BILL & MELINDA GATES foundation

The role of vector control in malaria eradication: Where are we?

Dr. Helen Jamet, April 2024

AGENDA

1. BMGF and Malaria PST Overview
2. Vector Control: Where are we?
3. Vector Control Innovations

What does BMGF do?

- We are a **private philanthropy** that supports partners around the world to do excellent work, largely in the global health and development space
- Our seven divisions collaborate with partners around the world to address issues we care about and drive change: Global Health, Global Development, Global Growth and Opportunity, Gender Equality, Global Policy and Advocacy and US Program.
- Our **malaria funding** supports large international organizations (e.g., WHO, GFATM), product development partners (e.g., MMV, IVCC) and providers of technical and other support (e.g., CHAI, ALMA, RBM Secretariat) across Africa
- Our **malaria program strategy team** works with global, regional and local partners who provide various services and technical assistance to country programs (e.g., campaign digitization, surveillance strengthening, modeling and analytics, molecular work, operational research)

Highlights for BMGF scope across all areas of work:

1,960
Total Grants

9
Offices worldwide, HQ in Seattle

141
Countries

1,217
Grantees

2,173
Alumni

$7.0B
Total Charitable Support in 2022

41
Program Strategies

1,818
Employees

For the year ended December 31, 2022. Amount in U.S. dollars.

Our malaria program strategy and goals aim for an eradication pathway that minimizes deaths

Three strategy goals define our Pathway to Eradication

1 Drive down burden

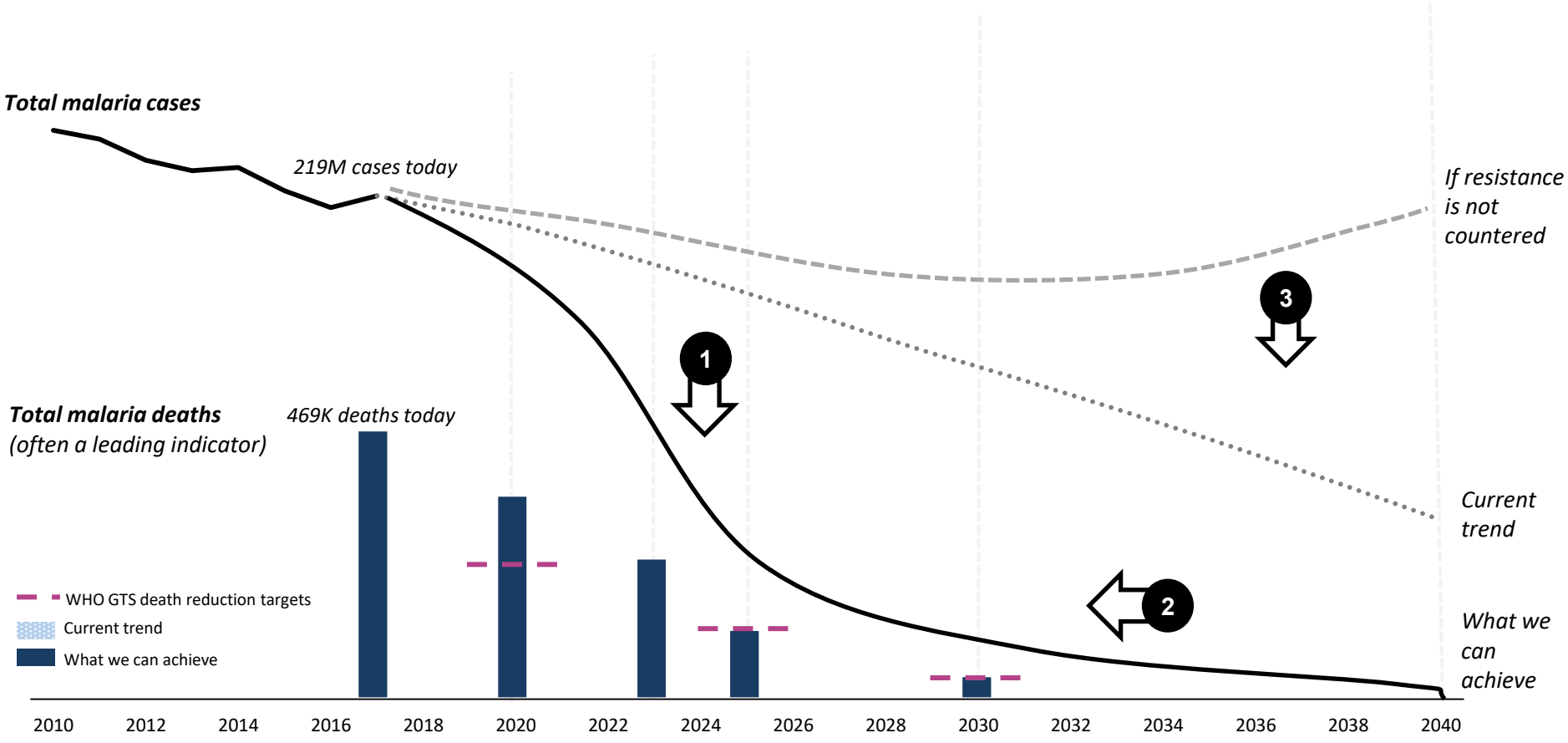
In the short- and medium- term, **scale surveillance + data-driven sub-national optimization, chemoprevention & case management in high burden settings** to reduce deaths and cases

2 Shorten the endgame

Create enabling environment for winning endgame in high endemic SSA by **investing in next-gen surveillance systems, MDR *Pf* elimination, and accelerating endgame R&D** today

3 Get ahead of resistance

Mitigate emergence of drug & insecticide resistance by **eliminating *Pf* in the GMS**, **developing a robust pipeline of AIs and analyzing entomological and genetic epi data** to quickly respond to biological threats (including resistance to insecticides in mosquitoes and resistance to diagnostic detection and drugs in the parasite) and to emerging species.



Overview of the foundation's malaria eradication investment portfolio

BMGF Malaria Eradication Direct Investment Budget and Example Grantees

(does not include our contribution to the Global Fund)

Over 2022-5, the Malaria PST has an approved budget of $1.16B, with a 2023 budget of $301M

Antimalarial Interventions

- ***Pf* & *Pv* diagnostics**
- **Pf drugs for treatment**
  - E.g., New drugs for resistance & S/MERC
- **Pv radical cure**
- **Lifecycle management**
- **Pf mAbs & drugs for prevention**
  - E.g., 2nd gen chemoprev.
- **Pf vaccine**

Vector Control

- **Insecticidal vector control**
  - E.g., dual AI LLINs, IRS, and ATSBs, launching new nets, tools for improved vector control surveillance
- **Modified mosquitoes**
  - E.g., Field sites, constructs for self-sustaining gene drive

Surveillance, Data, and Epidemiology

- **Routine systems and data**
- **Novel tools & strategies**
  - E.g., genetic epidemiology & EOCs
- **Surveillance partnerships**
  - E.g., Africa CDC
- **Data & modeling platforms**
  - E.g., Global transmission maps

Strategic Partnerships & Country Engagement

- **Subnational tailoring**
  - E.g., Data-based country planning (incl. high-burden geos)
- **Access to quality care**
- **Operational partnerships**
- **Market access & policy**
- **New product uptake**
  - E.g., Tafenoquine & G6PD test, new nets

Global Policy and Advocacy

- **Leadership & accountability**
  - E.g., RBM, ALMA, APLMA
- **Traditional donors**
- **Emerging donors**
  - E.g., China
- **Country political momentum**
- **Social acceptance of new tools**
  - E.g., Gene Drive

Digital Health for Malaria Eradication

- **Campaign digitization**
  - E.g., digital tools to track distribution and coverage of LLINs
- **Digital case management**
  - E.g., digital RDT readers
- **Innovation and R&D for malaria eradication**
  - E.g., software tools for vector identification

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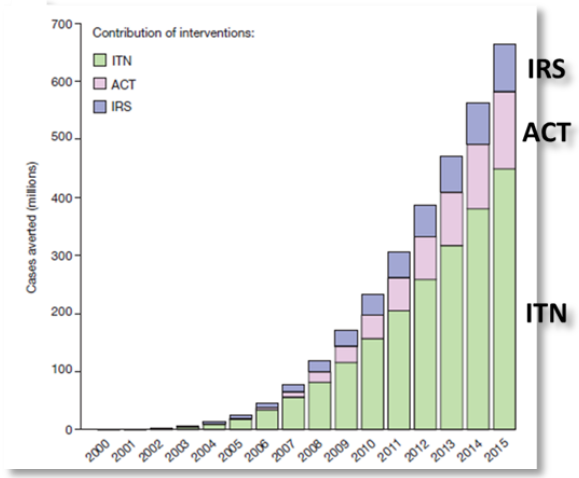
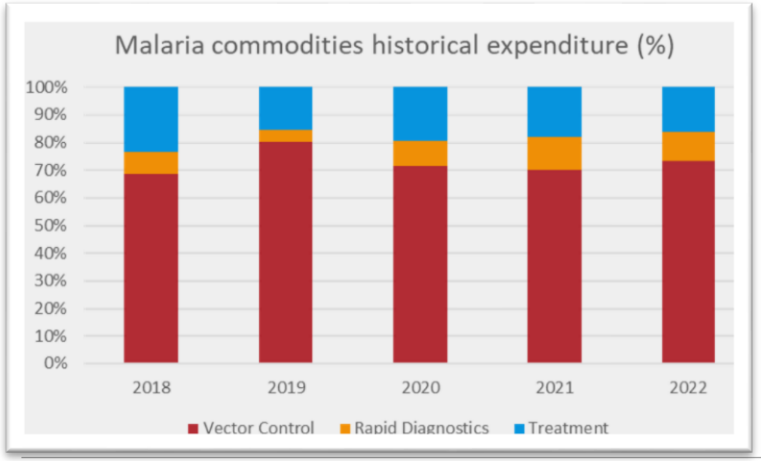
Why is there urgency for investment in vector control?

Since 2000, LLINs and IRS have contributed to the majority of malaria cases averted and are a significant part of malaria control budget



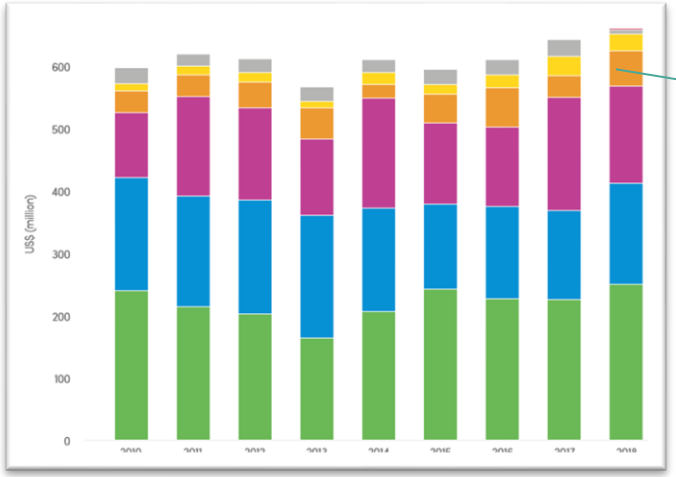
The effect of malaria control on Plasmodium falciparum in Africa between 2000 and 2015[1] is significant: **~80% of malaria cases averted are due to vector control interventions**



In terms of historical expenditure, **vector control commodities hold a significant portion of the budget for interventions**

Despite their important role in malaria control and addressing resistance across all malaria endemic areas, vector control tools made up only a small fraction of R&D funding, 2010–2018[3]….

Resistance in Anopheles mosquitoes to at least one class of insecticides is reported in **90% of malaria-endemic countries**, and **32% of the countries have reported resistance to all four classes[4]**.



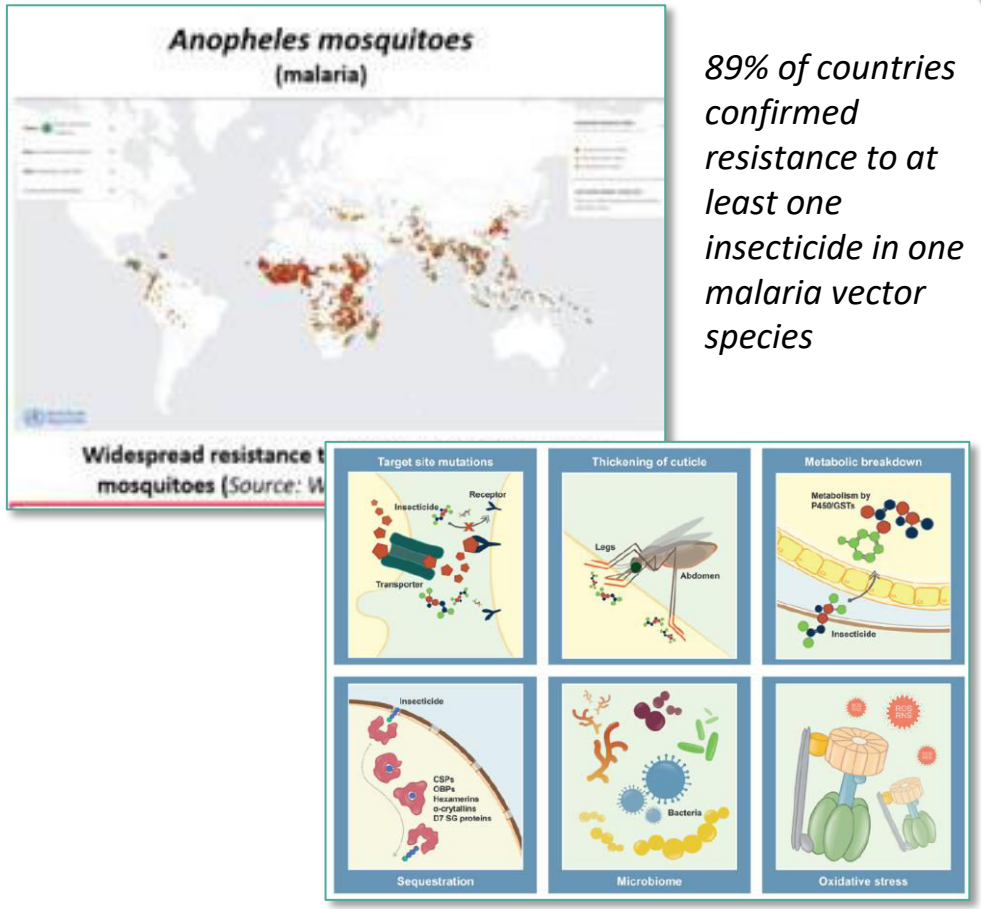
Budget for Vector Control R&D remains limited despite high impact of tools

- *Diagnostics*
- *Vector Control R&D*
- *Vaccines*
- *Basic research*
- *Drugs*
- *Unspecified*

1. Bhatt et al., Sept 2015 2. WHO Global report on insecticide resistance in malaria vectors, 2010-2016 3. WHO World Malaria Report 2019 4. IRS Mapper 2023

Value of innovation: Next generation bed nets helped mitigate intervention failure due to resistance

Risk: Failure of compounds in current pipeline

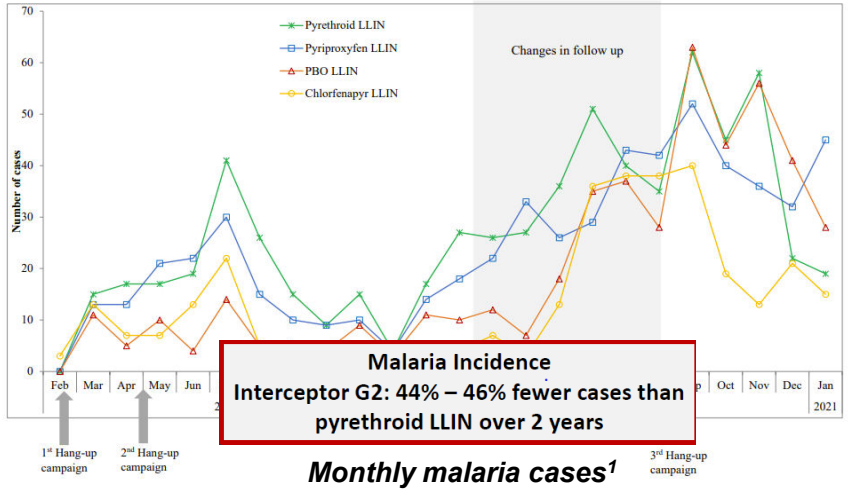


89% of countries confirmed resistance to at least one insecticide in one malaria vector species

Mitigation: Healthy product pipeline of novel chemistry

Next generation bednets (e.g. Interceptor G2, alpha-cypermethrin plus chlorfenapyr) have been shown to have a significant impact on malaria incidence and prevalence and be cost saving.

In Tanzania, the chlorfenapyr LLINs provided significantly better protection over 2 years than did pyrethroid LLINs; children aged 6 months to 14 years had 55% lower odds of having malaria 2 years after LLIN distribution, and children aged 6 months to 10 years had 44% lower malaria incidence over the 2 years[1].

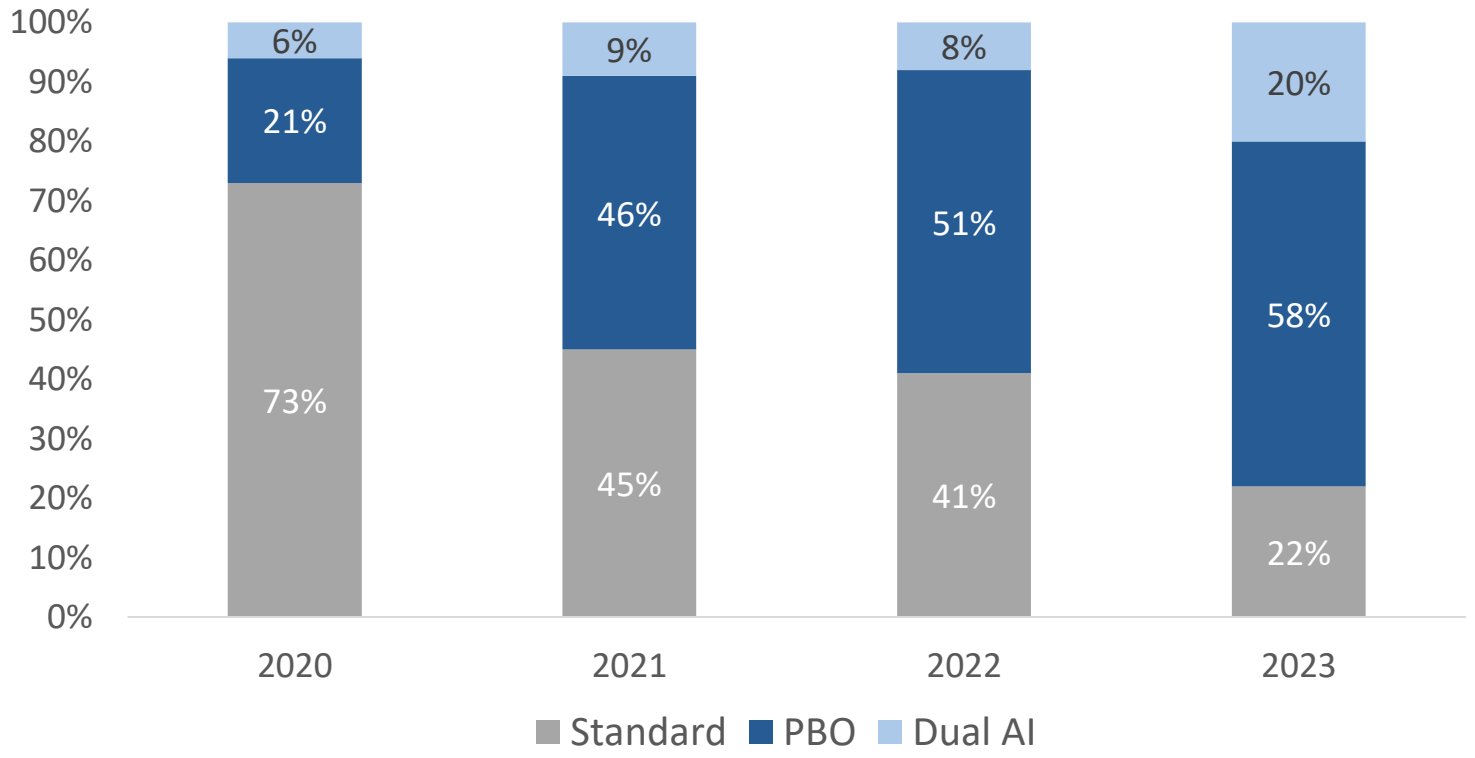


Monthly malaria cases[1]

1) Lancet. 2022 Mar 26;399(10331):1227-1241. doi: 10.1016/S0140-6736(21)02499-5. PMID: 35339225; PMCID: PMC8971961.

With the catalytic effect from the New Nets Project, next generation bed nets (PBO + Dual AI) now have ~80% market share

Market share by type of LLIN



Key takeaways

- **Dual AI represented 20% of LLIN supplied to Sub-Saharan Africa in 2023**, almost tripling market share since 2020
- The **New Nets Project,** led by IVCC and launched in 2018, had a **significant catalytic effect on the market**
- **Additional progress in 2023 will enable further market share growth**
  - New WHO recommendation of dual AI nets
  - Supplier diversification, with 2 manufacturers achieving PQ

Source: John Millener report, SSA, Key procurement agencies

Ongoing operational challenges are limiting progress against malaria…

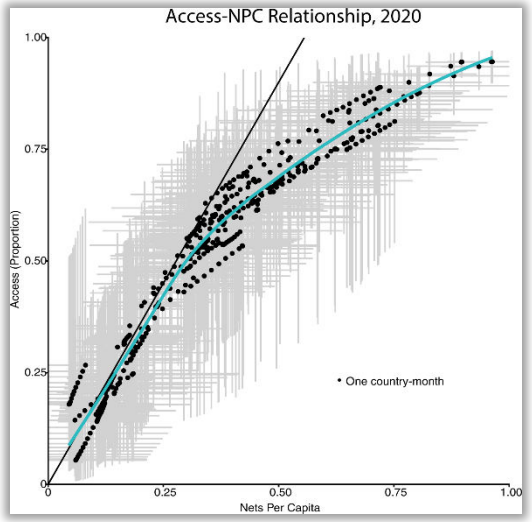
Ongoing operational challenges

While existing tools can work well in many contexts, **achieving the necessary coverage and usage levels is impossible in some geographies**

Operating environments in malaria endemic countries are complex, resulting in significant challenges for intervention delivery

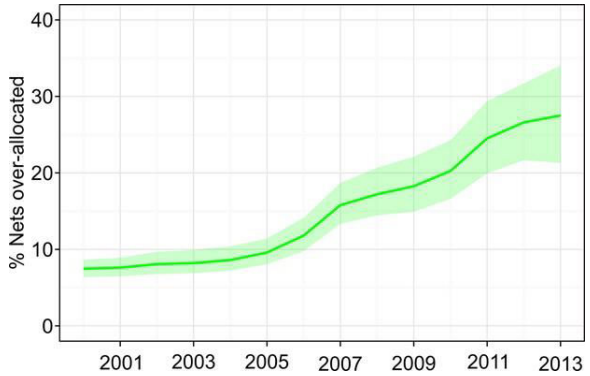
Inequity in approaches to intervention delivery **limits impact of interventions and concentrates burden** in high-risk populations

Decision-making is often not informed by data, leading to inefficient and less effective control strategies



Distributing additional bed nets per capita eventually results in diminishing returns, as operational and logistics challenges limit uptake

Overallocation of nets in Sub Saharan Africa has grown to 30%, a result of delivery inefficiencies



Figures sources: Bertozzi-Villa et al., Nature Communications 2021; Bhatt et al., "Coverage and system efficiencies of insecticide-treated nets in Africa from 2000 to 2017"

…and these challenges are compounded by new and growing threats

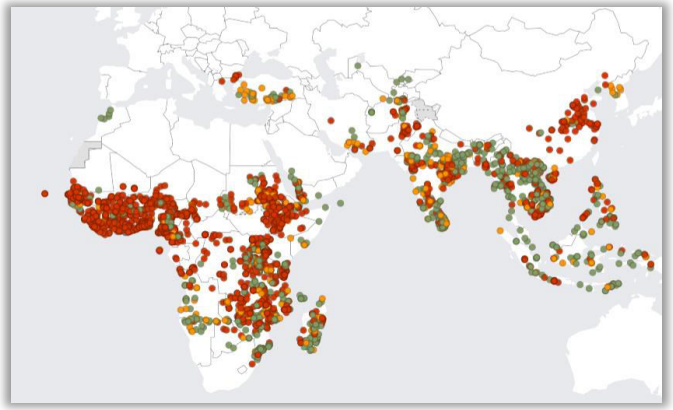
New and growing threats

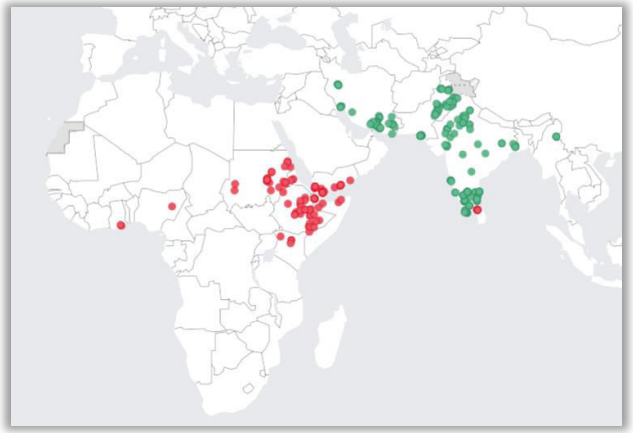
Resistance is expected to expand, limiting efficacy of existing toolkit and requiring new interventions to continue achieving progress

Newly emerging biological threats (e.g., expansion of *An. stephensi,* climate change) will also limit progress and require new approaches to intervention delivery in new geographies

While new tools are being developed, **our understanding of their comparative advantages and use cases is limited**

Resistance in Anopheles mosquitoes to at least one class of insecticides is reported in 90% of malaria-endemic countries…





…and new approaches will be required for other emerging threats, such as An. stephensi

Maps source: WHO Malaria Threats Map

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Vector control portfolio

Focus on tools and innovations for mosquito control, reflecting the PST's overall strategy in Malaria R&D.

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- **Insecticidal vector control**
  - E.g., dual AI LLINs, IRS, and ATSBs, launching new nets, tools for improved vector control surveillance
- **Genetic based vector control**
  - E.g., Field sites, constructs for self-sustaining gene drive

Surveillance, Data, and Epidemiology

- Surveillance, data use, and response
  - E.g., strengthening routine surveillance systems
- Molecular surveillance
  - E.g., genomics and informatics tools
- Modeling for malaria
  - E.g., geospatial and malaria modeling support

Strategic Partnerships & Country Engagement

- Sub-national tailoring
  - E.g., Data-based country planning
- Access to quality care
- Optimized prevention methods
  - E.g., scaling chemoprevention
- Global, regional, and country partnerships
  - E.g., technical support units, regional initiatives

Policy, Advocacy & Communications

- Leadership & accountability
  - E.g., RBM, ALMA, APLMA
- Traditional donors
- Emerging donors
  - E.g., China
- Country political momentum
- Social acceptance of new tools
  - E.g., Gene Drive

Digital Health for Malaria Eradication

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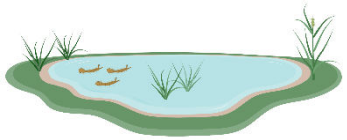
- Innovation and R&D for malaria eradication
  - E.g., software tools for vector identification

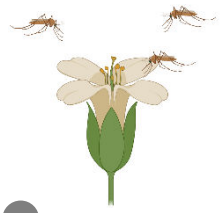
We invest in innovations across the mosquito life cycle and the entosurveillance cascade

xx Existing interventions / investments
xx Recent innovations / investments (deep-dives follow)

Mosquito life cycle



Development from egg to adult
- *LSM*
- *Tech-enabled LSM* 1



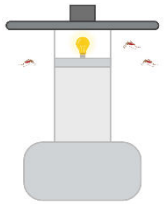
Sugar-feeding (throughout life)
- *ATSBs*

Mating
- *Genetic-based vector control* 2

Blood-feeding (female)
- *ITNs (e.g., dual AI)*
- *Endectocides*
- *Spatial repellents* 3

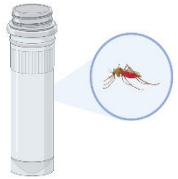
Resting (female, prior to egg-laying)
- *IRS*

Entosurveillance cascade

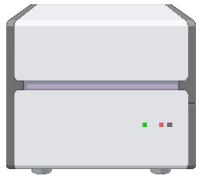


Mosquito collection
- *Simple traps (e.g., light trap)*
- *Human landing catch*
- *Smart traps (e.g., Premonition)*

Morphological identification
- *Field entomologist*
- *VectorCAM* 4



Sample preparation
- *Laboratory*
- *bCUBE* 5

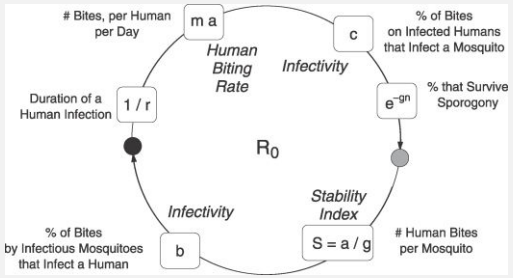


RT-PCR
- *Laboratory*
- *bCUBE* 5

1 Tech-enabled larval source management may facilitate a shift away from the “few, fixed, and findable” paradigm

LSM is not funded or widely recommended today given its limitations…

- **Challenges with scaled implementation:** Requires high-coverage of habitats every 2 weeks; WHO recommends LSM on habitats that are ‘**few, fixed, and findable**’
- **Other limitations:** LSM acts on linear term in R0 of vector-borne disease, in contrast to LLINs, which act on the exponential mortality term



…but technological advances could unlock new use cases and facilitate a shift away from the “few, fixed, and findable” paradigm

Remote sensing through satellites and drones

- Free and paid satellite imagery at varying resolutions
- Drone-based imaging
- Passive drone-based sensors for thermal and near infrared imaging
- Active drone-based sensors such as radar or lidar

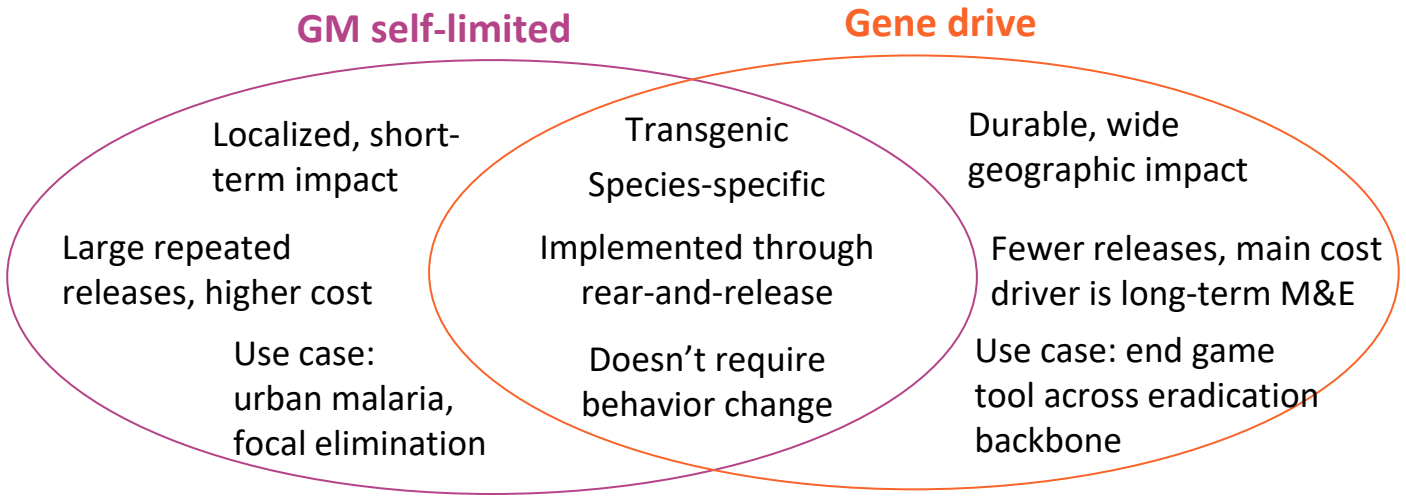
AI/ML algorithms to map productive habitats and generate delivery plans

- AI/ML algorithms including a variety of data (e.g., hydrology, topography, land cover, soil type) to identify productive larval habitats
- Algorithms to generate delivery plans

Drone-based or hybrid delivery models

- Fixed wing or quadcopter drones
- Aerial delivery
- Hybrid models (e.g., humans carry quadcopters in truck)

2 Genetic-based vector control could enable area-wide vector control, providing equitable protection and achieving significant impact



Epidemiological modeling predicts:

- **>50% of clinical cases averted** when primary vectors are targeted
- Layering preventative tools provides **additive impact**

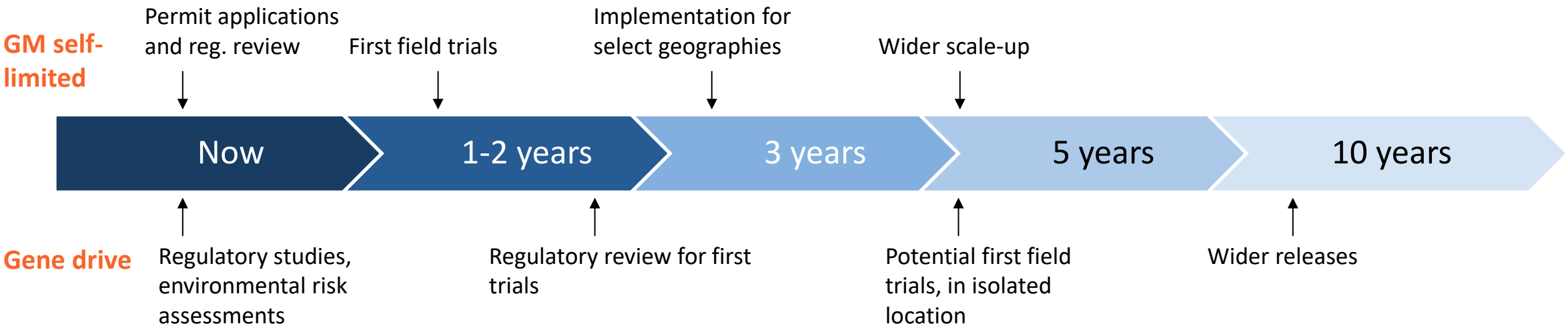
GBVC is meant to address 3 gaps:

1. Regions with outdoor biting and high transmission despite intervention scale-up
2. Hard-to-reach areas (gene drive)
3. Elimination and prevention of reintroduction

GBVC products currently under evaluation

Lab development	Regulatory approvals for field testing	Field trials	Implementation
TARGET MALARIA, UCI MALARIA INITIATIVE, transmission:zero *An. gambiae* gene drive	TARGET MALARIA *An. gambiae* self-limited OXITEC *An. albimanus* and *An. stephensi* self-limited	*No products for malaria control are in field trials*	OXITEC *Aedes aegypti* self-limited (DENV, ZIKV)

2 Genetic-based vector control is expected to reach scale in 5-10 years, though many questions and challenges remain



Remaining open questions

Funding

- How can we better understand the implementation costs of GBVC?
- How do we encourage other funders to become more involved in gene drive?
- Do we need to be funding more work on remediation or limited drives?

Logistics technologies

- How will rearing, transportation, release, and monitoring happen for gene drive, and do we need fund development of better technology now?

Engagement models

- How do we scale good models of stakeholder engagement to a larger audience?
- How do we ensure the gender equity & inclusion in gene drive research programs?

3 Spatial repellents developed by SC Johnson have emerged as a new intervention to target blood-feeding mosquitoes

Spatial repellent products

Spatial repellents are hung in semi-enclosed spaces (e.g., homes) to repel mosquitoes

Guardian™

Duration per unit:
Up to one year[1]

Mosquito Shield™

Duration per unit:
Up to one month[2]

Benefits and considerations

Highly efficacious, demonstrating in-field efficacy of one year (91% average reduction in bloodletting)

Long-lasting and easy to deliver and install, increasing likelihood of uptake

Commitment to local manufacturing by SC Johnson, beginning investment in Kenya

May 2025 target for inclusion in WHO guidance and PQ of products

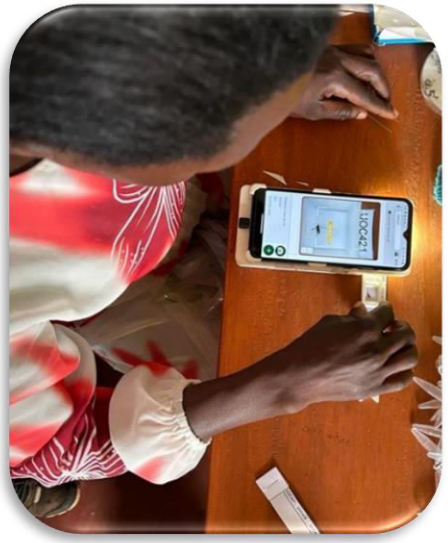
1. 91% reduction in blood-feeding, Ifakara Health Institute, Tanzania, 2022-23
2. 73% reduction in blood-feeding, Ifakara Health Institute, Tanzania, 2019

Source: SC Johnson

4 VectorCAM leverages AI/ML to address pain points in the morphological identification process for low-resource settings

What is VectorCAM?

A low-cost handheld field tool that will enable community health workers to morphologically identify mosquito species, thereby increasing surveillance coverage and timely reporting.



VectorCAM benefits

- ✓ **Task shift vector species identification process** to unskilled workers/ volunteers and enable capacity at scale
- ✓ **Reduce costs of sentinel site operations** (by avoiding expert travel & time, and/or costs associated with molecular identification)
- ✓ **Add capability to identify & flag presence of invasive species** that are programmatically important (e.g., *An. stephensi* alert)
- ✓ **Automate and digitize aggregate reporting,**thereby enabling access to timely and accurate entosurveillance data

Components optimized for low-resource settings

Locally-running AI algorithm can work offline

Android app that can run on a low-cost smartphone

Low-cost, low-maintenance hardware

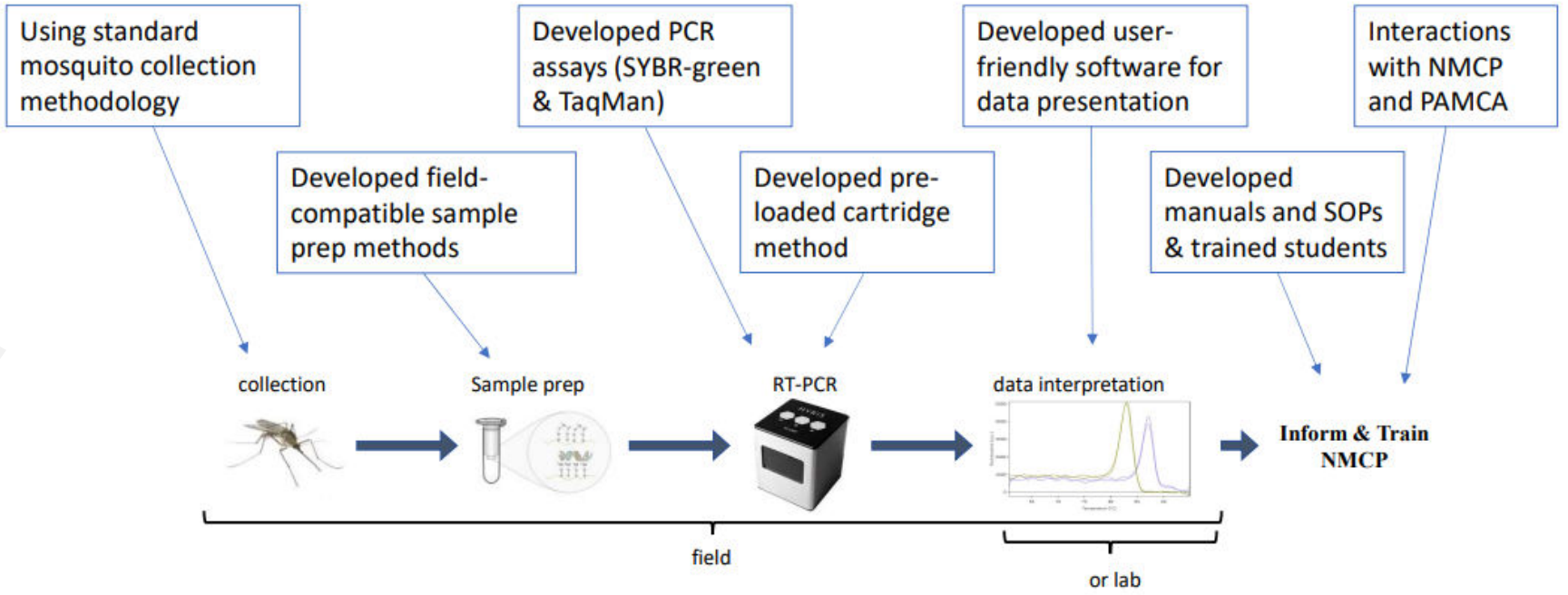
5 bCUBE is an RT-PCR machine that can be used in the field, accelerating processes for insecticide resistance surveillance

Objectives of the bCUBE project

- Develop a qPCR-based diagnostic system for mosquito insecticide resistance marker monitoring at the sample collection side in the field
- Eliminate need for sample transportation and analysis at a central lab, which typically results in a 6-12 month delay in informing IRS campaign decisions by NMCPs

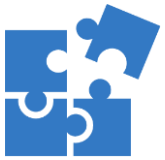
bCUBE has achieved significant process to date

Potential next steps include a collaboration with VectorCAM and a pilot to compare outcomes to a traditional entosurveillance workflow



Tools we have today will not be sufficient to eradicate malaria by target timelines…

…but rapid investment by the global community in transformational tools can bend the curve toward eradication



New tools are becoming available, and as the toolkit grows we need to clarify when and where they should be deployed

We need to **collaborate more effectively** to streamline introduction and scaling of these new tools

To address new and growing challenges and shorten the endgame, we need to **align on an accelerated plan**

Thank you for your time!