

The Resilience Against Future Threat through vector control (RAFT) consortium invites you to a panel discussion and reception on

Anopheles stephensi in Africa: why does this invasive vector matter for the future of malaria control?

Anopheles stephensi is an invasive vector with a unique ability to breed in man-made containers, and thus transmit malaria in highly-urbanised environments. Malariologists have been assuming that ongoing urbanisation across Africa would contribute substantially to the elimination of malaria in Africa. Unfortunately, the arrival and spread of *An. stephensi* in Africa means that this path towards elimination can no longer be assumed. Without action now, we will find ourselves forced to accept the presence of *An. stephensi* in Africa, and the long-term consequences, which are likely to get worse as urbanisation proceeds.

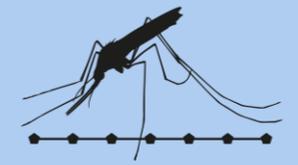
The reception will be hosted by James Sunderland MP and supported by the All-Party Parliamentary Group on Malaria and Neglected Tropical Diseases.

Venue The Attlee Suite, Portcullis House, London UK

Date 10 January 2024, Wed

Time 16:15 PM – 18:00 GMT

RSVP <https://tinyurl.com/raft-appg-stephensi>



RAFT
RESILIENCE AGAINST
FUTURE THREATS



Dr Seth Irish
World Health Organization



Dr Fitsum Tadesse
London School of Hygiene and
Tropical Medicine & Armauer
Hansen Research Institute,
Ethiopia



Professor Jo Lines
RAFT & London School of Hygiene
and Tropical Medicine

Anopheles stephensi: an emerging threat

Parliamentary Reception on *Anopheles stephensi* in Africa: why does this invasive vector matter for the future of malaria control?

Attlee Suite, London, UK

Fitsum G Tadesse (PhD)
10 January 2024



PMI

U.S. PRESIDENT'S
MALARIA INITIATIVE

LED BY



BILL & MELINDA
GATES *foundation*



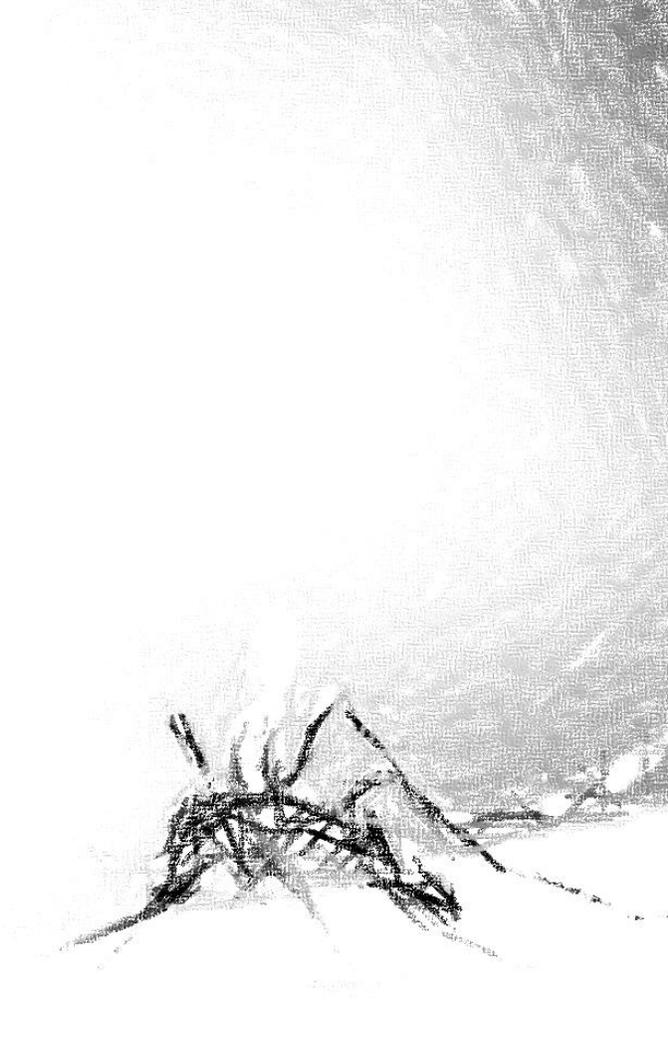
Some of the questions upon detection of the invasive mosquito in Africa

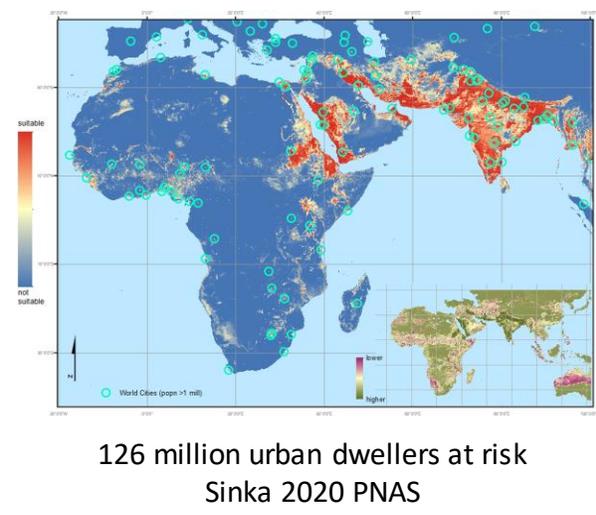
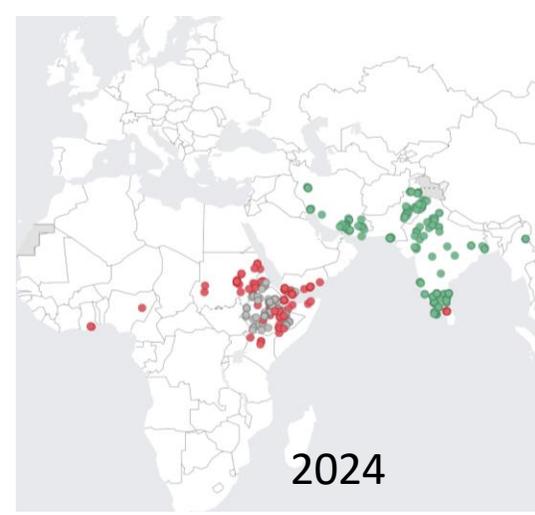
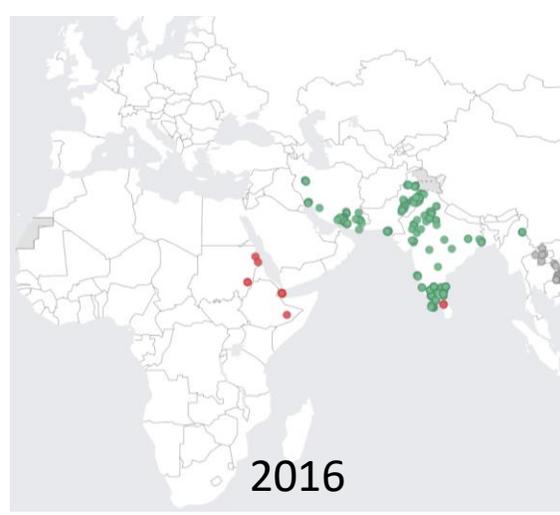
Is it just one more mosquito in a continent that hosts the most competent malaria vectors?



Question #1

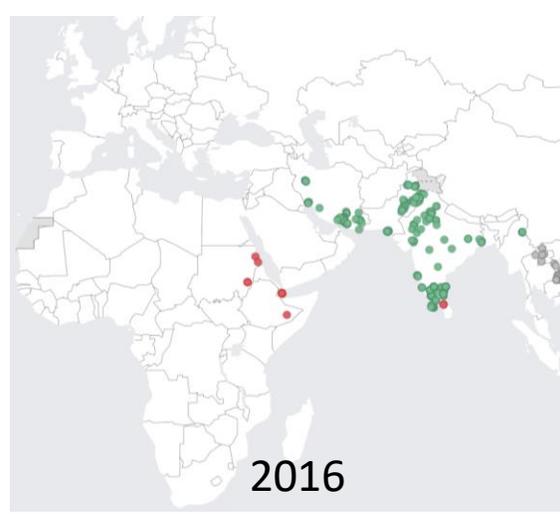
Would *An. stephensi* spread to a wider geography in the continent?



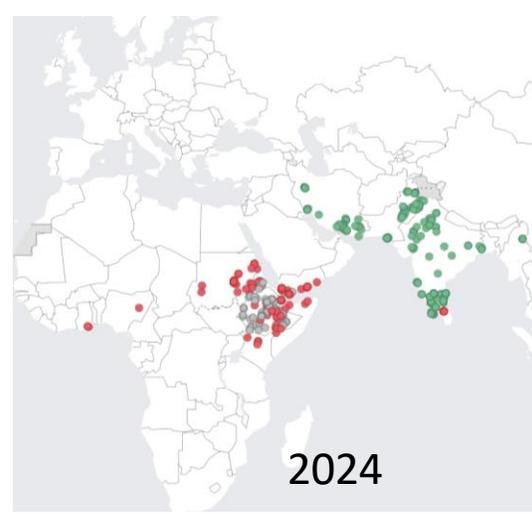




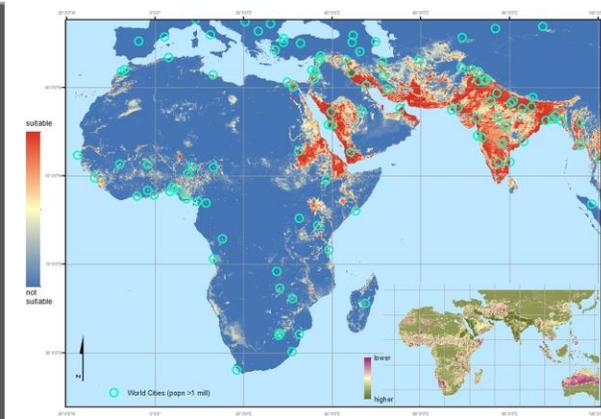
2012



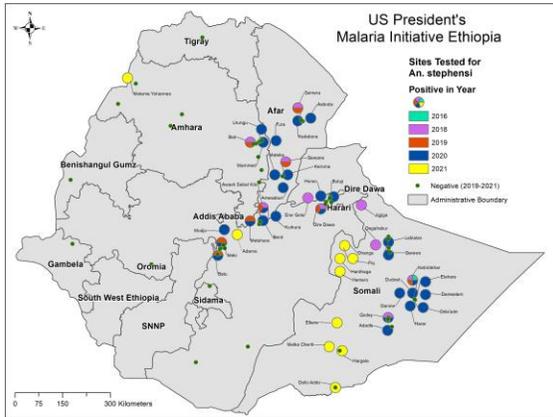
2016



2024



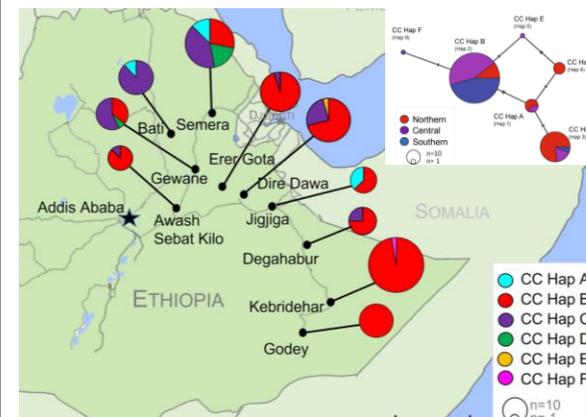
126 million urban dwellers at risk
Sinka 2020 PNAS



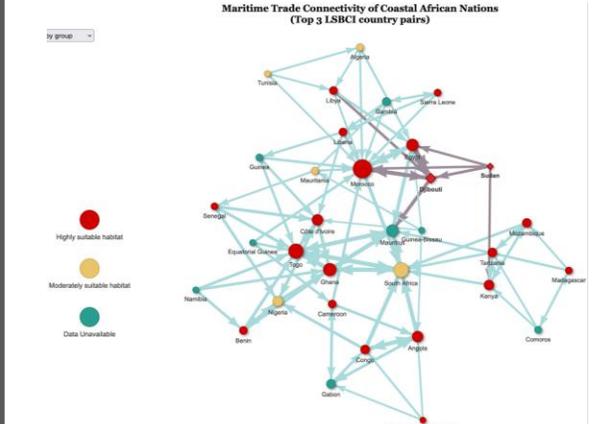
Expansion of *An. stephensi* in Ethiopia
US President's Malaria Initiative Ethiopia



An. stephensi in rural settings
Balkew 2021 Malar J



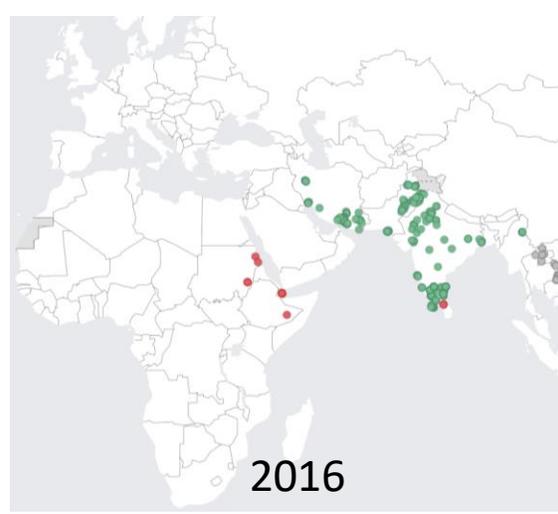
Multiple introduction and expansion
Carter 2021 Par Vect



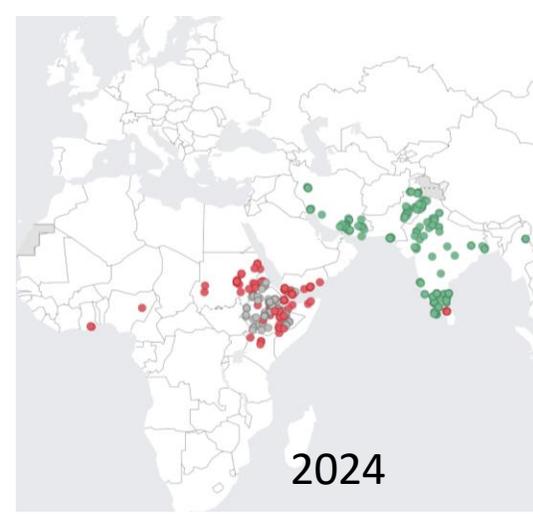
Marine cargo and *An. stephensi*
Ahn 2023 Sci Rep



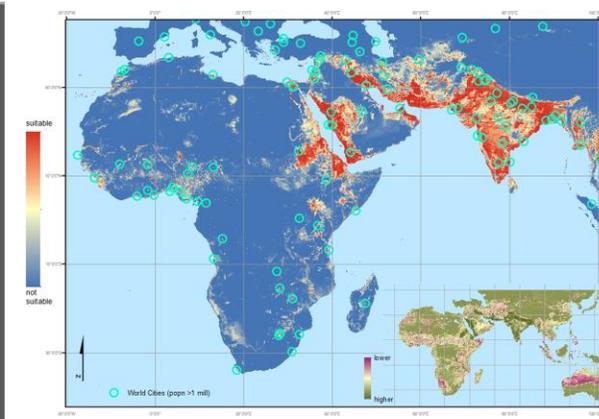
2012



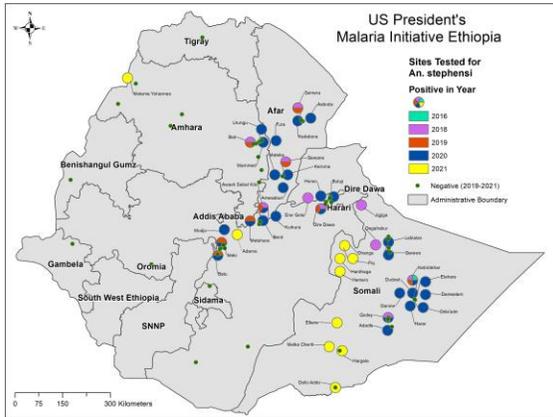
2016



2024



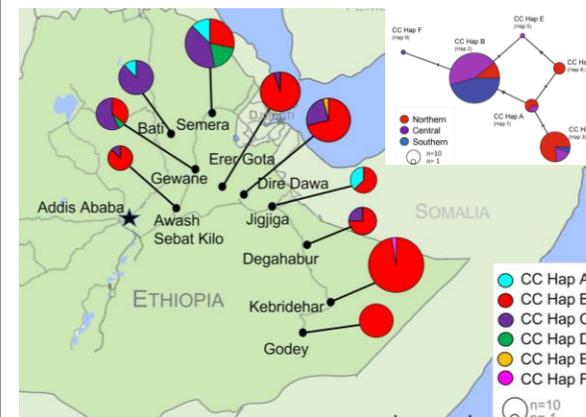
126 million urban dwellers at risk
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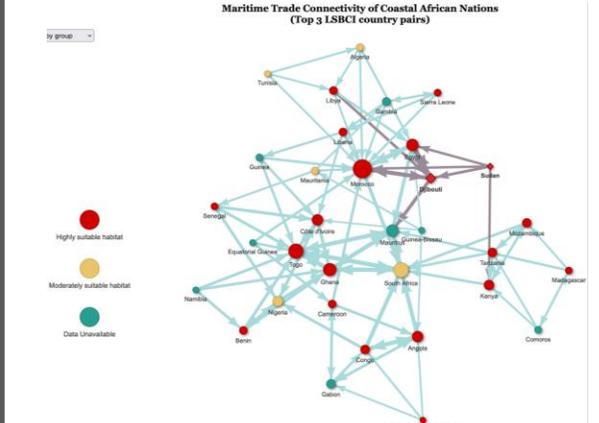
Expansion of *An. stephensi* in Ethiopia
US President's Malaria Initiative Ethiopia



An. stephensi in rural settings
Balkew 2021 Malar J



Multiple introduction and expansion
Carter 2021 Par Vect



Marine cargo and *An. stephensi*
Ahn 2023 Sci Rep

Malaria Policy Advisory Committee Meeting
2-4 October 2019, Geneva, Switzerland
Background document for Session 7



Meeting report of the WHO technical
consultation on the spread of *Anopheles stephensi*

25-27 June 2019, Geneva, Switzerland



Action plan for the integrated surveillance and control of
Anopheles stephensi and *Aedes aegypti*, with a targeted
elimination of *An. stephensi* in Ethiopia, 2022-2026



Question #2

Would *An. stephensi* be competent enough to support transmission of African parasites?

Local adaptation of parasites and mosquitoes has a role to play in limiting the contribution of an invasive mosquito to transmit allopatric parasite populations.

Hume 2007 Malar J

Receptive



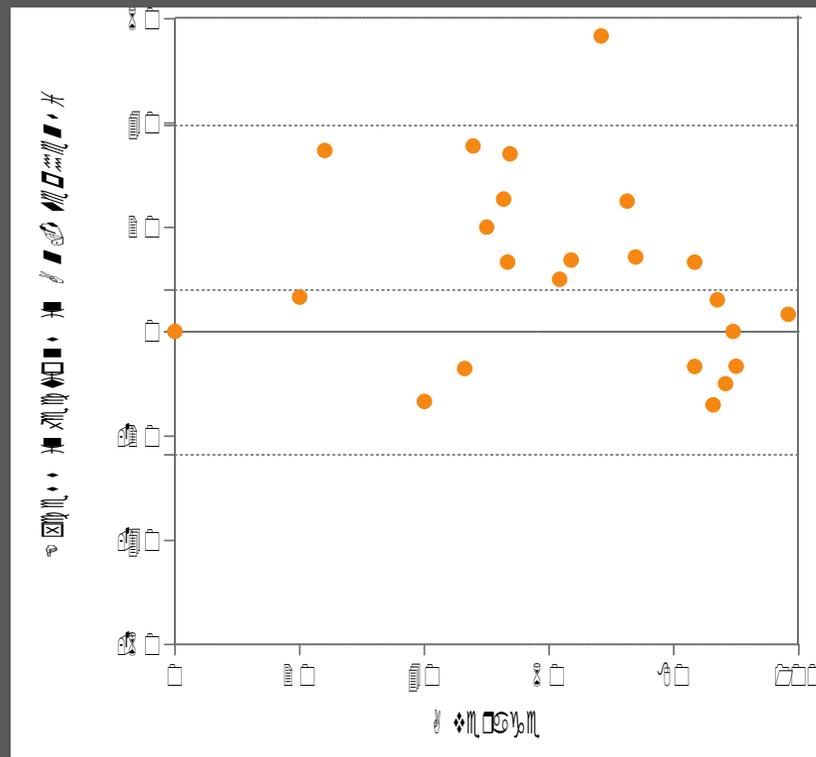
Refractory

An. freeborni, indigenous to North America, is highly susceptible to many species of *Plasmodium* from widely separated geographical areas

Indigenous European mosquitoes are almost completely refractory to tropical *P. falciparum* infection

An. stephensi is highly permissive to local isolates

Tadesse 2020 Emerg Infect Dis

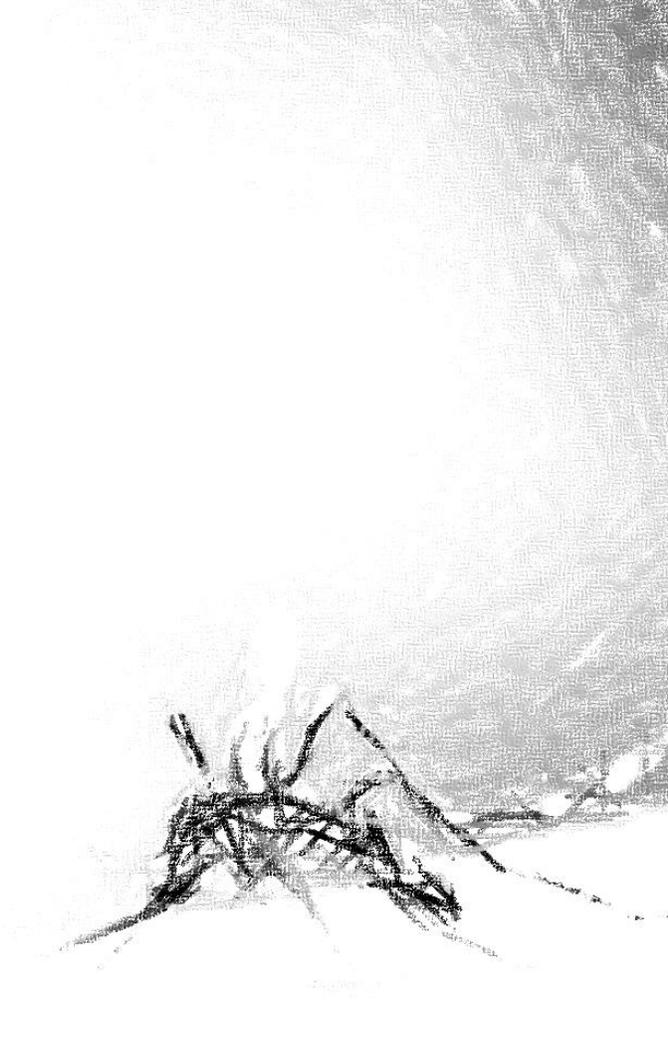


Oocyst
OR 2.0 (95% CI 1.5-2.6)

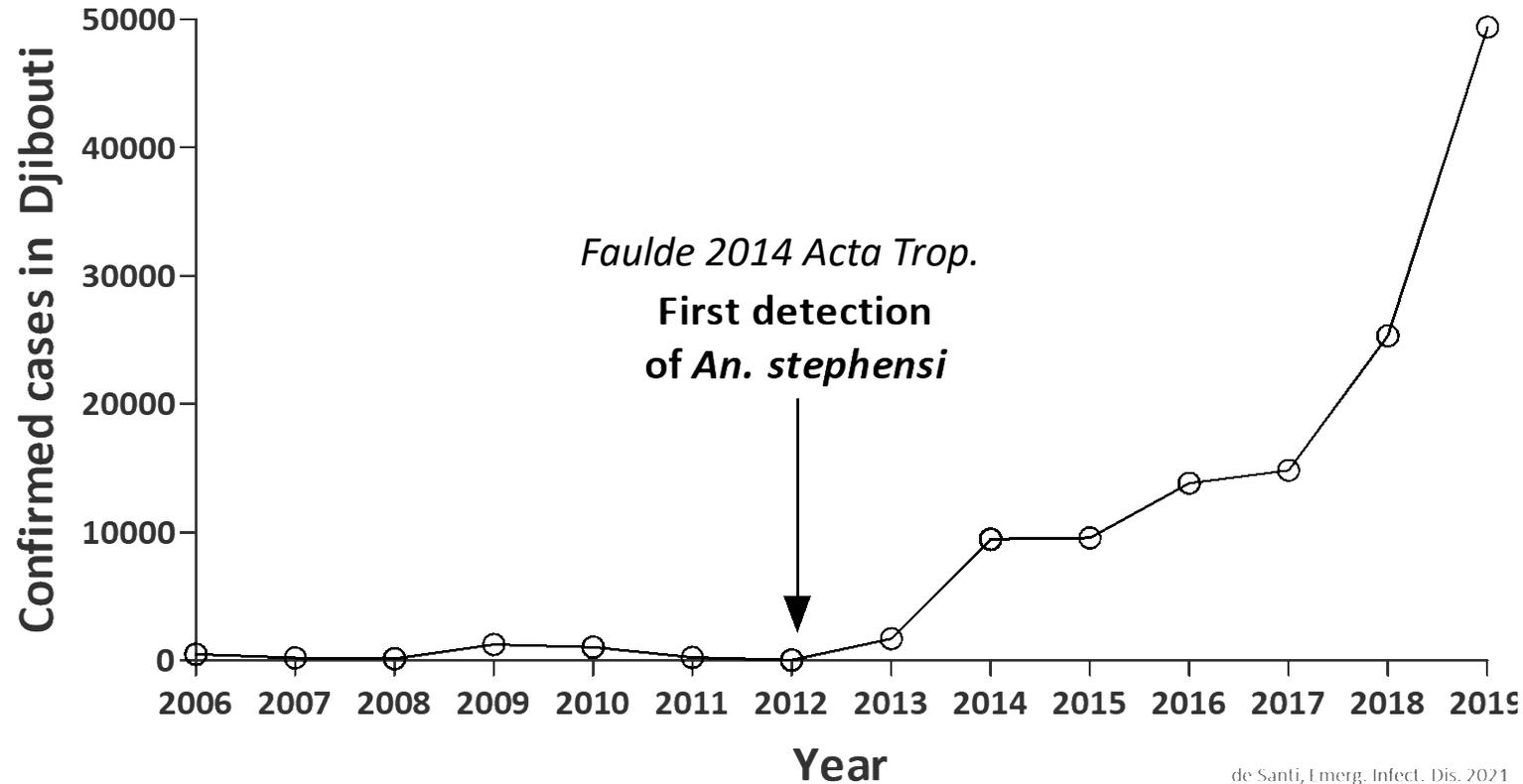
Sporozoite
OR 4.6 (95% CI 2.2-9.9)

Question #3

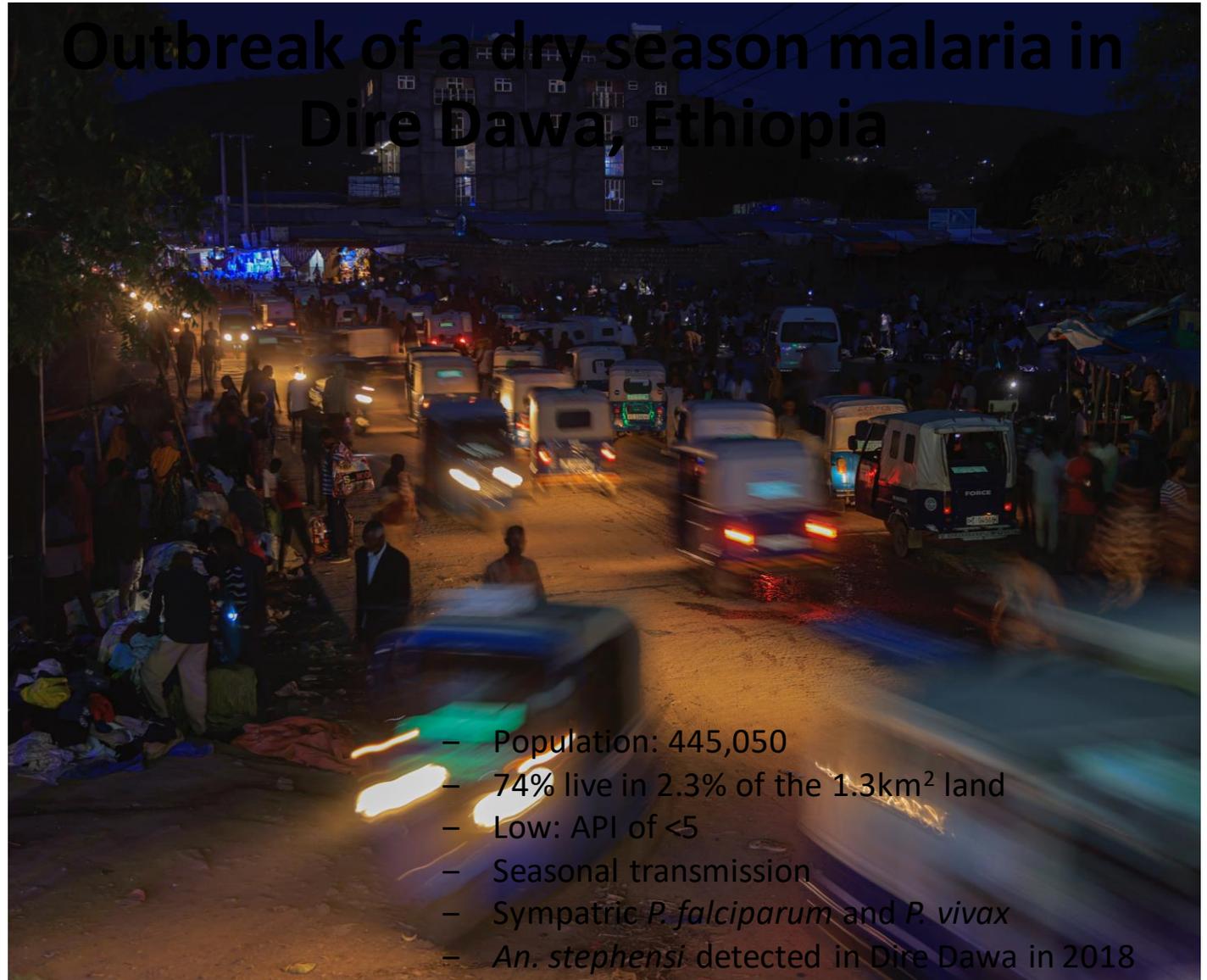
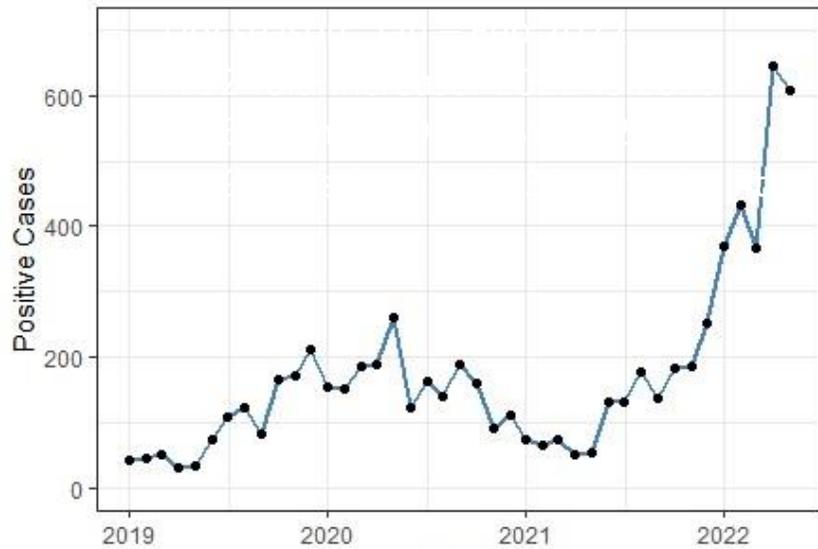
Would *An. stephensi* play a role in local malaria transmission – in a unique way?

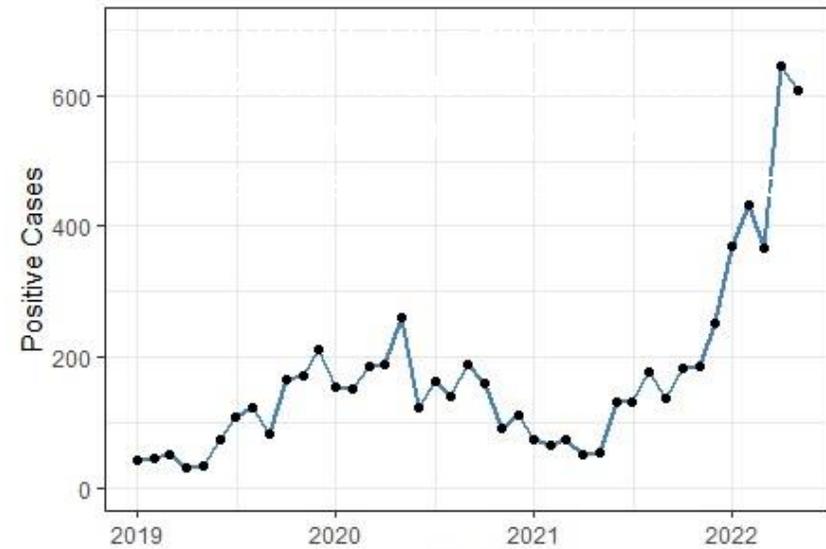


The establishment of *An. stephensi* in Djibouti was epidemiologically linked with an upsurge in malaria



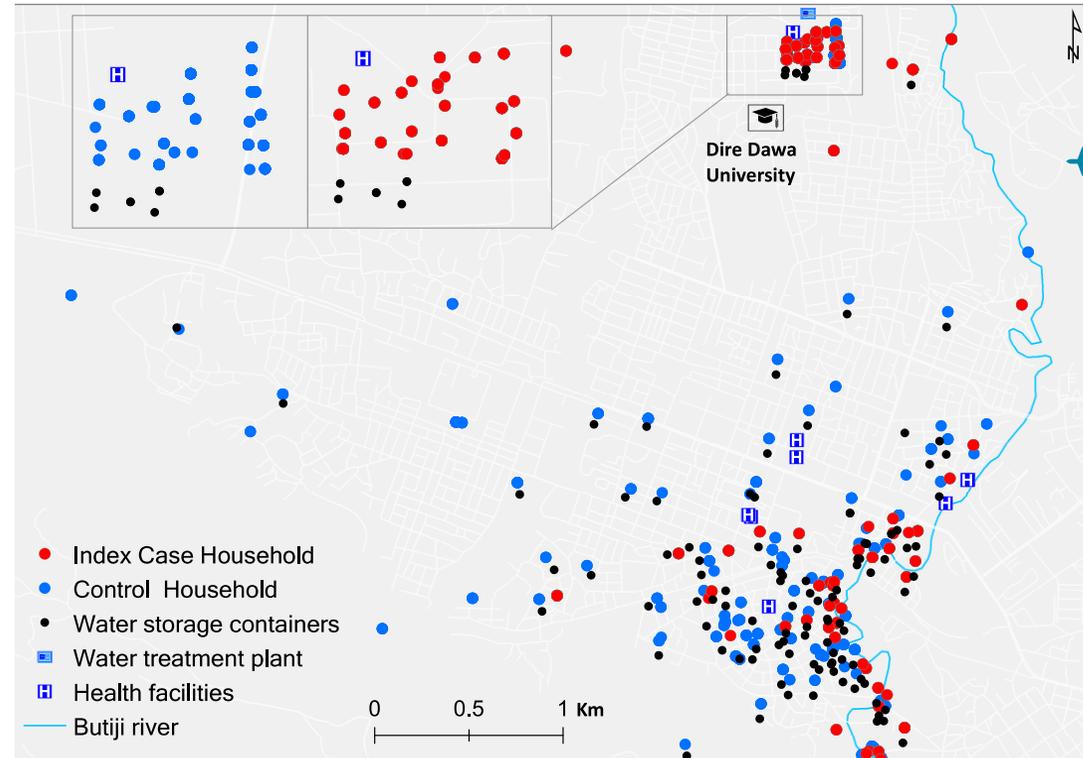
- *An. stephensi* – year-round presence
- *Pf* and *Pv* reported in mosquitoes
- *Pv* for the first time in 2016 - 17% - 37% in 2017





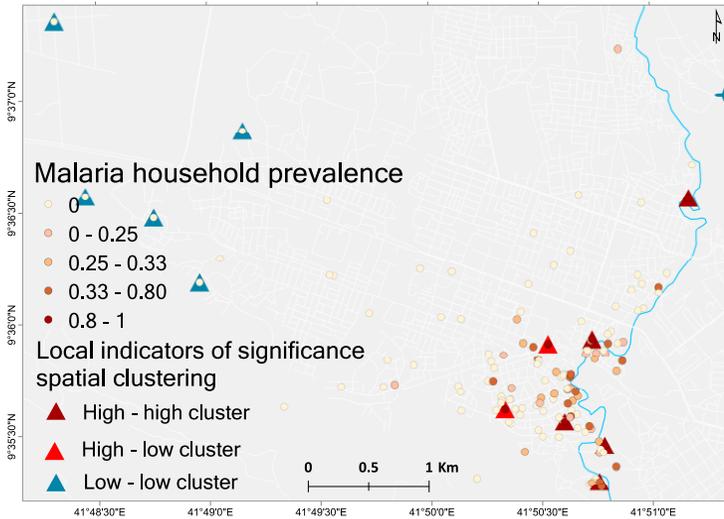
Emiru et al. 2023 Nat Med

Case control study in Dire Dawa: April to July 2022

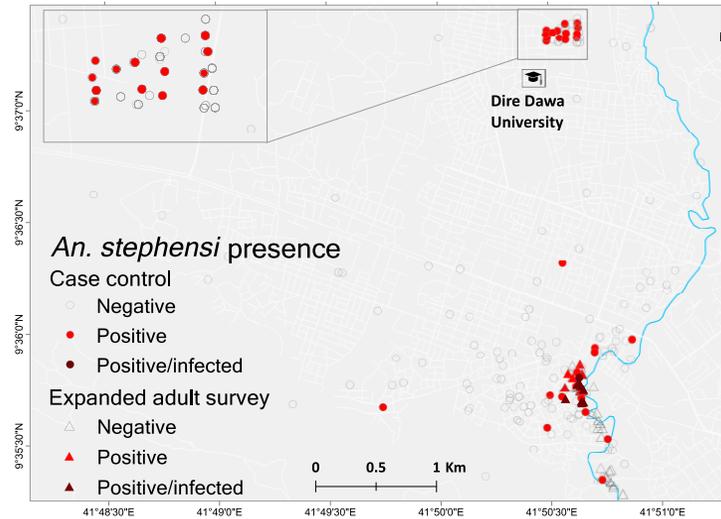


- 101 index cases
- 235 close contacts
- 187 controls
- 429 close contacts
- Adult surveys within the compound
- Larvae surveys within 100m radius

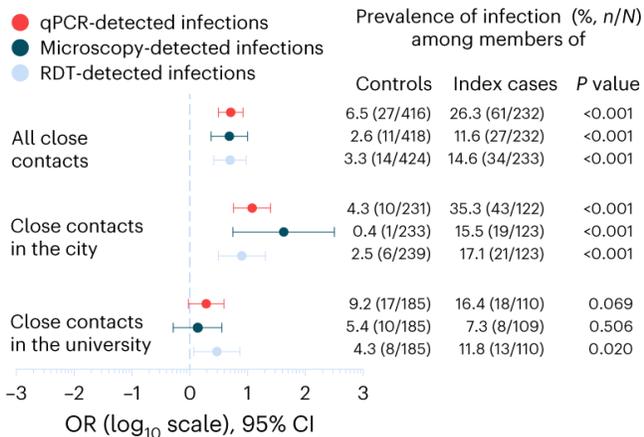
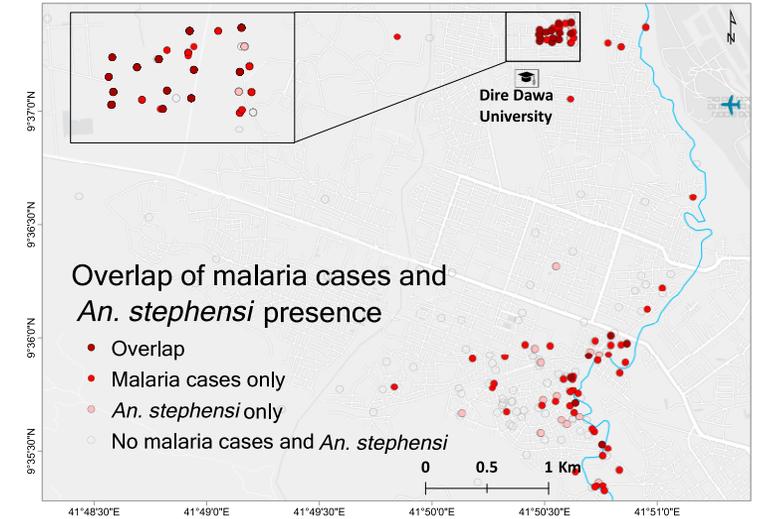
P. falciparum infections highly cluster around the index cases



Household members of malaria cases experience higher mosquito exposure



Areas with higher *P. falciparum* and *An. stephensi* abundance overlap



Anopheles larvae (*An. stephensi*):

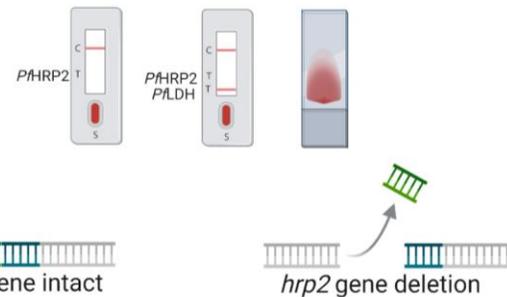
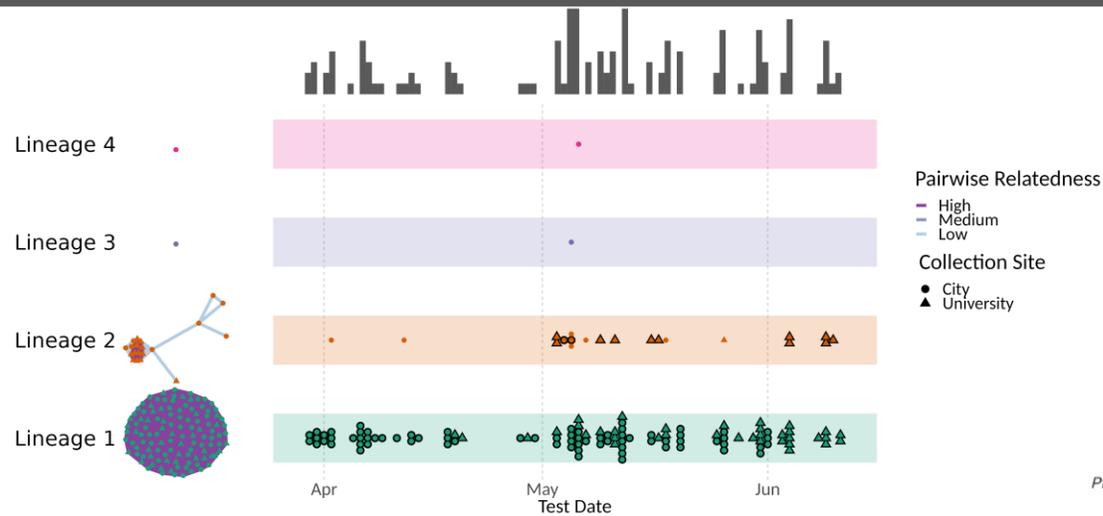
- Manmade: the only species detected
- Butiji river: 57% of the larvae

Adult mosquitoes

- Case control: All were *An. stephensi*
- *Aedes aegypti*: 21% (62/290) of the households
- Resting sites: Animal shelters 75%

An. stephensi mosquitoes were the only ones infected with *P. falciparum*

Convergence of biological threats to malaria at a smaller geography

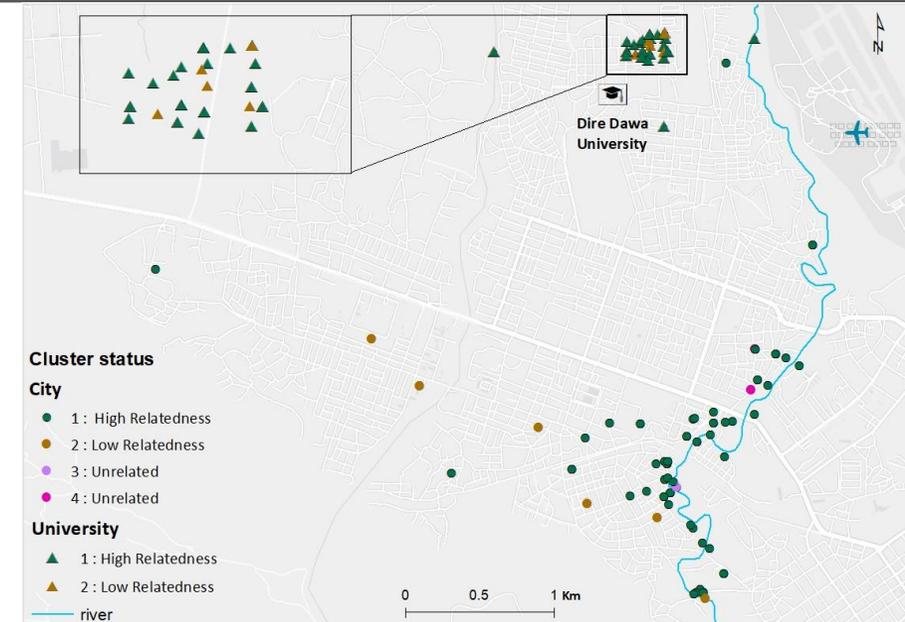


Lineage 1 infections (n=109)

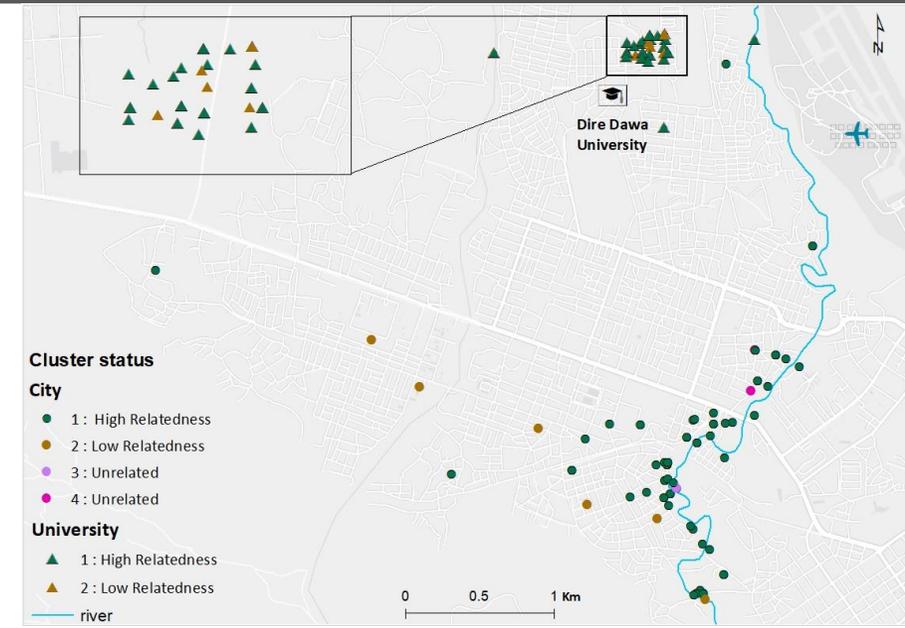
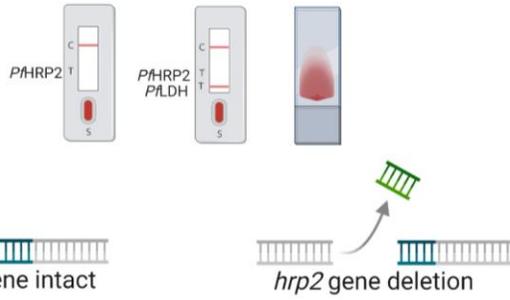
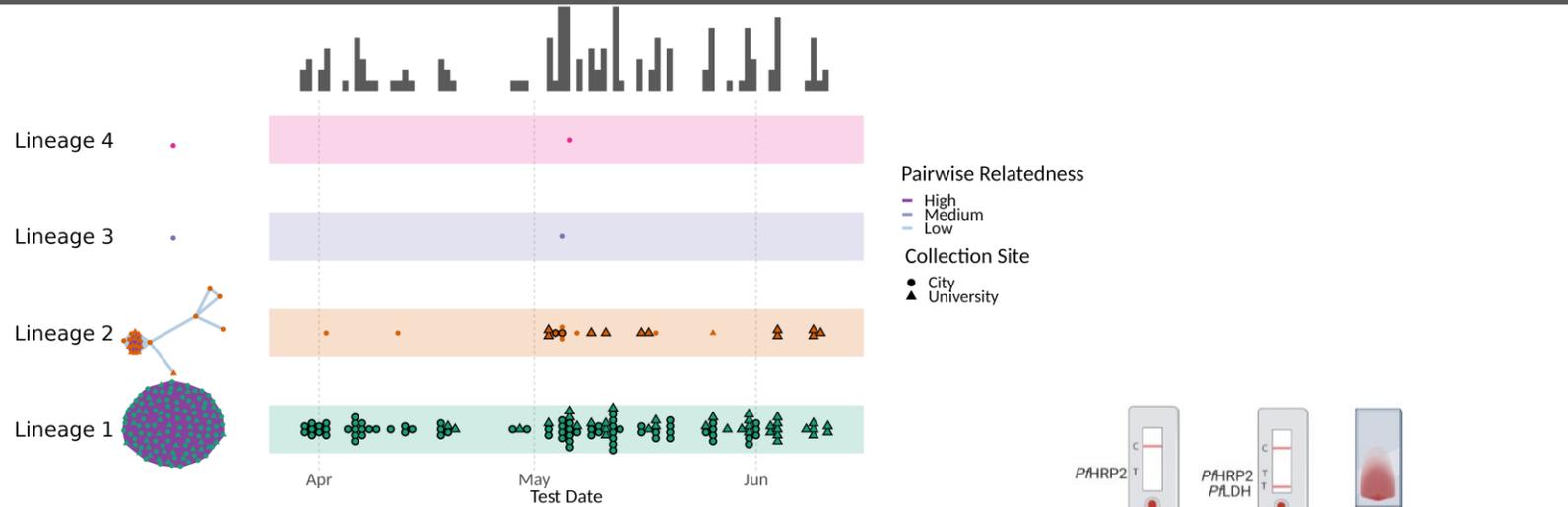
- No *pfhrp2* deletions
- Most were detectable by RDT (72%, 78/109)
- Only 2.8% contained the *kelch13* R622I mutation

Lineage 2 infections carried, 14/20

- *pfhrp2* and *pfhrp3* gene deletions
- Negative HRP2-based RDT but microscopy positive
- R622I mutation in the *kelch13* gene



Convergence of biological threats to malaria at a smaller geography



Lineage 1 infections (n=109)

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- R622I mutation in the *kelch13* gene

Emiru et al. 2023 Nat Med



Question #4

Would the existing interventions work well to target this mosquito?

***An. stephensi* evades standard vector control tools:**

- Unique ecology: Bites mainly animals and rests mostly in animal shelter
- Resistance to many of the currently available insecticides

Yared, Malar J 2020

Carbamates (bendiocarb and propoxur)
Pyrethroids (deltamethrin and permethrin)
DDT and malathion
Pirimiphos-methyl

Balkew, Malar J 2021

Pyrethroids, carbamates and organophosphates
Pre-exposure to PBO – increased susceptibility to pyrethroids
Larvae – susceptible to temephos

Teshome, Malar J 2023

IRS: propoxur, bendiocarb, pirimiphos-methyl
LLINs: alpha-cypermethrin, deltamethrin and permethrin



Question #5

Would the spectrum of the problem be limited in the typical settings in Africa?

- Populations with strong malaria control program are now affected (French Armed Force in Djibouti)

de Santi 2021 Emerg Infect Dis

- In ~40% of the time, *An. stephensi* is detected with *Ae. Aegypti*

Balkew 2021 Malar J

Tadesse 2021 Emerg Infect Dis

Conclusions

The spread of *An. stephensi* in rapidly expanding urban settings could pose a challenge to malaria control programs for many reasons

- Ability to exploit manmade containers that are abundantly present in rapidly expanding urban settings

1. Preference for manmade containers



- Resistant to many of the currently available chemicals that we use in insecticides and nets

2. Evades standard vector control tools



- It thrives in urban environments through different seasons

3. Year-round persistence



- Efficiently transmits both *P. falciparum* and *P. vivax*

4. Efficiently transmits both *Pf* & *Pv*



- Not only a container breeder
- Not only an urban vector
- Bites both humans/animals
- Rests mostly in animal shelter

5. Large behavioral variation



Carter 2018 Acta Trop
Balkew 2020 Parasit Vector
Tadesse 2021 Emerg Infect Dis
Balkew 2021 Malar J
Yared 2020 Malar J
Teshome 2023 Malar J

WHO response to the spread of *An. stephensi*



Dr Seth Irish

All Party Parliamentary Group

10 January 2024

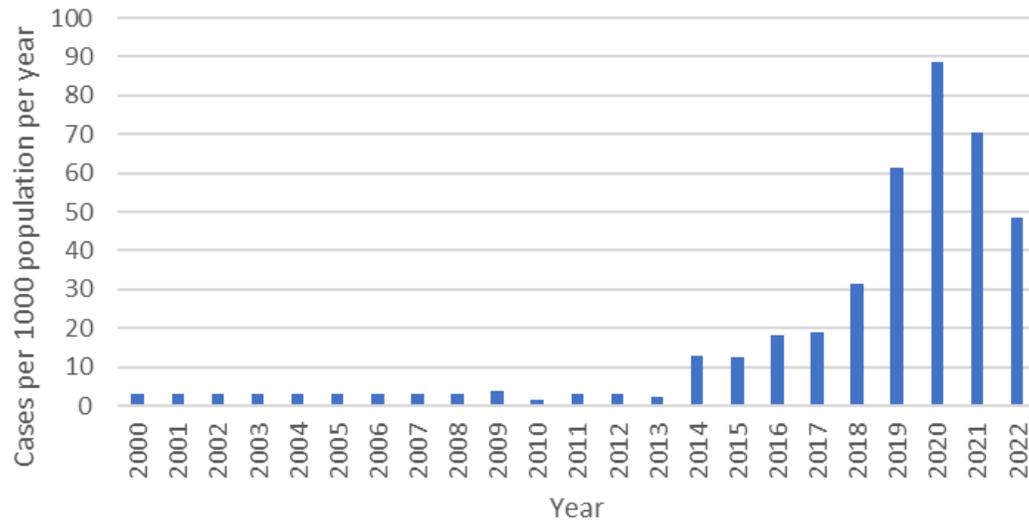
Global **Malaria** Programme



World Health
Organization



Djibouti annual parasite index



First record of the Asian malaria vector *Anopheles stephensi* and its possible role in the resurgence of malaria in Djibouti, Horn of Africa

Michael K. Faule^{a,b,*}, Leopoldo M. Rueda^c, Bouh A. Khaireh^d

^a Central Institute of the Bundeswehr Medical Service, Department of Medical Entomology/Zoology, PO Box 7340, D-56065 Koblenz, Germany

^b Institute of Medical Microbiology, Immunology and Parasitology, University Clinics Bonn, D-53105 Bonn, Germany

^c Walter Reed Biostatistics Unit, Entomology Branch, Walter Reed Army Institute of Research, 503 Robert Grant Avenue, Silver Spring, MD 20910, USA

^d Department of Infectious Diseases, Epidemiology and Clinical Research, Djiboutian Armed Forces Health Service, Djibouti City, Republic of Djibouti

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Plasmodium falciparum malaria
Outbreak
Djibouti

ABSTRACT

Anopheles stephensi is an important vector of urban malaria in India and the Persian Gulf area. Its previously known geographical range includes southern Asia and the Arab Peninsula. For the first time, we report *A. stephensi* from the African continent, based on collections made in Djibouti, on the Horn of Africa, where this species' occurrence was linked to an unusual urban outbreak of *Plasmodium falciparum* malaria, with 1228 cases reported from February to May 2013, and a second, more severe epidemic that emerged in November 2013 and resulted in 2017 reported malaria cases between January and February 2014. *Anopheles stephensi* was initially identified using morphological identification keys, followed by sequencing of the Barcode cytochrome c-oxidase I (COI) gene and the rDNA second internal transcribed spacer (ITS2). Positive tests for *P. falciparum* circumsporozoite antigen in two of six female *A. stephensi* trapped in homes of malaria patients in March 2013 are evidence that autochthonous urban malaria transmission by *A. stephensi* has occurred. Concurrent with the second malaria outbreak, *P. falciparum*-positive *A. stephensi* females were detected in Djibouti City starting in November 2013. In sub-Saharan Africa, newly present *A. stephensi* may pose a significant future health threat because of this species' high susceptibility to *P. falciparum* infection and its tolerance of urban habitats. This may lead to increased malaria outbreaks in African cities. Rapid interruption of the urban malaria transmission cycle, based on integrated vector surveillance and control programs aimed at the complete eradication of *A. stephensi* from the African continent, is strongly recommended.

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1. Introduction

The Republic of Djibouti is a small country (43°00' E, 11°30' N; 23,200 km² total area; 860,000 estimated population) located on the Horn of Africa (World Factbook, 2013; WHO, 2014). According to WHO data, *Plasmodium falciparum* malaria is exclusively transmitted by *Anopheles arabiensis* Patton and *Anopheles gambiae* Giles in Djibouti (WHO, 2014). Although the Horn of Africa is known to be highly susceptible to mosquito-borne infectious diseases, Djibouti was formerly thought to be a meso- to hypo-endemic country

with unstable malaria transmission (Carteron et al., 1978; Fox et al., 1989, 1991). Low levels of *P. falciparum* malaria endemicity in 2007 were also predicted for this area after employing a global mapping approach based on 7953 *P. falciparum* parasite rate surveys (Hay et al., 2009). The last malaria epidemic occurred in Djibouti City from March to June 1999 (Rogier et al., 2005). Since then, malaria cases had dropped to an incidence rate of <1/1000 persons/year (Ollivier et al., 2011). Studies further revealed that Djibouti was entering a malaria pre-elimination phase because conditions for its eradication had been established (Noor et al., 2011; Khaireh et al., 2013).

From January to May 2013, Djibouti experienced an unusual urban outbreak of *P. falciparum* malaria, with 1228 reported cases, of which 1016 (82.7%) were from Djibouti City alone (United Nations, 2013). Beginning in late January 2013, approximately 100 imported cases occurred in Dikhil State among a nomad

* Corresponding author at: Central Institute of the Bundeswehr Medical Service, Department of Medical Entomology/Zoology, PO Box 7340, D-56065 Koblenz, Germany. Tel: +49 261 400 6950; fax: +49 261 400 7084.
E-mail address: Michael.Faule@bundeswehr.org (M.K. Faule).

Meeting report of the WHO technical consultation on the spread of *Anopheles stephensi*

25-27 June 2019, Geneva, Switzerland

1. Background

In recent years, *Anopheles stephensi*, an efficient urban malaria vector for both *Plasmodium falciparum* and *P. vivax*, has been reported in four countries outside of the previously known geographical range, which was considered to be confined to certain countries in South-East Asia and large parts of the Arabian Peninsula.

The first detection outside the traditional geographical range was reported in Djibouti in 2012, in an area between Djibouti City and the Somali border (1). A follow-up study from 2013 to 2017 confirmed the presence of *An. stephensi* mosquitoes in Djibouti City 2017 (2). In addition, in 2016, the vector was detected for the first time in Mannar Island in Sri Lanka, five years after the country achieved zero malaria transmission (3). Subsequently, *An. stephensi* was reported in Ethiopia's Somali Regional State (4) and, most recently, in the Red Sea and Gedaref states in East Sudan (Ayman Ahmed, personal communication).

Experiences gained within the traditional geographical range of *An. stephensi* have shown that it can be a highly efficient malaria vector, particularly when it establishes itself in urban environments. Some of the *An. stephensi* specimens collected in Djibouti City were positive for *P. falciparum* sporozoites. The presence of this vector has been linked to the unusual urban malaria outbreak in Djibouti City in 2012.

The detection of *An. stephensi* in countries outside its established range poses a potential threat to malaria control and elimination. In Sri Lanka, the emergence of this vector could jeopardize efforts to prevent the reintroduction of malaria. In Africa, given the rapid and uncontrolled growth of cities, the potential establishment of this vector in urban environments could put at risk the reductions in malaria burden achieved since 2000.

2. Objectives of the Technical Consultation

The World Health Organization (WHO) plays a key role in monitoring threats to malaria control, elimination and prevention of re-establishment, and in providing guidance to Member States on how to manage these threats. Recognizing the emergence and spread of *An. stephensi* through the Horn of Africa and Sudan as a potential threat, WHO convened a Technical Consultation to assess the current evidence on this potential threat and to define a response strategy.



Theme:  Invasive vector species

Map: Vector occurrence

FILTER DATA

Vector species: all

Years

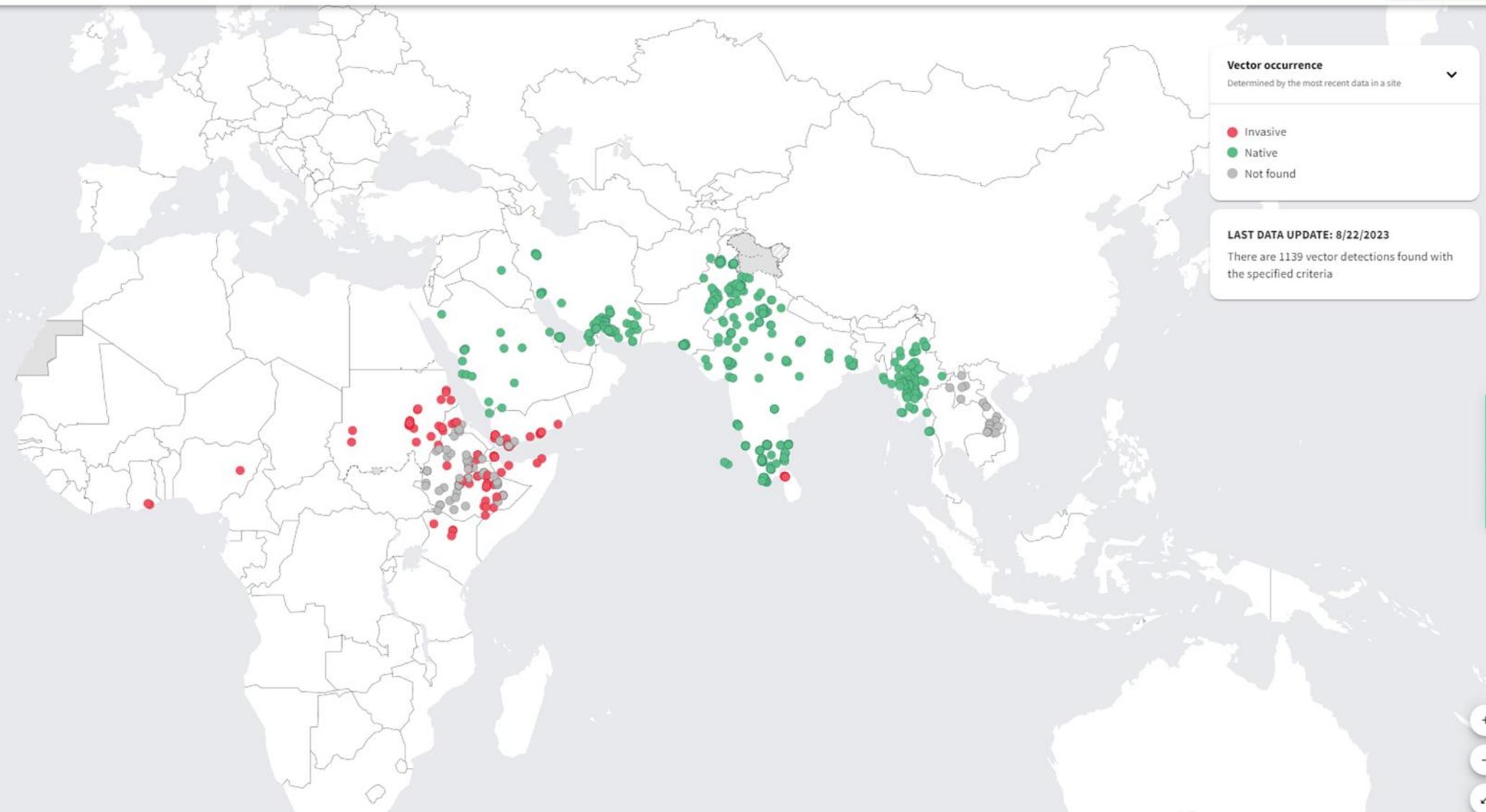
1984 2023

1984 2003 2023

Play animation

If you have detected invasive *Anopheles* vector species please report to us through the [reporting form](#)

FILTER LOCATION (OPTIONAL)



Vector occurrence

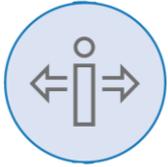
Determined by the most recent data in a site

- Invasive
- Native
- Not found

LAST DATA UPDATE: 8/22/2023

There are 1139 vector detections found with the specified criteria

REPORT BUGS



Information exchange



Increasing collaboration



Strengthening surveillance



Prioritizing research



Developing guidance

WHO initiative to stop the spread of *Anopheles stephensi* in Africa

2023 update

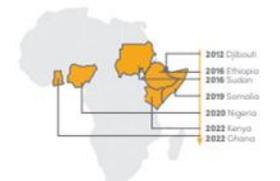
Anopheles stephensi at a glance

Anopheles stephensi is a mosquito species that is capable of transmitting both *Plasmodium falciparum* and *P. vivax* malaria parasites. It was originally native to South Asia and parts of the Arabian Peninsula but has been expanding its range over the last decade, with detections reported in Djibouti (2012), Ethiopia and Sudan (2016), Somalia (2019), Nigeria (2020) and Ghana and Kenya (2022). To date, it remains unclear when and via which route these countries were invaded. Although *An. stephensi* has likely spread to other African countries, it has yet to be detected as systematic, large-scale surveillance of the vector is still in its infancy.

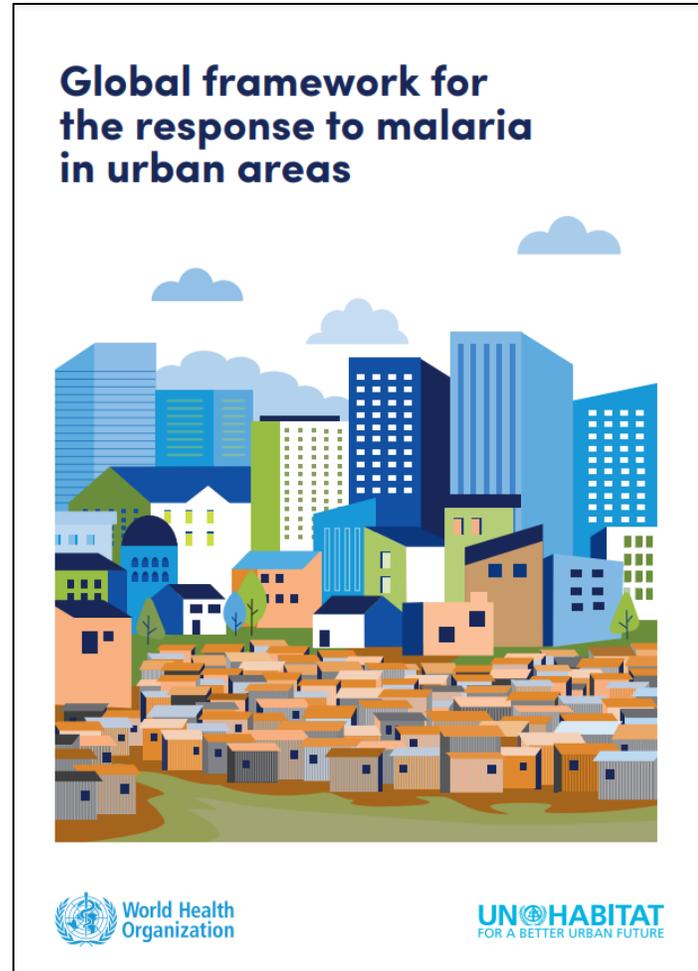
Anopheles stephensi has the capacity to thrive in urban and man-made environments, setting it apart from the other main mosquito vectors of malaria that primarily breed in naturally occurring waterbodies in rural areas. Where *An. stephensi* has been reported in Africa, it has been found to be resistant to many of the insecticides used in public health, posing an added challenge to its control.

The invasion of *An. stephensi* in sub-Saharan Africa – where the burden of malaria is highest and over 40% of the population lives in urban environments – is particularly worrying. Since 2012, *An. stephensi* is thought to have contributed to a resurgence of malaria in Djibouti City and at least one outbreak of the disease in Ethiopia. While the overall contribution of *An. stephensi* to malaria transmission in the region is unclear, the rapid growth of many African cities, coupled with the invasion and spread of this highly efficient and adaptable malaria vector, could undermine the gains made in reducing the burden of the disease.

Spread of *Anopheles stephensi* in Africa



- Role of municipalities in malaria control
 - Water storage / water systems
 - Construction
 - Education
 - Waste management
 - Agriculture
 - *Aedes aegypti* and other mosquitoes





- MS Teams call every quarter for updates on *An. stephensi*
- Those interested in joining can send me an email:
 - irishs@who.int

Thank you

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The Long-Term Significance of *Anopheles stephensi* in Africa

Parliamentary
Reception on
Anopheles stephensi

January 10th
2024

Jo Lines



www.lshtm.ac.uk/raft

The Long-Term Significance of *Anopheles stephensi* in Africa



Effects of Development and their role in Elimination



The strategic impact of *stephensi* likely to grow and grow



-- over time, and



-- as we approach elimination;

Why worry ?

Does *stephensi* matter so much?



The African vectors are *Anopheles gambiae* and *An funestus*



They are the world's BEST vectors = most efficient at transmitting the parasite.



Hence Africa has 90% of global malaria deaths!

The addition of another species of lower efficiency:

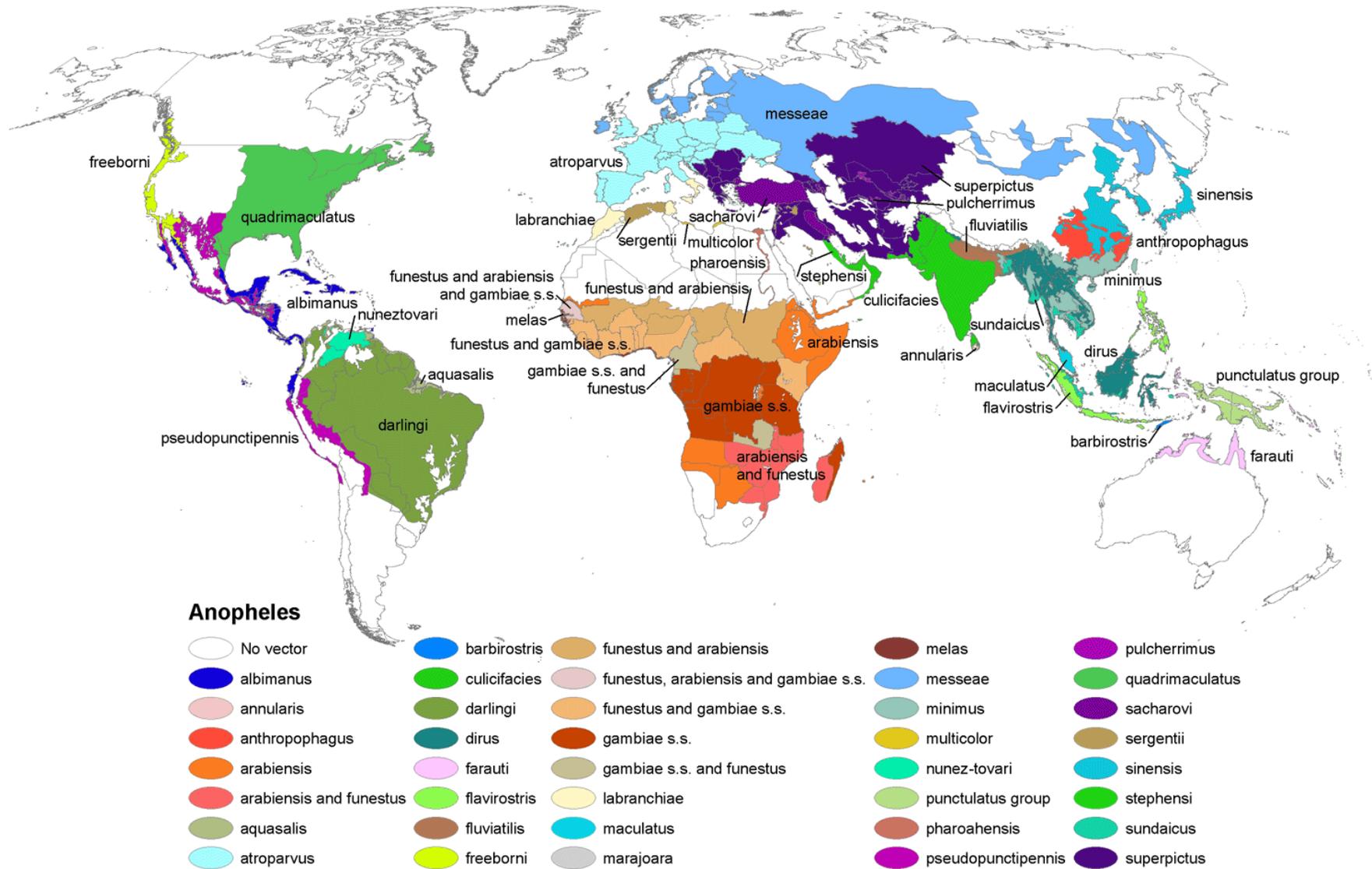


obviously not ideal,



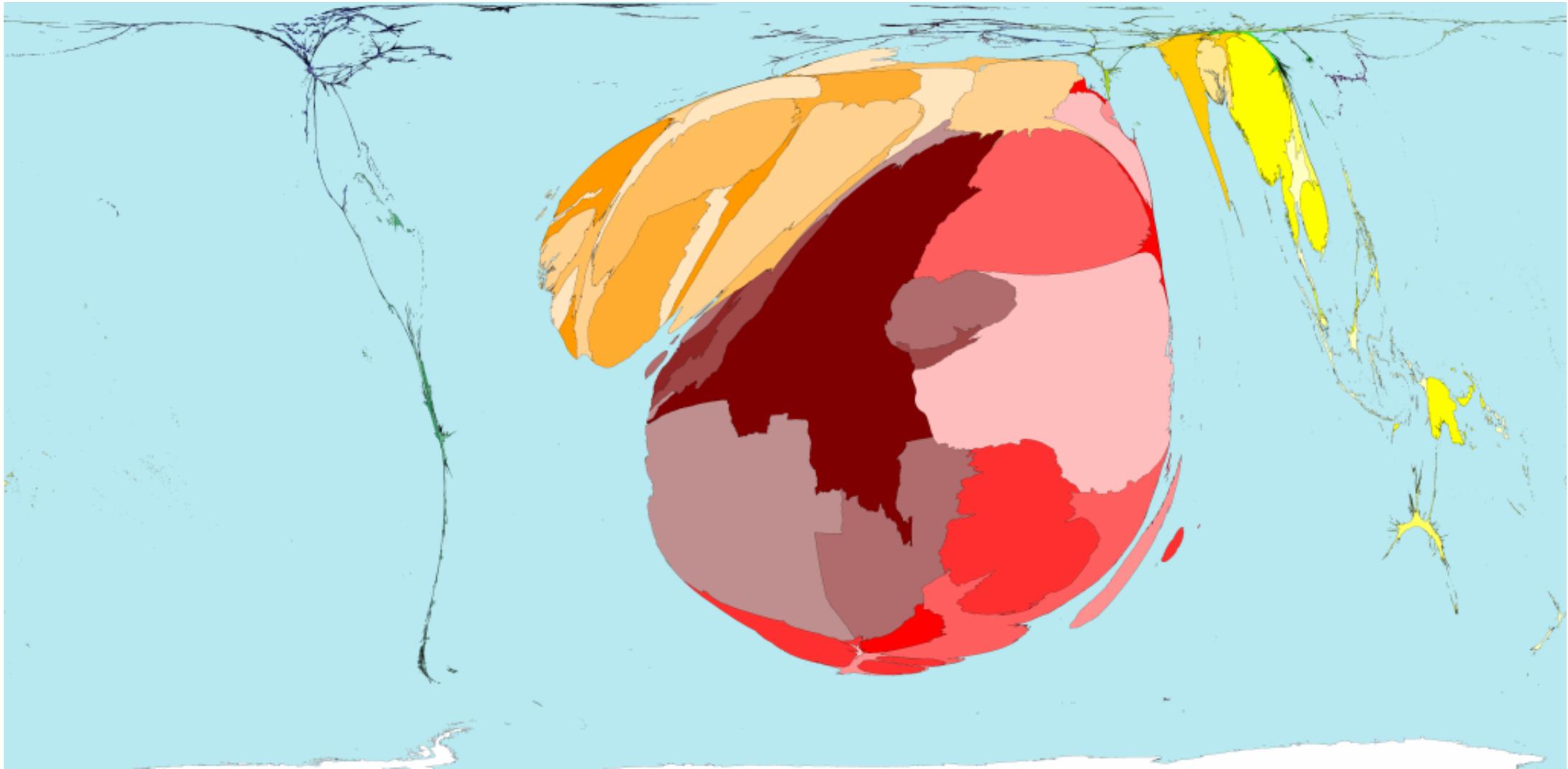
but surely not decisively disastrous?

Global distribution of primary malaria vectors



Kiszewski et al. (2004) AMJTMH 70: 486-498

The *Anopheles gambiae* problem:
Global distribution of malaria deaths in 2004



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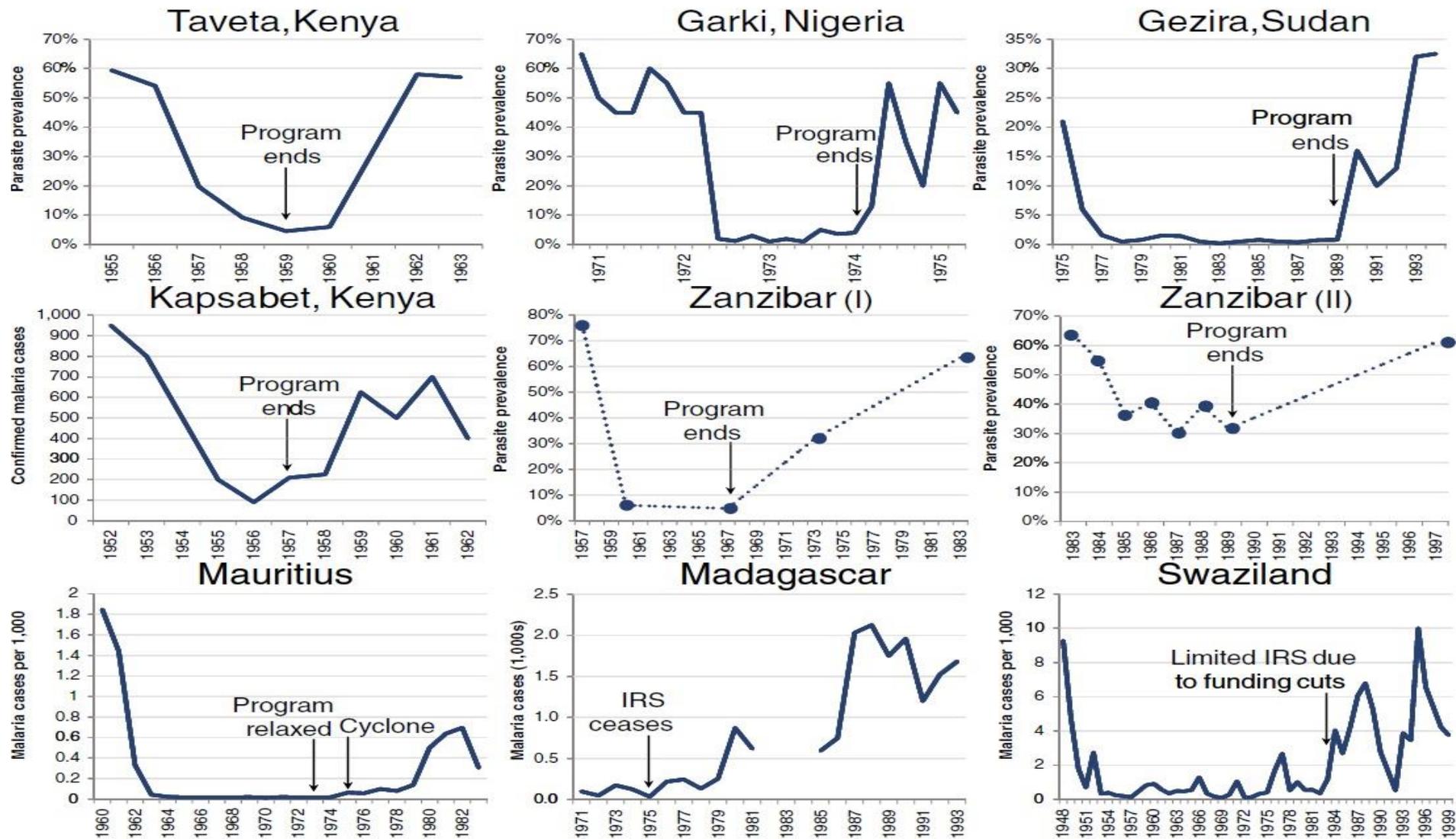


obviously not ideal,



but surely not decisively disastrous?

Coverage and resurgence: we cannot relax the pressure



Urbanisation in Africa (so far): building malaria **out**



African vectors cannot breed in polluted water, or in man-made containers.



Hence, urbanisation reduces malaria transmission: towns have less transmission, big city centres are often malaria-free. In these extremely urbanised settings, the absence of malaria is already a stable state.



Hence there is an unspoken underlying assumption that eventually, the process of development (especially urbanisation) will drive malaria out of Africa.



Urbanisation in India: building malaria in



In India, the main vectors of malaria are *Anopheles culicifacies* in rural areas and *Anopheles stephensi* in towns and cities.

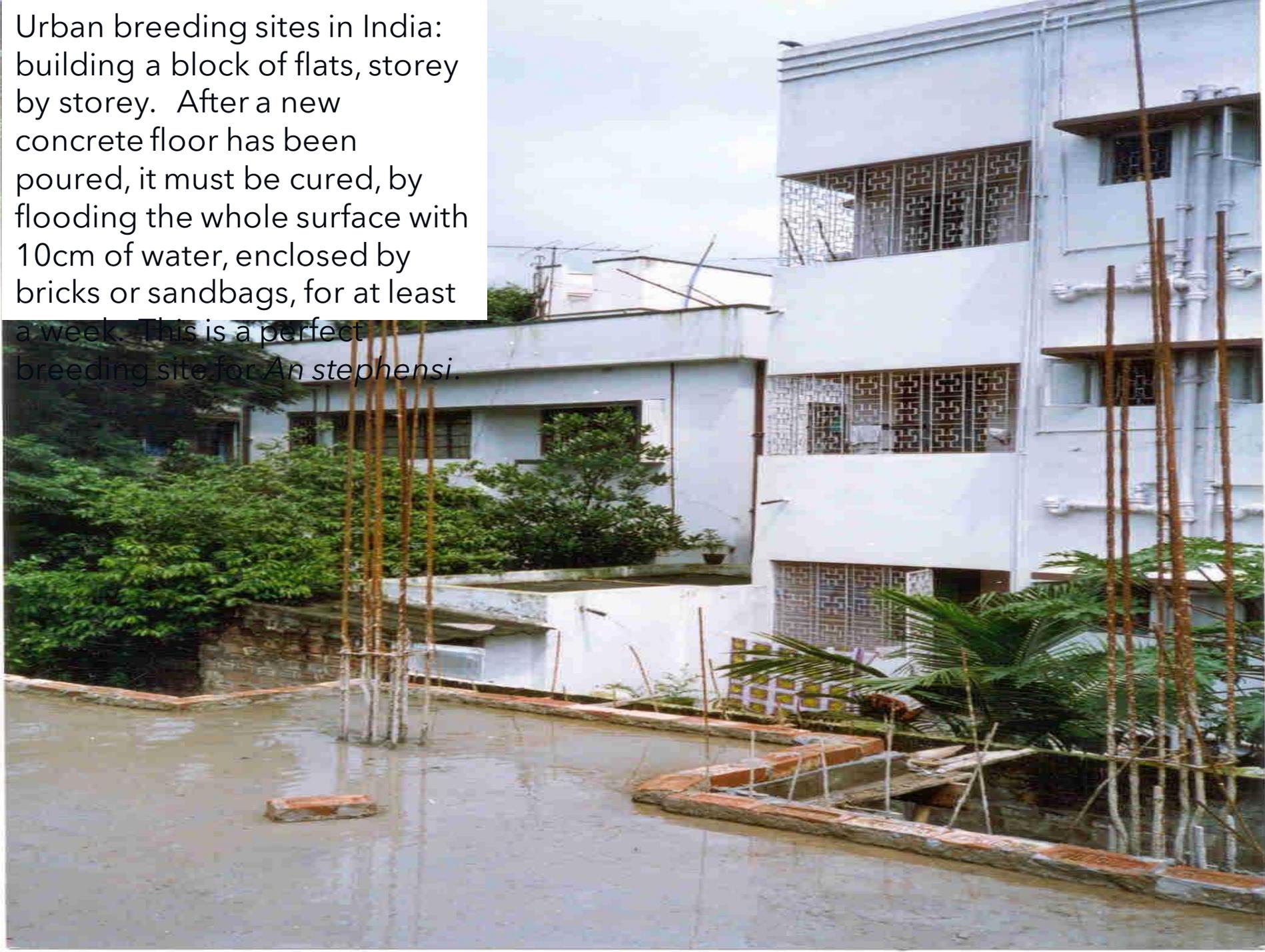


Anopheles stephensi breeds happily in man-made containers, especially water storage tanks of all kinds.



Hence, in India, urbanisation increases malaria transmission: many large towns have more transmission than the surrounding villages.

Urban breeding sites in India: building a block of flats, storey by storey. After a new concrete floor has been poured, it must be cured, by flooding the whole surface with 10cm of water, enclosed by bricks or sandbags, for at least a week. This is a perfect breeding site for *An stephensi*.



Previous success stories of Malaria Elimination elsewhere



Malaria Programmes have stressed the need for intersectoral action to avoid “malariogenic” activities:



Europe: drainage and barns for over-wintering cattle



Italy after WW2: “bonification”



USA: Tennessee Valley Authority and screen doors

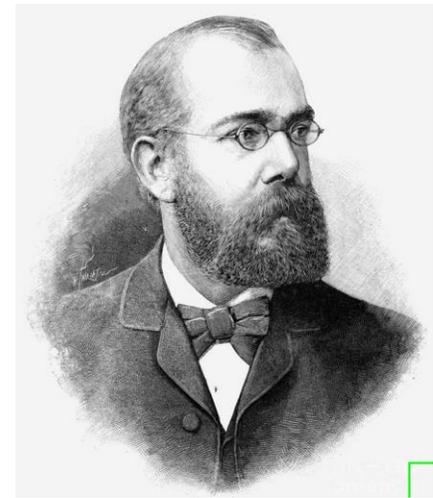


China: rice-growing methods, wet-dry irrigation, fish+rice cultivation

Medical vs Social vs Environmental

Robert Koch:

- “Malaria is a Medical Problem”
 - Treat the patient, not the mosquito



Angelo Celli, Manson et al.

- “Malaria is a Social Disease”
 - Malaria flees before the Plough
 - Bonification = housing, landscape, wages



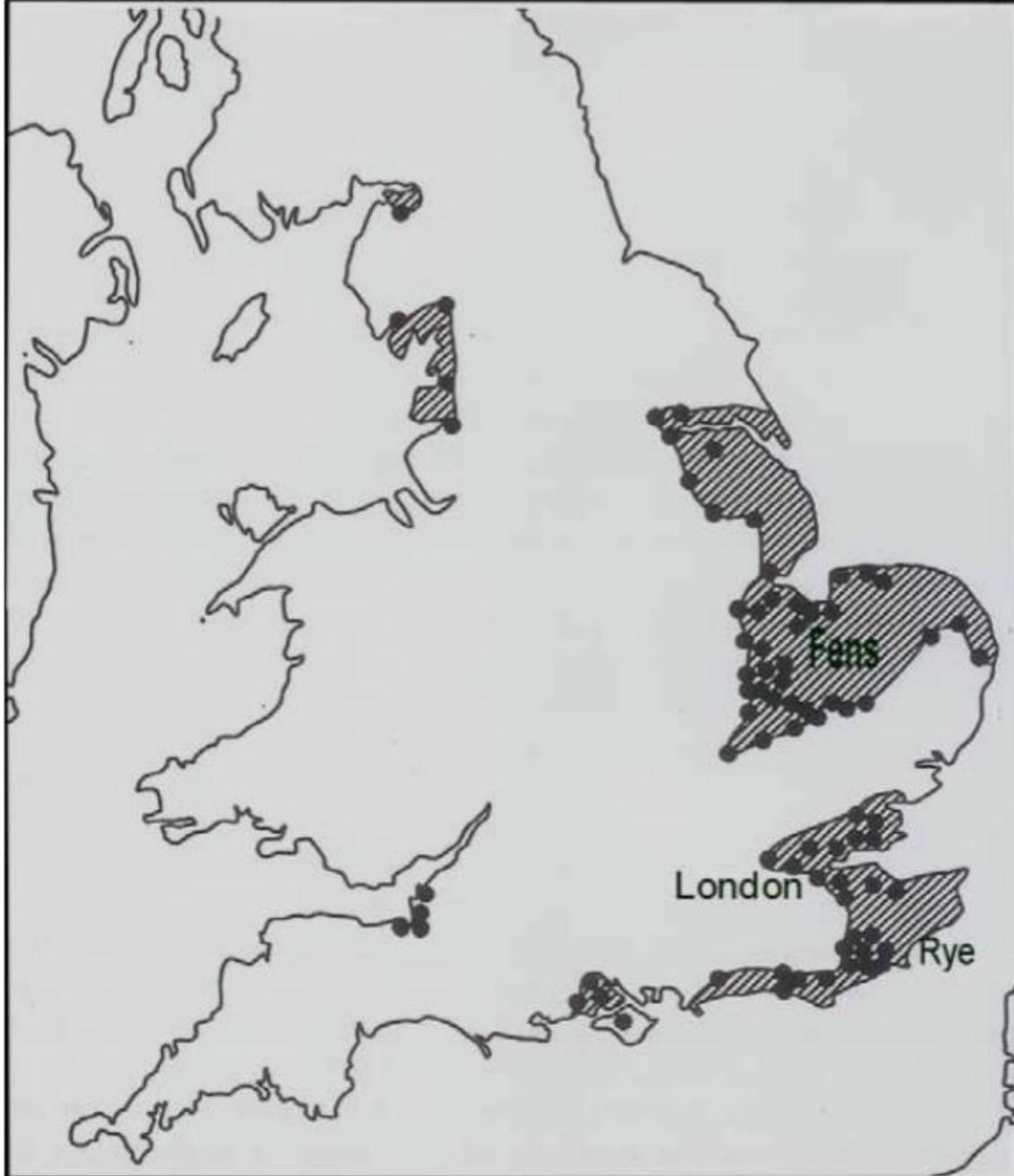


Figure 4. Geographical Distribution of malaria in England in the 1860s

Lt-Colonel SP James 1929

“...the diminution of local malaria in England was due neither to natural causes nor to the intentional application of any particular preventive method reputed to be specific, but to progressive improvements of a social economic, educational, medical, and public health character.”

Question Point

- In the past, successful elimination programmes have actively:
 -  discouraged development activities that build malaria IN and
 -  encouraged those that build malaria OUT
 -  much harder with *stephensi*!
- Is it too late to get rid of *stephensi* completely?
- How they do it in Agriculture:
 - E.g. the New World Screwworm in Libya
 - Modern genetic control methods aiming for 100% extinction in Africa

Convergence of biological threats to the fight against malaria in the Horn of Africa

Monday 15 January at 13.00 GMT
Online | LSHTM

Dr Fitsum Tadesse, Research Fellow
Malaria Centre, LSHTM

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