The New Role of *in-vitro* Diagnostics in the Reality of Public Health Programs around the World

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The International Diagnostics Centre
www.idx-dx.org

IVDs in Public Health Programmes

- **Disease Control and Prevention – need to increase access**
  - 90-90-90 Targets for HIV, including HIV self testing
  - Dual and Triple elimination of HIV, Syphilis and Hepatitis B
- **Global Health Security Agenda – need to develop better tests**
  - Antimicrobial resistance (AMR)
  - Global health emergencies
- **Assuring quality of IVDs pre- and post market**
- **The Way Forward**

Innovations in Diagnostics

- **Patient-centred**
- **Value for money**
- **Evidence-based**
- **Quality-assured**
- **Enables linkage to care**

- **Improving access**
  - Point-of-care tests
  - Dried Blood spots
- **Enabling technologies**
  - Connectivity solutions
  - Supply chain

The Ideal Diagnostic Test

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A = Affordable

S = Sensitive

S = Specific

U = User-friendly

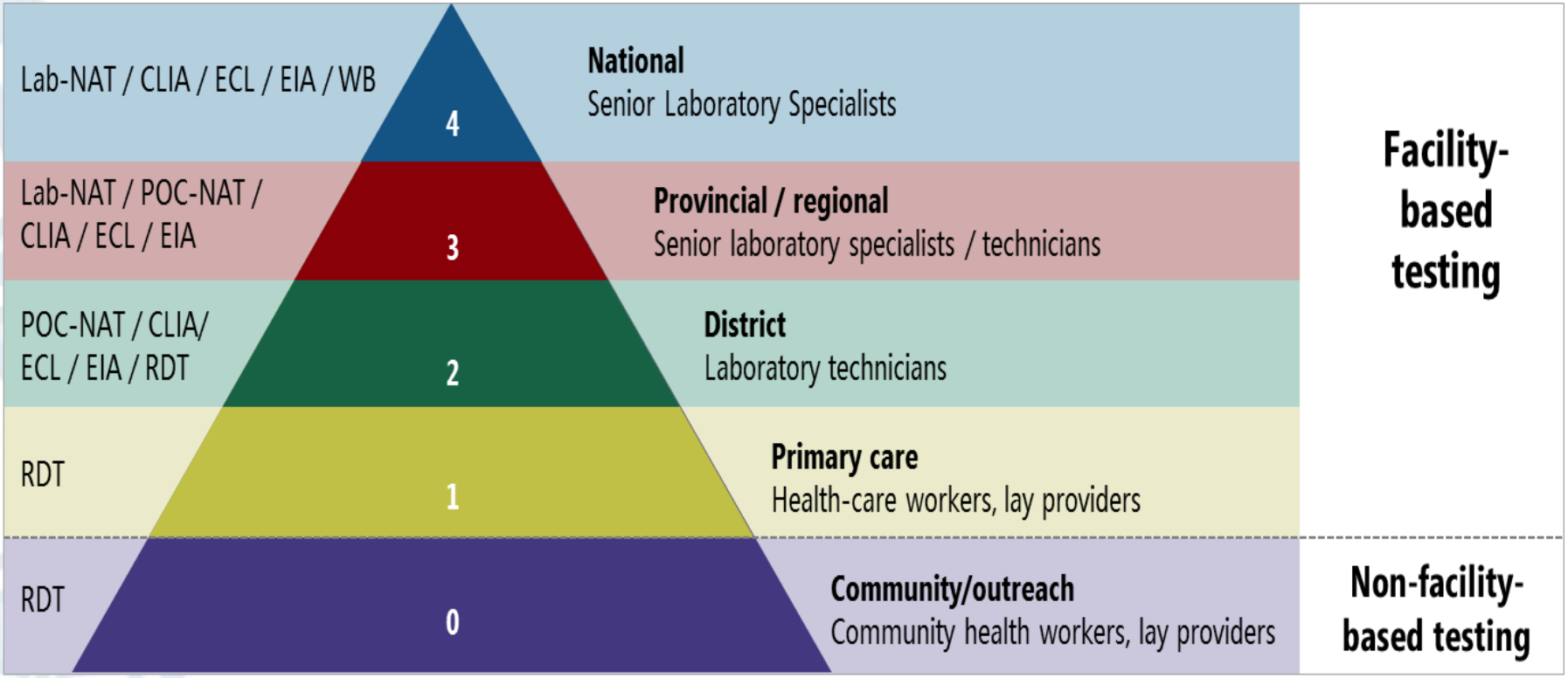
R = Rapid and robust

E = Equipment-free

D = Deliverable

- ✓ **Affordable**
- ✓ **Accurate**
- ✓ **Accessible**

A Tiered Testing Service with Test Format Menu and Staff Competencies



NAT: Nucleic acid tests: Lab-NAT: laboratory-based; POC-NAT: at point-of-care;
CLIA: chemiluminescence immunoassay; ECL: electrochemiluminescence immunoassay;
EIA: enzyme immunoassay; RDT: rapid diagnostic test

Source: WHO Hepatitis Programme

Diagnostics:
Access vs Accuracy vs Affordability

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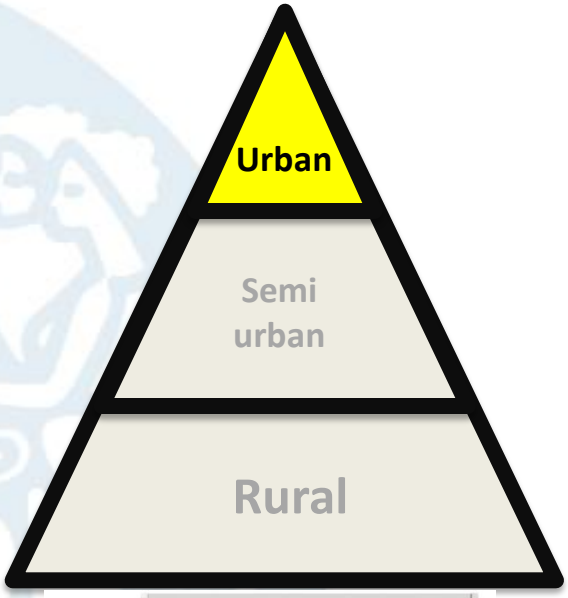
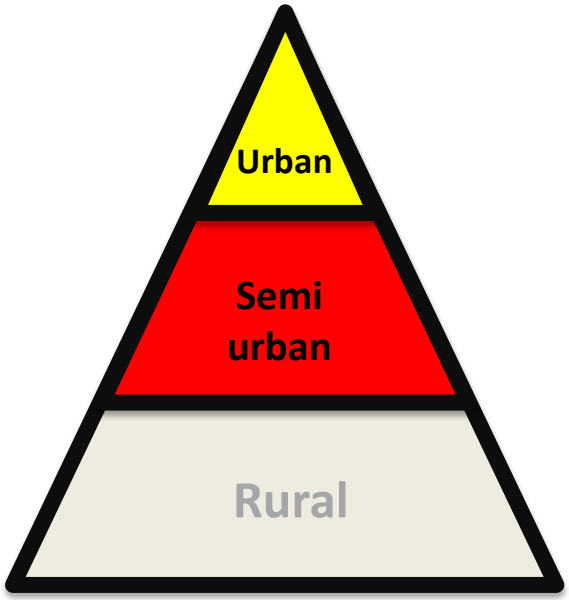


Accurate ✓✓✓

Cheap ×

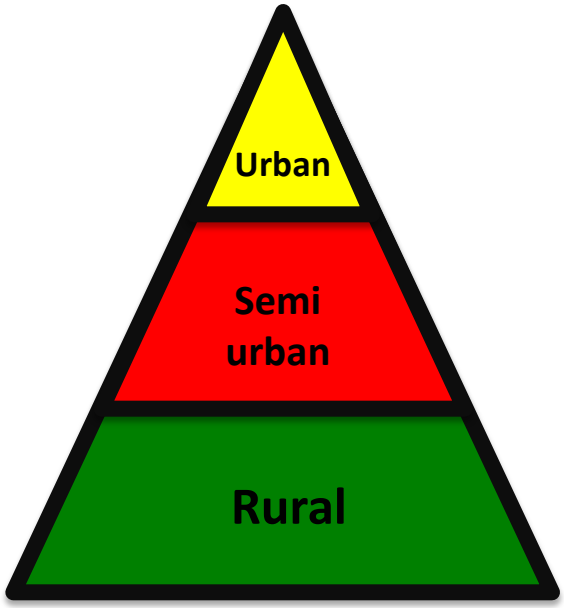
Fast/simple ×



Accurate ✓✓

Cheap ✓

Fast/simple ✓

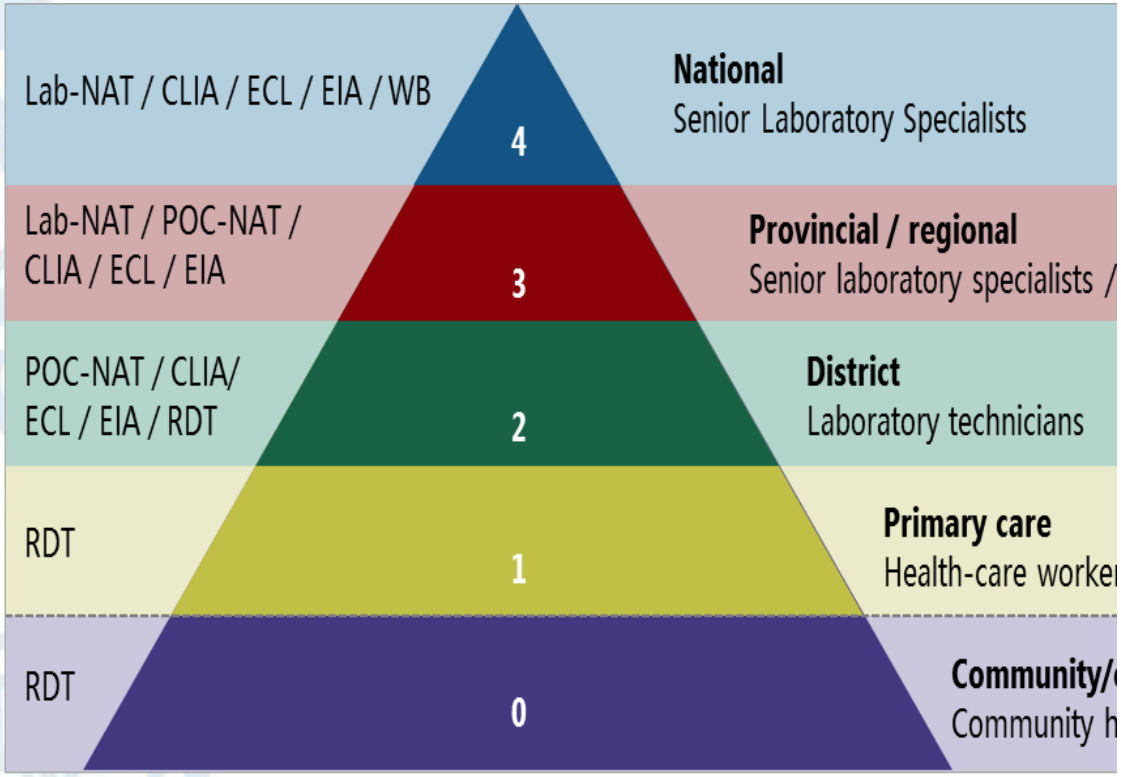


Accurate ✓

Cheap ✓✓

Fast/simple ✓✓

Trade-off between Access vs Sensitivity



	Sensitivity			
Access	**100**	**90**	**80**	**70**
100	100	90	80	70
90	90	81	72	63
80	80	72	64	56
70	70	63	56	49
60	60	54	48	42
50	50	45	40	35
40	40	36	32	28
30	30	27	24	21
20	20	18	16	14
10	10	9	8	7

Current HCV Testing Scenario

Stage of diagnosis	Type of diagnostic	Number required	Price per test (USD)	Total price (USD)
Confirmation of HCV	Immunoassay	1	~5-10	~5-10
	Qualitative assay	1	~40-50	~40-50
Treatment decision	Genotype test	1	~20-500	~20-500
	Quantitative assay (viral load)	1	~20-80	~20-80
	Liver function test	1	~100-300	~100-300
Treatment monitoring and post-treatment	Viral load assay	2	~20-80	~40-160
			TOTAL PRICE	**~220-1,100**

Hepatitis C Medicines and Diagnostics:
A Scoping Report 2013

Innovations in Diagnostics Linked to Advances in Therapeutics

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- **Liver function tests**:

Safer, more effective treatments will reduce the need for staging liver damage, making all patients potentially eligible for treatment, regardless of disease stage.

- **Genotyping tests:**

Pan-genotypic drugs will soon be available, eliminating the need to determine patients' genotype before treatment.

- **Viral load quantitation**:

With highly effective treatments (simpler and shorter treatment regimens), viral load quantitation to monitor treatment efficacy may no longer be necessary.

This will simplify physicians' decision and patient management as well as limit the number of diagnostic tests required to initiate treatment.

The Future of HCV Testing

Hepatitis C Medicines and Diagnostics:
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Future Testing Scenario:

Stage of diagnosis	Type of diagnostic	Number required	Price (USD)
Confirmation of HCV	POC qualitative RNA assay	1	~10-40
Treatment monitoring	POC qualitative RNA assay	1	~10-40
Post treatment	POC qualitative RNA assay	1	~10-40
		TOTAL PRICE	**~30 - 120**

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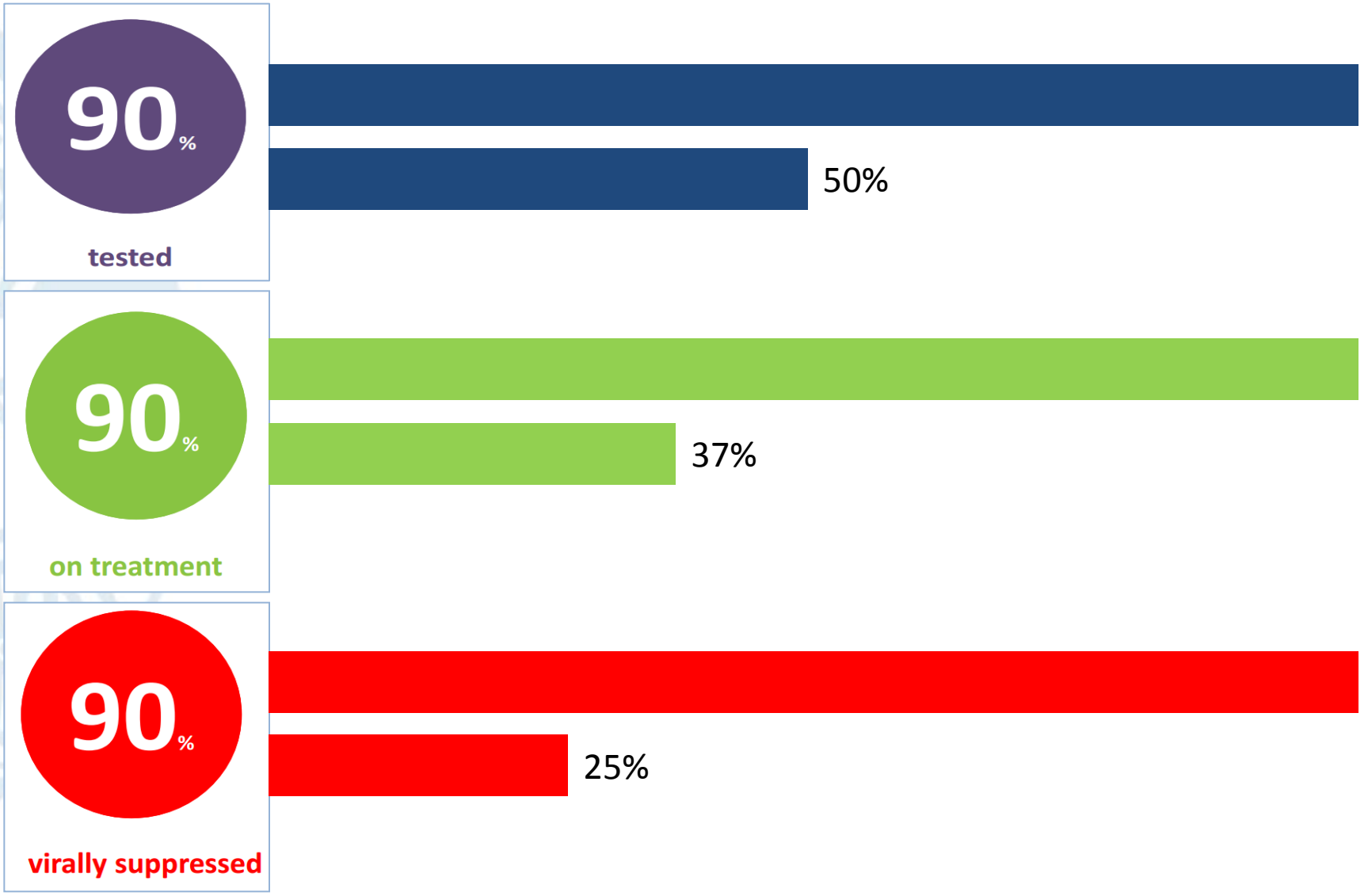
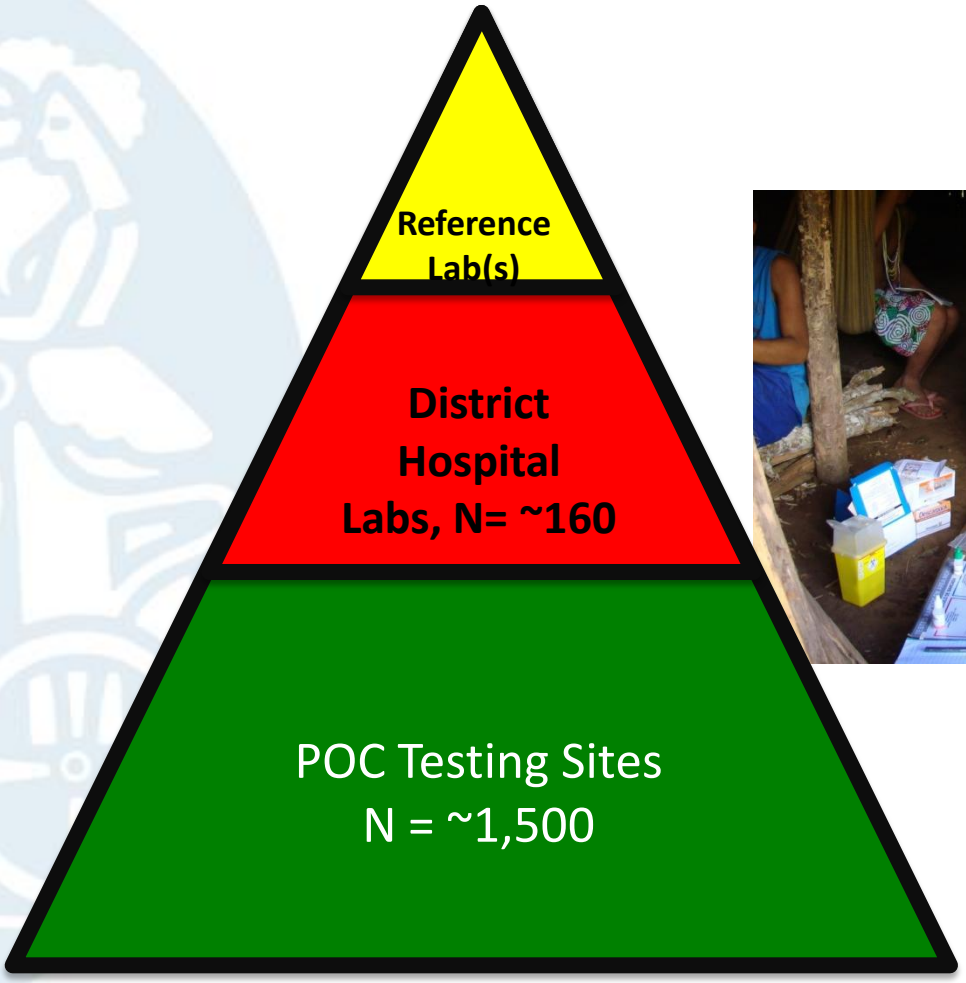
Accuracy vs Access

Risks vs Benefits

UNAIDS/WHO 2020 Targets for HIV

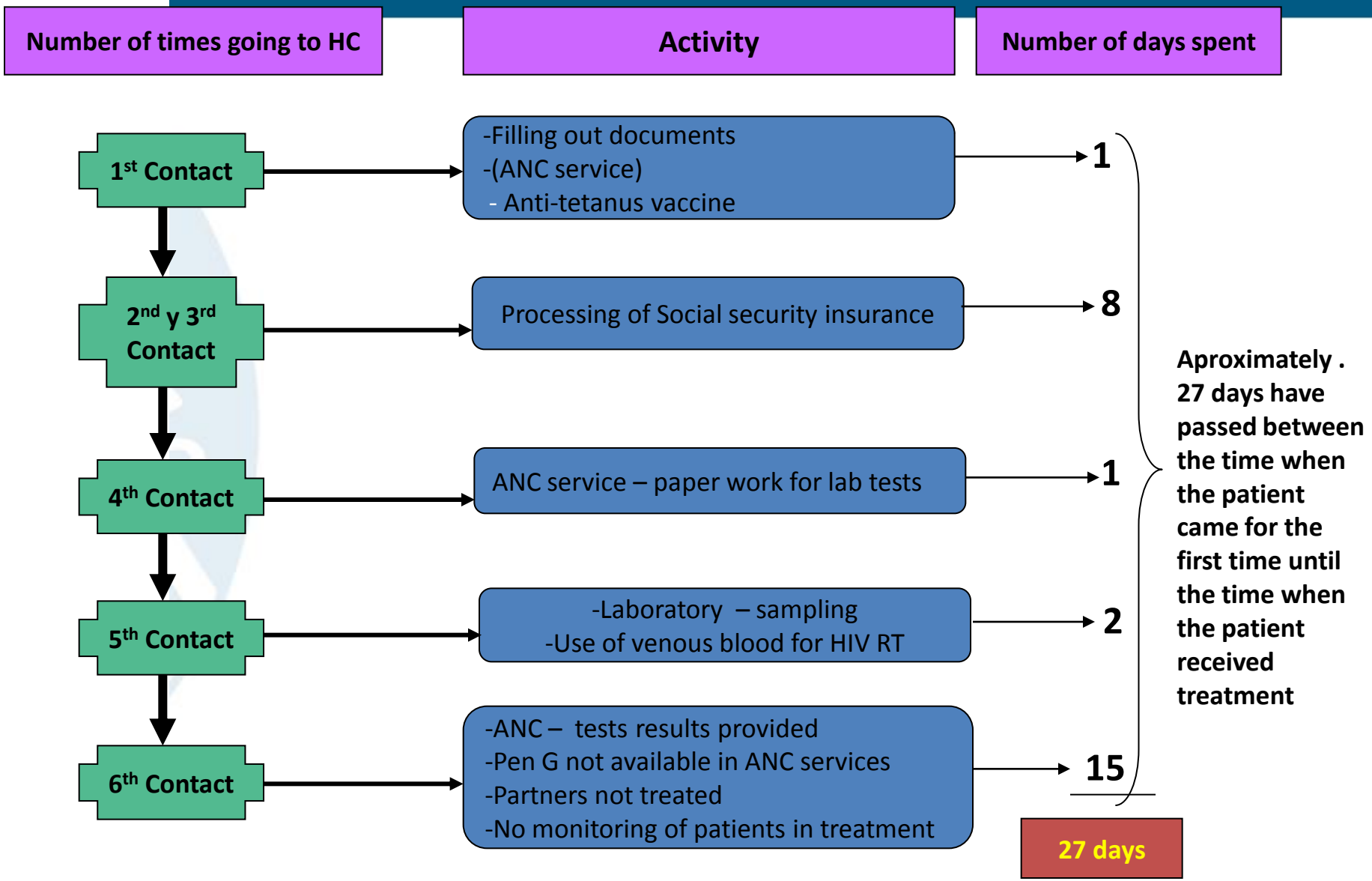


Point-of-Care Tests: Quality Assurance Challenges



PERU Cisne Project: Prenatal Syphilis Screening Summary

Garcia et al PLoS One. 2013



FDA approves Oral HIV Tests for home use, July, 2012

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Aspirin? Check. Shampoo? Check. Free HIV Test — Check?

LWA / GETTY IMAGES

Source: time.com

Oct 22, 2013: European Parliament votes favourably for home use of IVDs

Performance of the oral HIV Test

Performance Measure*	Professional Use OraQuick Test Performance (2-sided 95% CI**)		Over-the-Counter OraQuick Test Performance (2-sided 95% CI**)	
	Minimum FDA Recommended Performance	**Evaluation Results**	**Minimum FDA Recommended Performance**	**Evaluation Results**
Sensitivity	**98%** (lower bound of the 2-sided 95% CI)	99.3% (**98.4** - 99.7%)	**95%** (lower bound of the 2-sided 95% CI)	92.98% (**86.64** – 96.92%)
Specificity	**98%** (lower bound of the 2-sided 95% CI)	99. 8% (**99.6** – 99.9%)	**95%** (lower bound of the 2-sided 95% CI)	99.98% (**99.90** – 100%)

* Compared to a blood based HIV test

**95%CI = 95% Confidence Interval

Risk Benefit analysis

- The FDA performed a risk analysis to understand the public and individual health implications of approving a test with these performance characteristics.
  - estimated the net transmissions averted
  - The impact of switching from professional testing to self-testing
  - The impact of who will use the test
  - Do the benefits outweigh the risks?

- **A risk assessment model showed that in the first year of use, there would be:**
  - **A net increase of ~4,500 new HIV infections identified among those not aware of their HIV status**
  - **~ 2,700,000 who would test negative.**
  - **~4,000 transmissions would be averted , outweigh the individual risk of increased numbers of false negative results (approximately 1,100).**

- Individual risk remained which prompted FDA to address this risk through messages in the test kit labeling:
  - A positive result with this test does not mean that you are definitely infected with HIV, but rather that additional testing should be done in a medical setting.
  - A negative result with this test does not mean that you are definitely not infected with HIV, particularly when exposure may have been within the previous three months.
  - Testing is recommended if you test negative and continue to engage in behavior that puts you at risk for HIV infection.
  - A negative result does not imply it is safe to engage in risk behavior for HIV infection.

The Dual Elimination Dashboard

www.idc-dx.org

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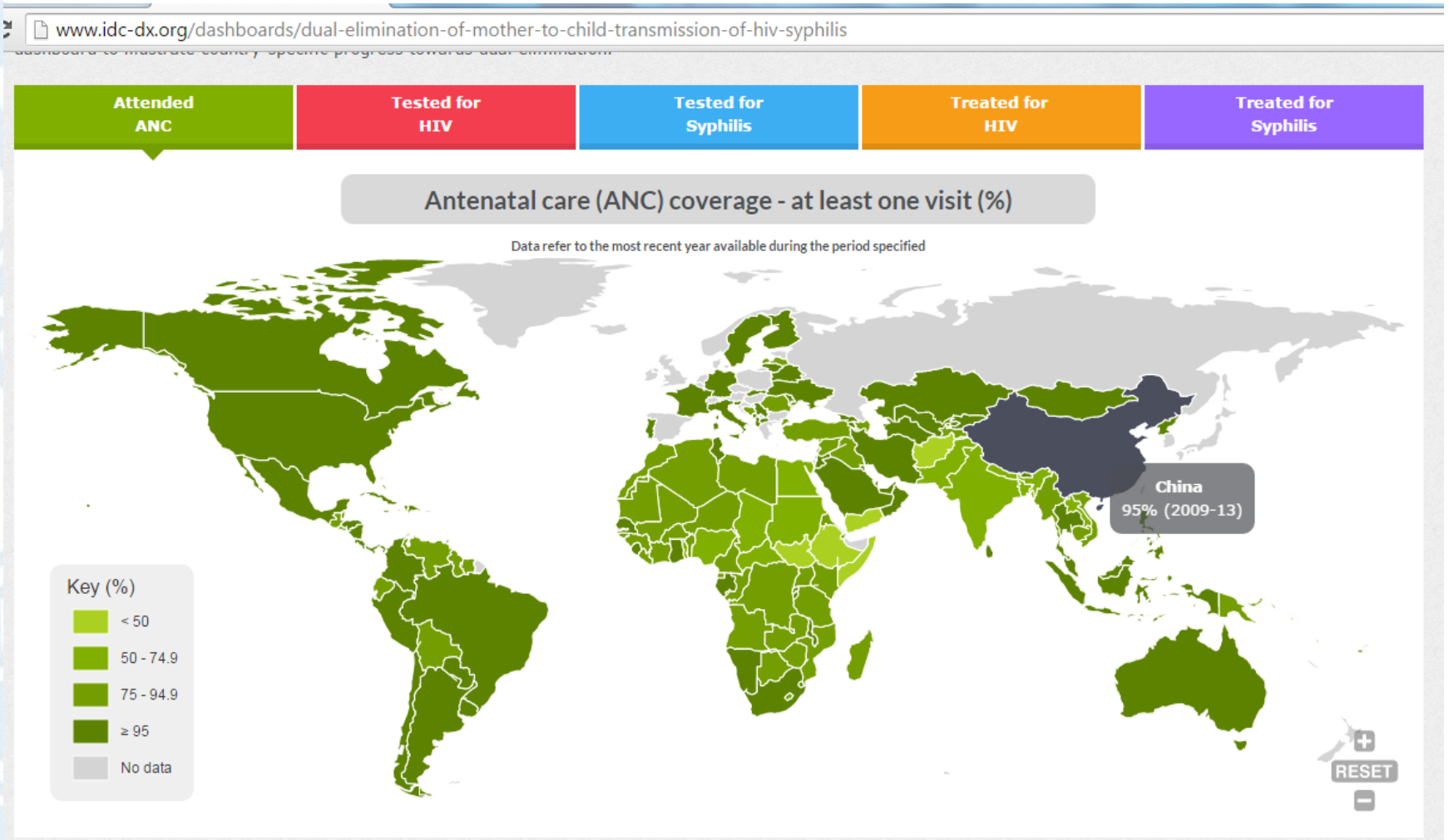
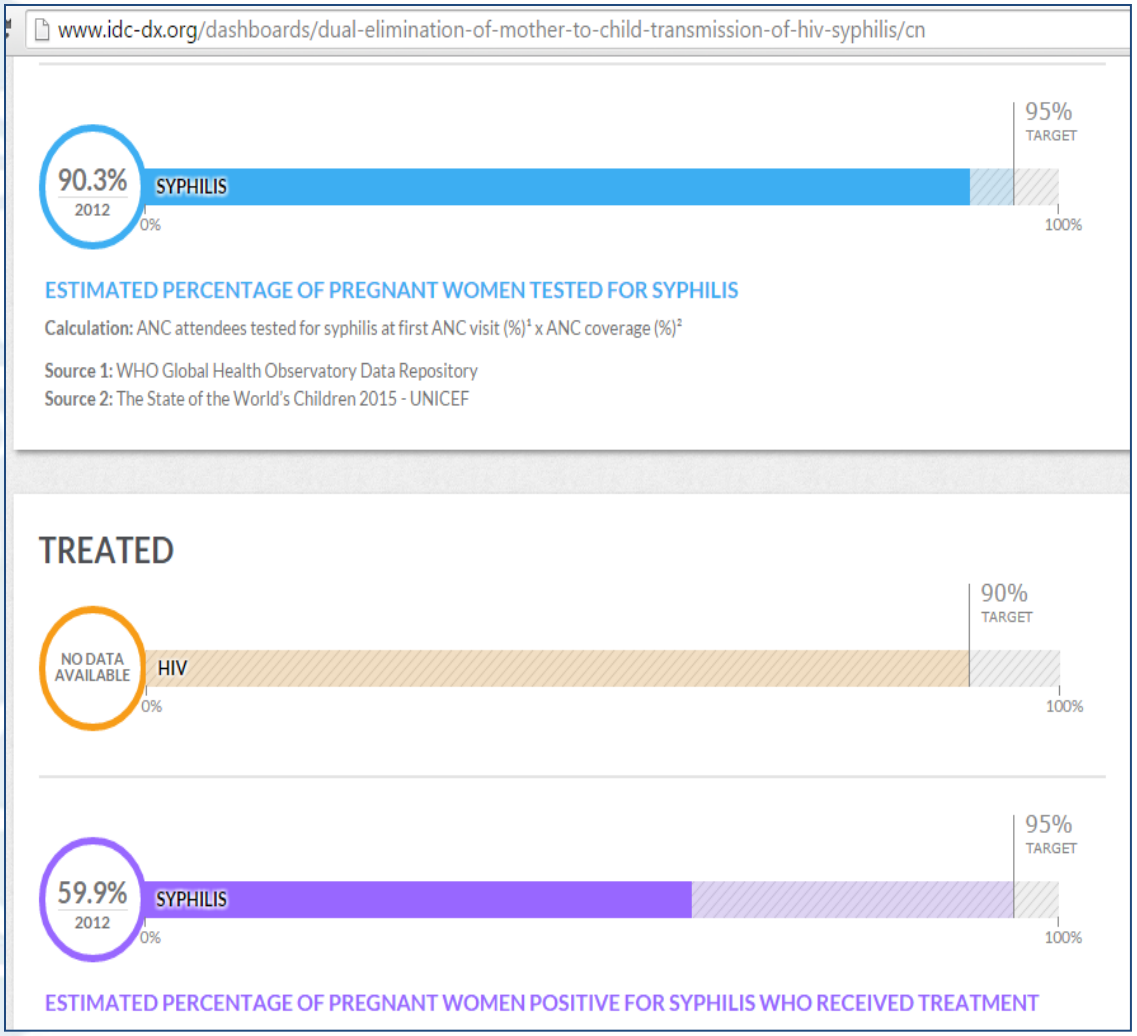
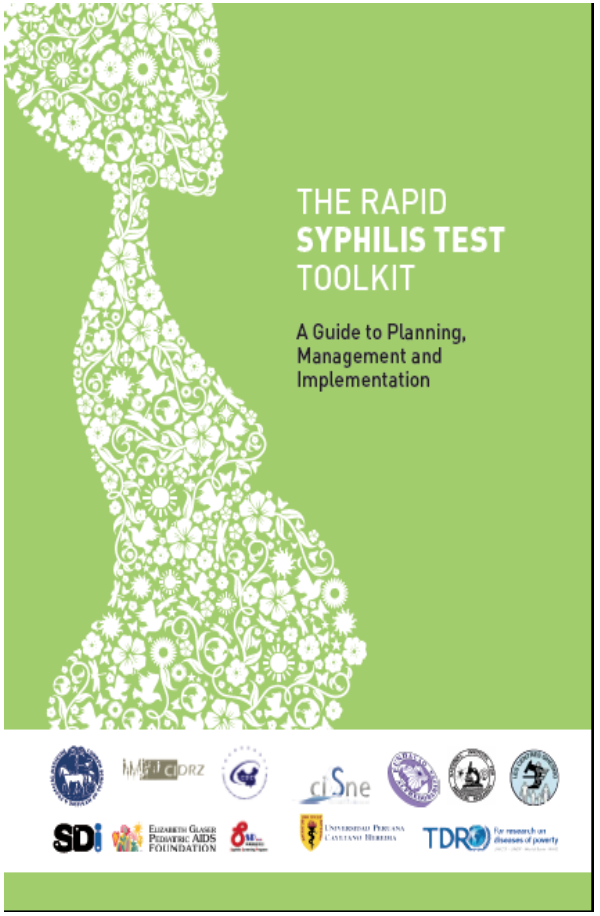


Elimination Dashboard & Toolkit





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Lives lost/year attributable to Antimicrobial Resistance by 2050

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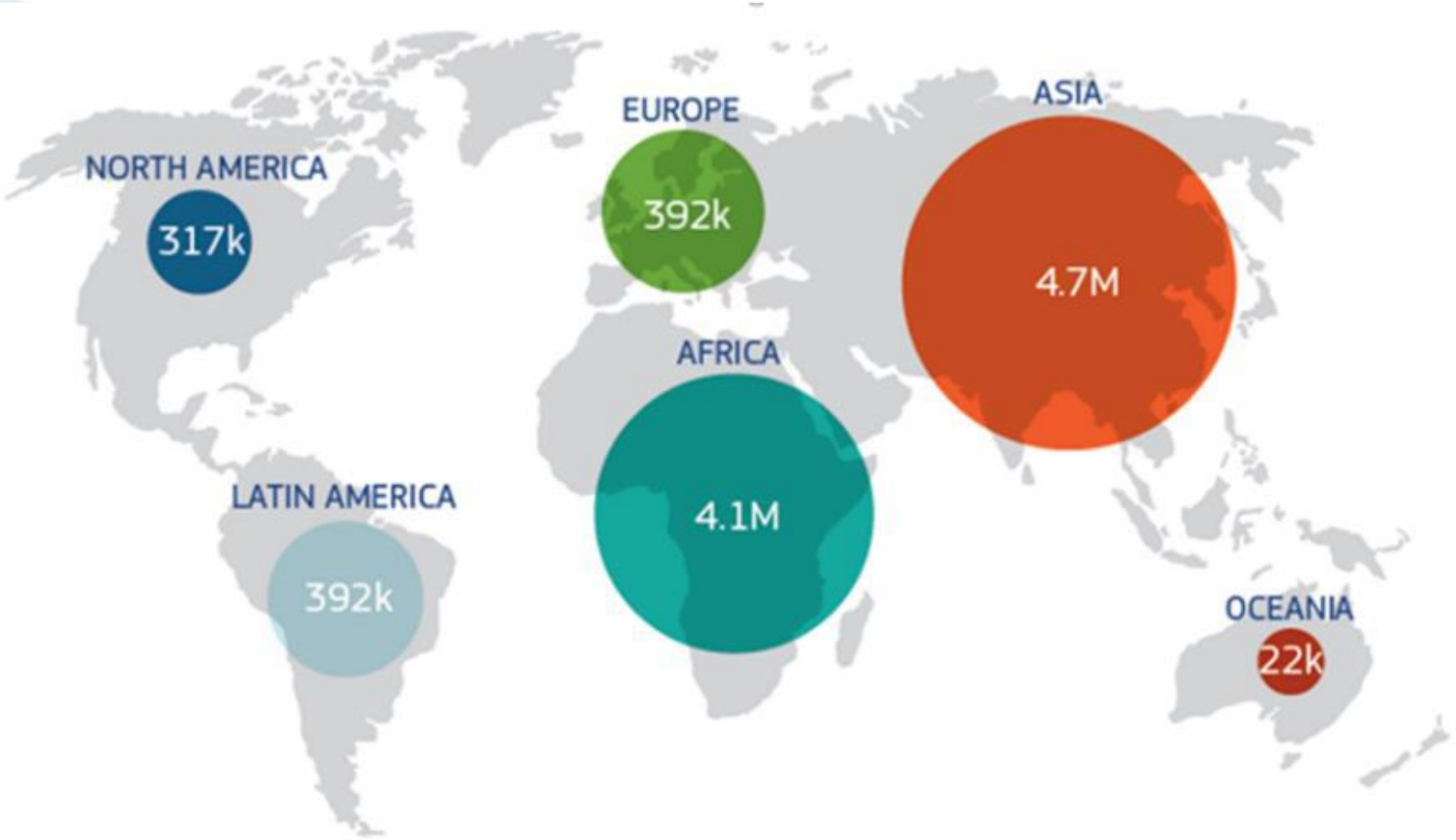


(Source: European Commission)

Introduction of Malaria Rapid Tests

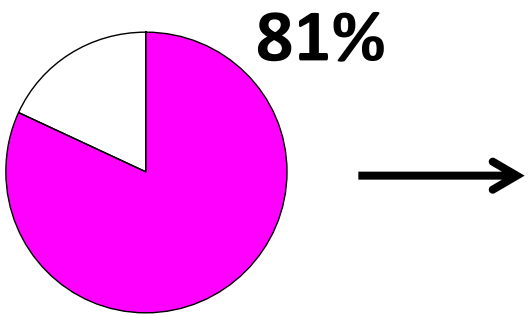
Antibiotic prescription study in Dar es Salaam

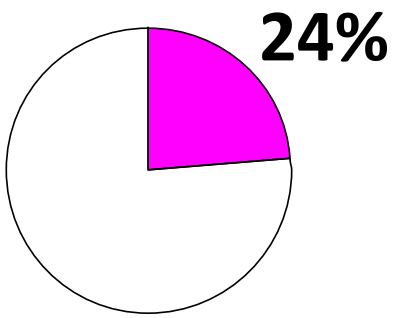
Proportion of febrile patients receiving:

Before RDT implementation

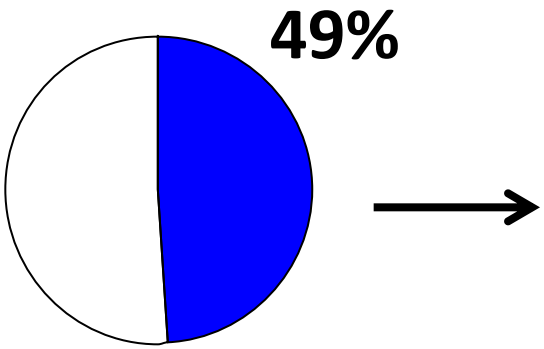
After RDT implementation

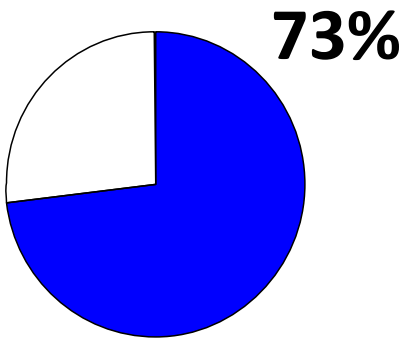
Antimalarials





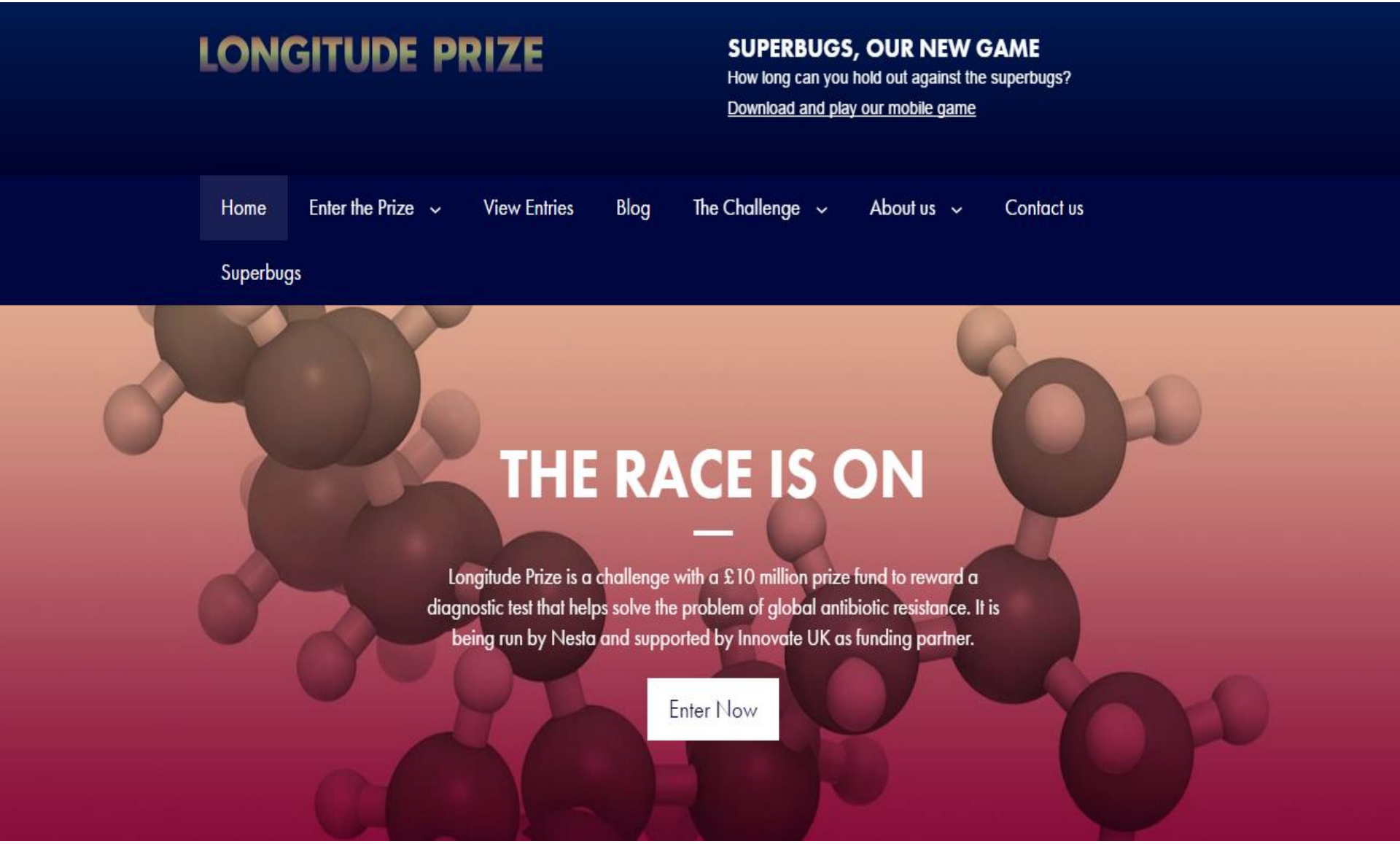
Antibiotics





D'Acremont et al, 2010

The UK Longitude Prize



Longitude Prize Award Criteria

NEEDED

Improve the antibiotic treatment decision of a globally-occuring problem

ACCURATE

Eliminate harmful treatment decisions and give confidence to the user

AFFORDABLE

Affordable for purchase and use everywhere that it is needed

RAPID

Under 30 minutes from sample collection to result

EASY-TO-USE

Can be used and interpreted anywhere in the world without advanced medical resources

SCALABLE

An original idea with a plan for full-scale manufacture and distribution

SAFE

The benefits of using the test far outweigh any risks associated with it

CONNECTED

In-built data-recording and transmission capability

PROTOTYPE

Have at least three copies of your prototype that is ready for clinical trials

European Commission

Horizon **Prize**

BETTER USE OF ANTIBIOTICS

$20m NIH Prize

Request for Comment for: Antimicrobial Resistance Rapid, Point-of-Care Diagnostic Test Challenge

Purpose & function	**Which pathogens?**	**Sample matrix**	**Settings**	**Ease-of-use**
Diagnostic performance	**Tradeoffs**	**Cost**	**Other characteristics**	
Key technologies	**Interest in competing**	**Use**	**Barriers**	

https://www.challenge.gov/challenge/request-for-comment-for-antimicrobial-resistance-rapid-point-of-care-diagnostic-test-challenge/

Global Health Emergencies: Need for Open Technology Platforms

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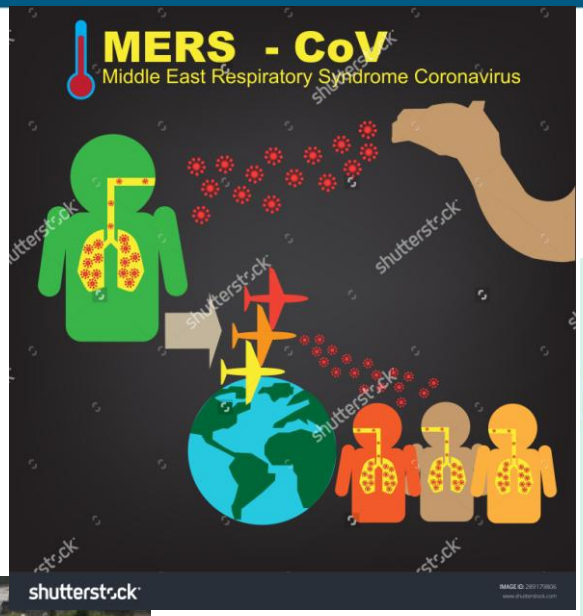

Source: J. Whitehorn

Developing an Early Warning System for Infectious Diseases in the United Kingdom

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Microsoft

UCLPartners
Academic Health Science Partnership

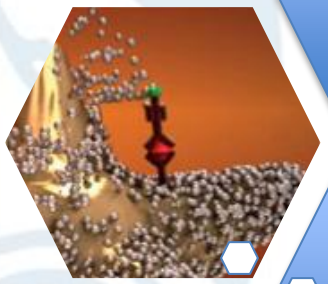
NHS

OJBIO
MOBILE DIAGNOSTICS

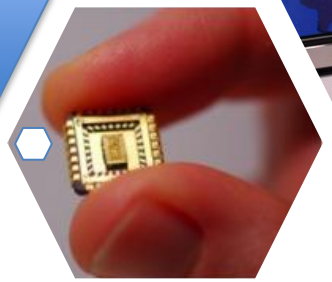
Surrey University

London School of Hygiene and Tropical Medicine

UCL



Newcastle University



Imperial College London

Public Health England

Cepheid

O2 Telefónica

Avacta

FAB
MIXED-SIGNAL FOUNDRY EXPERTS

CAMBRIDGE LIFE SCIENCES

Zurich Instruments

MOLOGIC
an Alere company

EPSRC
Engineering and Physical Sciences Research Council

i-sense

Early-Warning Sensing Systems for Infectious Diseases

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NHS

Clinical Care

Helping patients gain faster access to care

Accurate Information
Electronic prescriptions

Public Health England

Public Health

Protecting the public
Monitor interventions

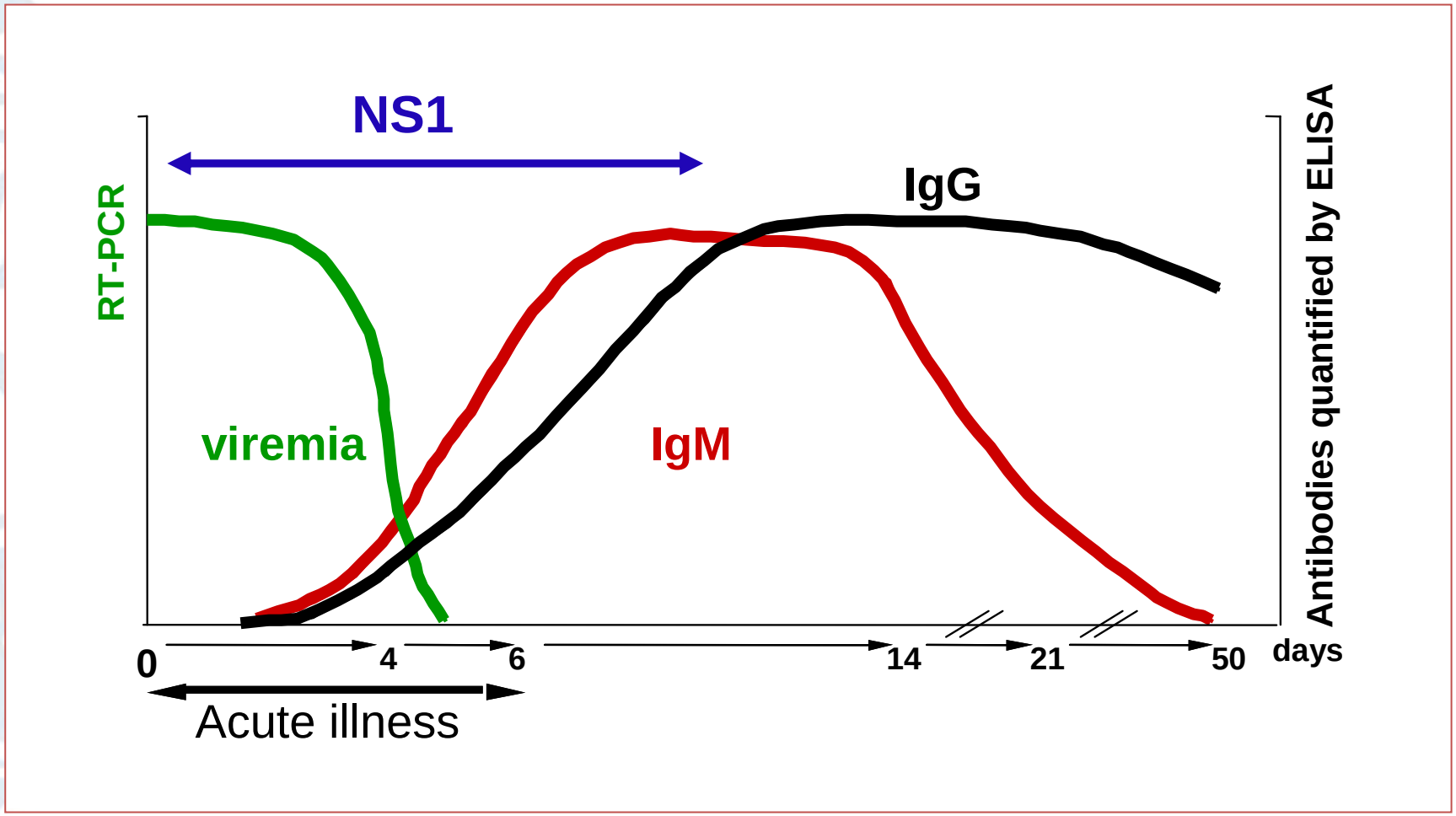
Prevention Programmes
Local information

Early Detection

Rapid Response

EPSRC
Engineering and Physical Sciences Research Council

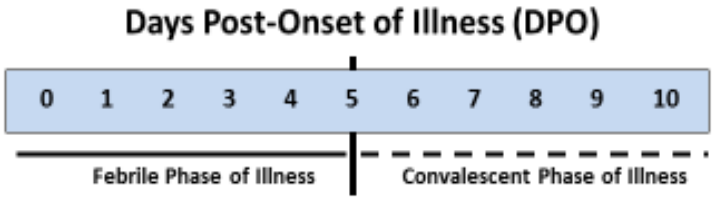
Doing the Right Test at the Right Time



Reimagining the Future of the Diagnosis of Viral Infections

- 1,234 paired serum samples from laboratory confirmed dengue patients, archived between 2005-2011

- accurately identified >90% of primary and secondary dengue cases from a single serum specimen collected during the first 10 days of illness by using either:
  - **DENV real-time RT-PCR + IgM ELISA**
  - **DENV NS1 antigen ELISA + IgM ELISA**



Specimen from suspected dengue case by DPO	IgM anti-DENV	RT-PCR or NS1	Percent Positive	Decision
0-3	-	+	79-90%	One-Test
4-7	+	+	95-100%	Two-Test
>7	+	-	93-100%	One-Test

Hunsperger et al JID Mar 2016

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1% compromise in quality ?
PP-TEB
TRANSBRASIL
Slide from Antoine Pierson

Connectivity Solutions

The need is actually not for connectivity but for intelligence to improve the quality of testing and patient care

1. Quality Assurance, especially in the case of POCT
2. Patient treatment
3. Public health monitoring
4. Outbreak response
5. LI(M)S interfacing
6. Stock management
7. Operator performance; Instrument performance

Drones for Health in Malawi

Small, rotary-wing aircraft:

Cost: ~ $10,000
Payload : 5 lbs
Flight time: 30-60 min
Range: 20-60 miles

Operation: manual or pre-programmed for specific routes; need almost no room to land, and can even drop packages from a low hover; can deliver 100 HIV POC tests

Wearable Biosensors

Summary: Investing in diagnostics can strengthen health systems

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- Many communities in developing countries lack access to laboratories and diagnostics. Simple affordable point-of-care tests are now available. Risk vs benefit analysis need to be considered in regulatory approval
- Assuring the quality of POC tests and testing is critically important. Connectivity solutions linking data from diagnostic laboratories and POC test readers/devices provide automated surveillance
- Diagnostics can now be used to monitoring quality of tests and testing, increasing the efficiency of health care systems including supply chain management, improving patient outcomes and empowering communities

Acknowledgement

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