Managing and maintaining diagnosis in the community

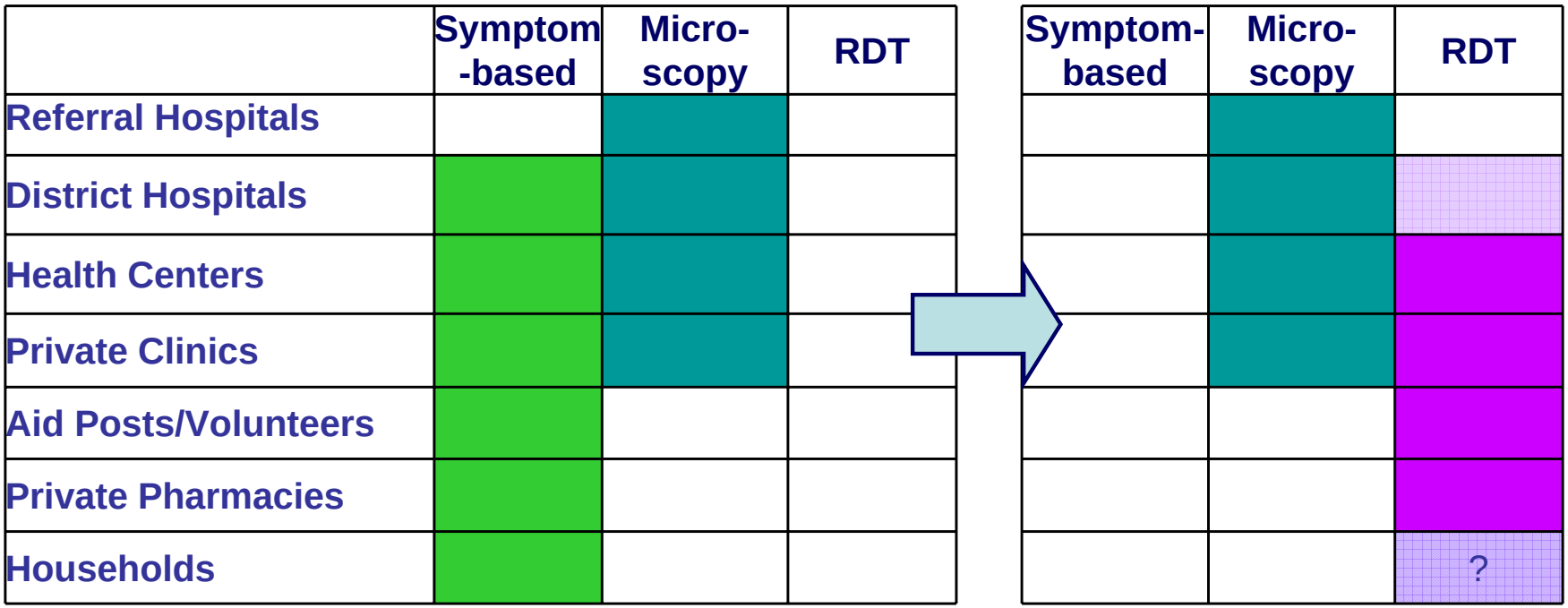
–

Sustaining gains

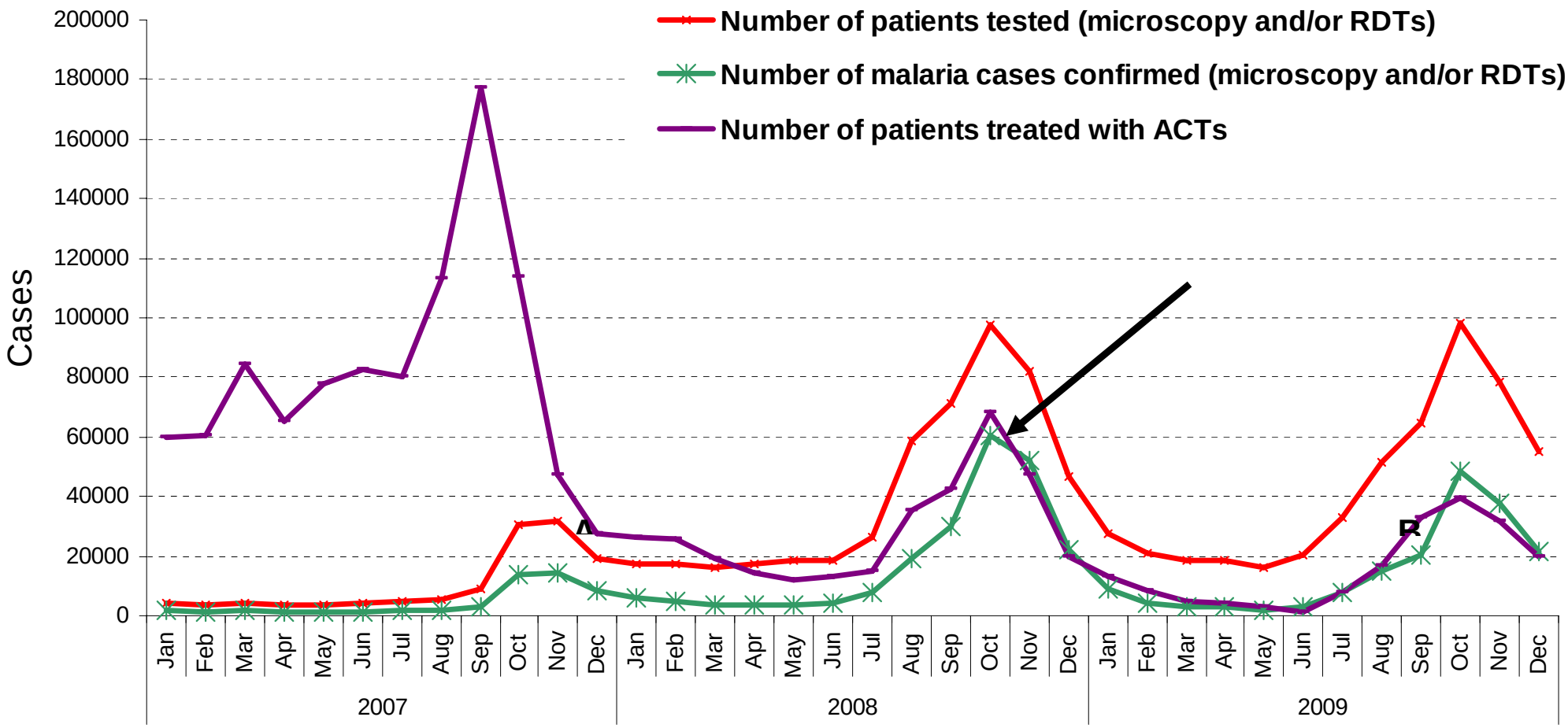
David Bell
WHO – Global Malaria Programme
International Malaria Colloquium 2010 (IMC 2010)
Bangkok. December 2010

Malaria Diagnosis, WHO, 2009

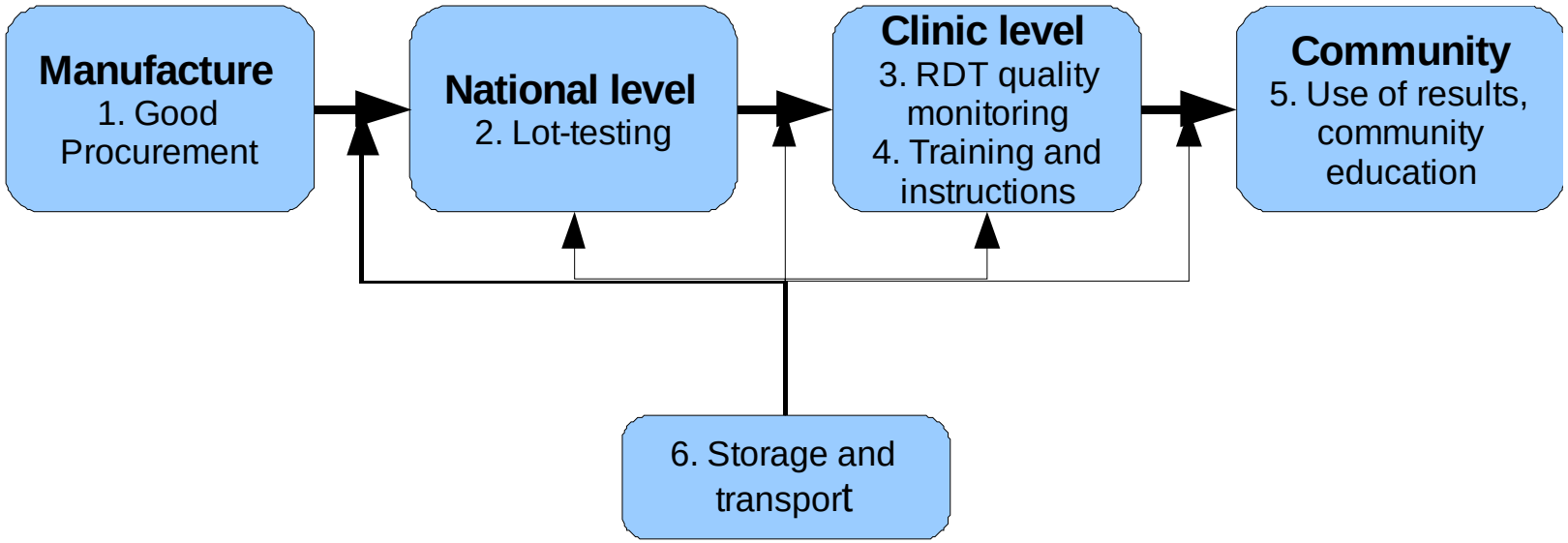
- **Prompt parasitological confirmation by microscopy or alternatively by RDTs is recommended in all patients suspected of malaria before treatment is started.**
- **Treatment solely on the basis of clinical suspicion should only be considered when a parasitological diagnosis is not accessible.**



Evolution of parasite based diagnosis in malaria in Senegal public health services 2007-2009.



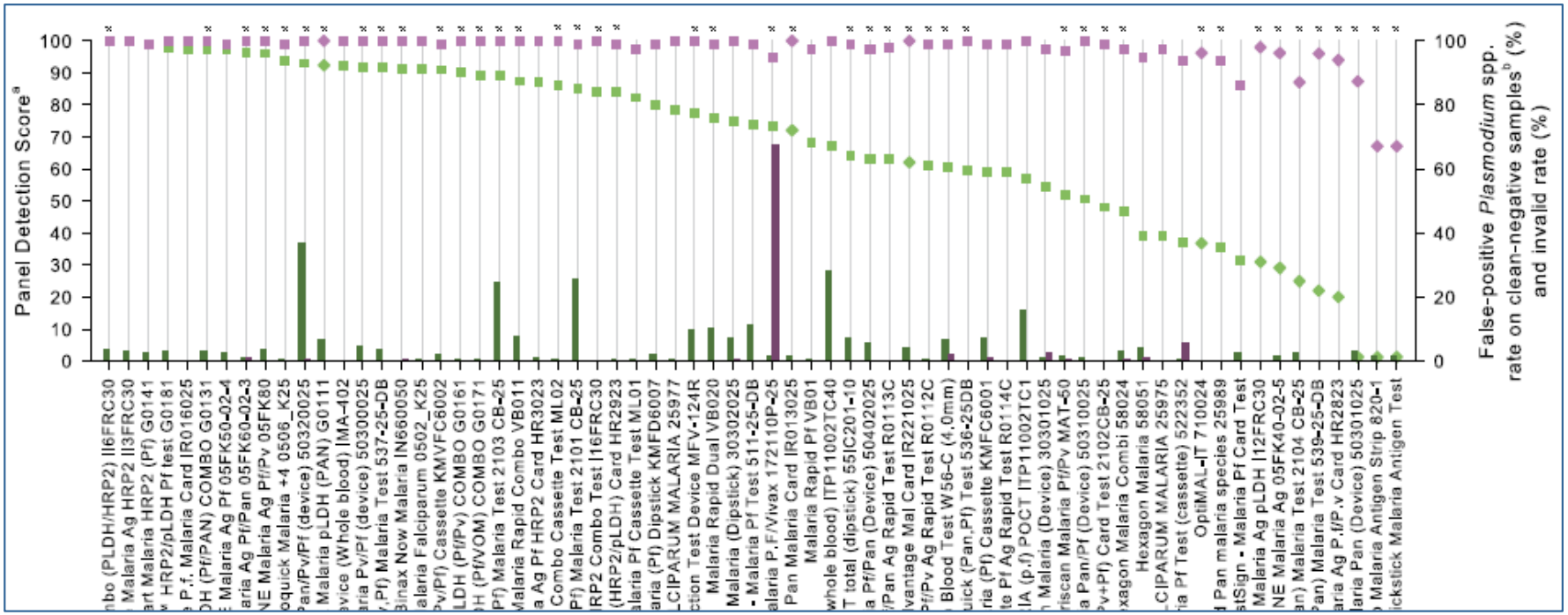
WHO-FIND malaria RDT evaluation programme



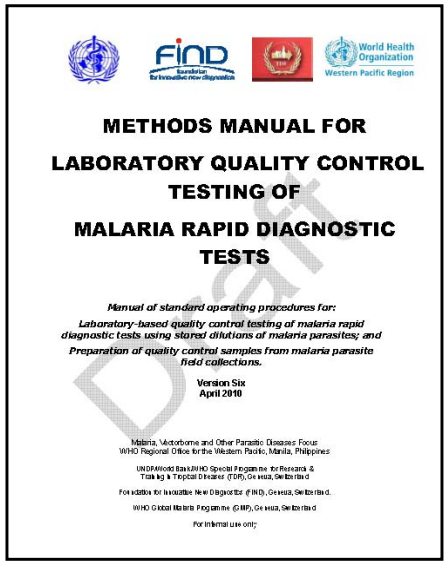
WHO malaria RDT product testing
Round 1 & 2 results

Rnd 1 (2008) 41 products
Rnd 2 (2009) 29 products
Rnd 3 (2010) 50 products

P. falciparum



Lot Testing



METHODS MANUAL FOR

LABORATORY QUALITY CONTROL TESTING OF

MALARIA RAPID DIAGNOSTIC TESTS

Manual of standard operating procedures for:

Laboratory-based quality control testing of malaria rapid diagnostic tests using stored dilutions of malaria parasites; and

Preparation of quality control samples from malaria parasite field collections.

Version Six
April 2010

Malaria, Vectorborne and Other Parasitic Diseases Focus
WHO Regional Office for the Western Pacific, Manila, Philippines

UNDP/World Bank/WHO Special Programme for Research & Training in Tropical Diseases (TDR), Geneva, Switzerland.

Foundation for Innovative New Diagnostics (FIND), Geneva, Switzerland.

WHO Global Malaria Programme (GMP), Geneva, Switzerland

For internal use only

Draft

2006: 41 lots

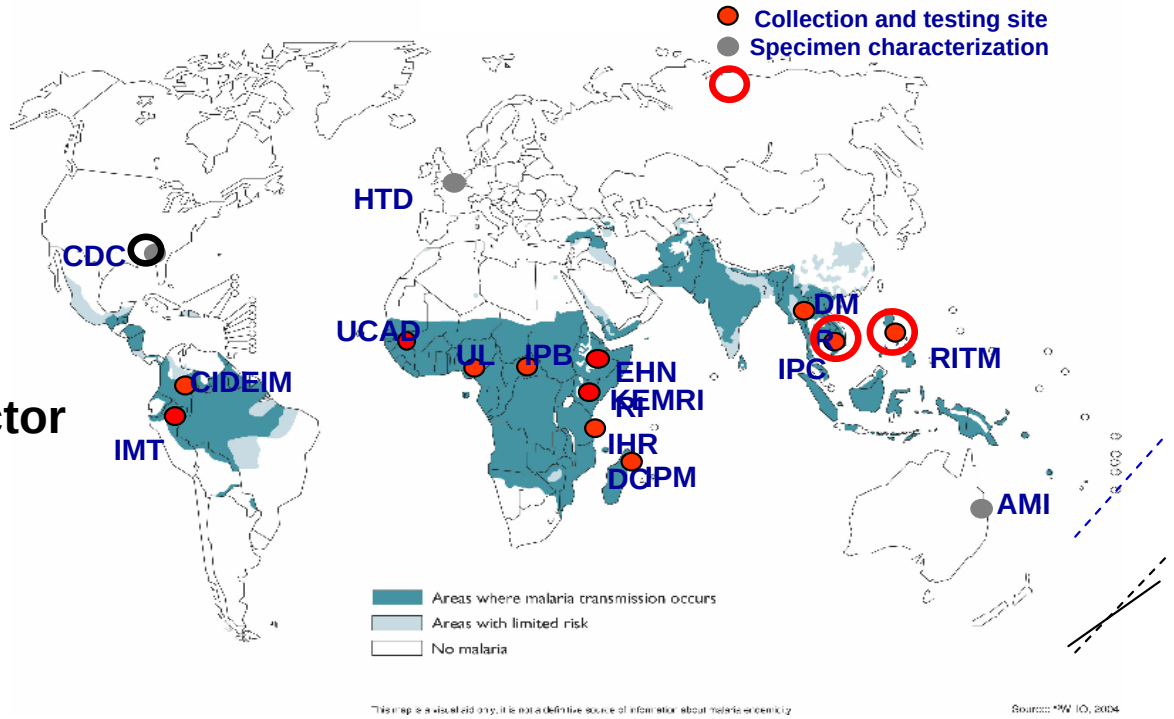
2007: 81 lots

2008: 167 lots

2009: 196 lots

2010: +++

(?15% of public sector procurement)



Future lot-testing panels

Recombinant-based panels, suitable for use at NMCP level.

Trials in 2011

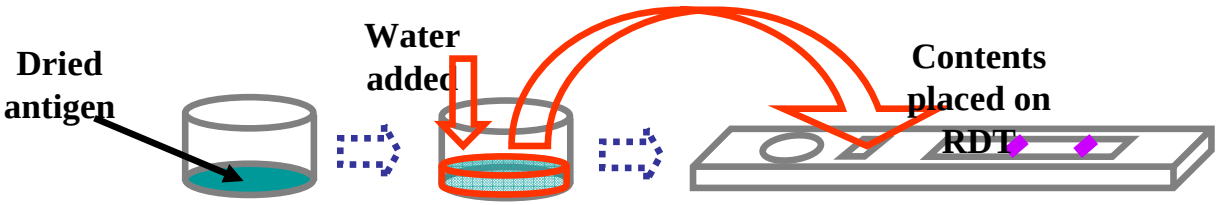
Community/clinic-level monitoring of RDT quality

Still a gap, but can:

- **Compare routinely with microscopy at sentinel sites (often difficult, works if good microscopy)**
- **Withdraw of RDTs from field for lab testing (working in some situations, but logistically difficult**

Future: Positive Control Wells

- **Under development by FIND, WHO, and partners**
- **Field implementation trials 2011**



Training and instructions - Zambia

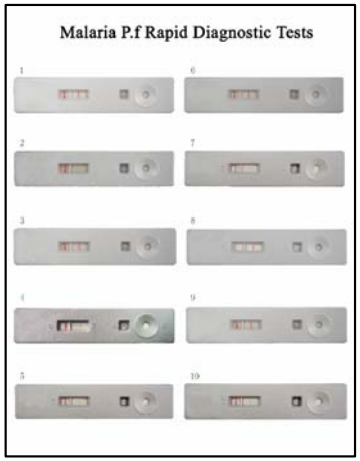
Suite of products:

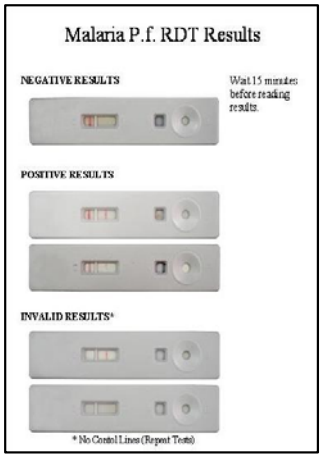
Job-aid

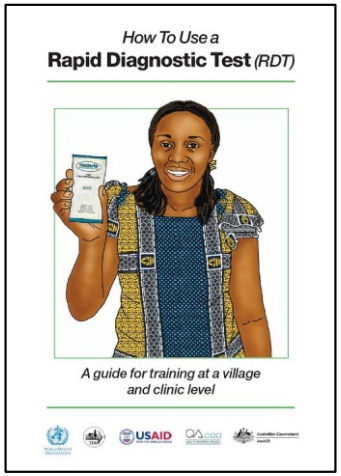
Training manual

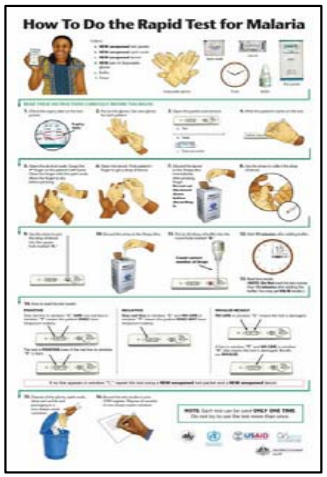
Photographic result guide

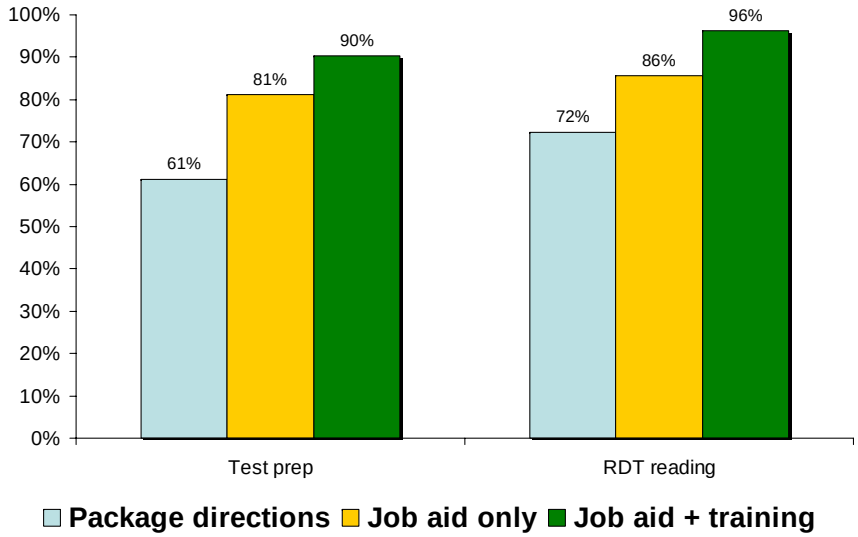
Proficiency tests



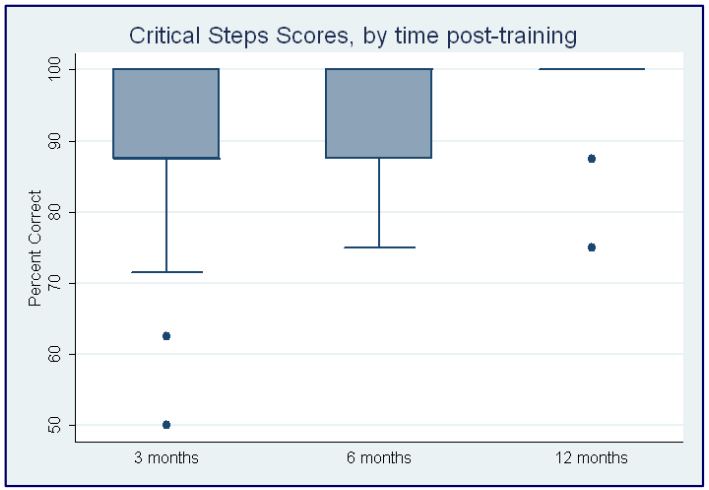








12 month follow-up 2008-9:
Performance of 'critical steps'



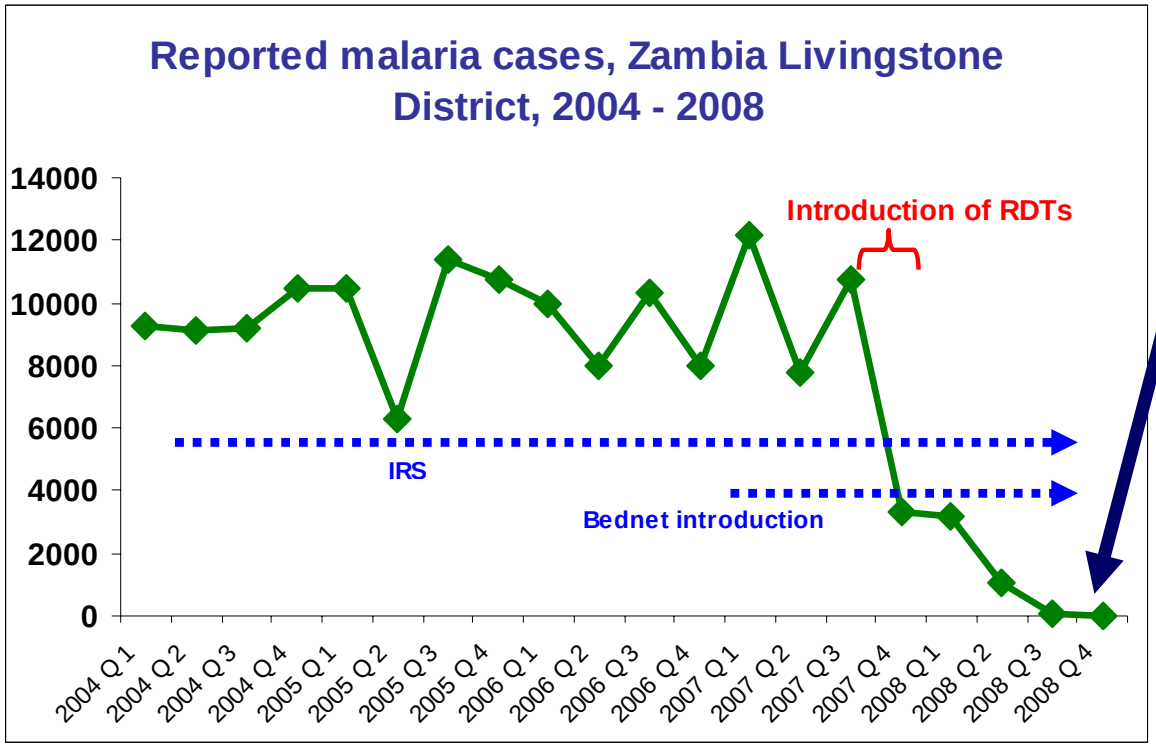
Zambia MoH, URC, WHO, TDR, FIND, Malaria Consortium

www.wpro.who.int/sites/rdt,

Courtesy: Malaria Consortium

Accurate malaria diagnosis <u>can</u> now be accessible to all.

Success. What next?



Successful intervention

10 cases per month.

Malaria now down from 1st to 16th district health priority….other disease priorities are more urgent

But the mosquitoes and the people are still there…

We have the tools to identify and manage malaria as a common disease

We need new tools and strategies to manage malaria as a rare disease

Challenges for low-prevalence malaria

- **Loss of interest**
  - **Few deaths**
  - **Little publicity**
- **Less finance available?**
  - **Priorities elsewhere (eg. GF, DFID strategy)**
  - **Fall-out from financial crisis**
- **Conditions for transmission remain**
  - **Vectors**
  - **People / immigration**
  - **LLINs will wear out after 3-5 years**

Maintaining very low transmission / elimination with current tools: Zanzibar

The costs of keeping R_0<1

Zanzibar elimination feasibility assessment

(with and without bednets long-term)

- **Population immunity drops**
- **Immigrants from malaria-endemic areas continue to arrive**
- **Vectors remain**

Who would pay for this when the excitement of elimination is over?

FIGURE 30: AVERAGE COST PER YEAR FOR THE DIFFERENT STAGES OF AN ELIMINATION PROGRAM WITH LLINS KEPT AT > 75% EFFECTIVE COVERAGE COMPARED TO SUSTAINED CONTROL

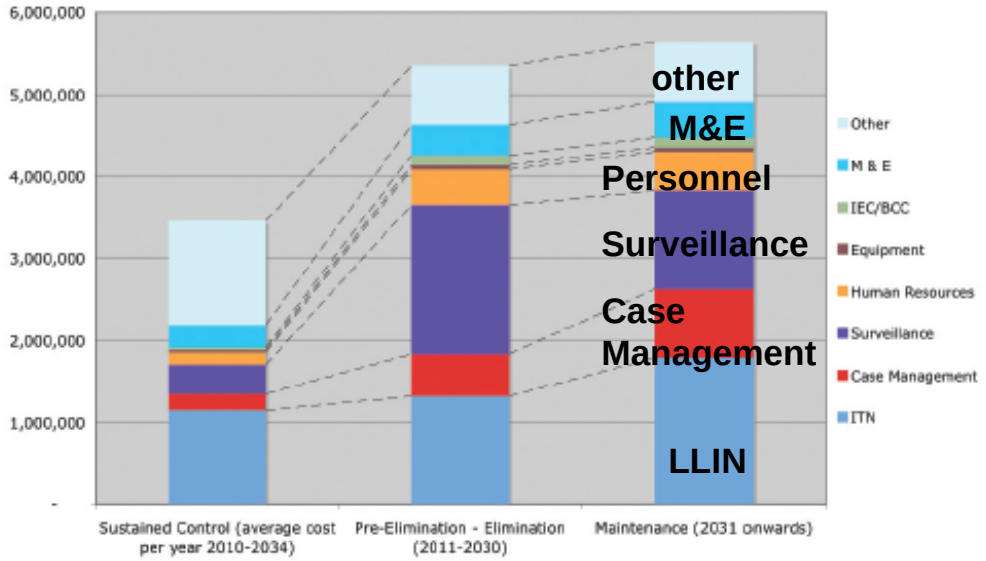
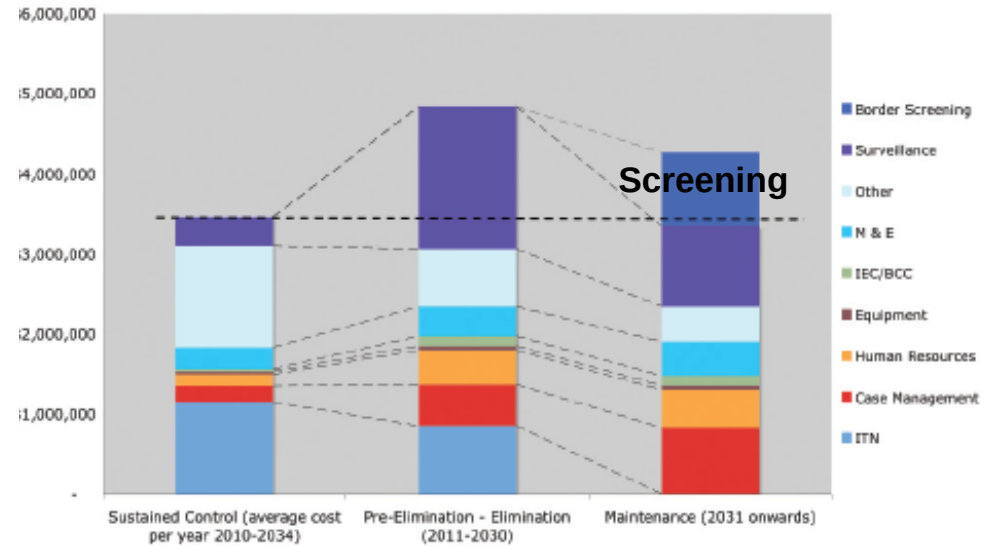


FIGURE 31: AVERAGE COST PER YEAR FOR THE DIFFERENT PHASES OF AN ELIMINATION PROGRAM WITH NO LLINS AFTER 2030, COMPARED TO SUSTAINED CONTROL



Source: Malaria Elimination in Zanzibar - Feasibility assessment. October 2009. Zanzibar Malaria Control Programme

Very low prevalence settings in resource-limited countries

- **Unlikely to sustain microscopy competence or infrastructure when slides ~always negative**
- **Difficult to maintain financing for RDTs for all febrile cases if results are nearly always negative**
- **Hard to maintain priority and enthusiasm within the MoH and within communities**
- **Unlikely to maintain adequate donor funding for conventional programme**

But

- **Still high probability of focal transmission and re-introduction outbreaks**

How to keep tools and workers in place?

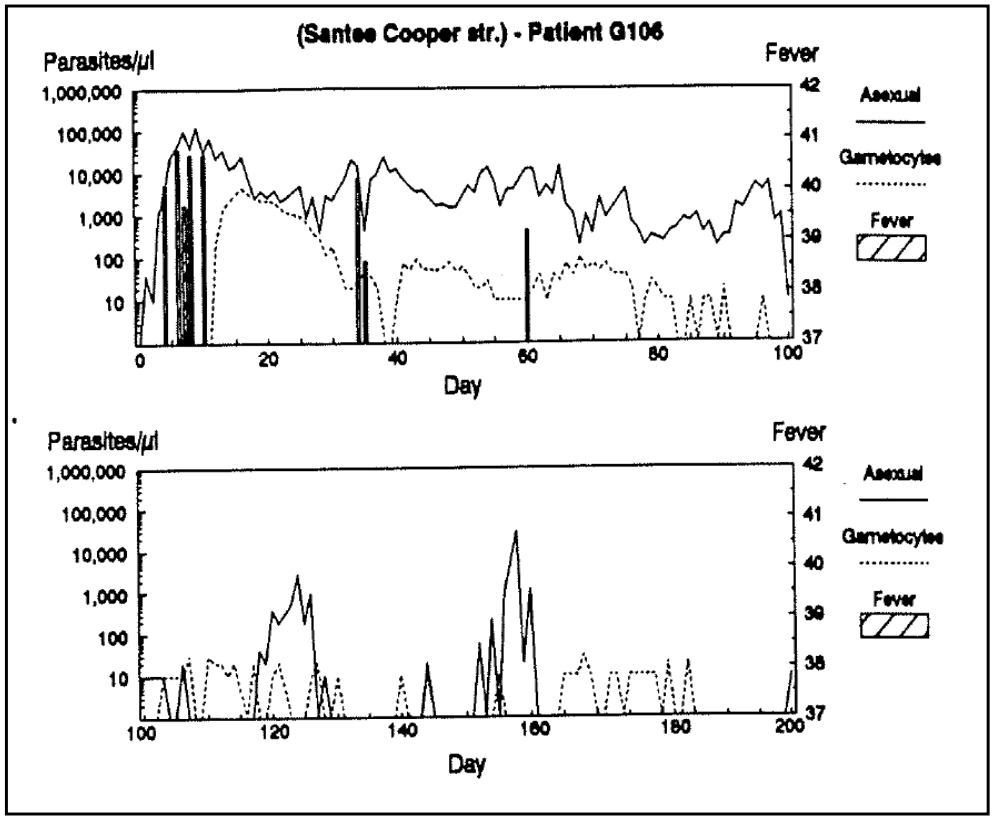
- **Diversify**
  - Malaria an essential part of broader effort (IMCI, EPI, new strategies for non-malarial febrile illness)

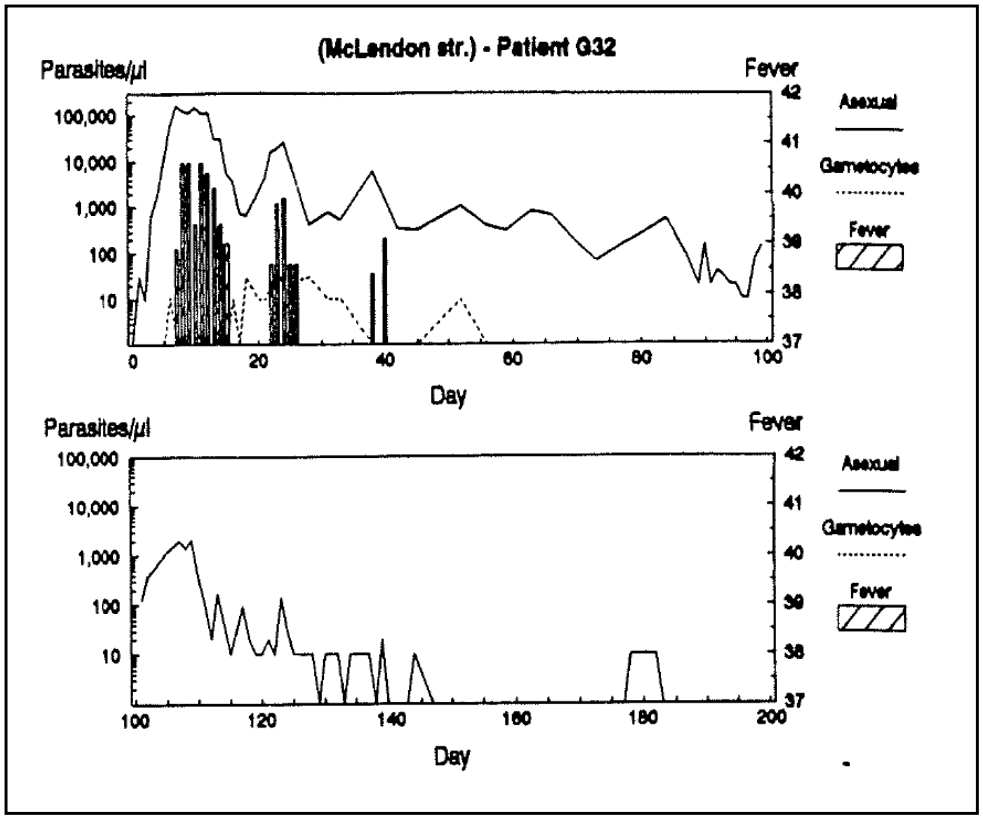
- **Focus efforts to areas of need**
  - New tools and strategies
    - Identify priority areas
    - Improve surveillance with real-time information
    - Need to detect ‘reservoirs’ that are maintaining transmission
    - Change funding structure to allow more flexibility

- **Programmes will have to be increasingly self-contained**
  - Communities will have to <u>want</u> to prioritize malaria
  - Can’t be imposed from outside
  - Need good communication

Untreated *P. falciparum* infections (Hidden reservoirs)

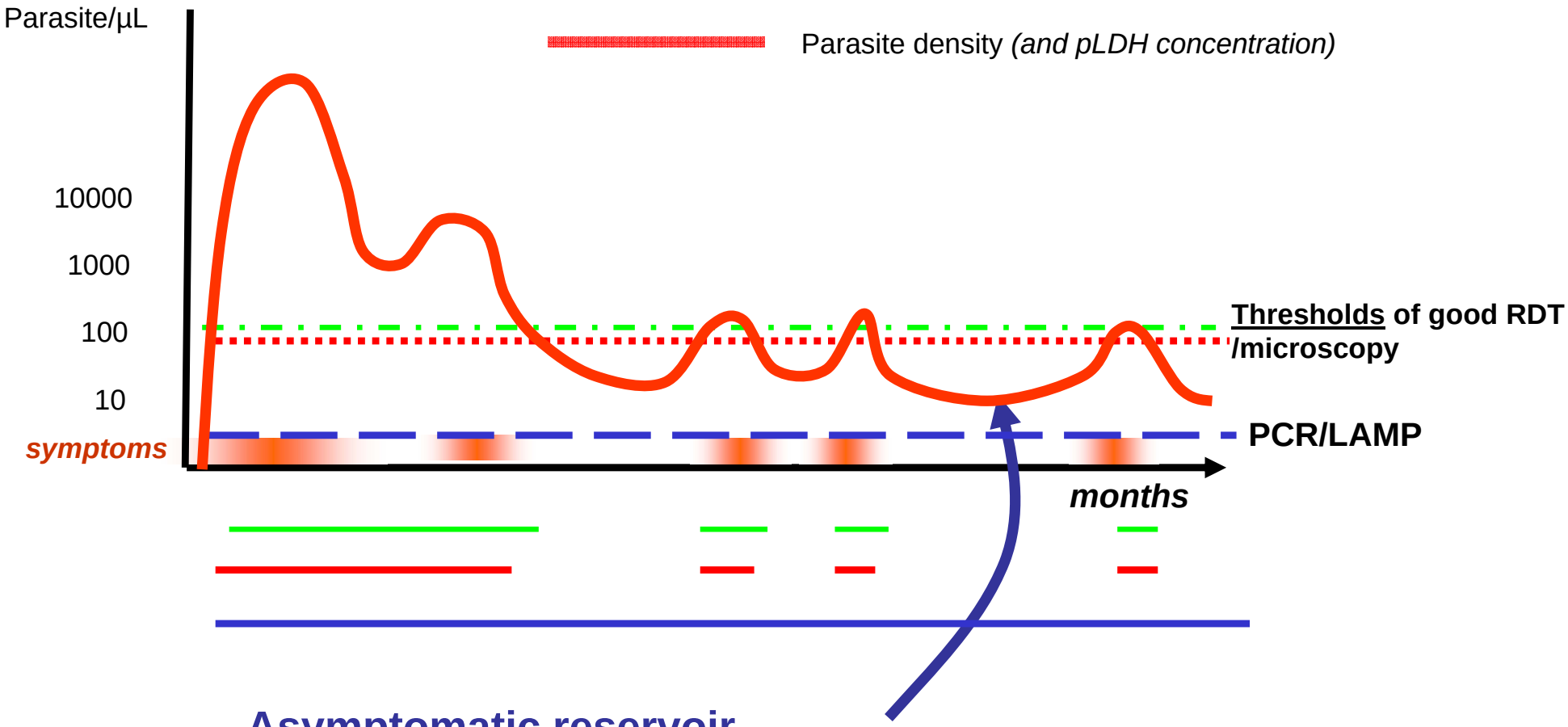
Examples of long-term course of untreated *P. falciparum* infections





Source: ***Therapeutic malaria in man: Sporozoite and blood-induced infections with Plasmodium falciparum. William E Collins and Geoffrey M Jeffrey. Unpublished.***

Untreated *P. falciparum* infections



Asymptomatic reservoir

Must be detected to assess true prevalence of parasitaemia, prevent re-introduction

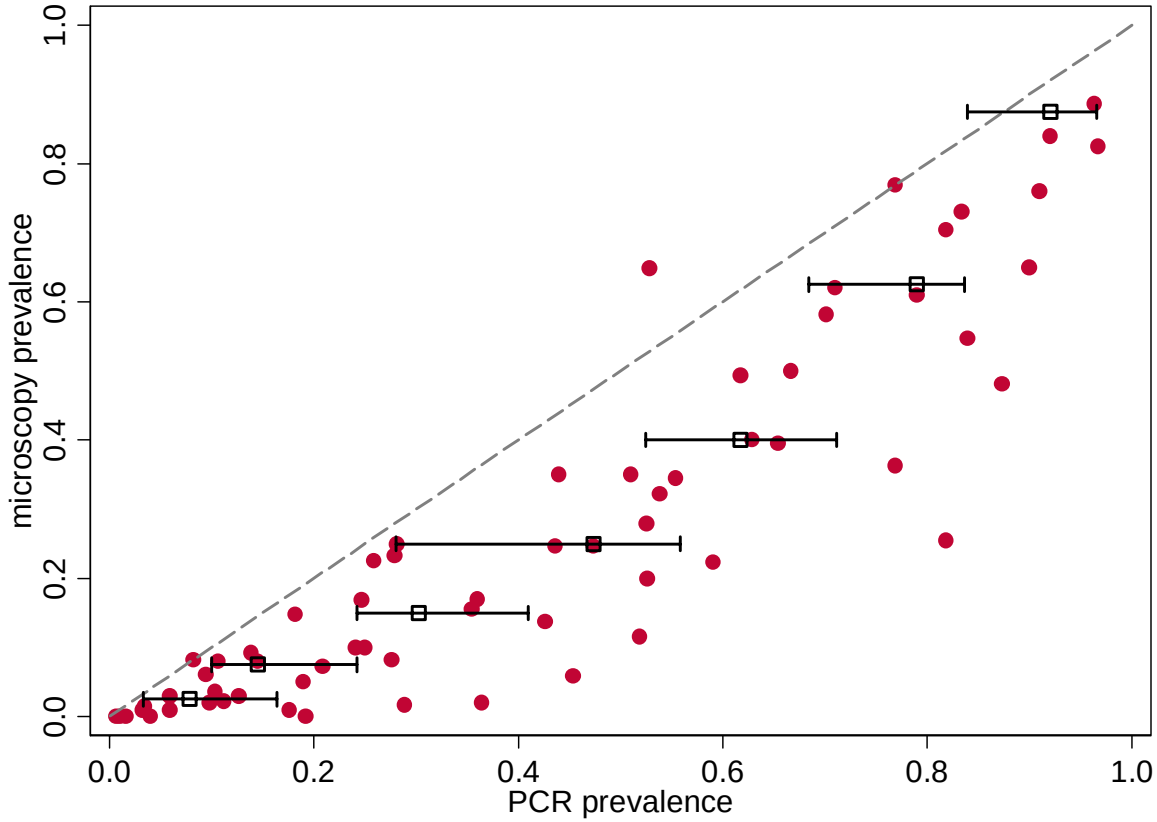
Must detect in field if case finding and treatment (FSAT) is employed

How common is sub-microscopic infection?

Meta-analysis of 72 studies of microscopy vs PCR

High transmission areas: Micro + 74.5% when PCR prevalence >75%

Low transmission areas: Micro + 12.0% when PCR prevalence <10%.



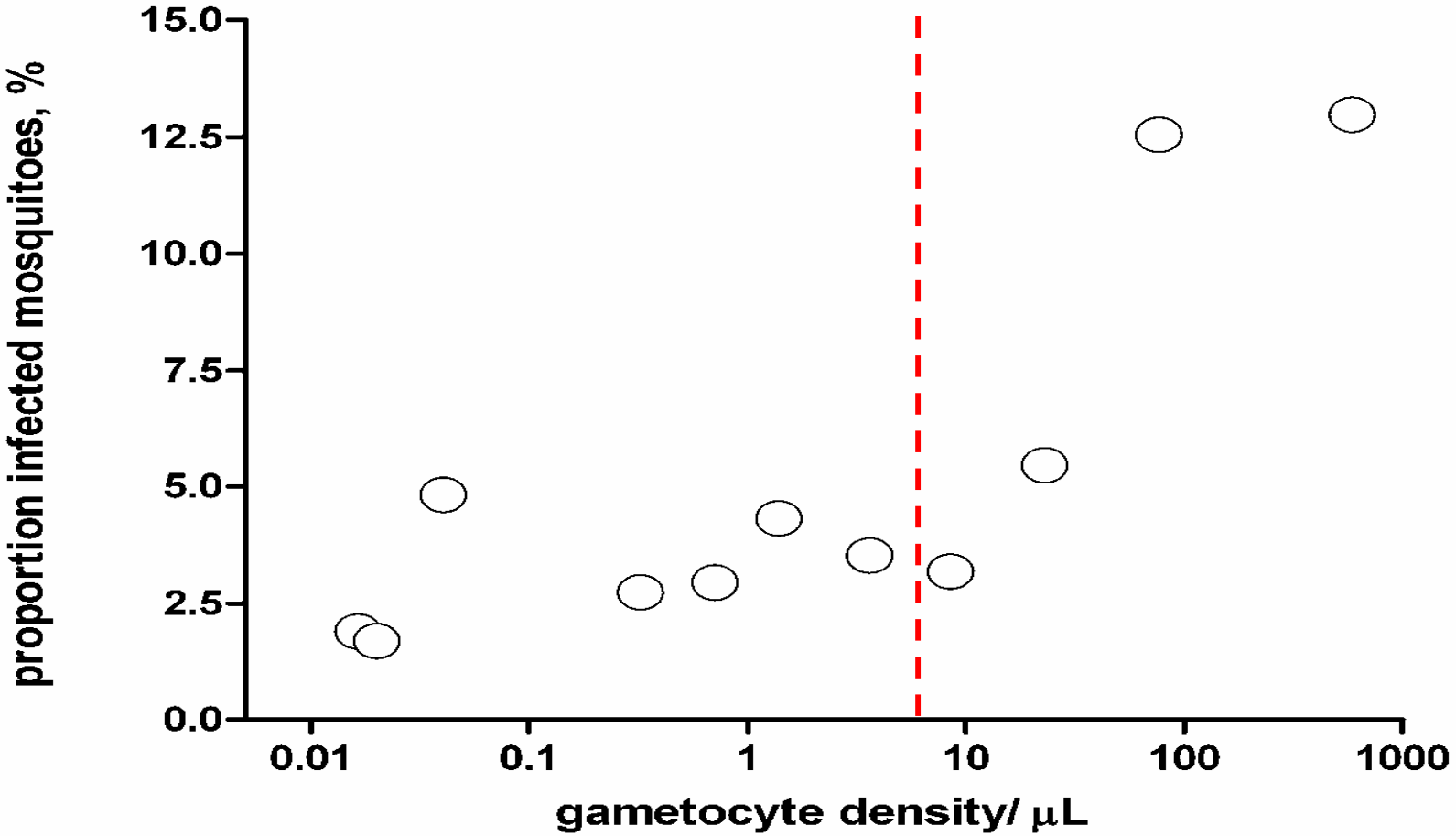
Microscopy prevalence	Median PCR prevalence (IQR)
75.0 - 100	92 (84.0-96.5)
50.0 - 74.9	79 (68.4-83.6)
30.0 - 49.9	61.7 (52.4-71.1)
20.0 - 29.9	49.9 (28.0-61.9)
10.0 - 19.9	35.4 (24.3-47.3)
5.0 - 9.9	14.5 (10.0-24.2)
0.0 - 4.9	10.4 (3.4-17.6)

Okell et al JID 2009

Results in MSAT/FSAT test in Phnom Damban, Cambodia

	1st test Nov. 08	2nd test May 09	3rd test May 10
Microscopy	22/416 **5.2%**	34/512 **6.6%**	5/375 **1.3%**
PCR	57/416 **13.7%**	49/512 **9.6%**	13/375 **3.5%**

Gametocyte infectivity



Bousema & Drakeley under review

Potential strategies in countries approaching elimination

Stratification based on surveys and surveillance

In regions with significant transmission:

1. **Continued case management diagnostic tools for symptomatic cases in high-priority areas (RDTs / microscopy)**

In regions with little or no transmission:

2. **A low-cost screening tool that can rapidly survey large areas to identify hot-spots of continued transmission**

3. **A highly sensitive field diagnostic tool to screen all people in identified hots-spots to detected and treat hidden reservoirs**

Survey tools to detect continuing transission

Serology

Screen large populations for signs of recent malaria transmission

Greece 1974: 15 years post E

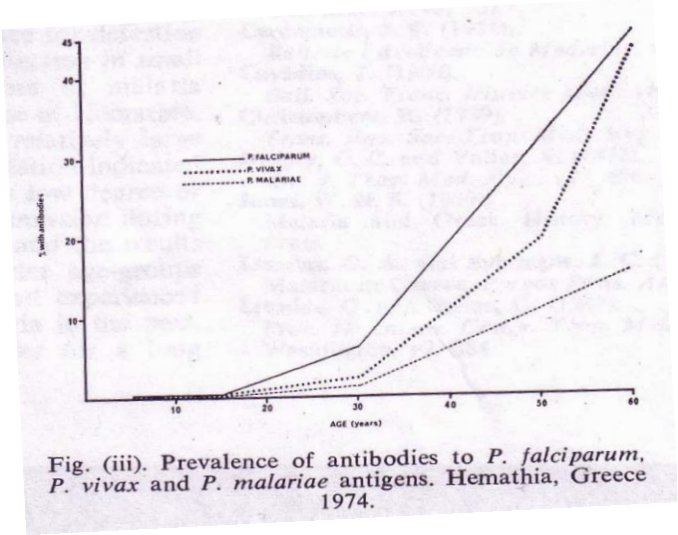


Fig. (iii). Prevalence of antibodies to *P. falciparum*, *P. vivax* and *P. malariae* antigens. Hemathia, Greece 1974.

Mauritius 1973: 5 years post E

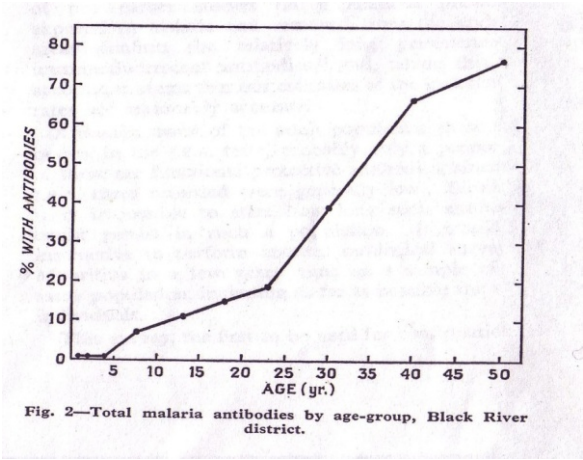
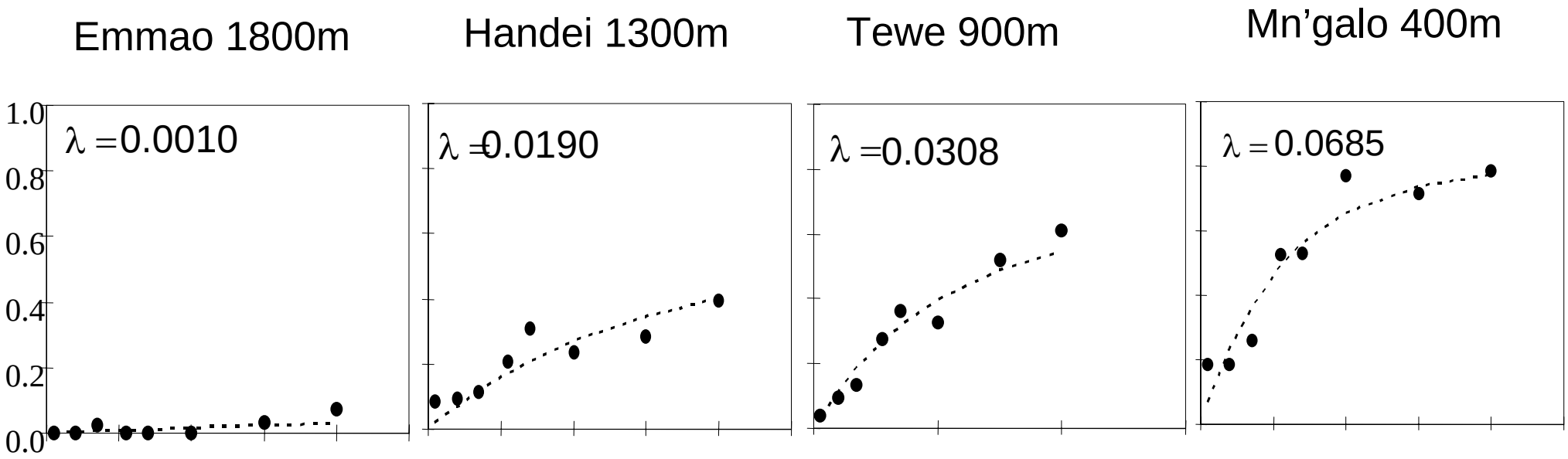


Fig. 2—Total malaria antibodies by age-group, Black River district.

Measuring transmission through serology

The rate of sero-conversion is linked to the transmission intensity (NE Tanzania)



Drakeley et al 2005

Finding and eliminating hidden parassite reservoirs in transmission foci

Will need field molecular diagnostic tools to detect very low parasite densities…

Need to determine where this is needed, where it is not

Eg. IPC model (Cambodia)

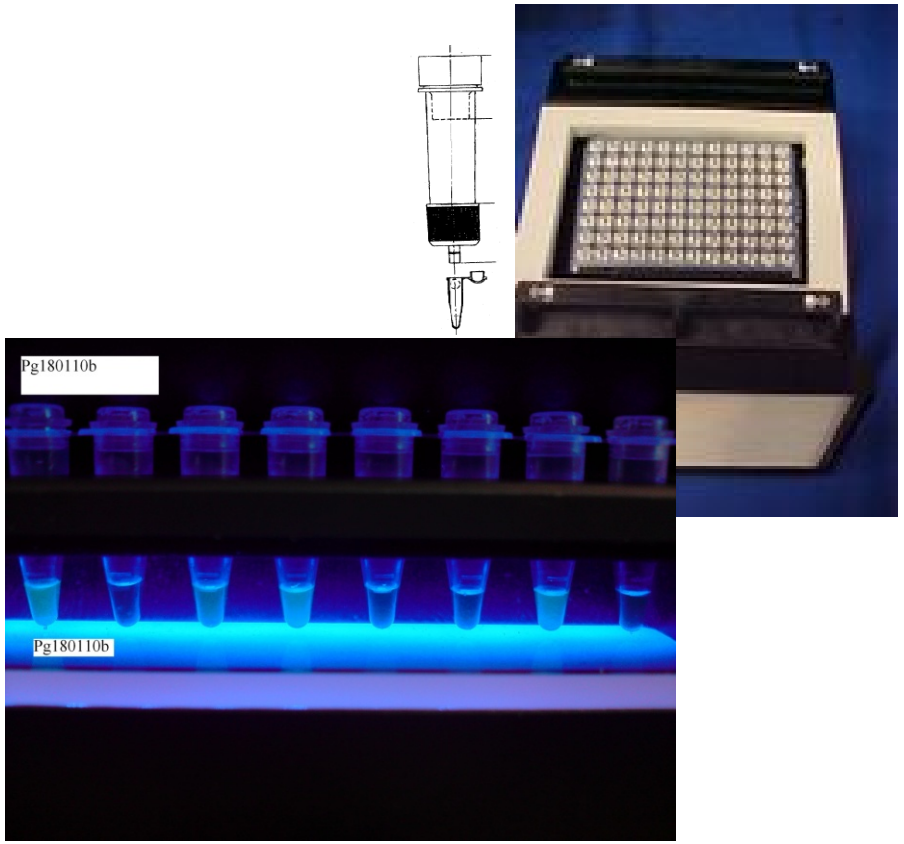
High through put PCR with rapid communication to field

Eg. Malaria LAMP

Detects 1 parasite/µL

Potential for district / clinic level use

Find and treat malaria 'carriers'



Diagnostics R&D funding

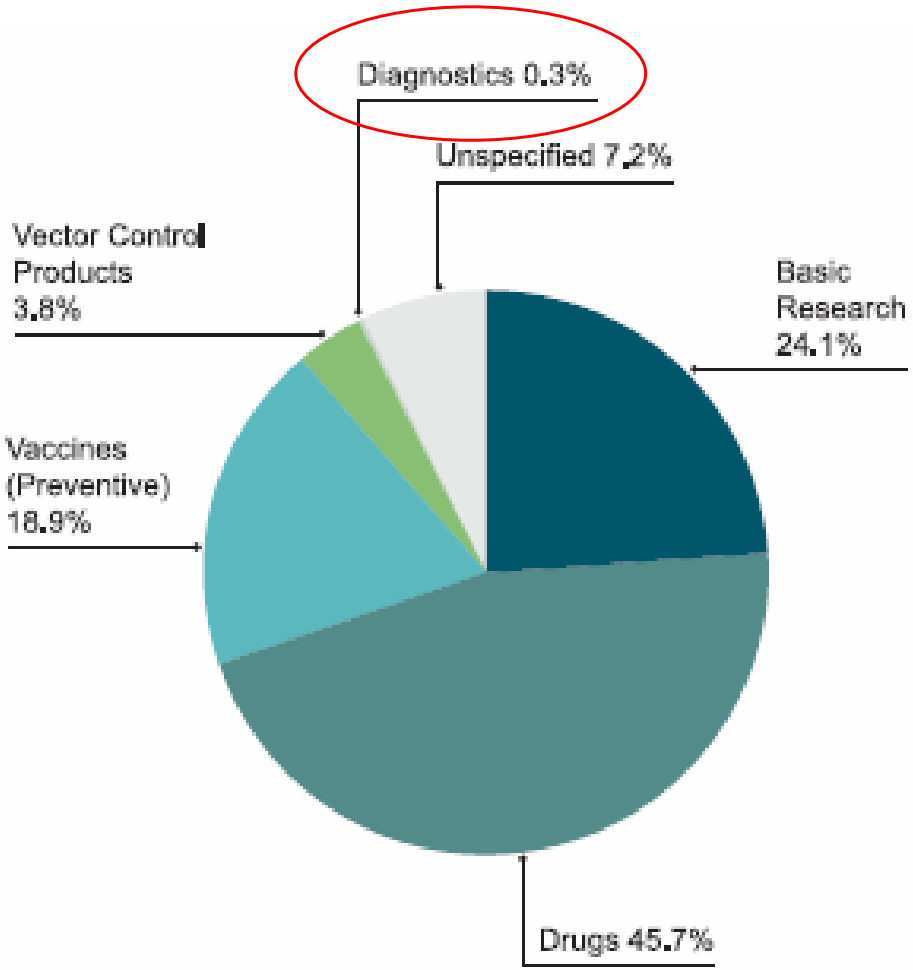
The needle in the pie chart

Malaria R&D research funding 2007

Top 12 funders:

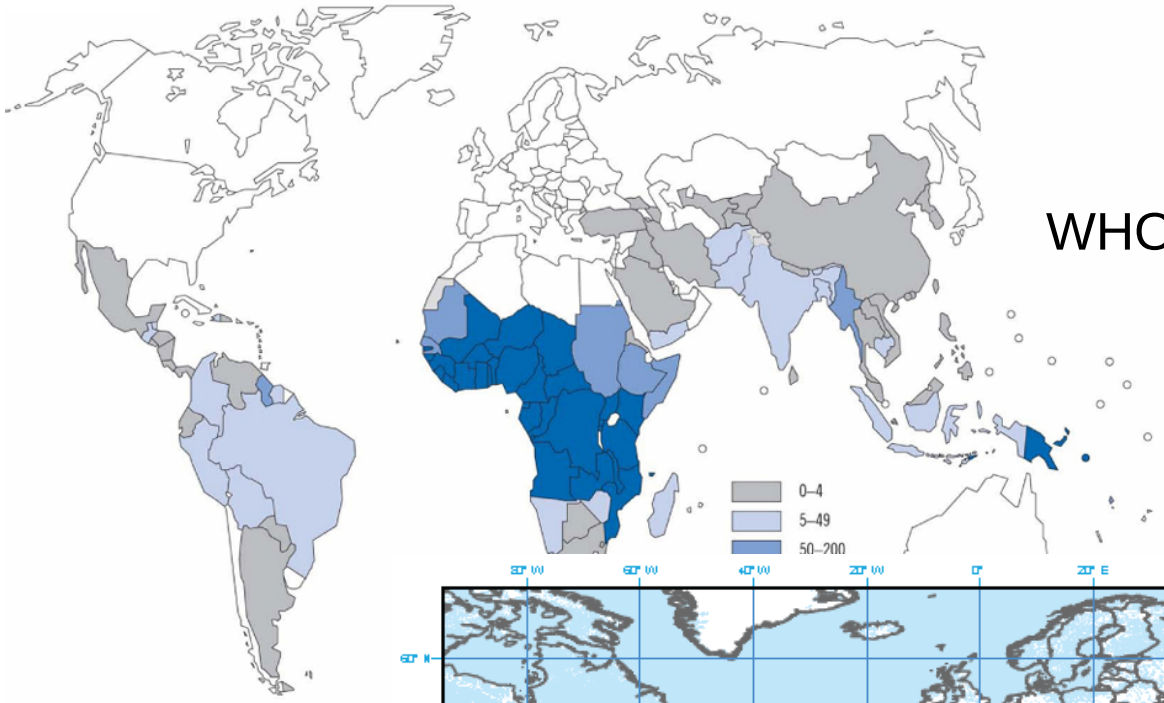
$484 M

- **Drug development $214M**
- **Diagnostics $1.6M**

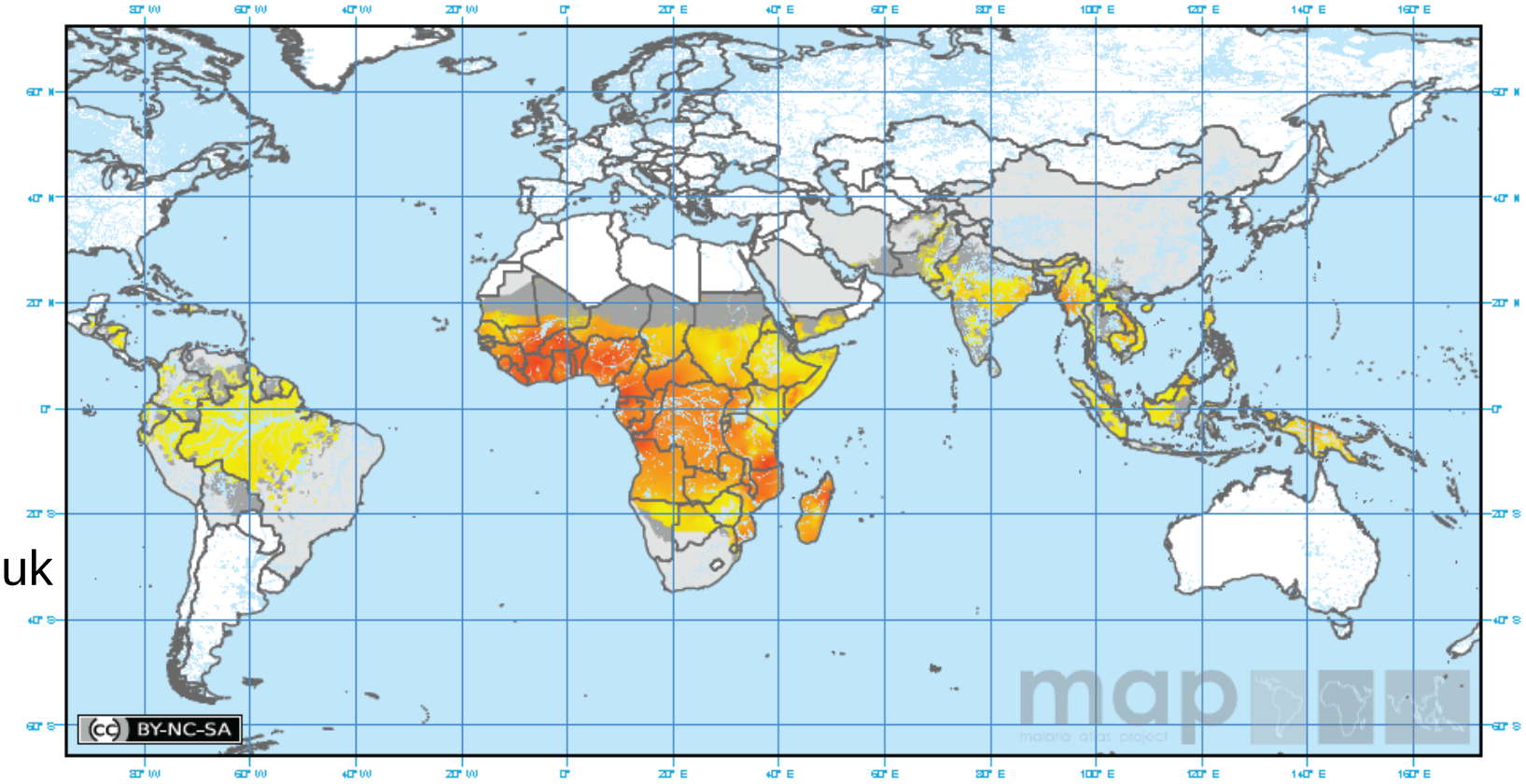


The George Institute: http://www.georgeinstitute.org.au/sites/default/files/pdfs/G-FINDER_2008_Report.pdf

Current maps of malaria incidence

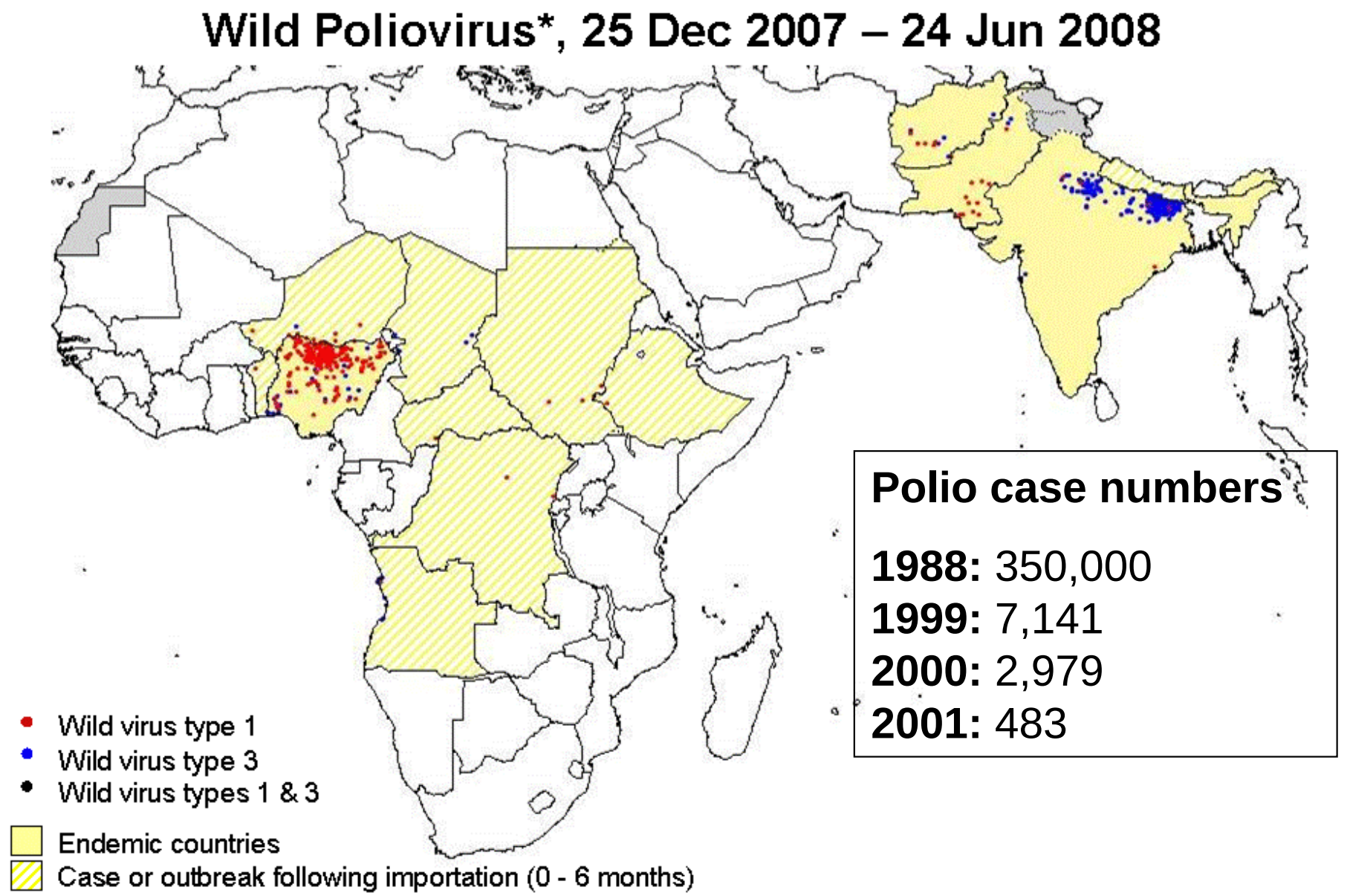


WHO 2009



www.map.ox.ac.uk
2009

Possible future for malaria??



Polio case numbers

1988: 350,000
1999: 7,141
2000: 2,979
2001: 483

Thank you

Acknowledgements:

- **FIND**
- **TDR (Jane Cunningham)**
- **LSHTM (Chris Drakeley)**
- **Malaria Consortium (Helen Counihan)**
- **URC (Steve Harvey)**