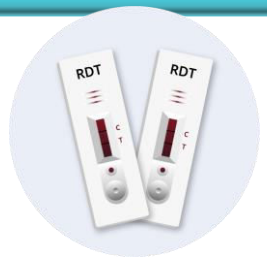
Update on Malaria Diagnosis: Successes and Challenges

Anderson Chinorumba

Parasitological Diagnosis

All cases of suspected malaria should have a quality-assured parasitological test to confirm the diagnosis

WHO recommends either light microscopy or rapid diagnostic tests (RDTs) for malaria diagnosis



Test results should be available within a short time (< 2 hours) of the patient presenting

- Antimalarial treatment should be limited to cases with positive tests
- However, in patients with suspected severe malaria and or other high-risk groups, absence or delay of parasitological diagnosis should not delay an immediate start of antimalarial treatment

- Patients with negative results should be assessed for other causes of fever and treated appropriately
- If the initial test is negative in patients with symptoms compatible with severe malaria, repeat parasitological tests can be done at 6-12h intervals

Parasitological diagnosis

- At present, molecular diagnostic tools based on nucleic-acid amplification techniques (e.g. loop-mediated isothermal amplification or polymerase chain reaction [PCR]) do not have a role in the clinical management of malaria.
  - Except in specific situations, such as the use of PCR to detect *P. knowlesi* infections.
- Recurrent Malaria - Microscopy or LDH-based RDTs
- Diagnosis of *P. vivax*, *P. ovale*, and *P. malariae* mixed infection - microscopy.
- Severe Malaria - microscopy is preferred.
- Rapid diagnostic tests based on immunochromatographic methods are relatively insensitive for detecting *P. malariae* and *P. ovale* parasitaemia
- Areas with *P. vivax* - combination RDT be used that allows detection of *P. vivax* (pLDH antigen from *P. vivax*) or pan-malarial antigens (Pan-pLDH or aldolase).

Considerations for Diagnostics

	Microscopy	Rapid diagnostic tests
Hospitals	++++	++
Designated laboratories	++++	+
Health facilities	++	++++
Community health workers	+	++++
Follow-up of patients	++++	−

Successes in Malaria diagnosis

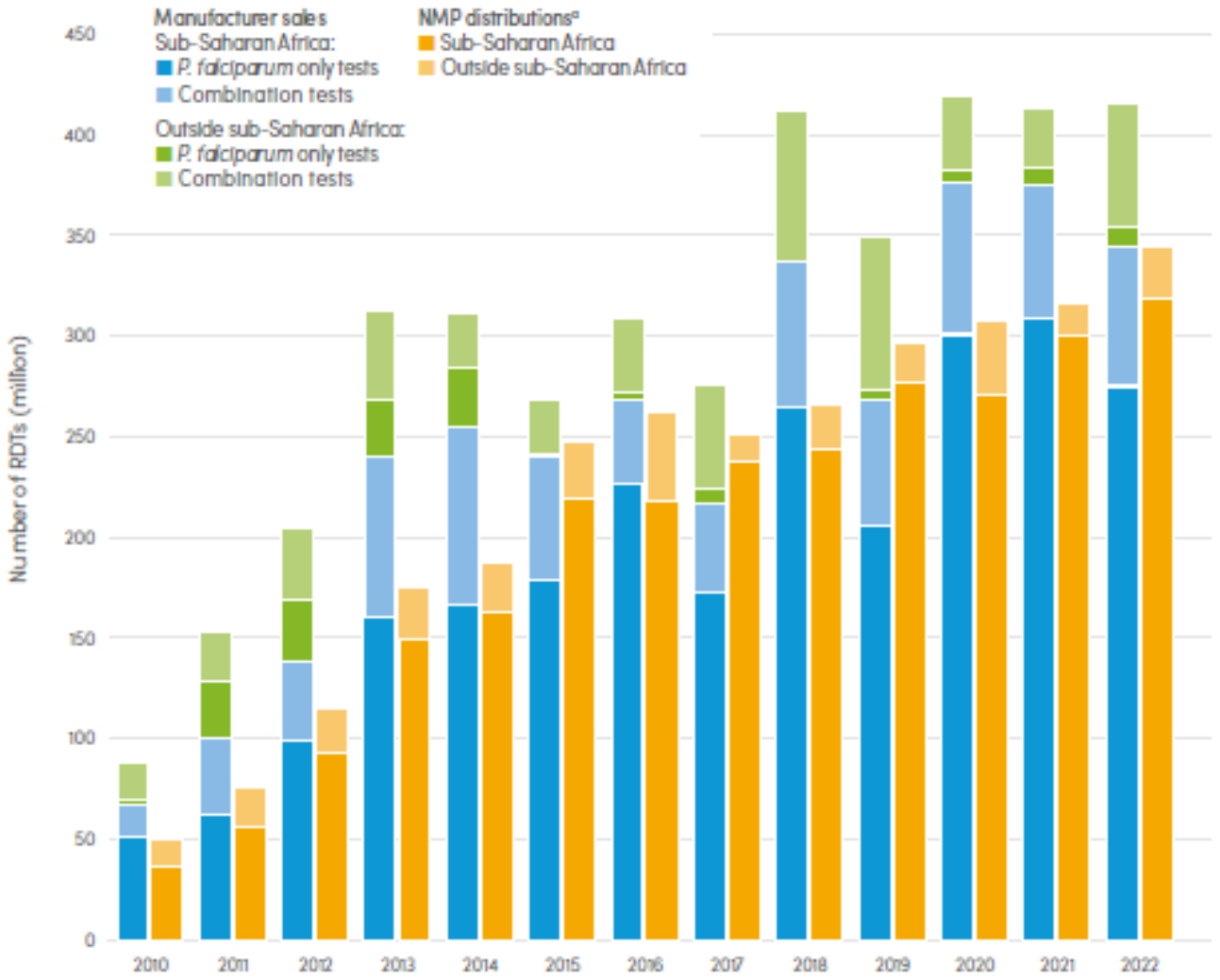
Diagnostic Policies

- Dissemination and adoption of guidelines on malaria diagnosis
  - Rolling out of RDTs and microscopy in different settings.
  - Development and adoption of QA/QC guidelines.

- Procurement of quality malaria IVDs.
  - Procurement of good quality RDTs
  - Procurement of good quality microscopes and availability in facilities

Fig. 7.6.

Number of RDTs sold by manufacturers and distributed by NMPs for use in testing suspected malaria cases, 2010–2022[a] *Sources: NMP reports and sales data from manufacturers eligible for the WHO Malaria RDT Product Testing Programme.*



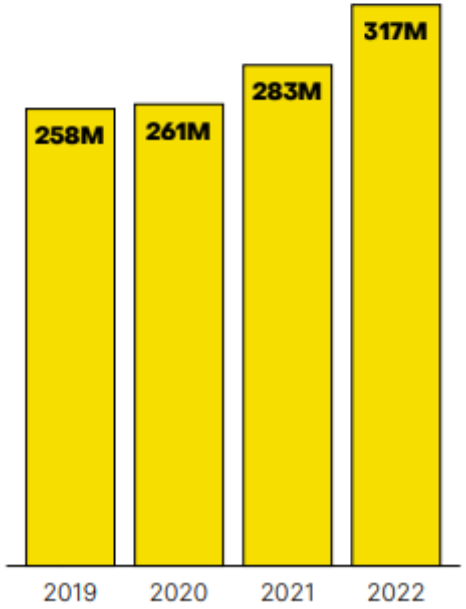
NMP: national malaria programme; *P. falciparum*: *Plasmodium falciparum*; RDT: rapid diagnostic test; WHO: World Health Organization.

[a] NMP distributions do not reflect RDTs that are still in storage and are yet to be delivered to health facilities and to community health workers.

- Globally, 3.9 billion rapid diagnosti
with 82% of these sales being in su
2.9 billion RDTs – 90% in sub-Saharan
- In 2022, 415.5 million RDTs were sold b

- The rate of diagnosis among childre
increased from a median of 30% a
improvement in case management

Suspected malaria cases that receive a parasitological test



ever and for whom care was sought
est household surveys, indicating an
ate levels of diagnostic services.

ere sold by manufacturers in 2010–2022,
. In the same period, NMPs distributed

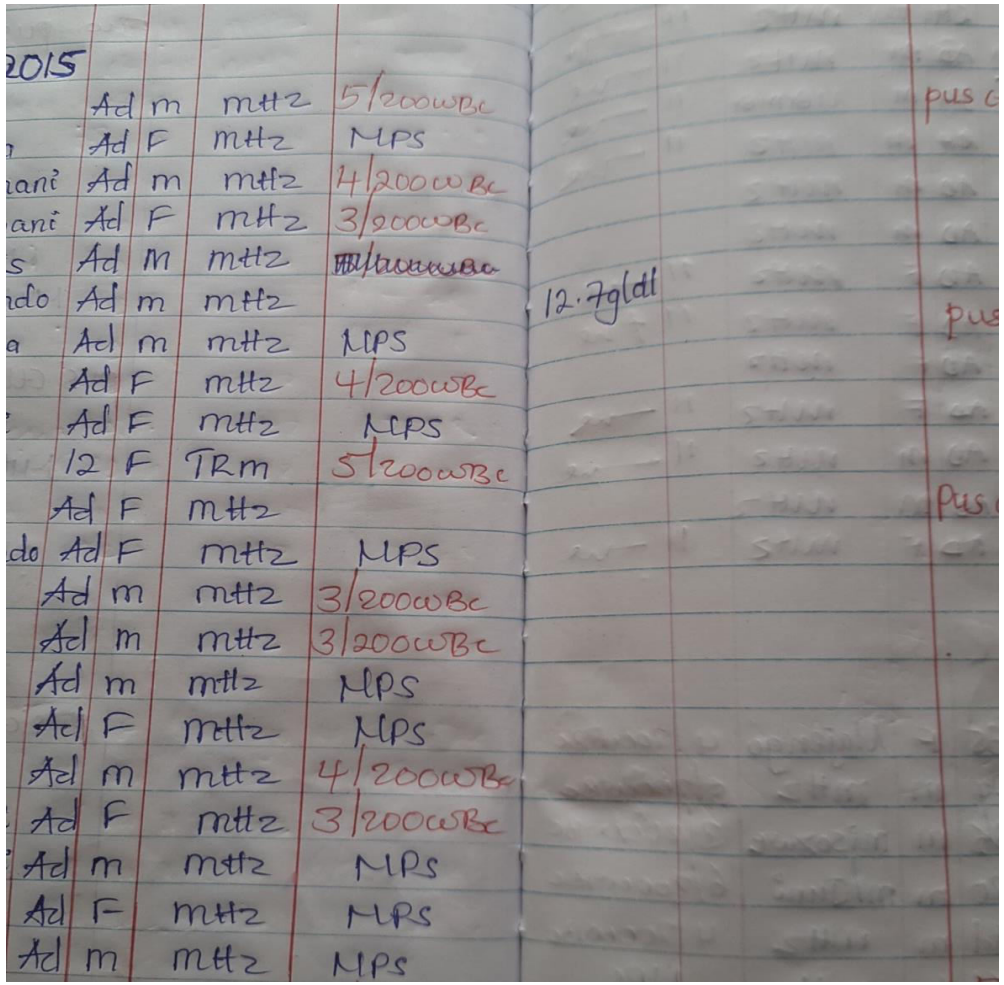
llion were distributed by NMPs.

World Health Organization

Challenges in Malaria diagnosis

Quality of Microscopy

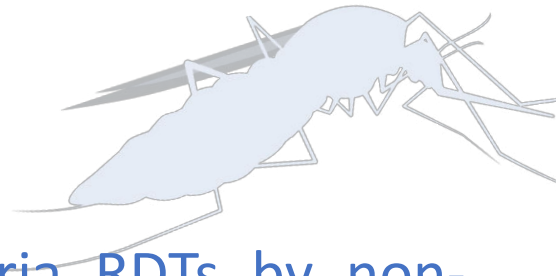
- The quality of malaria microscopy remains inadequate
  - Competency of microscopists – Detection, Species identification and Parasite quantification.
  - Reporting of microscopy results.



Health facility code ..... Date Opened.....

		RESULTS							
Age/Sex	Health Facility/Department	Day	Date Received	MPS /NMPS	Species	Parasite density (p/ul)	Gametocytes? Yes/No	Date and Time results entered	Test Performer
	Pandamakoge	~~D0~~	14/01/21	MPS	P.f	4668	NO	15/01/21	R.m
		~~D3~~	17/01/21	NMPS					K.M
		~~D7~~							
		D14							
		D21	10/2/21	NMPS				10/2/21	R.sa
		D28	17/2/21	NMPS				18/2/21	Imm
35/M	KPH/OPD	~~D0~~	15/01/21	MPS	P.f	3400	NO	17/01/21	KM
		D3	18/01/21	MPS	P.f	988	NO	19/01/21	R.m
		D7	22/01/21	MPS	P.f	106	NO	25/01/21	R.m
		D14	29/01/21	NMPS				29/01/21	BN
		D21							
		D28							
31/M	OPD	~~D0~~	16/01/21	MPS	P.f	5006	NO	16/01/21	K.M
		D3	19/01/21	MPS	P.f	1398	NO	20/01/21	R.m
		D7							
		D14							
		D21							
		D28							

Regulatory Frameworks



Failure of regulatory frameworks to support performance of malaria RDTs by non-laboratory personnel due to:

- Out-dated and often multiple regulations and regulators with often conflicting interests – Professional bodies vs Regulators (IVDs, Pharmacy, Premises).
- Professional Boundaries - No policies to support task shifting.

No Harmonization on IVD regulations and poor enforcement

- Lack of control and/or monitoring of the importation of diagnostic products.
- Regulators lack capacity to enforce regulations resulting in widespread non-compliance.

Weak Public Health Structures

Weak or absent public health sector structures to support/supervise/monitor the quality of diagnostic services

Poor training programs for the performance of both microscopy and RDTs

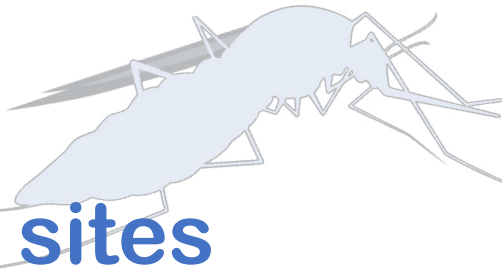
Lack of capacity to update providers on changes to algorithms and guidelines

Inadequate QA/QC systems

Poor EQA programs for testing facilities

Inadequate post market surveillance of diagnostic reagents and RDT kits in many developing countries

Inadequate Infrastructure

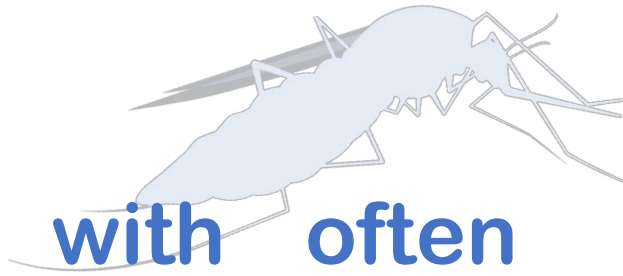


- Barriers to performing RDTs in non-laboratory sites
  - Most non laboratory sites were not designed to accommodate malaria RDT testing.
  - Poor infrastructure (space, lighting, table surface etc).

- Waste Management
  - Poor waste collection, Storage, Transportation and Disposal practices.
  - Challenges with safe storage of waste by CHWs


COMBIART
PRAZIQUANTEL CAPLETS USP
PedZinc
OMEGA

Complex Private sector



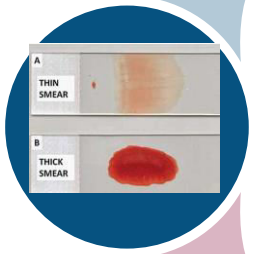
- Availability of a huge private sector with often unregistered/ unregulated facilities that are outside most governments' capacity to inform, update, monitor and regulate.
  - This causes non-adherence to diagnostic and treatment algorithms and guidelines
- A lot of unfair business practices
  - No parasitological confirmation of malaria
  - RDT leakages from the public sector
  - Use of unregistered and cheaper diagnostic reagents and RDT kits

Workload and/or Inadequate Personnel

Laboratory Organization

Equipment

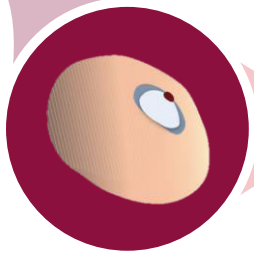
Type of Blood Films



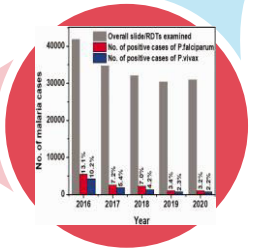
Factors determining the time required to examine a given set of malaria microscopy slides

Competency

Parasite Density



Slide Positivity Rate



Minimum time required to examine a thick blood film

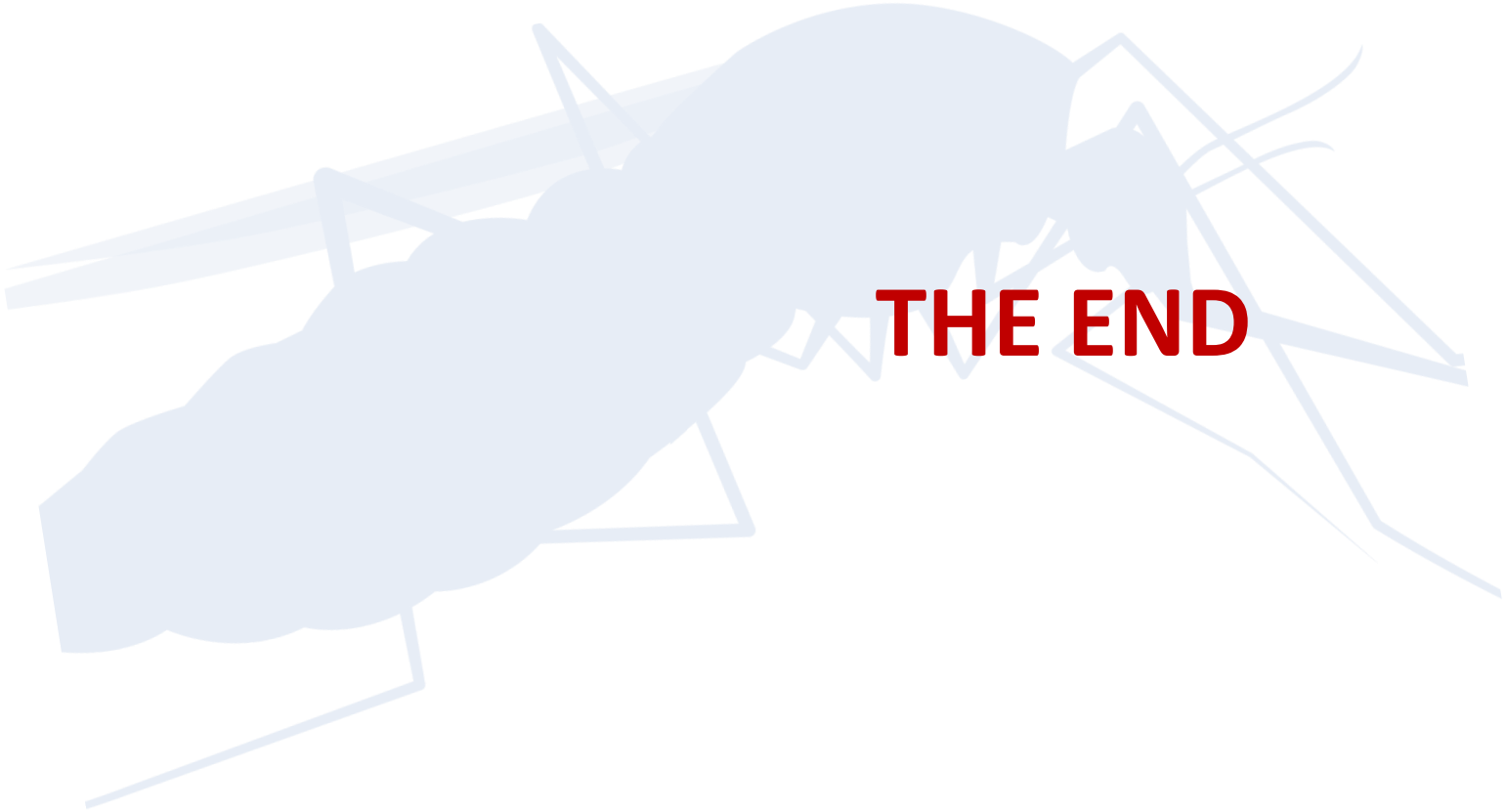
Activity	Minimum time required
Locating and placing the slide on the microscope stage	5 s
Focusing x10, then adding oil and focusing the x100 objective	10 s
Microscopic examination of a high-density positive thick film to determine positivity or negativity	10 s
Microscopic examination of a low-density positive thick film to determine positivity or negativity	2–6 min
Microscopic examination of a negative thick film	6 min
Counting of the number of parasites/200 WBC in a positive film	10 min
Recording the result in a register	20 s

Estimated maximum numbers of slides that can be examined in a workday

Slide positivity rate	10%	20%	30%	40%	50%
No counting					
Slides per hour	10	10.5	11.1	11.7	12.3
Slides per 4 h	40	42	44.4	46.8	49.2
Slides per 6 h	60	63	66.6	70.2	73.8
Counting					
Slides per hour	9	8.5	8.1	7.6	7.3
Slides per 4 h	36	34	32.4	30.4	29.2
Slides per 6 h	54	51	48.6	45.6	43.8

Emerging Threats

- HRP2/3 Gene deletions



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