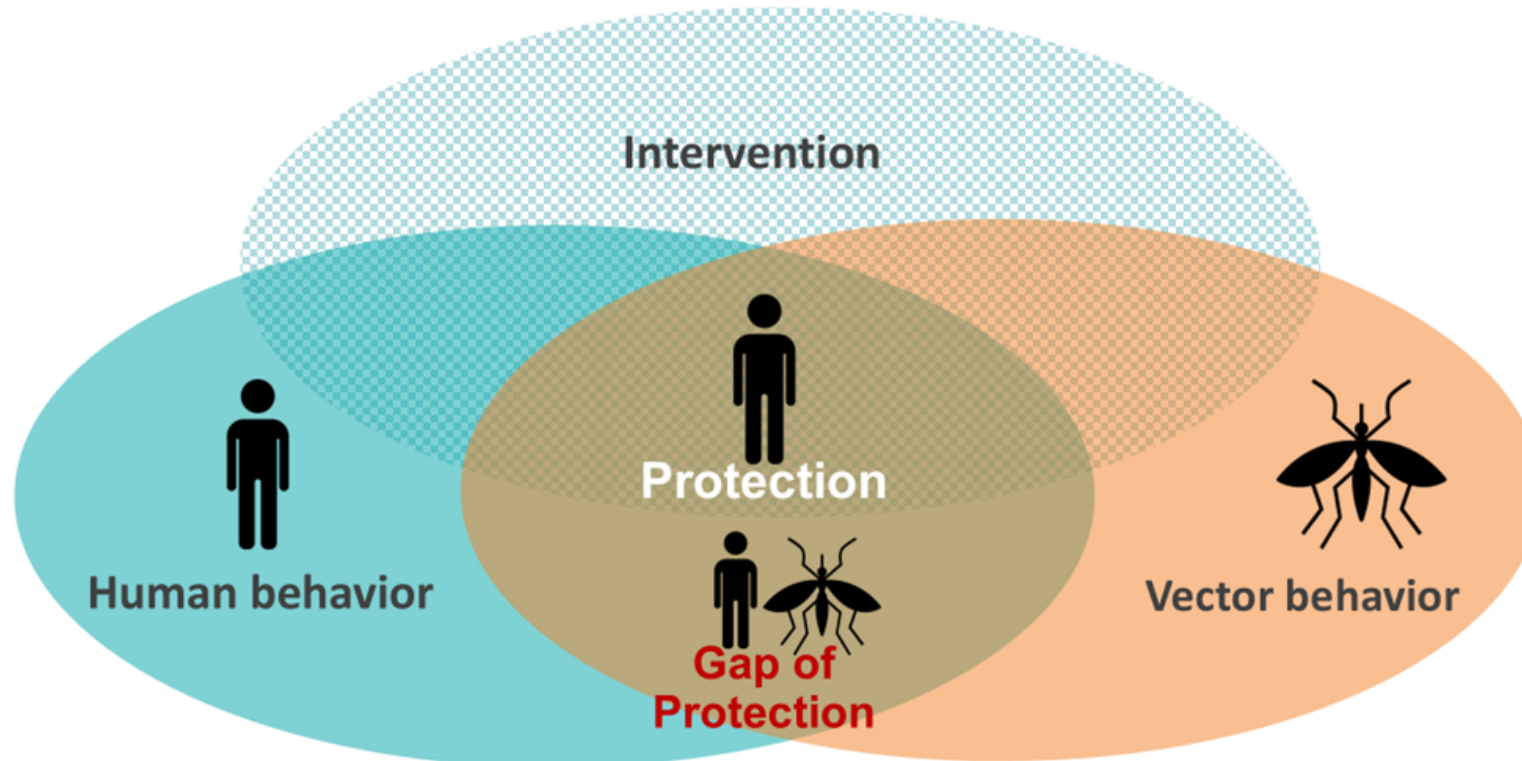
Genetics-Based Incidence



New approach taking into account the human behaviours

Integrating human behavior into the determination of protection gaps

- Vector control interventions **target** specific vector behaviours
- Interventions only protect populations from mosquito bites **ONLY** when human behavior, vector behavior and the intervention overlap.



TEAM: Together Everyone Achieves More



HARVARD T.H. CHAN
SCHOOL OF PUBLIC HEALTH



REACH MALARIA



Swiss TPH



Gates Foundation



President's Malaria Initiative



Yale

