Swiss TPH
Swiss Tropical and Public Health Institute
Schweizerisches Tropen- und Public Health-Institut
Institut Tropical et de Santé Publique Suisse

Associated Institute of the University of Basel

Department of Epidemiology and Public Health
Health Interventions Unit
New Vector Control Interventions Group

Building on Success – Malaria Control and Elimination
Swiss TPH Winter Symposium 2016

New tools and innovations in vector control

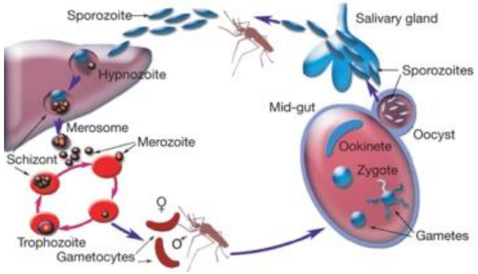
Sarah Moore

IFAKARA HEALTH INSTITUTE
research | training | services

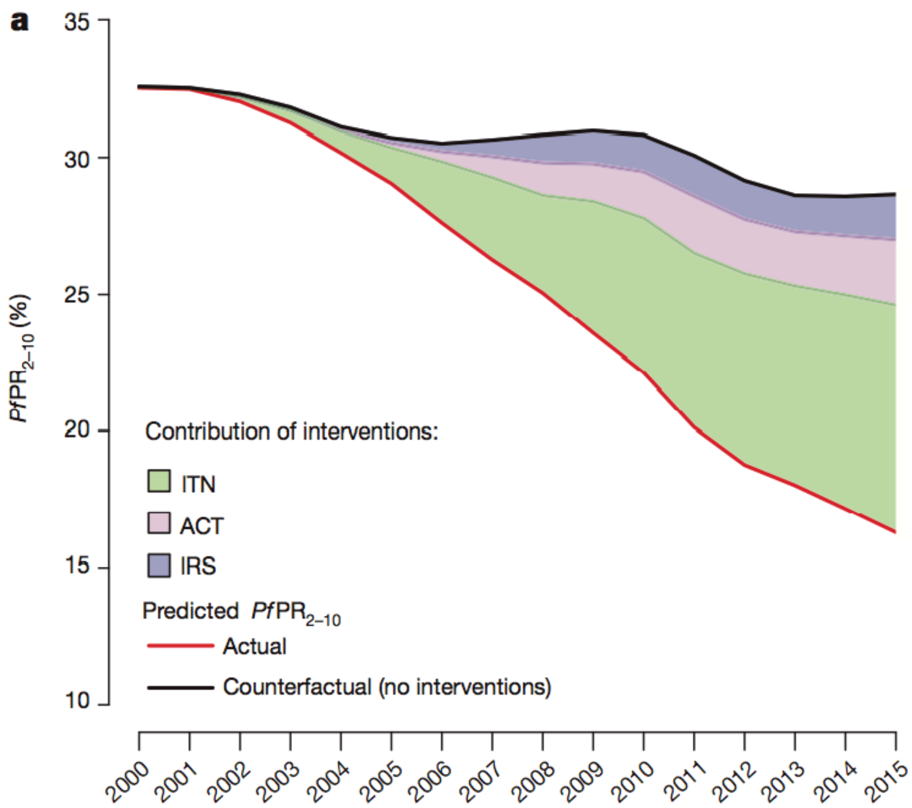
What is a new Tool?

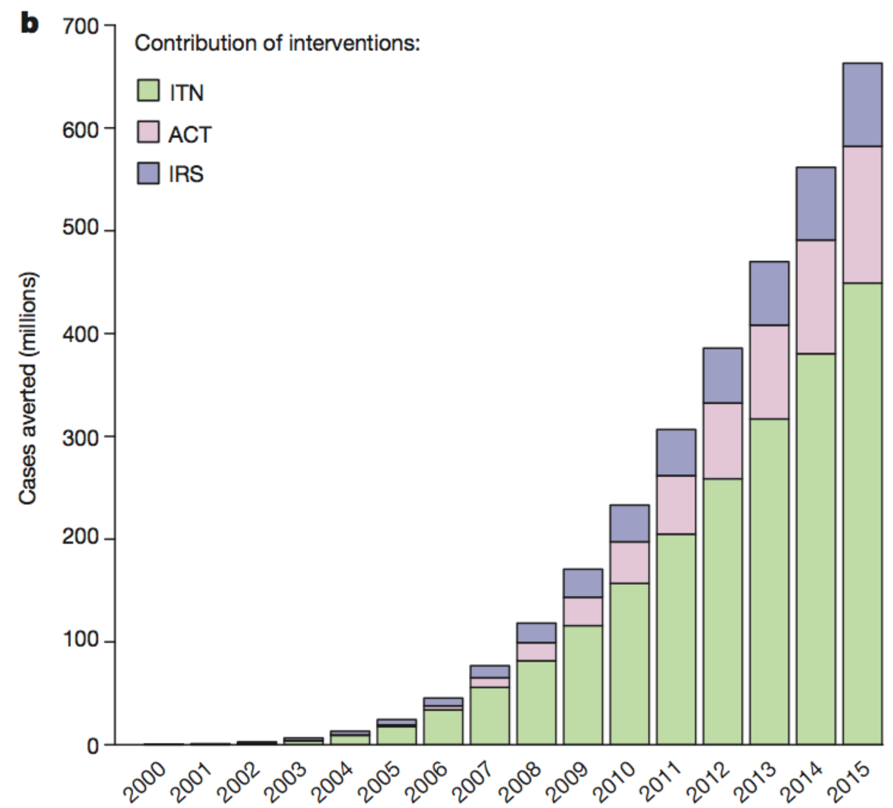
- A product class or product claim in vector control
- Shares a *common entomological mechanism of action* to reduce infection
- It requires evidence of epidemiological efficacy to substantiate product claims for impact on disease.
- May have several product claims, which need specific evaluation methods and assessment of impact.
- New interventions may require new evaluation methods and new guidance for deployment.






Vector control really works when you use the right tool





We estimate that interventions have averted 663 (542– 753 credible interval) million clinical cases since 2000. Insecticide-treated nets, the most widespread intervention, were by far the largest contributor (68% of cases averted). Bhatt et al (2015) Nature 526

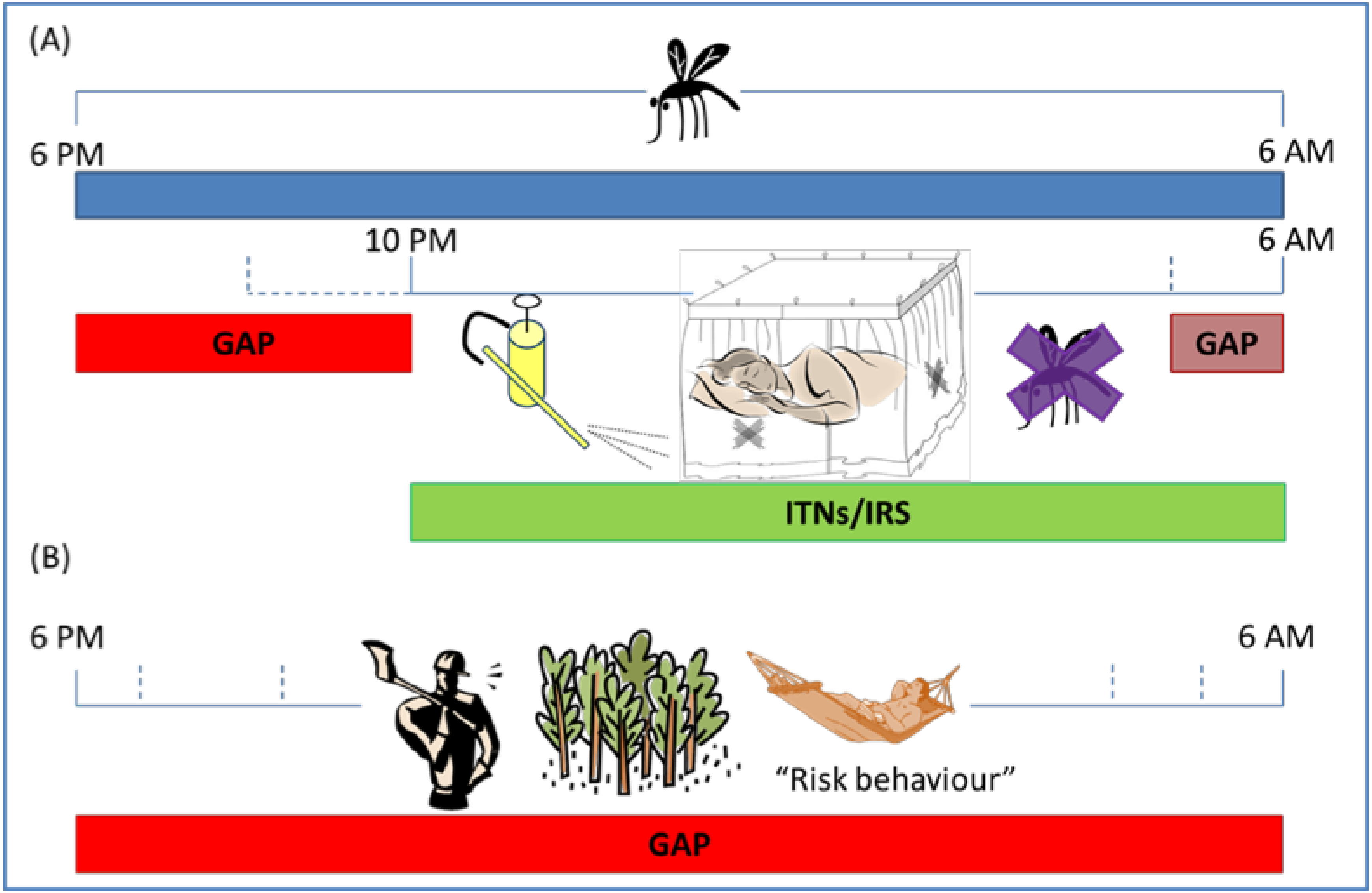


Figure 2. Protection 'gap' when only indoor insecticide-based vector control measures are applied. Anophelines generally bite between 6pm and 6am. ITNs will only protect from infective bites that are acquired indoors, and during sleeping time. IRS only target mosquitoes that rest indoors. Therefore, there is a gap in protection both indoors and outdoors before and after people go to bed (A), but also for people conducting outdoor activities during the night (i.e. 'risk behaviour') (B).

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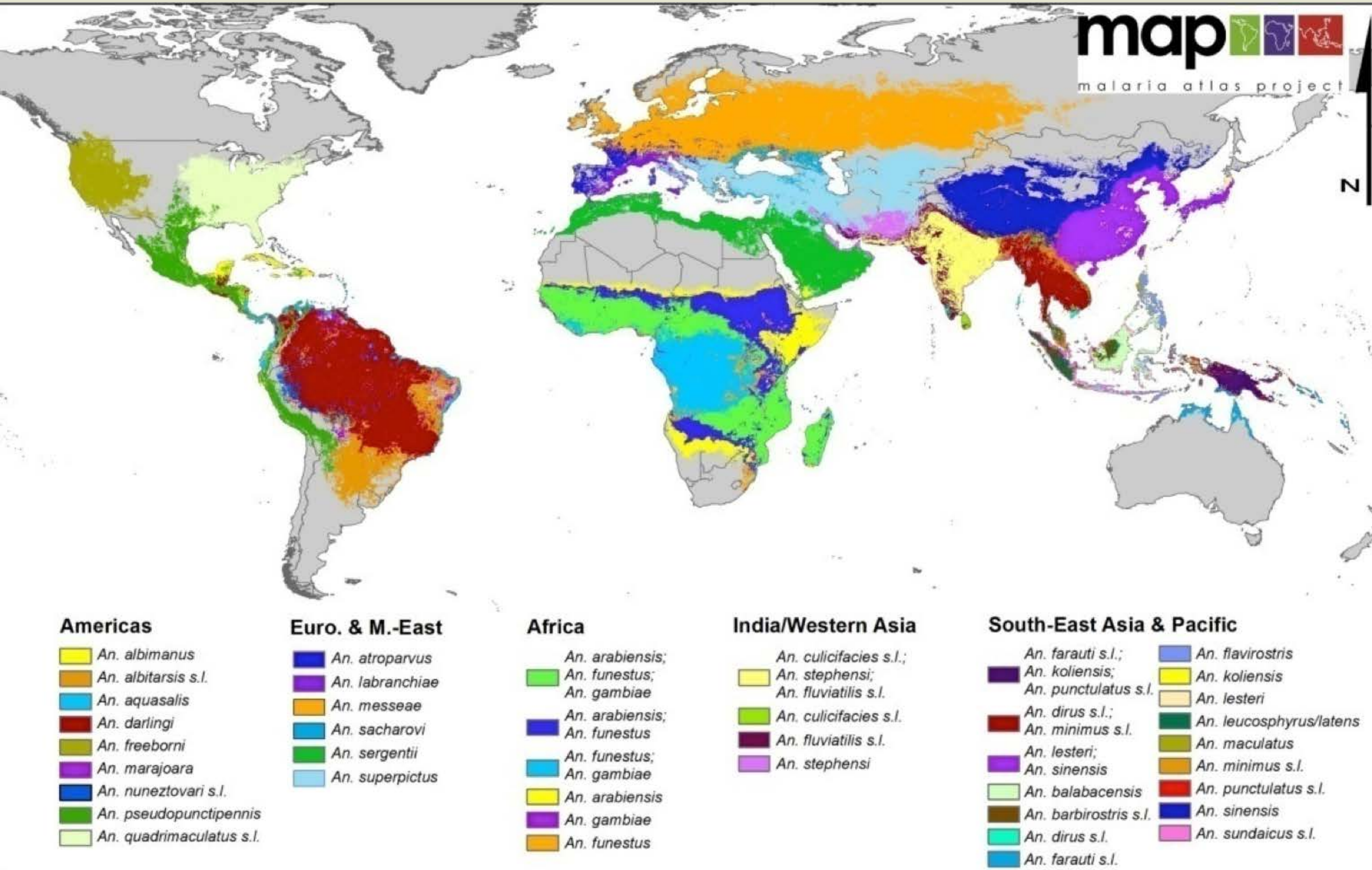
map
malaria atlas project
N
Americas
An. albimanus
An. albitarsis s.l.
An. aquasalis
An. darlingi
An. freeborni
An. marajoara
An. nuneztovari s.l.
An. pseudopunctipennis
An. quadrimaculatus s.l.
Euro. & M.-East
An. atroparvus
An. labranchiae
An. messeae
An. sacharovi
An. sergentii
An. superpictus
Africa
An. arabiensis; An. funestus; An. gambiae
An. arabiensis; An. funestus
An. funestus; An. gambiae
An. arabiensis
An. gambiae
An. funestus
India/Western Asia
An. culicifacies s.l.; An. stephensi; An. fluviatilis s.l.
An. culicifacies s.l.
An. fluviatilis s.l.
An. stephensi
South-East Asia & Pacific
An. farauti s.l.; An. koliensis; An. punctulatus s.l.
An. dirus s.l.; An. minimus s.l.
An. lesteri; An. sinensis
An. balabacensis
An. barbirostris s.l.
An. dirus s.l.
An. farauti s.l.
An. flavirostris
An. koliensis
An. lesteri
An. leucosphyrus/latens
An. maculatus
An. minimus s.l.
An. punctulatus s.l.
An. sinensis
An. sundaicus s.l.

When Bill Gates and his wife Melinda visited Tanzania mid last year, an entomologist at the Ifakara Health Institute in Dar es Salaam told them that "Mosquitoes are smart…we must be smarter."

Prosper Chaki present his findings to Bill and Melinda Gates

"The Red Queen has to run faster and faster in order to keep still where she is. That is exactly what you all are doing!"

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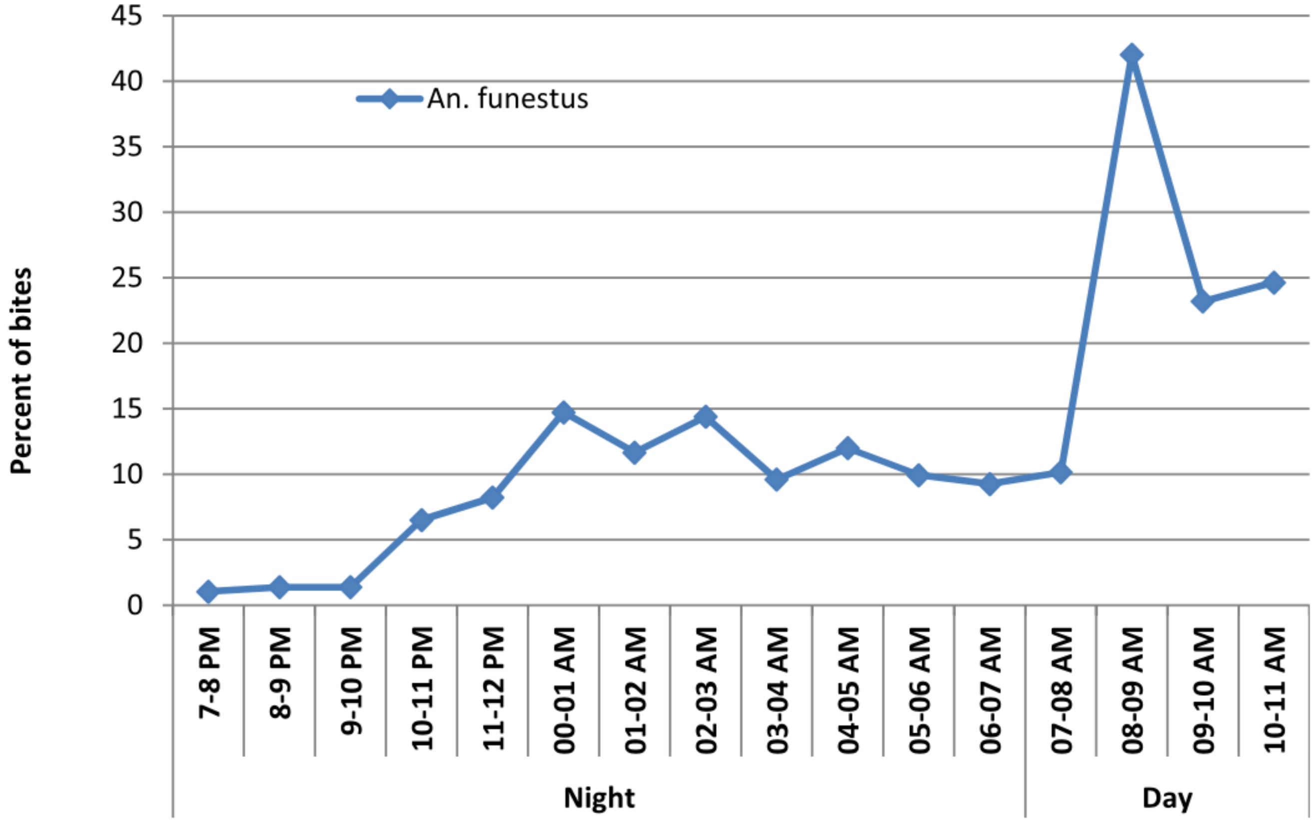
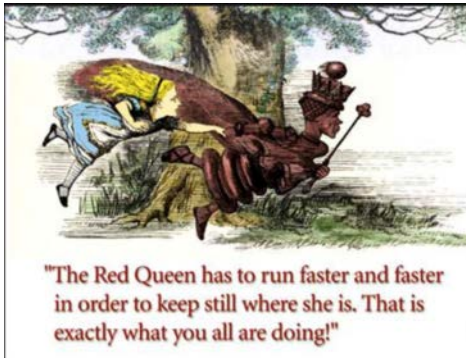


Figure 2 Trends in the biting cycle of *Anopheles funestus* night and dayly human landing catche after the implementation of LLINs (cumulated number of bites of *An. funestus* per hour by total number of bites per night x 100).

Sougoufara et al. Malaria Journal 2014, 13:125



New vector control tools in process and timelines for policy development

Tool	Prototype	1: Concept	2: Efficacy (Ento)	3: Efficacy (Epi)	Risk Assess.	Specifi-cations	Policy Review
Resistance targeting products	PermaNet 3.0 LN	✓	✓	*?*	✓	✓	**?**
Microbial Control	Wolbachia	✓	✓	**on going**	**on going**	**on going**	***2017***
Spatial Repellents	Transfluthrin passive emanator	✓	✓	**on going**	***planning***		***2017***
Vector traps for disease management	A LOT / TNK / AGO / In2Trap	✓	✓	**on going**	***planning***		***2018***
Systemic insecticides	Rodent bait	✓	✓	**on going**			***2018***
Lethal House Lures	Eave tubes and bricks	✓	✓	**on going**			***2019***
Genetic manipulation	OX513A Aedes aegypti	✓	✓	**on going**	**on going**	**on going**	***2017***
Attract and kill baits	Attractive Toxic Sugar Bait	✓	✓	**on going**			***2019***

Slide courtesy of Raman Velayudhan

Operational

New Tools Currently in the Development pipeline

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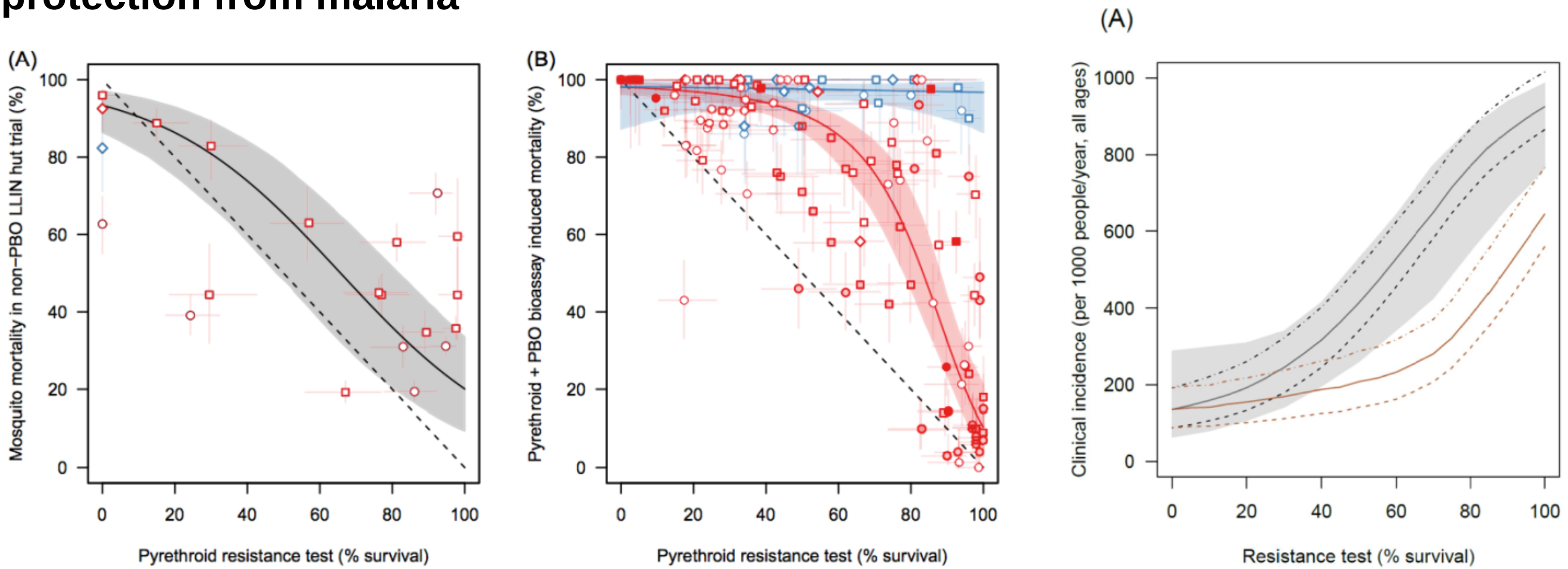
New Generation Bednets – data from a modelling study predicts increased protection from malaria



As resistance (x) increases, the mosquito mortality (y) declines

As resistance (x) increases, the mosquito mortality (y) declines more slowly with PBO added

As resistance (x) increases, the number of clinical cases in a population (y) increases

Churcher et al. eLife 2016;5:e16090. The impact of pyrethroid resistance on the efficacy and effectiveness of bednets for malaria control in Africa

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Impact of PermaNet 3.0 on entomological indices in an area of pyrethroid resistant *Anopheles gambiae* in south-western Nigeria

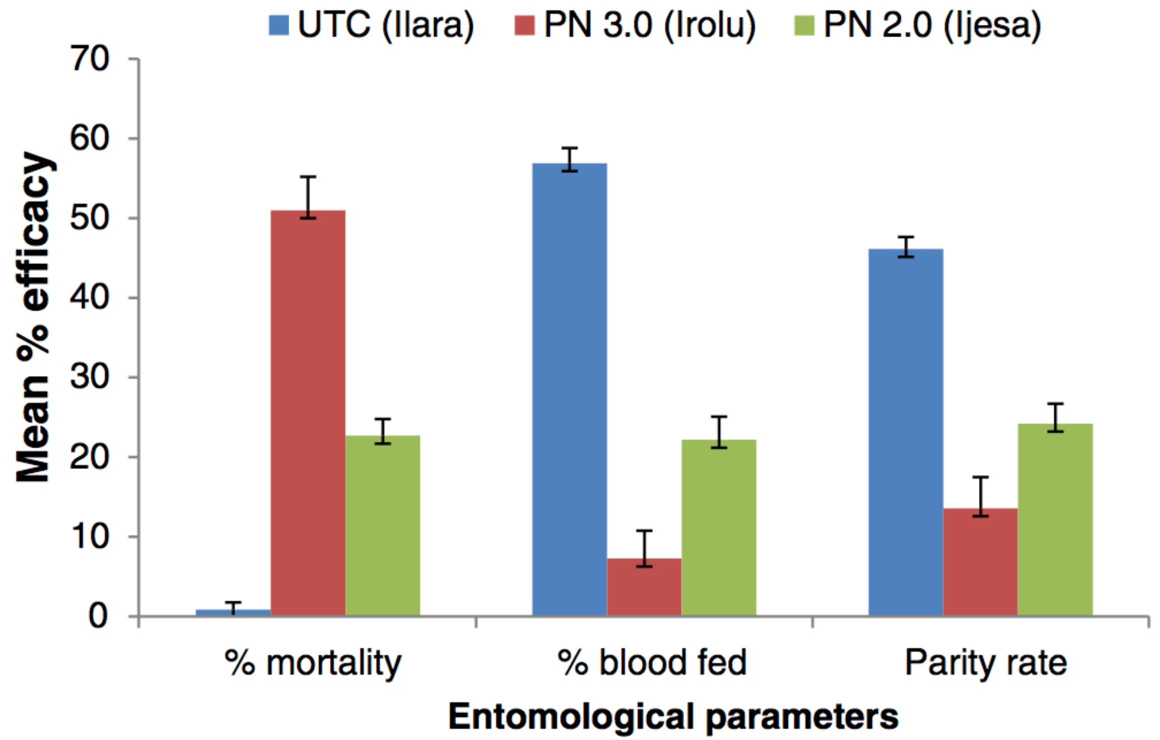

Figure 4 **Geometric mean of percentage mortality, blood feeding and parity rate for *An. gambiae s.s.* collected indoor during 12-months post intervention at Ilara, Irolu and Ijesa.**

Awolola et al. Parasites & Vectors 2014, 7:236

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Global **Malaria** Programme

WHO-COORDINATED MULTI-COUNTRY EVALUATION

Implications of insecticide resistance for malaria vector control

NOVEMBER 2016

✔

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IVCC Strategic Roadmap

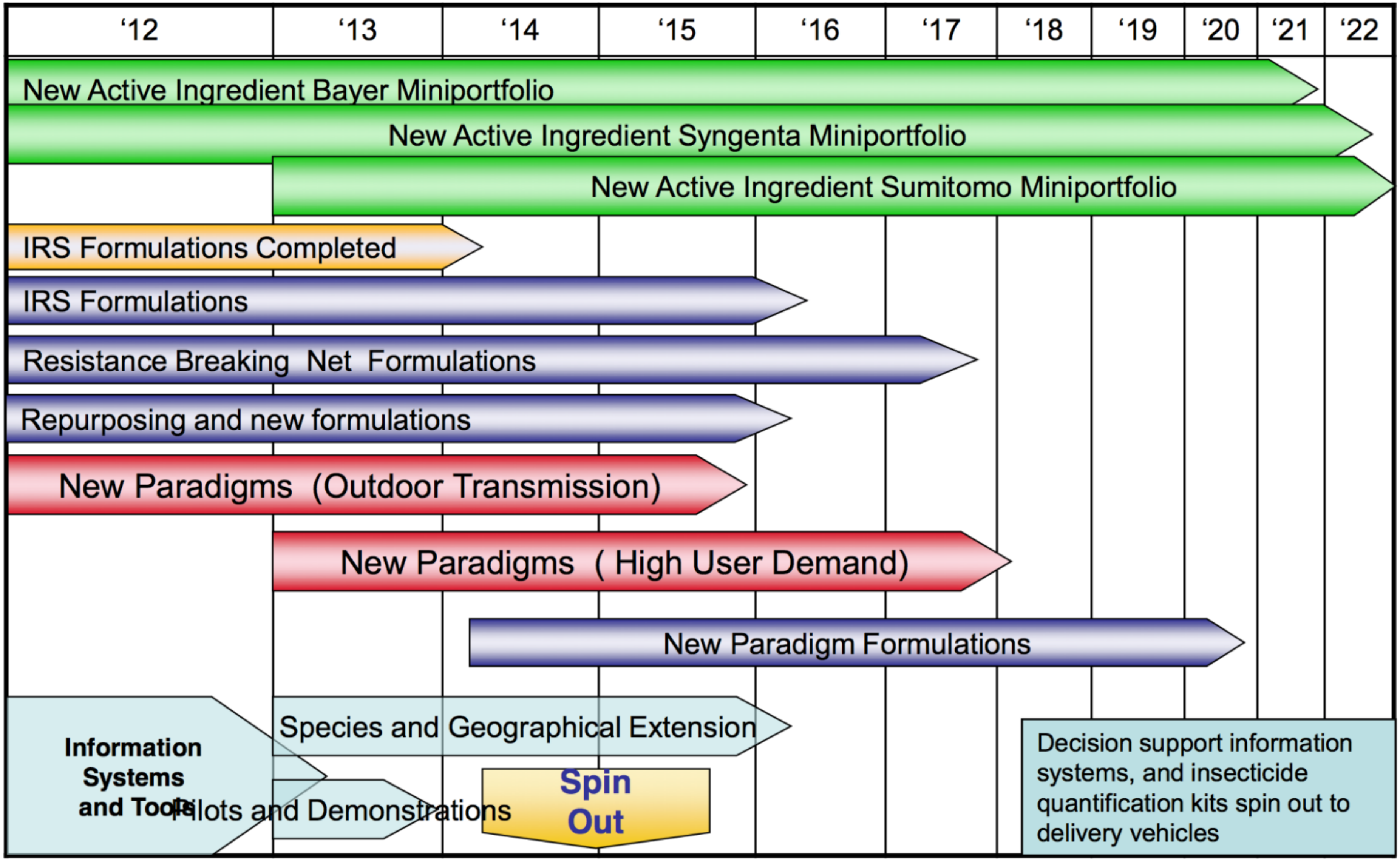
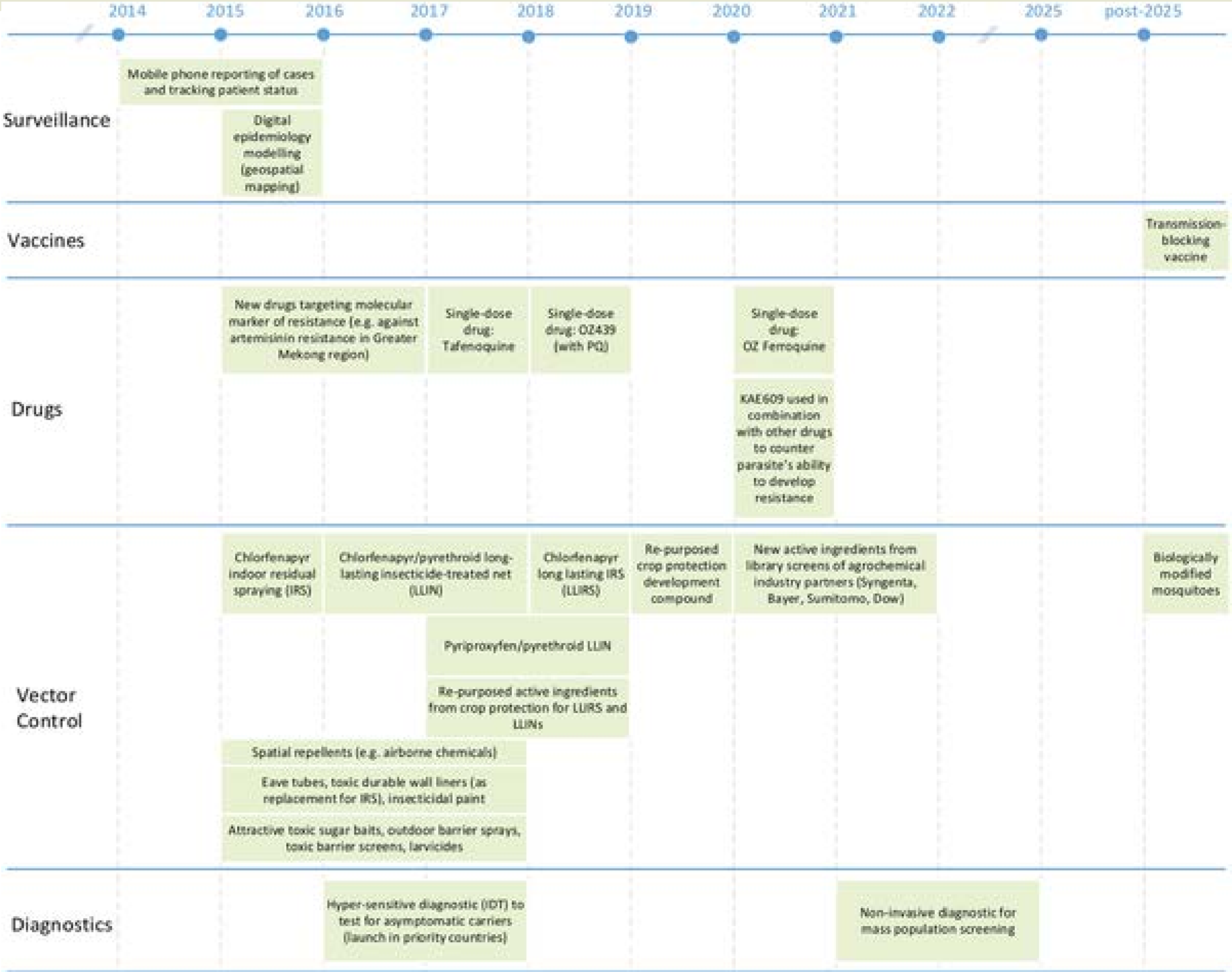


Fig 1. Projected time periods for introduction of novel malaria technology.



Hemingway PLOS Biology 14(3): e1002380. doi:10.1371/journal.pbio.1002380

NgenIRS

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Saving lives and improving health by making the best insecticides available to control malaria.

4,500,000	compounds reviewed
100,000	primary screened
20,000	secondary screened
27	chemical classes
9	in final review stage
3	for full development

Eave Tubes

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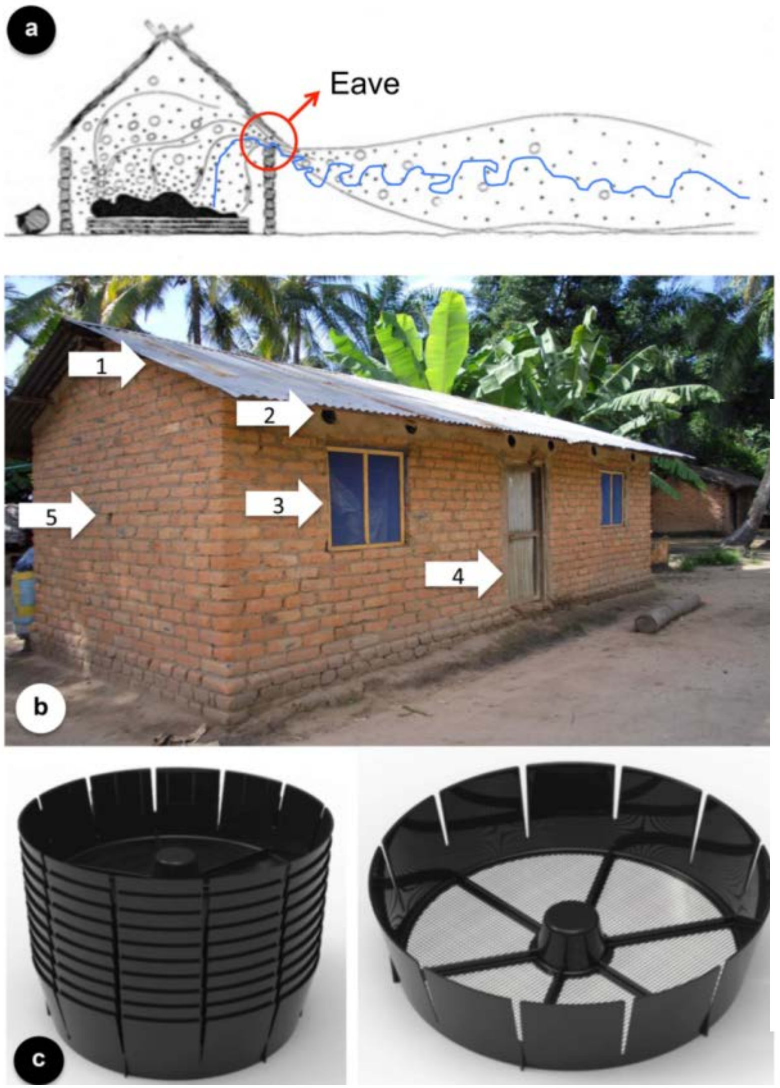
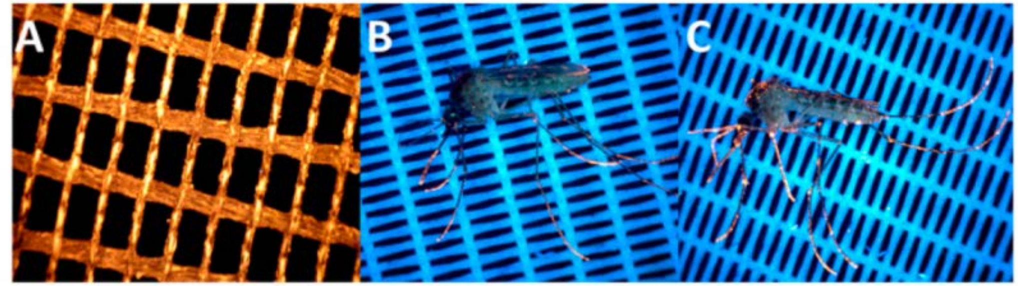
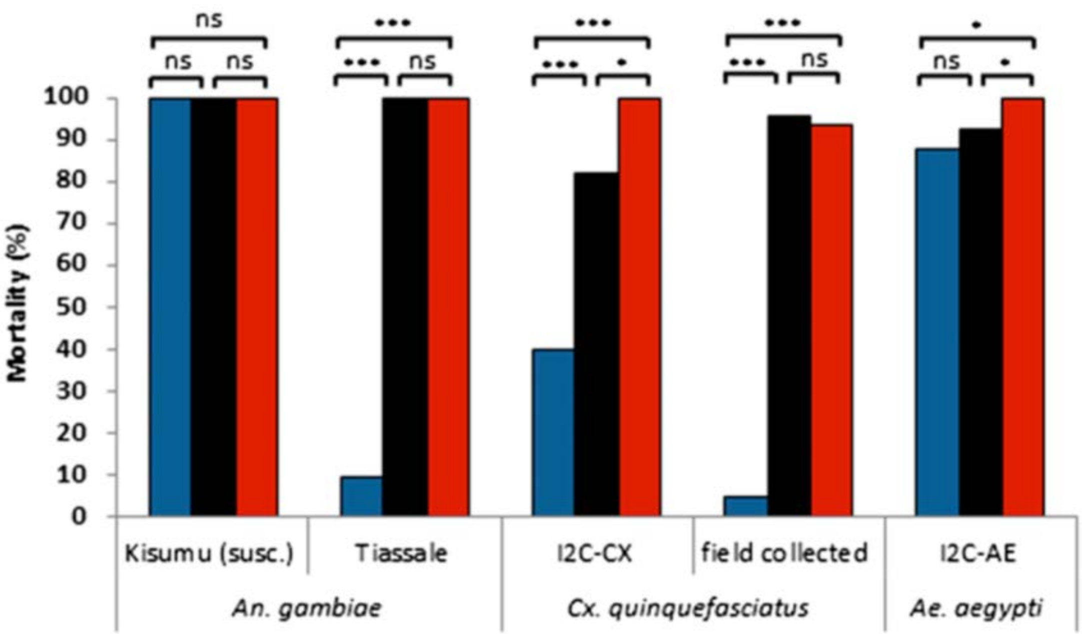
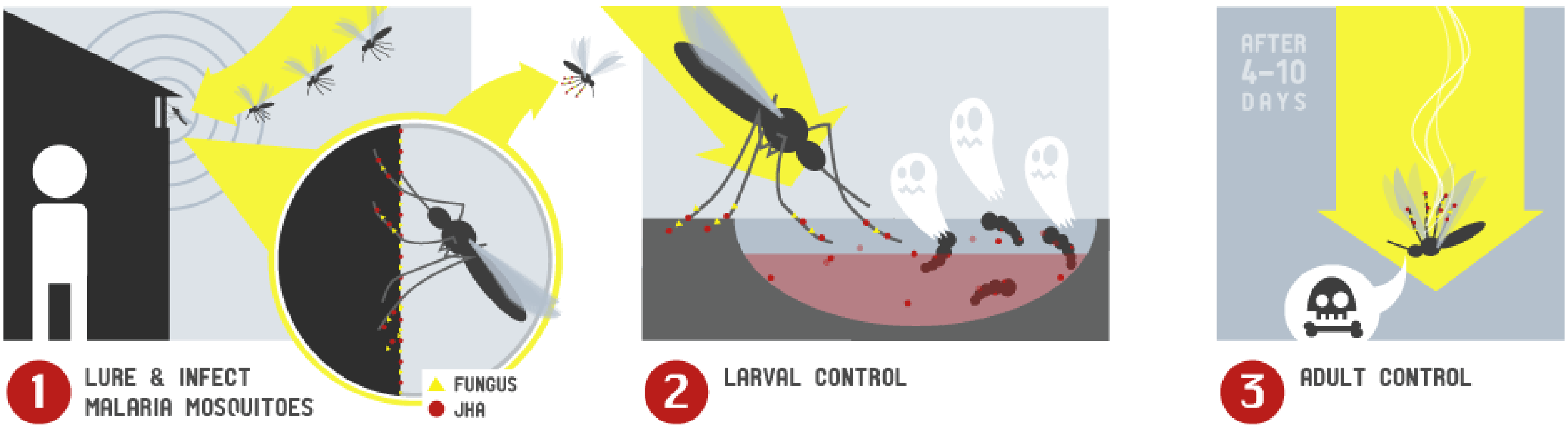






Andriessen (2015) *Proc Natl Acad Sci U S A* **112**(39):12081-12086. / Knols (2016) **Eave tubes for malaria control in Africa: an introduction**. *Mal J* , **15**:404.



Mosquito contamination with eave tubes

Entomopathogenic fungus

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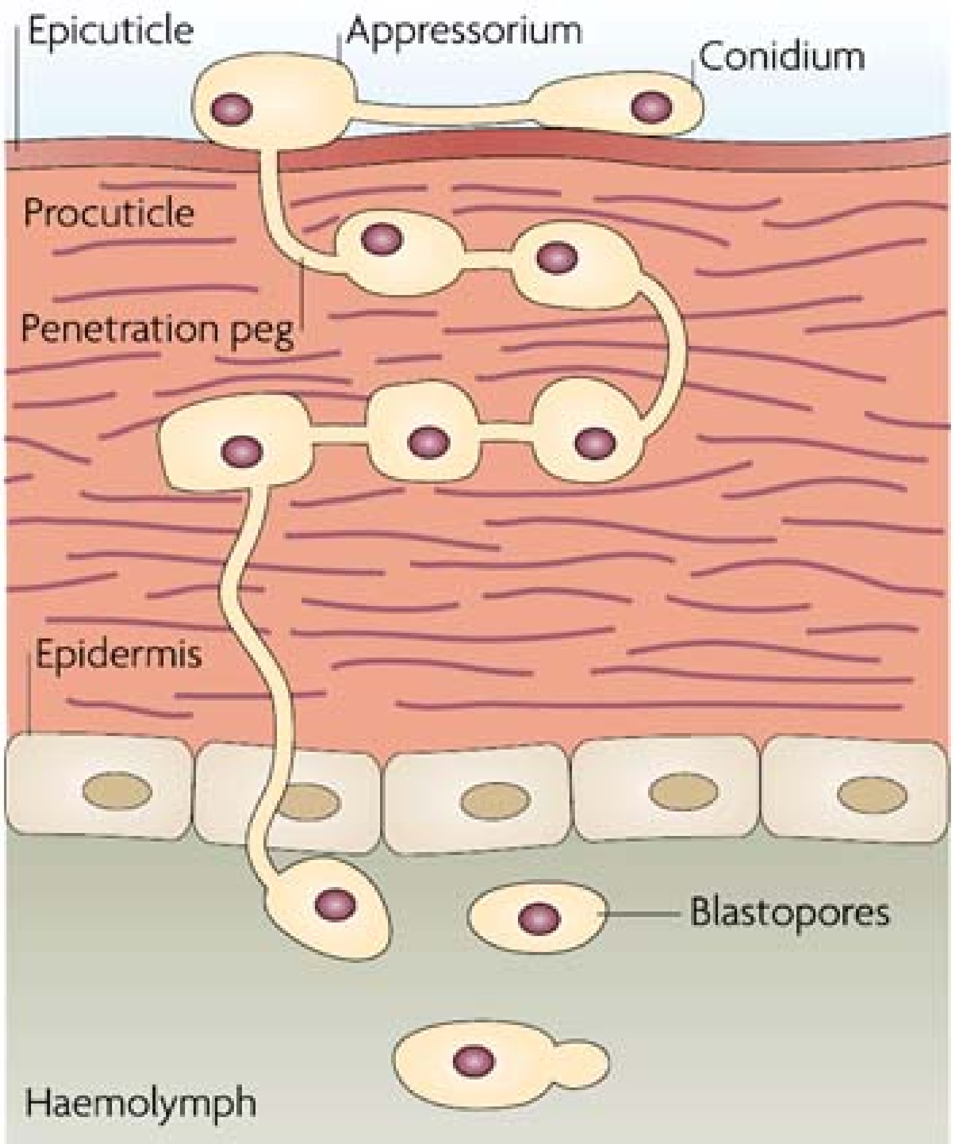
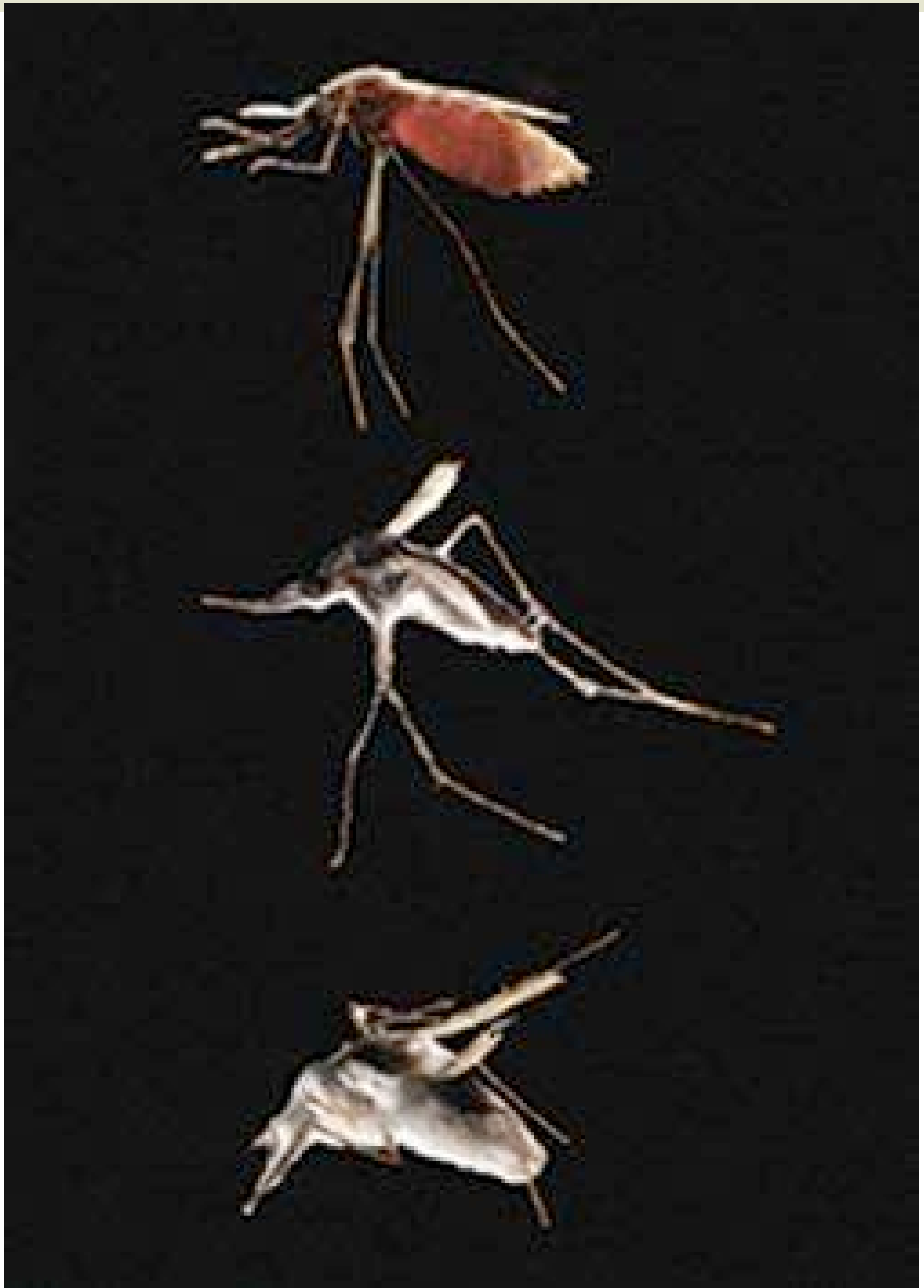
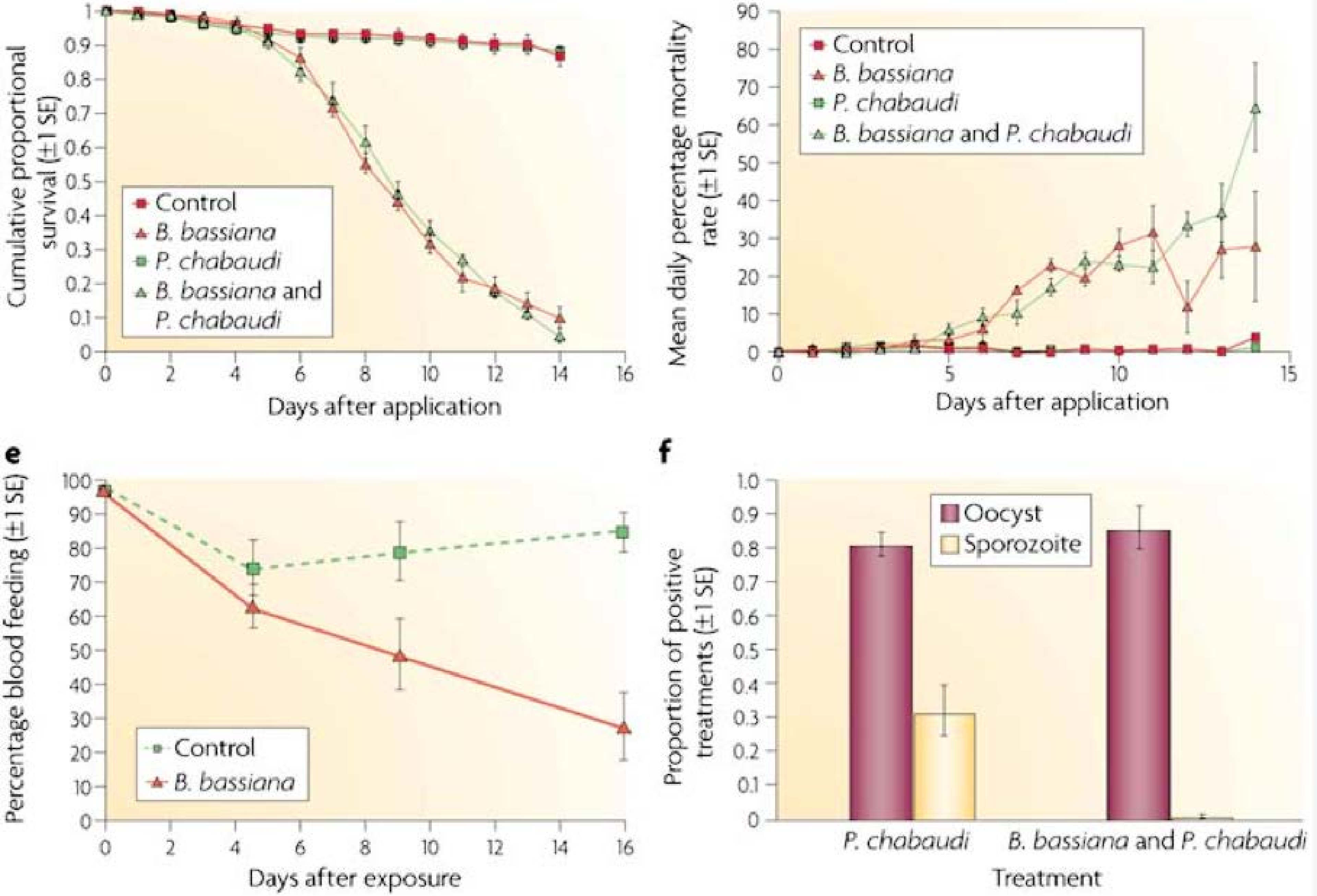





Cumulative proportional survival (±1 SE)
Days after application
Control
B. bassiana
P. chabaudi
B. bassiana and P. chabaudi
Mean daily percentage mortality rate (±1 SE)
Days after application
Control
B. bassiana
P. chabaudi
B. bassiana and P. chabaudi
e
Percentage blood feeding (±1 SE)
Days after exposure
Control
B. bassiana
f
Proportion of positive treatments (±1 SE)
Oocyst
Sporozoite
P. chabaudi
B. bassiana and P. chabaudi
Treatment

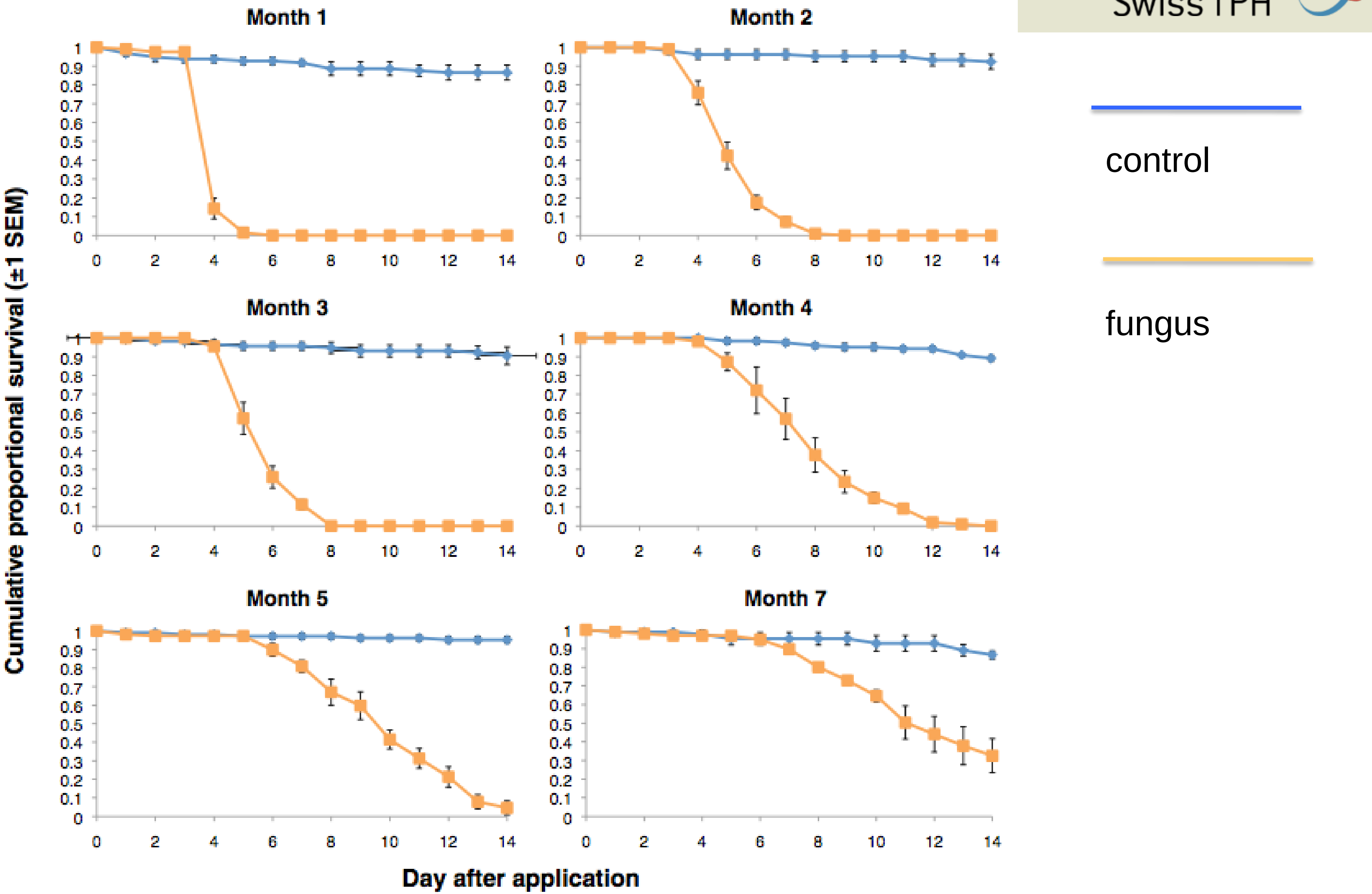
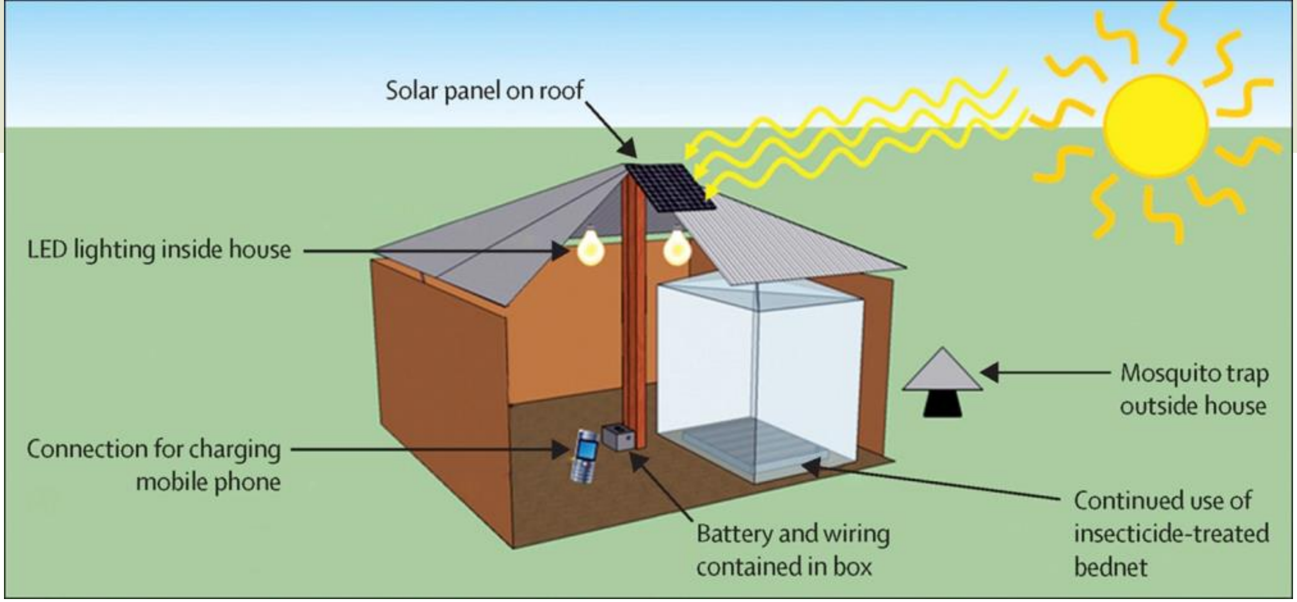
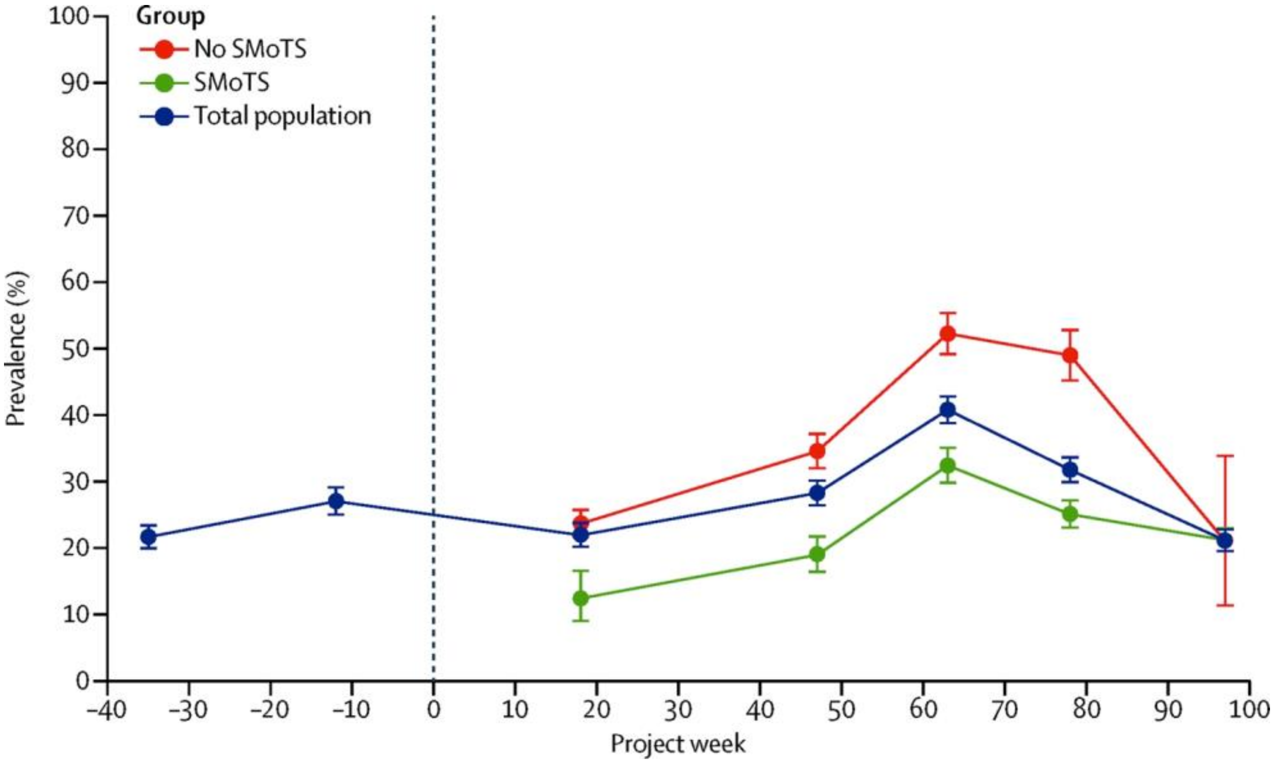


Figure 5 Cumulative proportional survival of *Anopheles gambiae* exposed to spores of *B. bassiana*. Control tiles were left untreated. Exposures were carried out monthly after an initial post application assessment (Day 1 – not shown, see Table 5) for seven months. Blue and orange curves show survival for the control and *B. bassiana* treatments respectively.





The Lancet 2016 388, 1193-1201DOI: (10.1016/S0140-6736(16)30445-7)

EACo MoPP: The East African Collaboration on Mosquito Push-Pull

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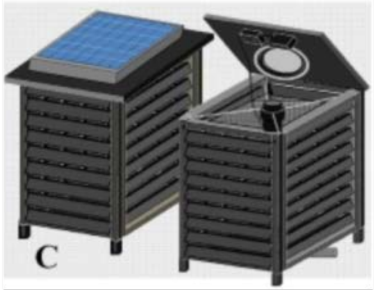
- PUSH and PULL devices will be evaluated in semi-field conditions in Tanzania and Kenya for their ability to reduce human landing rates

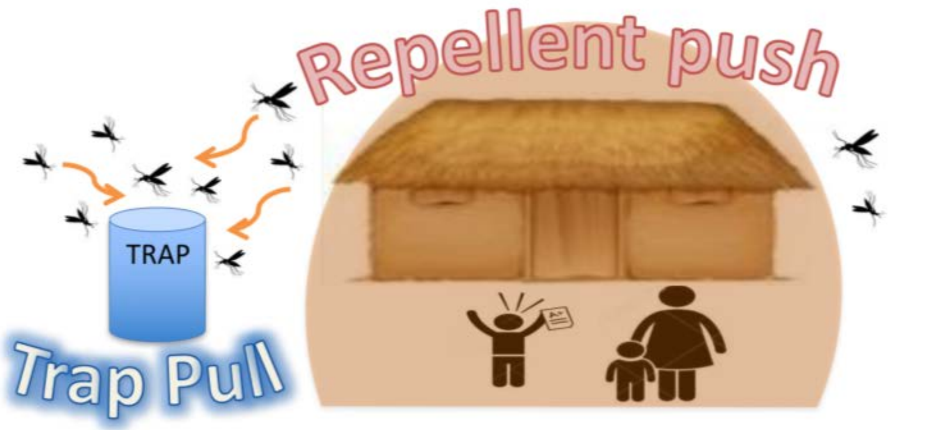
- The optimal combination of devices will then be evaluated in the field

- The project contains a large modelling and economic component to determine i PUSH-PULL will be a viable vector control intervention.

Suna Trap

Ifakara Mosquito Landing Box





ATSB Attractive toxic sugar baits

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The Concept:

Westham INNOVATIONS

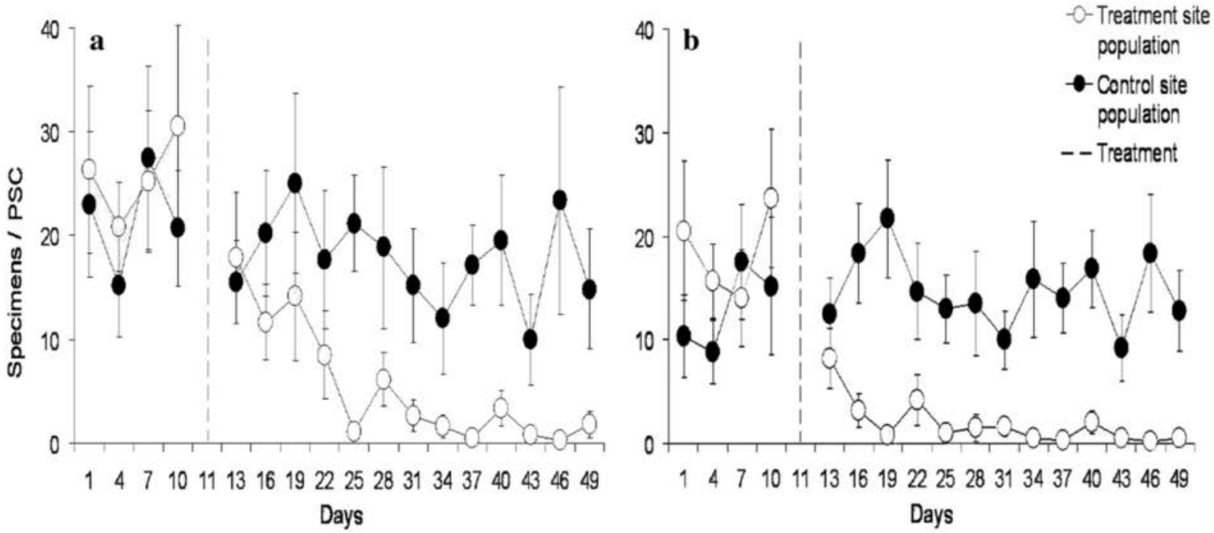
"using a mosquito's own drive for daily sugar meals against itself"

Once attracted mosquitoes feed and are exposed to a low level dose of insecticide within the bait.

but

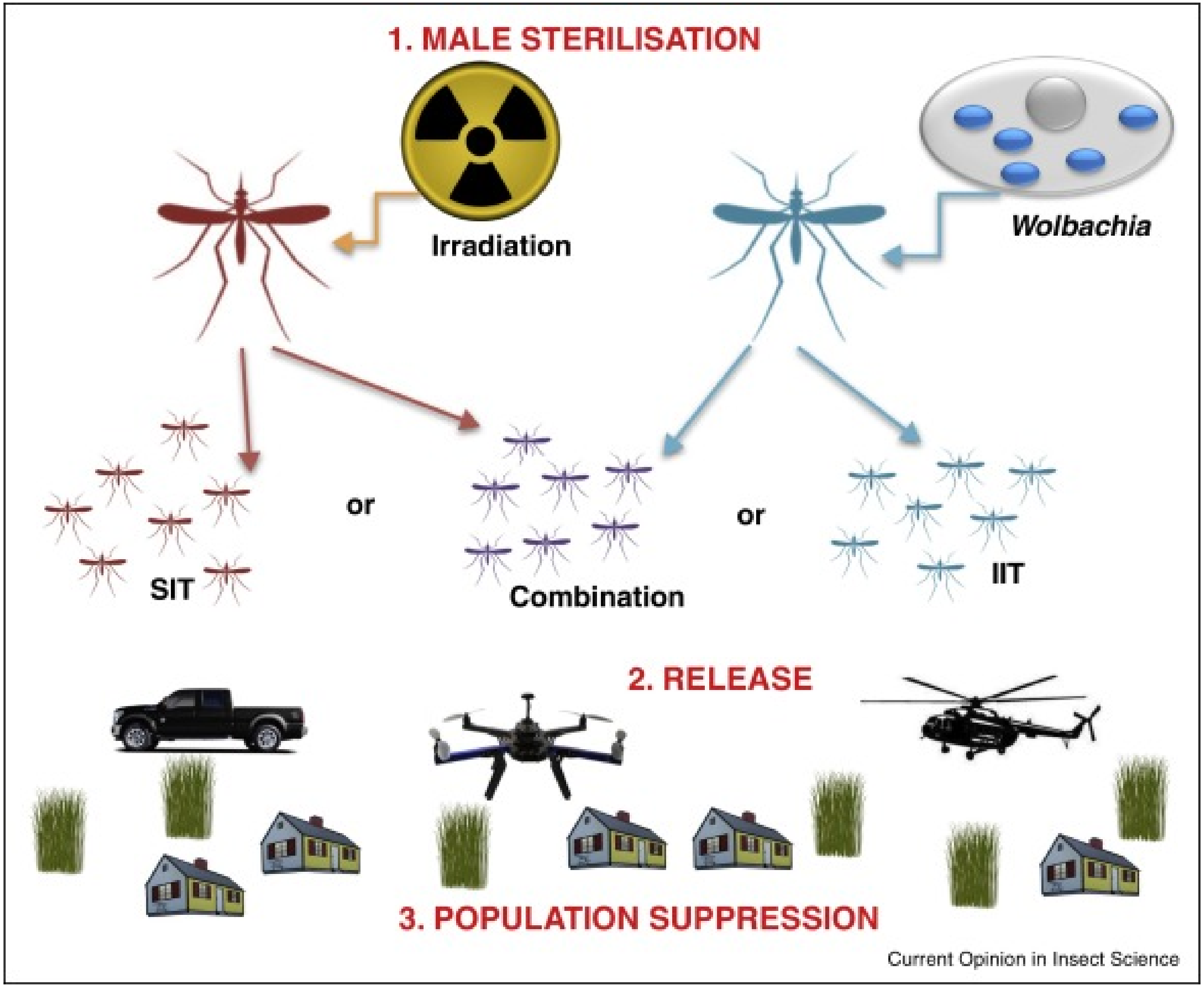
ATSB competes in the field directly with natural sugar sources, accordingly the

quality of the Attractant is crucial.



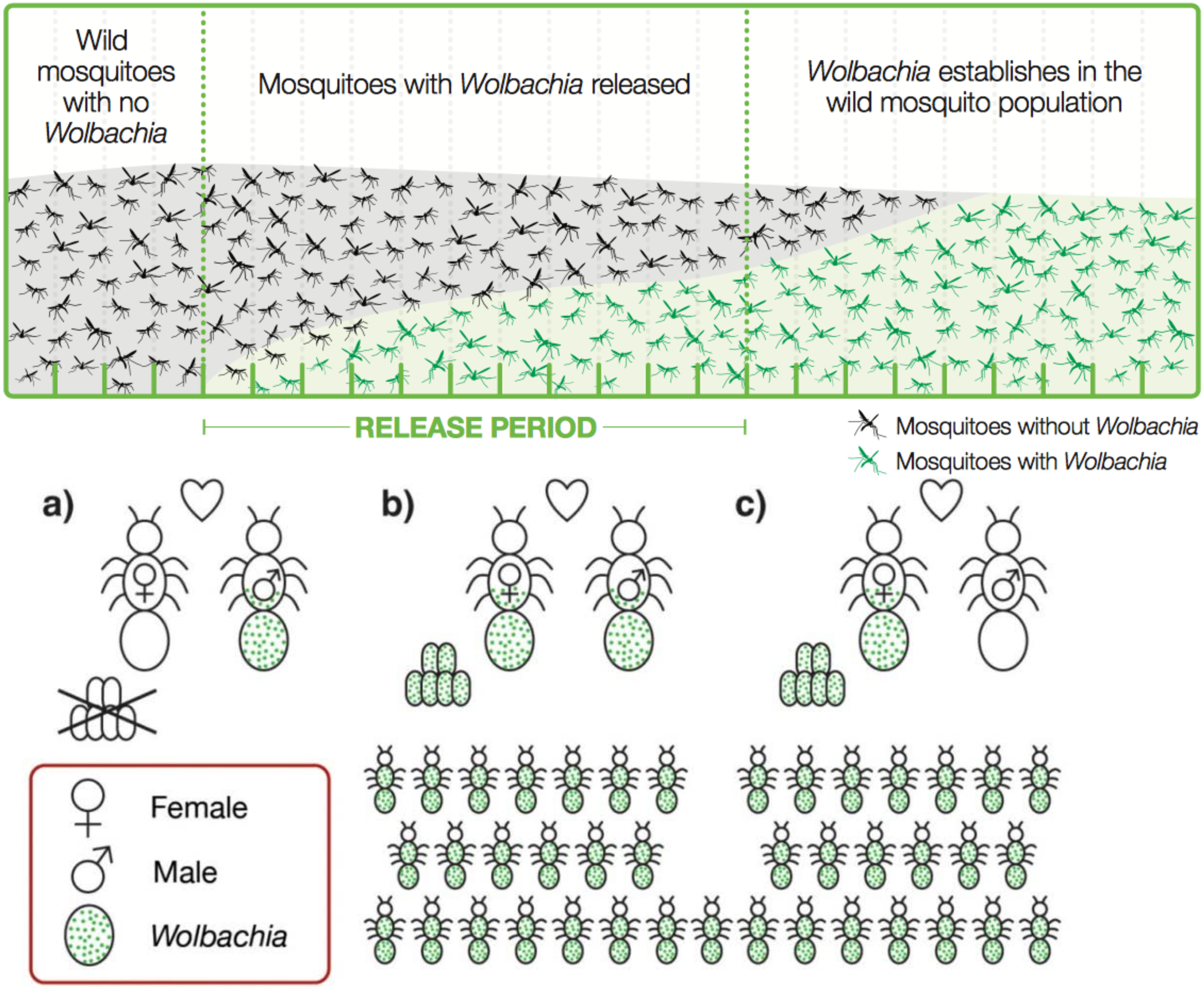
Qualls **Indoor use of attractive toxic sugar bait (ATSB) to effectively control malaria vectors in Mali, West Africa**. *Malaria Journal* 2015, **14**(1):301.

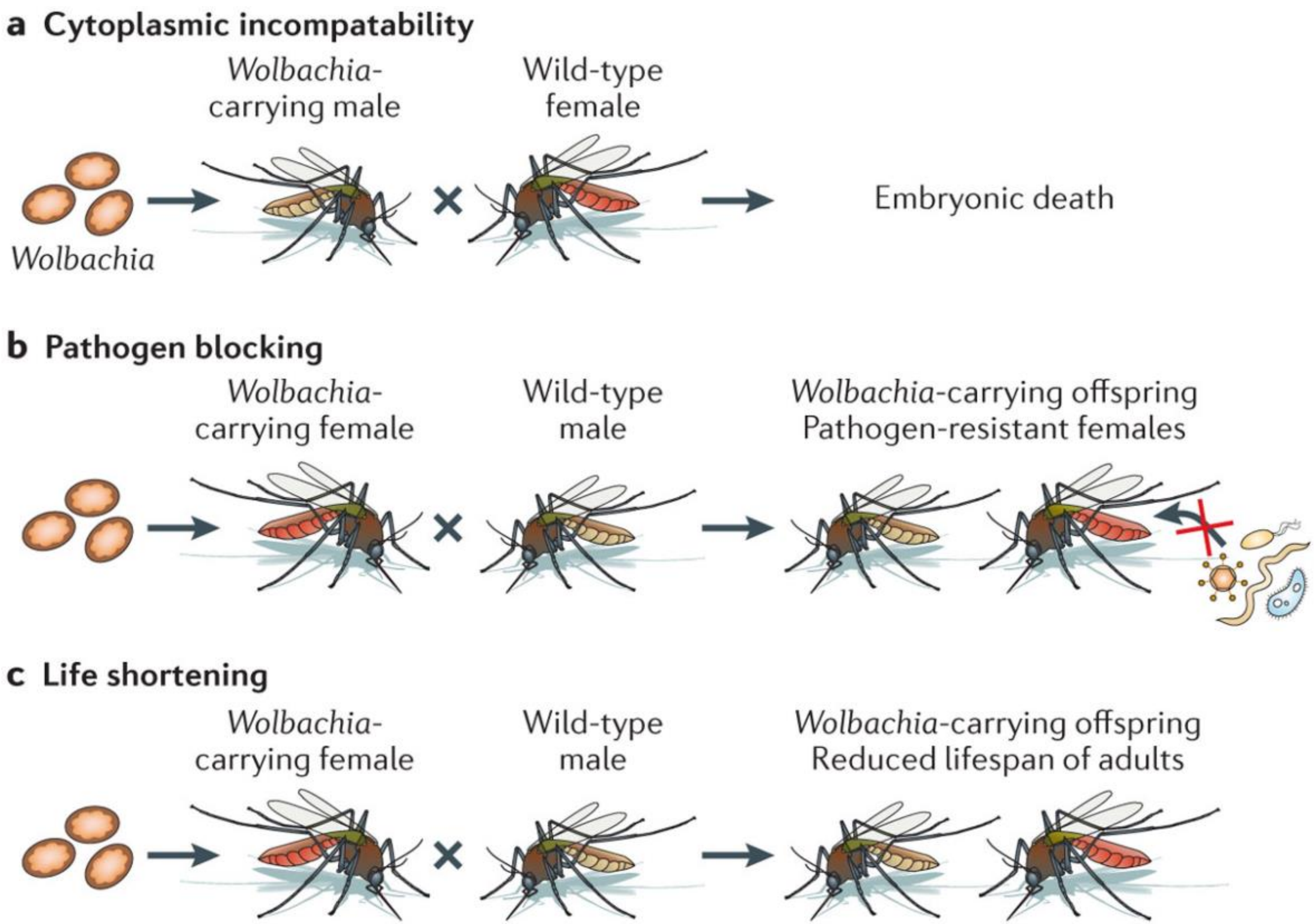
Release of modified insects



Sterile Insect Technique (SIT) Incompatible Insect Technique (IIT)

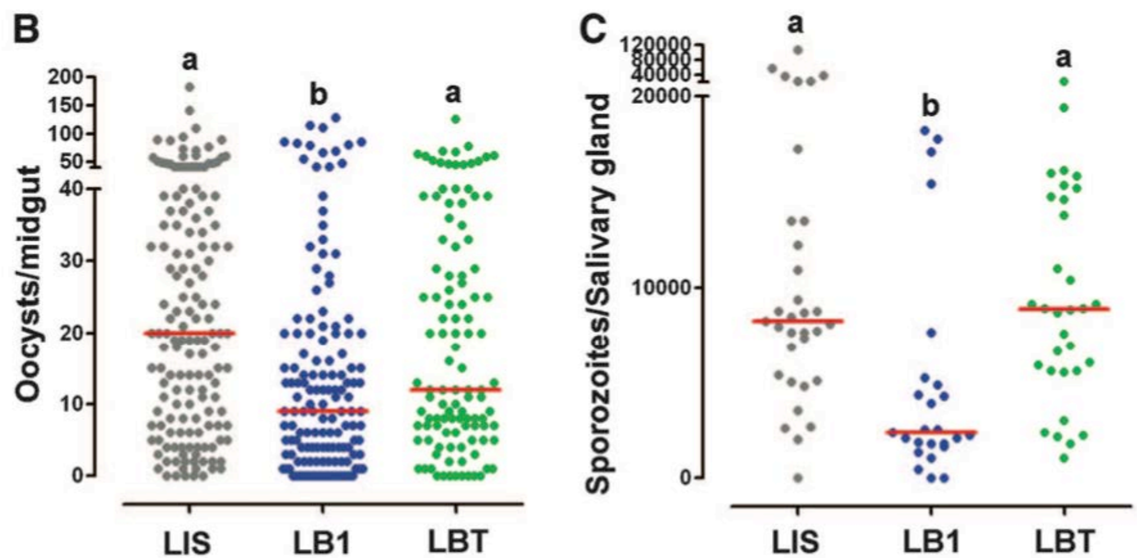
How *Wolbachia* establishes in a local mosquito population

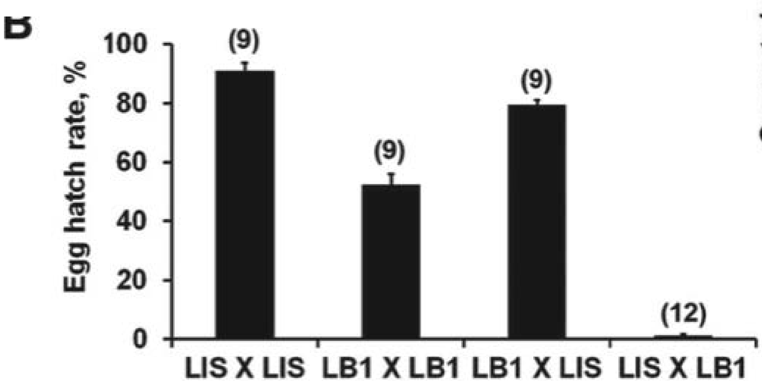


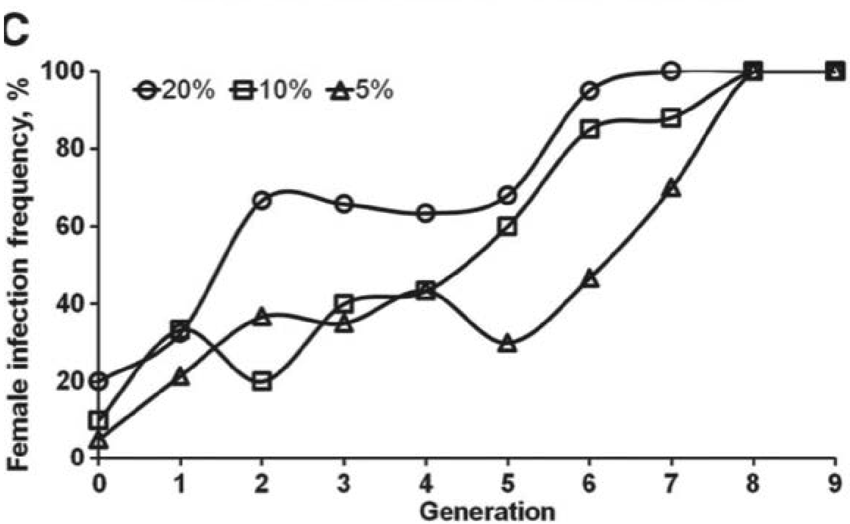


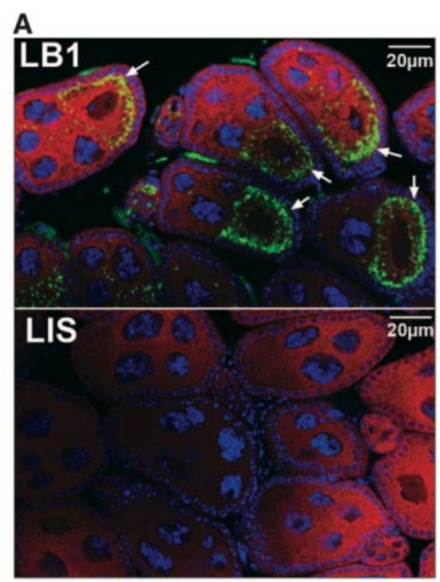
Nature Reviews | Microbiology

Bian et al **Wolbachia invades *Anopheles stephensi* populations and induces refractoriness to Plasmodium infection**. *Science* 2013, **340**(6133):748-751.









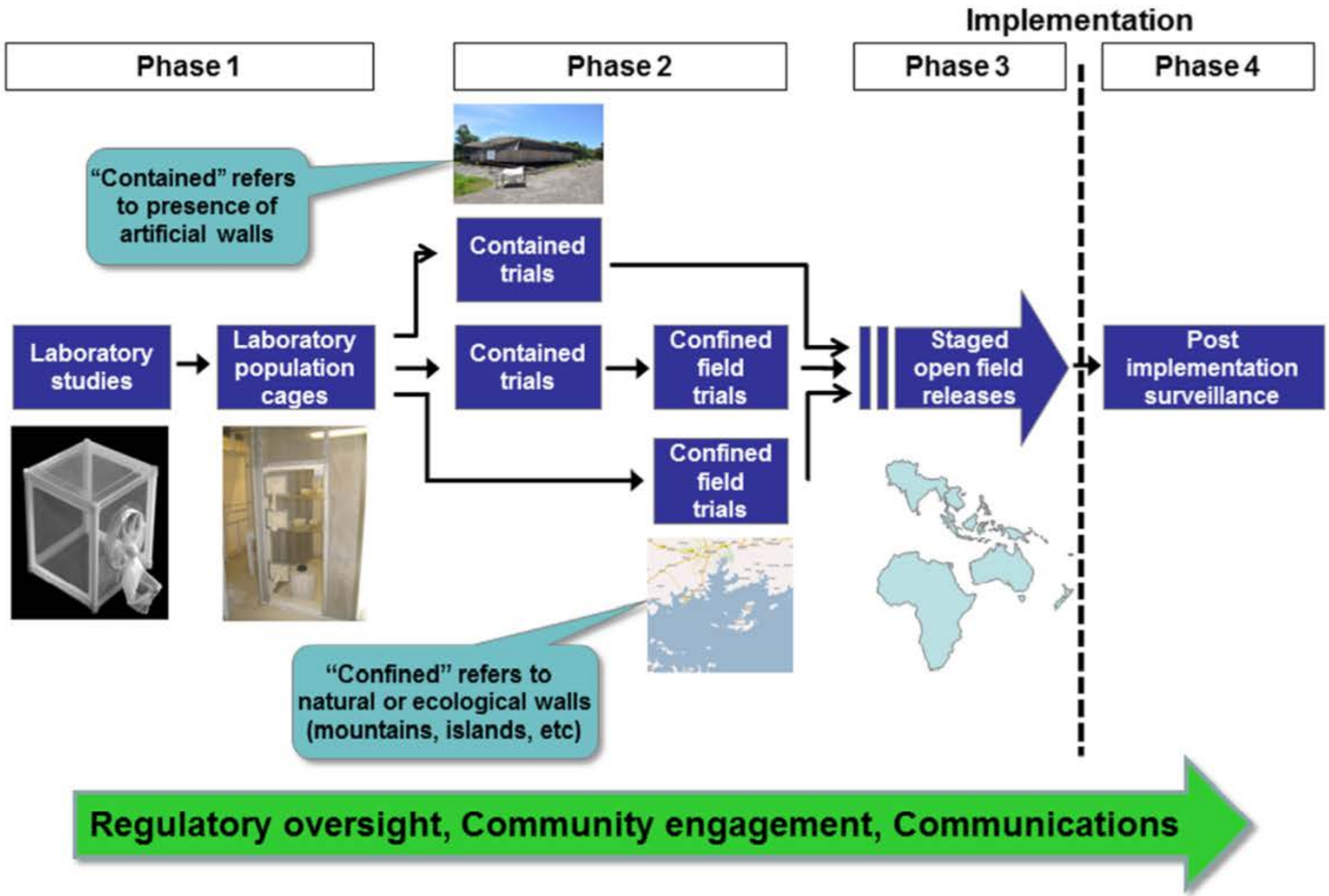


FIGURE 19.2 Phased testing of genetically engineered mosquitoes. A proposed scheme for the phased testing of genetically engineered mosquitoes was developed by working groups at the WHO [43]. Phase 1 is carried out entirely in the laboratory and includes the original development of the transgenic strains and small/large cage trials to estimate fitness. Phase 2 takes place in a field setting and may be either contained or confined. Phase 3 is an open field release with either or both entomological and epidemiological end points. Phase 4 is the implementation phase with the intent to achieve a sustained epidemiological impact. Regulatory oversight, community engagement, and communications should initiate early in the program. *Image adapted from Ref. [43].*

ELIMINATE DENGUE
OUR CHALLENGE

Wolbachia naturally occur in up to

60%

of insect species


Community open day at our lab in Yogyakarta


Rearing mosquitoes with *Wolbachia* in Rio de Janeiro


We work with schools and families to measure how children get dengue in Nha Trang

Project sites around the world

We began field trials of *Wolbachia* in 2011, with our first city-wide trial starting in 2014 in Northern Australia.

Plans for large-scale trials in several of our project sites are underway and scheduled to commence in 2016-17.

Queensland, Australia

Sustaining high levels of *Wolbachia* five years after the first mosquito releases in Cairns. There is no evidence of local dengue transmission in release areas.

Rio de Janeiro, Brazil

Trials in Tubiacanga and Jurujuba have paved the way for expansion into larger areas of Rio de Janeiro.

Antioquia, Colombia

Adapting our approach for use in high density, urban environments and preparing for expansion in the state of Antioquia.

Yogyakarta, Indonesia

City-wide efficacy trial underway following successful small-scale trials in Yogyakarta.

Nha Trang, Vietnam

Preparing for field trials in four pilot areas of Nha Trang following a field trial in Tri Nguyen Island.

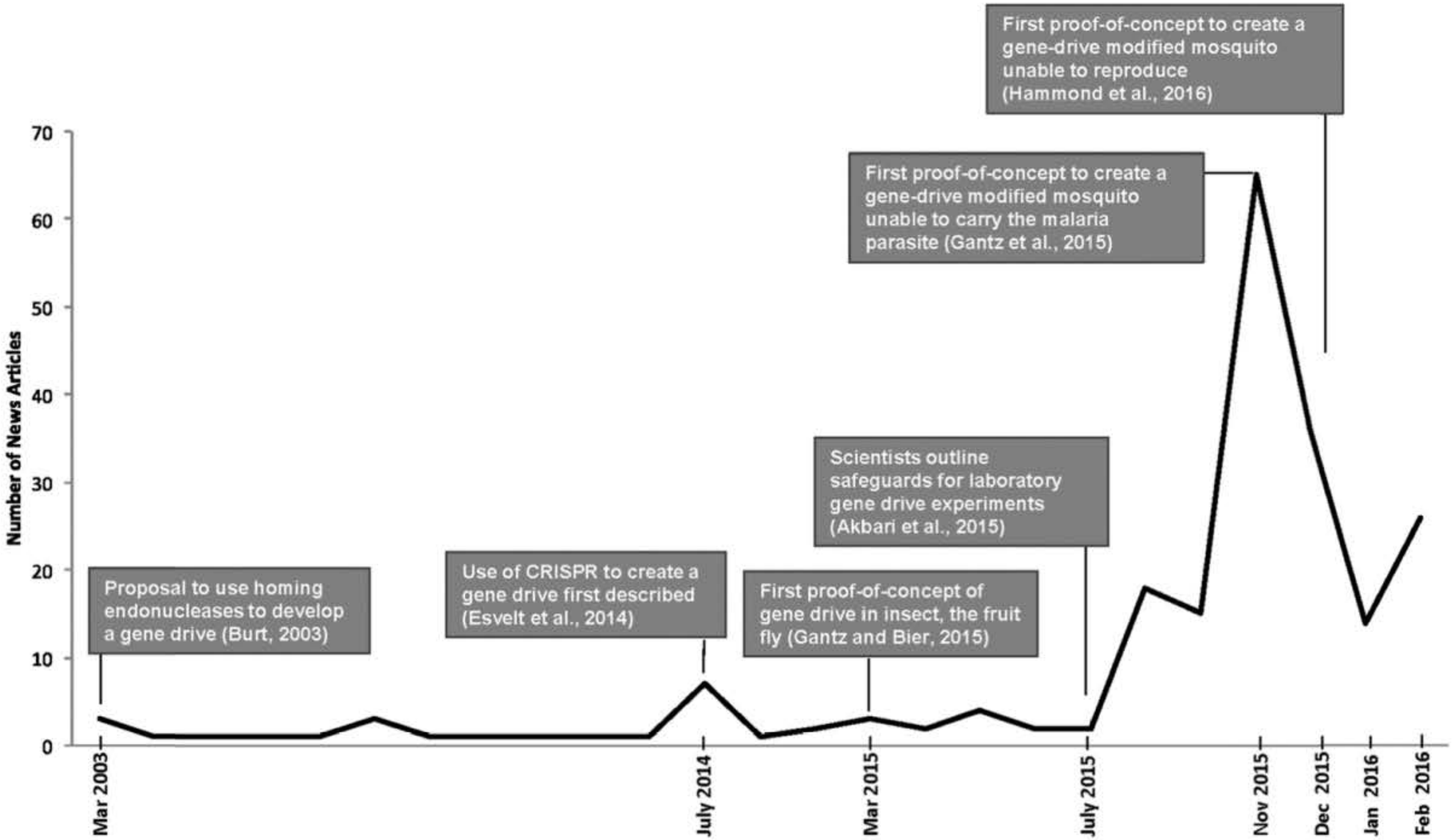
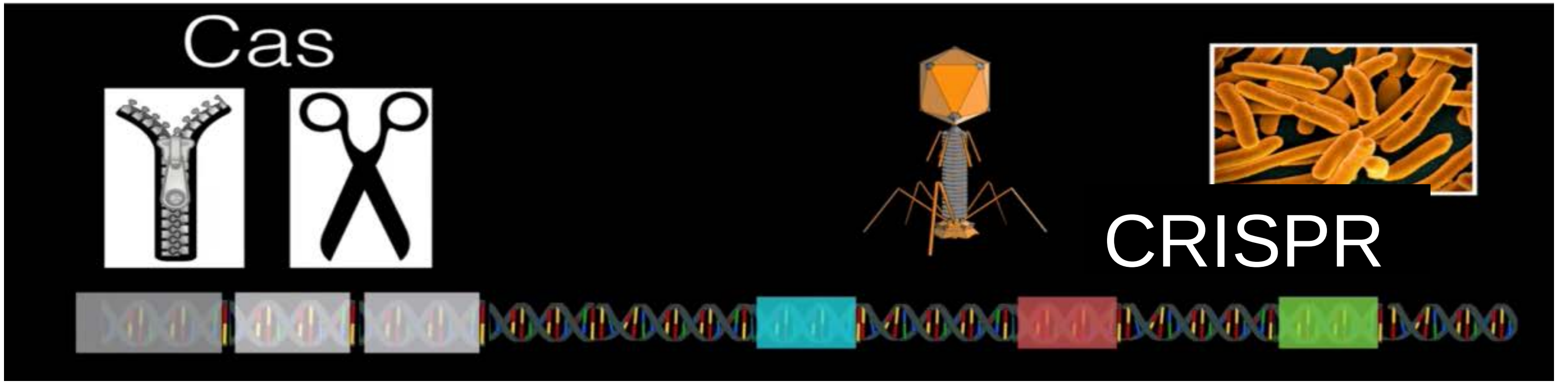
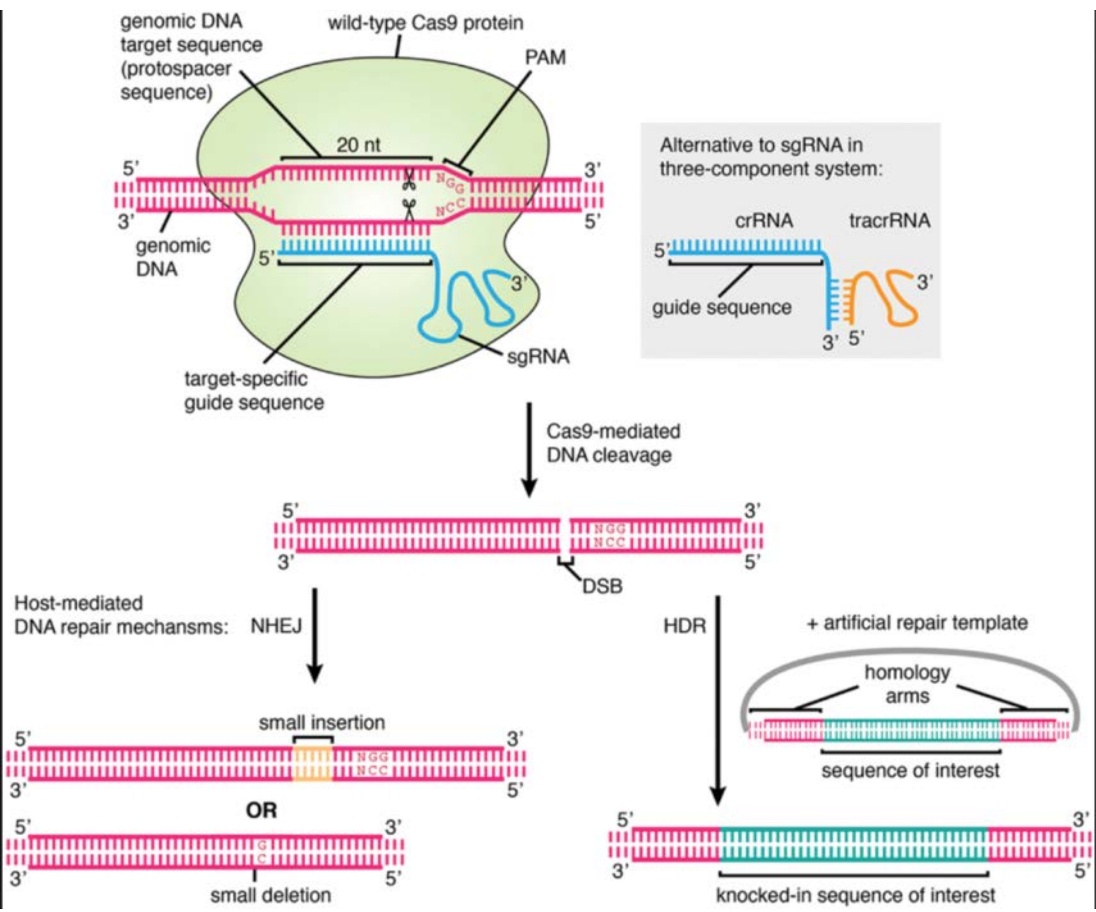
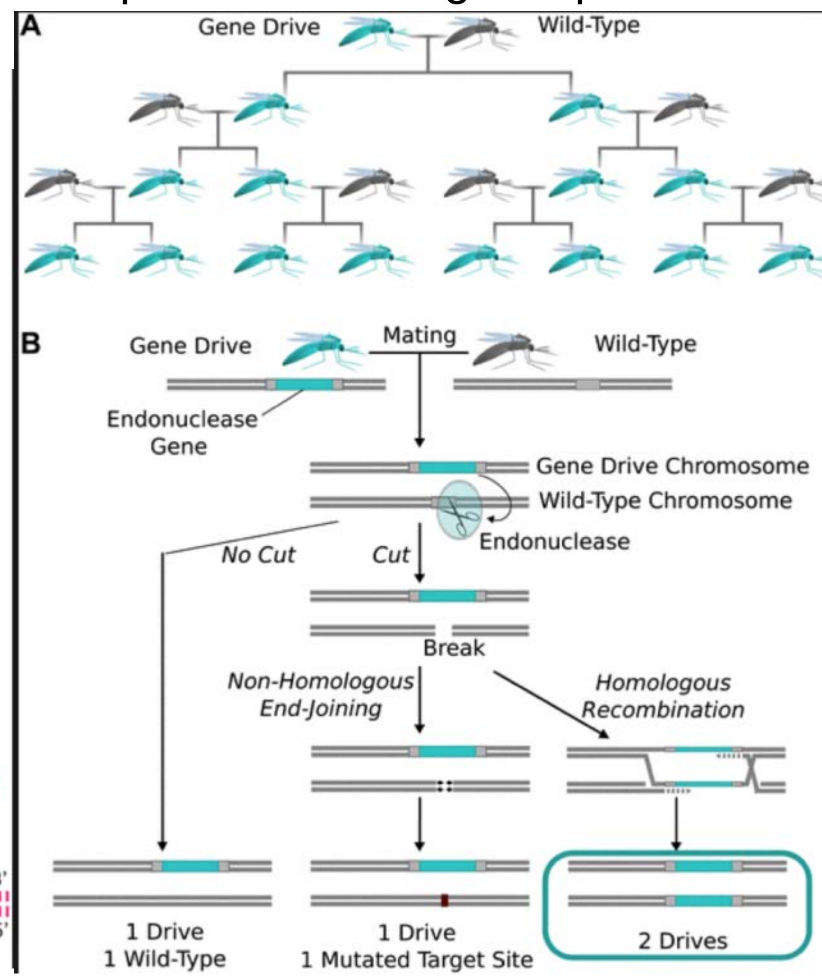


FIGURE 1-3 Timeline of published news articles about gene drive research (2003-2015). Boxes highlight select scientific publications on advances in gene drive research. Source: LexisNexis, 2016. Limited to top 20 daily circulating newspapers, press releases, and select science publications. Search terms: Gene Drive or Mutagenic Chain Reaction.



Clustered regularly-interspaced short palindromic repeats + CAS 9 guide protein





Population alteration

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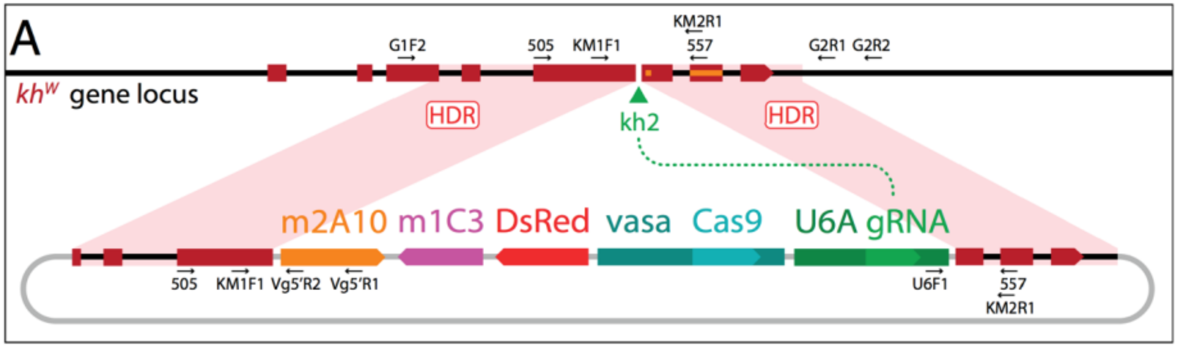
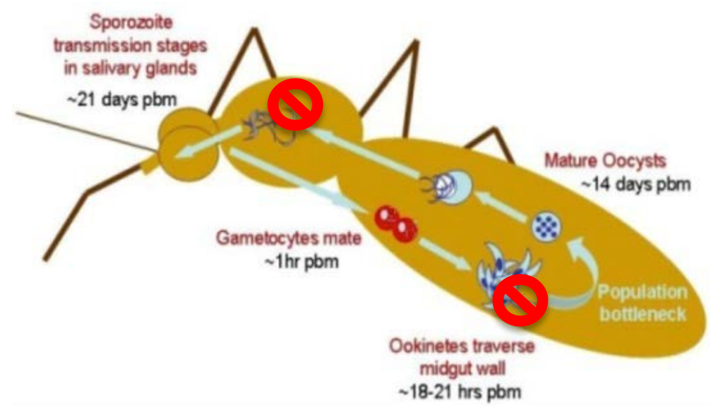
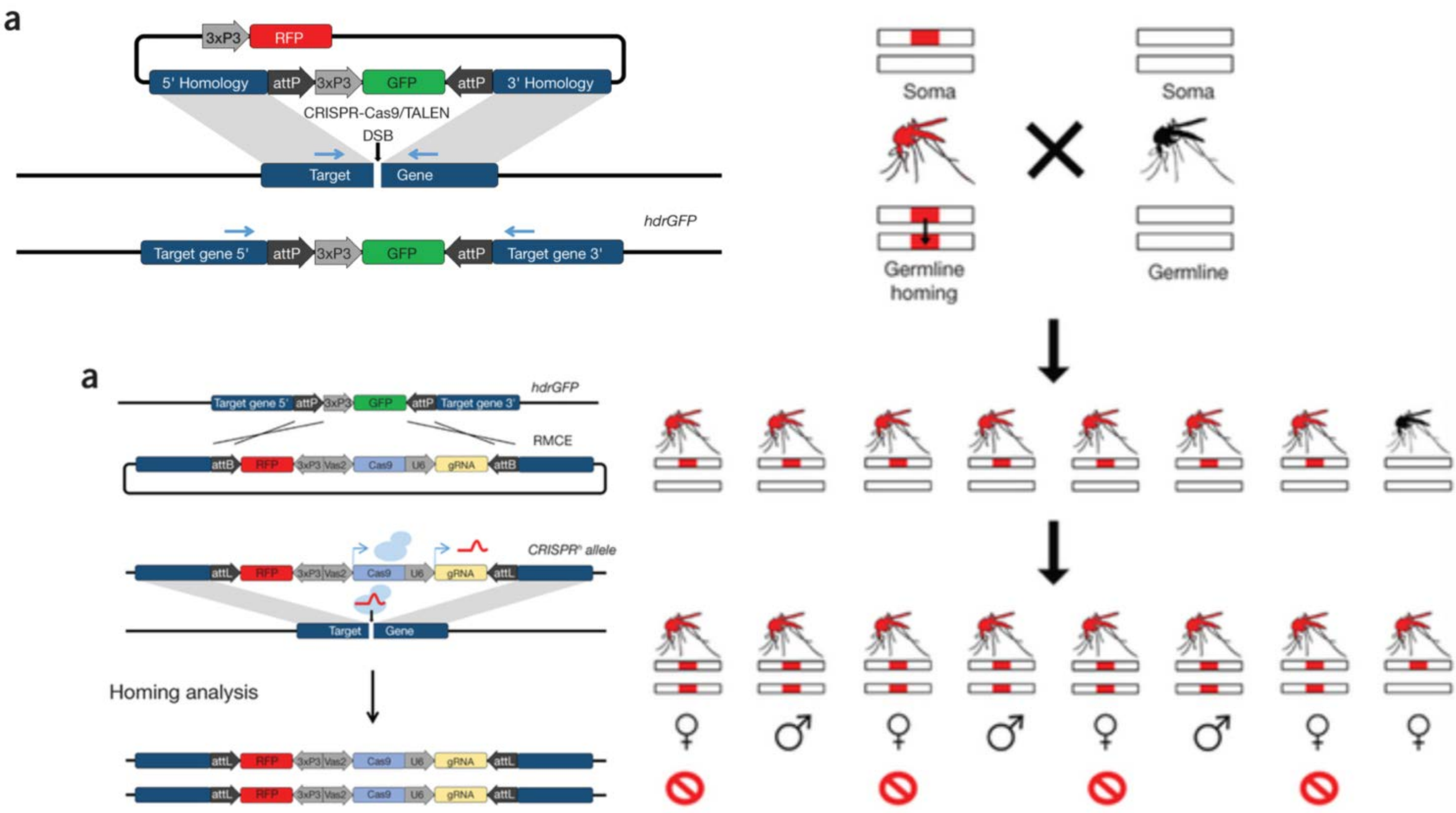




Gene	Outcome	Under control of
m1C3	Neutralise ookinetes – targets Chitinase 1	***An. gambiae*** **carboxypeptidase A (AgCPA) and** ***An. stephensi*** **Vitellogenin 1 (AsVg1) genes**
m2A10	Inhibit salivary gland invasion (circumsporozoite protein)	
Cecropin A	Antimicrobial	
DsRed	Dominant marker gene	
U6A	Expression of guide RNAs (RNA polymerase-III) promoter	
vasa promoter	Germline expression of Cas9 endonuclease	
CAS 9	endonuclease	
gRNA	Guide RNAs	

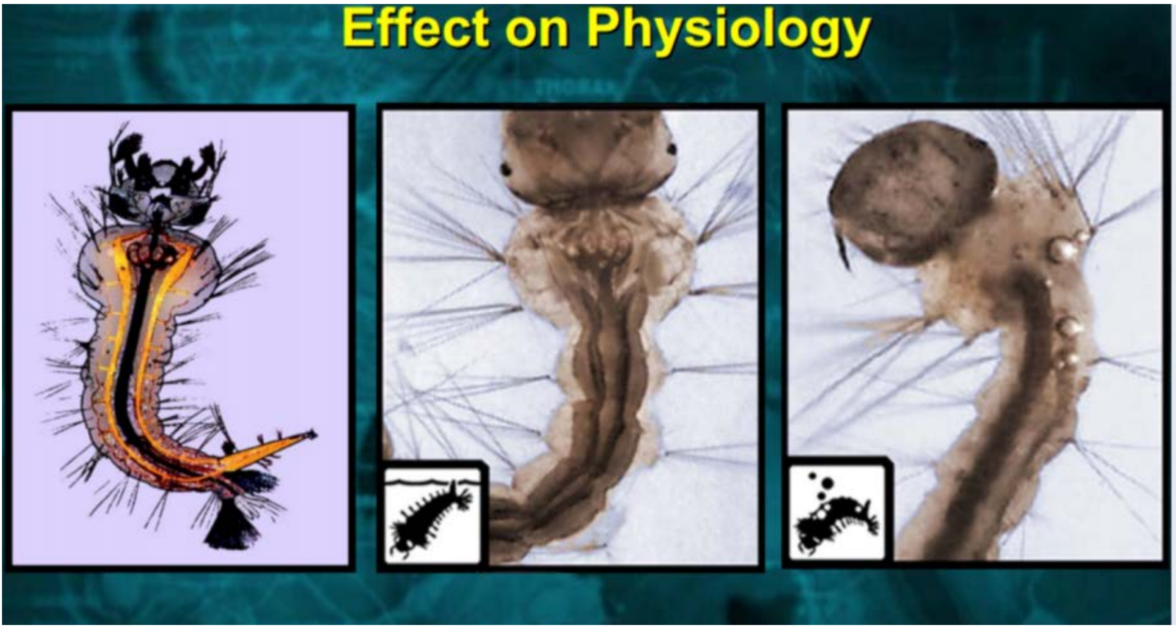
Gantz (2015) pnas.1521077112, Isaacs (2012) pnas.1207738109

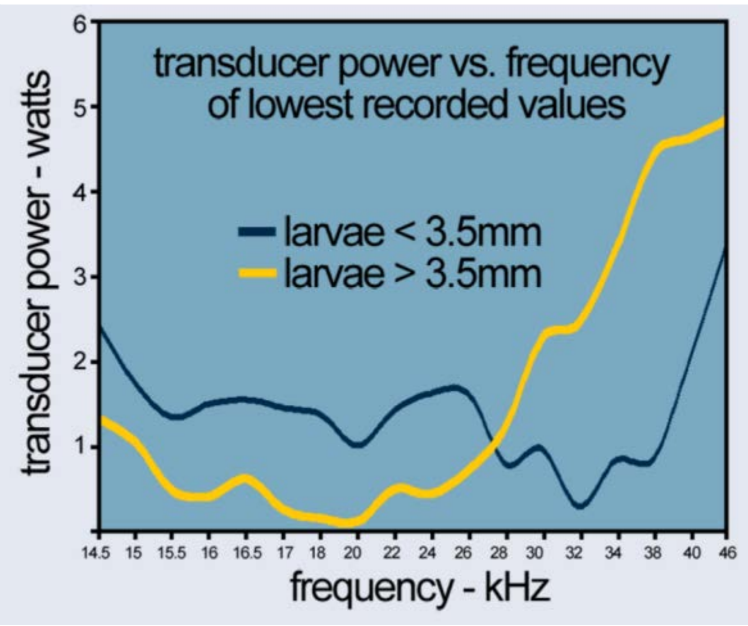
CRISPER CAS 9 for gene editing to induce sterility



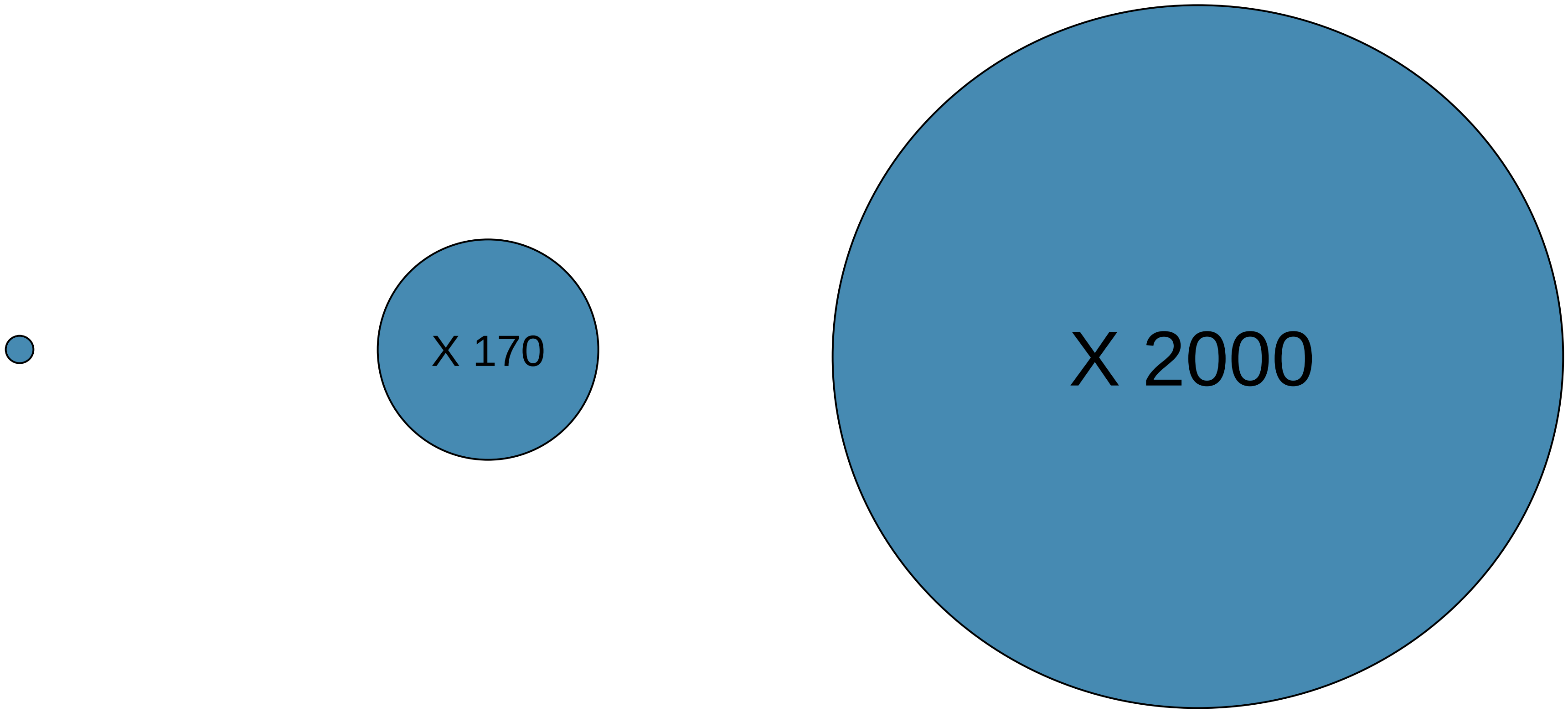
Hammond et al Nat Biotechnol. 2016 January ; 34(1): 78–83

Acoustic Larvicides





Cost of generating solid evidence versus current and future vector control investments



Cost of ITN trials: <10 mio USD

Investment to-date in LLINs (2004-2010): USD 1.7 Billion (WHO 2009)

Future investments: 1 Billion per year for 2011-2030 USD 20 Billions GMAP 2008