How will Rapid Diagnostics Revolutionise Healthcare in the Coming 5-10 years?

Rosanna W Peeling
Professor and Chair, Diagnostic Research
Director, International Diagnostics Centre

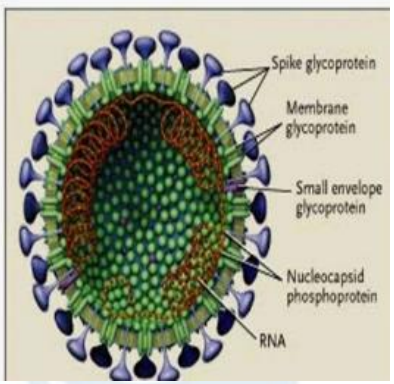
www.idx-dx.org

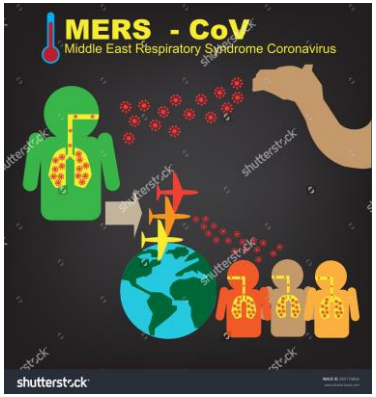
Plan of Presentation

- **Why do we need rapid diagnostics?**
  - Epidemic preparedness
  - Antimicrobial resistance
  - Improve access and health system efficiencies towards universal health care
- **Performance and operational characteristics of rapid diagnostics**: access vs accuracy
- **Diagnostics to revolutionise health care will require the convergence of**:
  - biotechnology advances
  - digital technology
  - artificial intelligence and machine learning
  - Faster regulatory approval and policy development process
- **The future is in our hands**

Global Health Emergencies:
Viral epidemics - more frequent and severe

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE





2003-4
SARS

Needed a new test

2012
MERS-CoV

Needed a new test

2013
EBV

Needed a faster NAT and more sensitive antigen test

2015-6
ZikaV

Needed a more sensitive antigen test and more specific antibody test

Preparing for the Inevitable

- **As part of the R&D Blueprint for Actions to Prevent Epidemics, WHO has called for ideas for platform technologies to improve research and development preparedness against a set of priority infectious disease threats:**
  - **haemorrhagic fevers: Crimean-Congo haemorrhagic fever, Ebola and Marburg viruses, Lassa fever**
  - **Middle East respiratory syndrome coronavirus (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS)**
  - **Nipah and henipaviral diseases**
  - **Rift Valley fever (RVF)**
  - **Zika**
  - **Disease X for any unknown pathogen of epidemic potential**

https://www.who.int/blueprint/priority-diseases/en/

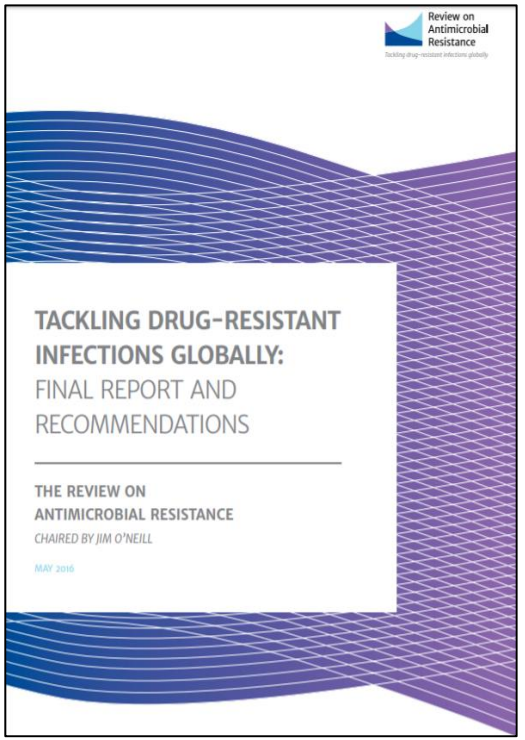
Antimicrobial Resistance (AMR)

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

According to the O'Neill Review on AMR:

- **In 2016, 1 person dies from AMR every 45 seconds**

- **If no action is taken, by 2050:**
  - **1 person dies from AMR every 3 seconds**
  - **AMR will cost 100 trillion USD**
  - **many infections will become incurable – threaten the practice of modern medicine**

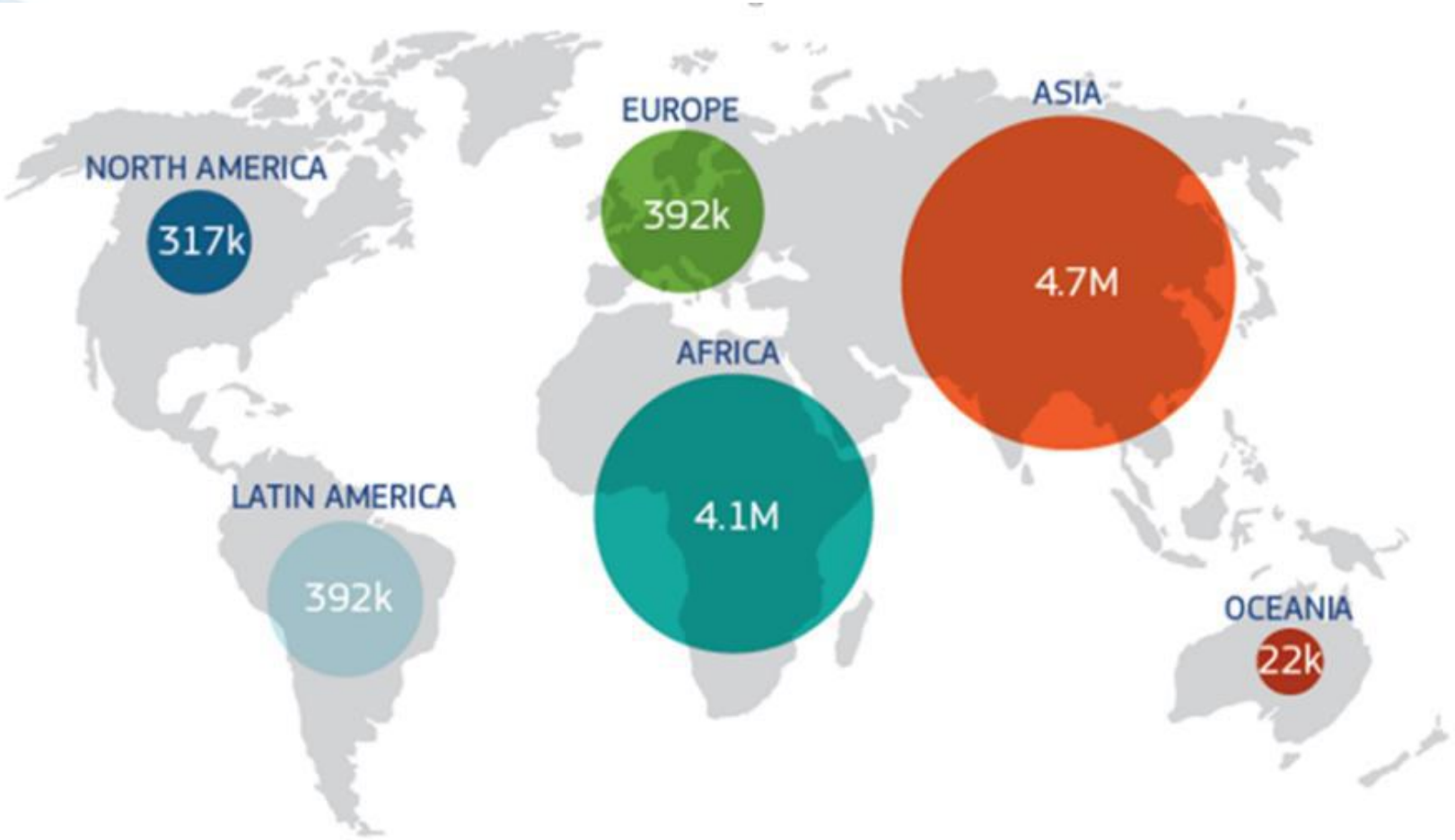


https://amr-review.org/

WHO: No action today, no cure tomorrow

Lives lost/year attributable to Antimicrobial Resistance by 2050

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE



(Source: European Commission)

Excessive Use of Antimicrobials has contributed to AMR

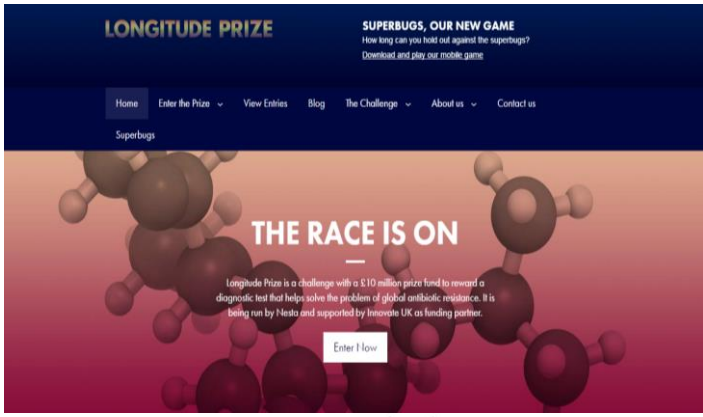
- **Urgent need for rapid diagnostics to guide appropriate use of antibiotics for common clinical syndromes:**
  - fever, pneumonia
  - diarrheal illness
  - urinary tract infections
  - sexually transmitted infections
  - sepsis

Data extracted from: Shapiro et al. Antibiotic prescribing for adults in ambulatory care in the USA, 2007-9. J Antimicrobial Chemoth 2013.

Investments in Diagnostics for AMR

Diagnostic tests or test systems are needed to:

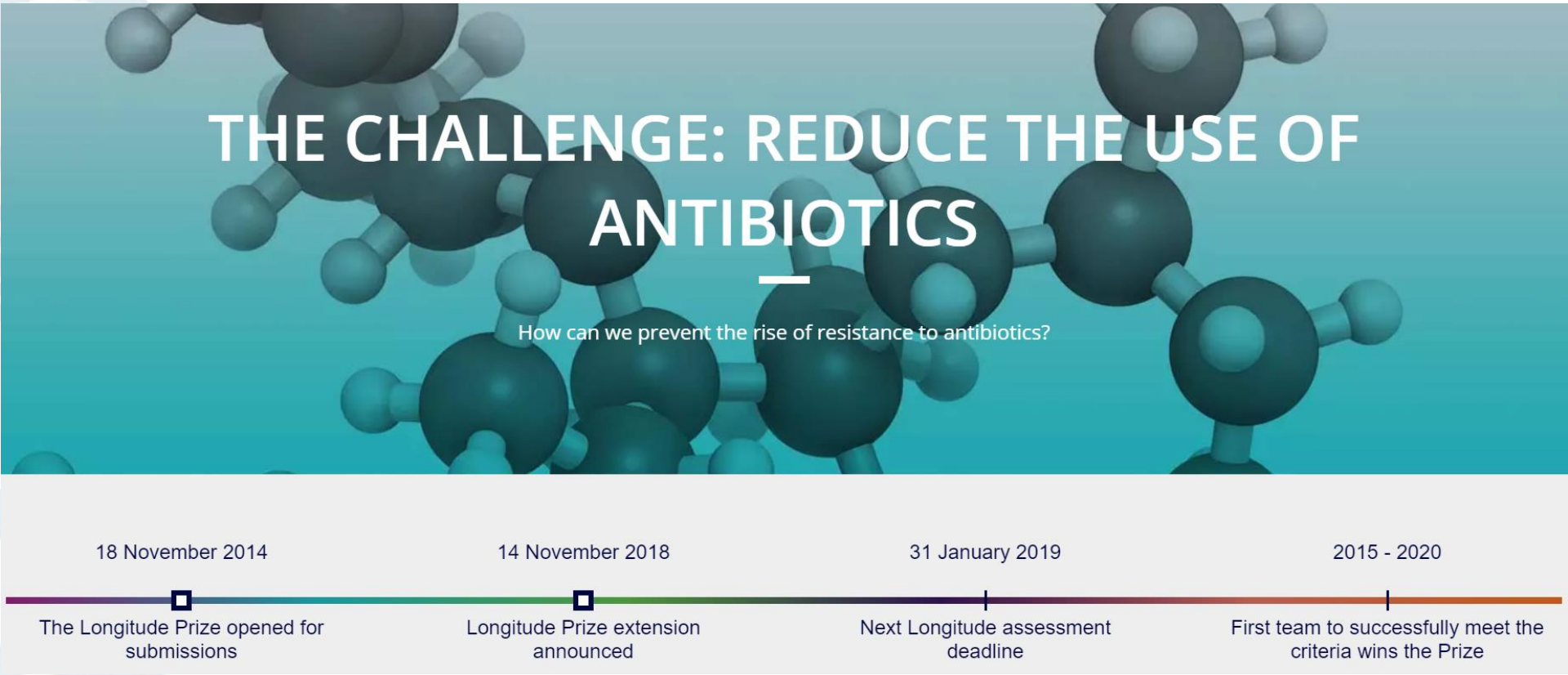
- improve patient management by more targeted use of antibiotics for common syndromes
- Enable AMR surveillance
- Assess the impact of AMR interventions



<u>Incentivising Rapid Test Development</u>:

- The UK Longitude Prize: £ 10 million
- The EC Horizon 2020 Prize: 1 million euros
- The US NIH AMR Prize of up to $ 20 million

Longitude Prize, £10 million



So far, 239 groups have registered and 13 Discovery awards have been given as seed funding

LONGITUDE PRIZE

WHAT KIND OF TEST COULD WIN?

ENVIRONMENTAL STABILITY

EASILY CARRIED

NO COLD CHAIN

NO MAINS POWER

THE WINNING TEST MUST BE...

NEEDED

Improve the antibiotic treatment decision of a globally occurring problem

ACCURATE

Eliminate harmful treatment decisions and give confidence to the user

AFFORDABLE

Affordable for purchase and use everywhere that it is needed

RAPID

Sample collection to result in less than 30 minutes

EASY TO USE

Can be used and interpreted anywhere in the world with minimal training

CONNECTED (OPTIONAL)

Tests with data-recording and transmission will be favoured

SAFE

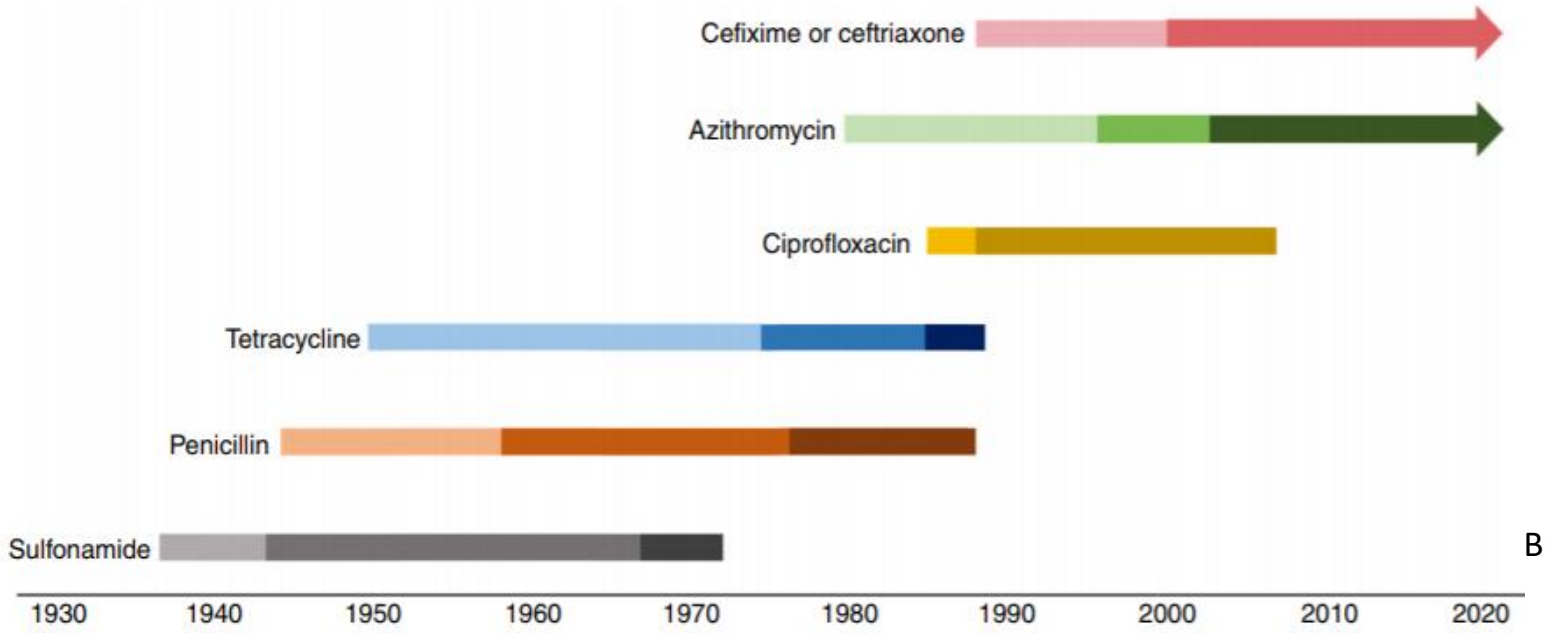
The benefits far outweigh any risks

SCALABLE

A plan for full-scale manufacture and distribution

The winning test will help reduce unnecessary use of antibiotics and/or help medical professionals know which antibiotic to use when.

A Rapid Test for Gonorrhoea



Brazil J Microbiol 2017

- **In the UK 33, 431 ceftriaxone treatments are given annually for gonorrhoea (2014)**
- **A modelling study showed that if a rapid test could detect:**
  - **GC + ciprofloxacin resistance, 66% of tx could be replaced by ciprofloxacin;**
  - **GC + penicillin resistance, 79% of current tx could be replaced by penicillin**

Rapid AMR tests can reduce loss to follow up, extend the life of our current last-line treatment, and is cost-saving

Ref: Turner KME, et al. BMJ Open 2017;7:e015447.

Sustainable Development Goals (SDGs): A Global Pledge to Leave No-One Behind

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

WHO Sustainable Development Goals.
http://www.who.int/sdg/targets/en/

Plan of Presentation

- **Why do we need rapid diagnostics?**
  - Epidemic preparedness
  - Antimicrobial resistance
  - Improve access and health system efficiencies towards universal health care
- **Performance and operational characteristics of rapid diagnostics:** access vs accuracy
- **Diagnostics to revolutionise health care will require the convergence of**:
  - biotechnology advances
  - digital technology
  - artificial intelligence and machine learning
  - Faster regulatory approval and policy development process
- **The future is in our hands**

ASSURED Tests to Improve Global Health

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

A = Affordable

S = Sensitive

S = Specific

U = User-friendly

R = Rapid and robust

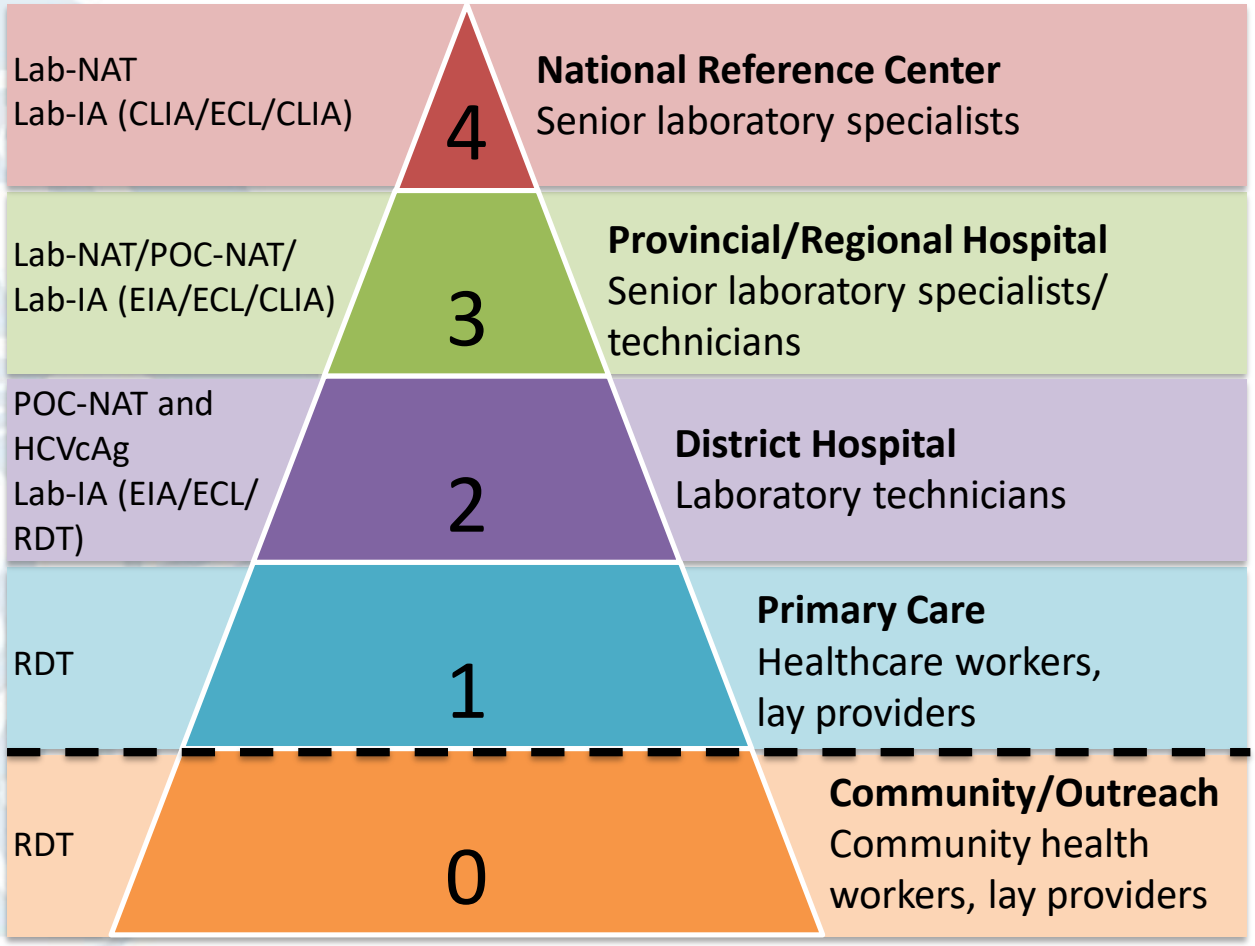
E = Equipment-free

D = Deliverable

- ✓ **Affordability**
- ✓ **Accuracy**
- ✓ **Accessibility**

Mabey D, Peeling RW, Ustianowski A, Perkins MD. Diagnostics for the developing world. Nature Rev Microbiol 2: 231-40, 2004.

Rapid Diagnostic Tests: Trade-Off between Access and Sensitivity



- No test is perfect
- We need to weigh acceptable risks vs incremental clinical benefit

Access	Sensitivity			
	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

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

WHO Guidelines on Hepatitis B and C Testing. Available at: http://apps.who.int/iris/bitstream/10665/254621/1/9789241549981-eng.pdf?ua=1 (accessed July 2018).

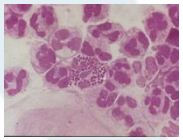
Diagnostics Methods:
Ease of Detection vs Confidence in Diagnosis

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

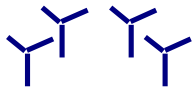
Confidence

DIRECT METHODS:
Pathogen Detection

INDIRECT METHODS:
Host Biomarkers





Microscopy	Culture	Genome detection	Antigen detection	Serology IgM	Serology IgG

Ease of detection

Time to Result:

Days/Hours → **Minutes**

Adapted with permission from J. Cardosa

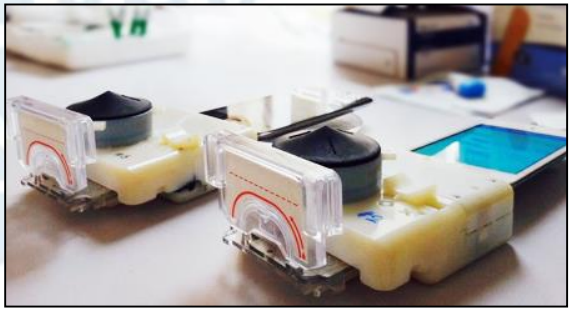
Plan of Presentation

- **Why do we need rapid diagnostics?**
  - Epidemic preparedness
  - Antimicrobial resistance
  - Improve access and health system efficiencies towards universal health care
- **Performance and operational characteristics of rapid diagnostics:** access vs accuracy
- **Diagnostics to revolutionise health care will require the convergence of**:
  - biotechnology advances
  - digital technology
  - artificial intelligence and machine learning
  - Faster regulatory approval and policy development process
- **The future is in our hands**

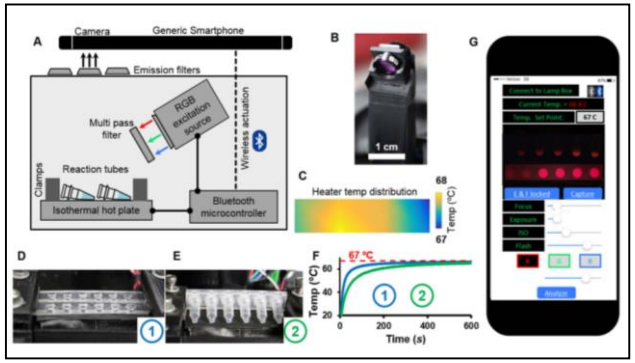
Explosion in Near-Patient Molecular Detection and Sequencing Technologies

Plug and play format:

- Minimal Hands on time
- Multiplex testing
- Rapid time to result
- Data transmission

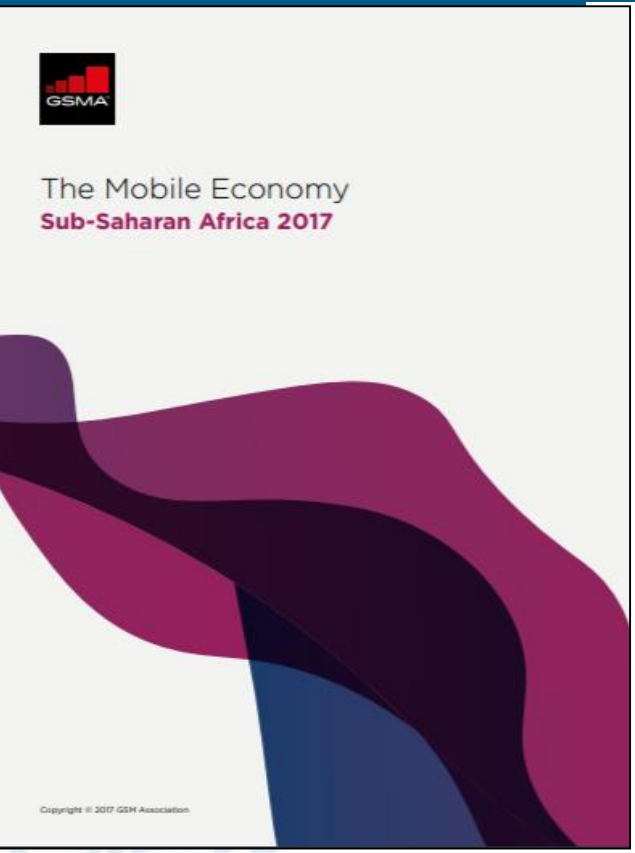


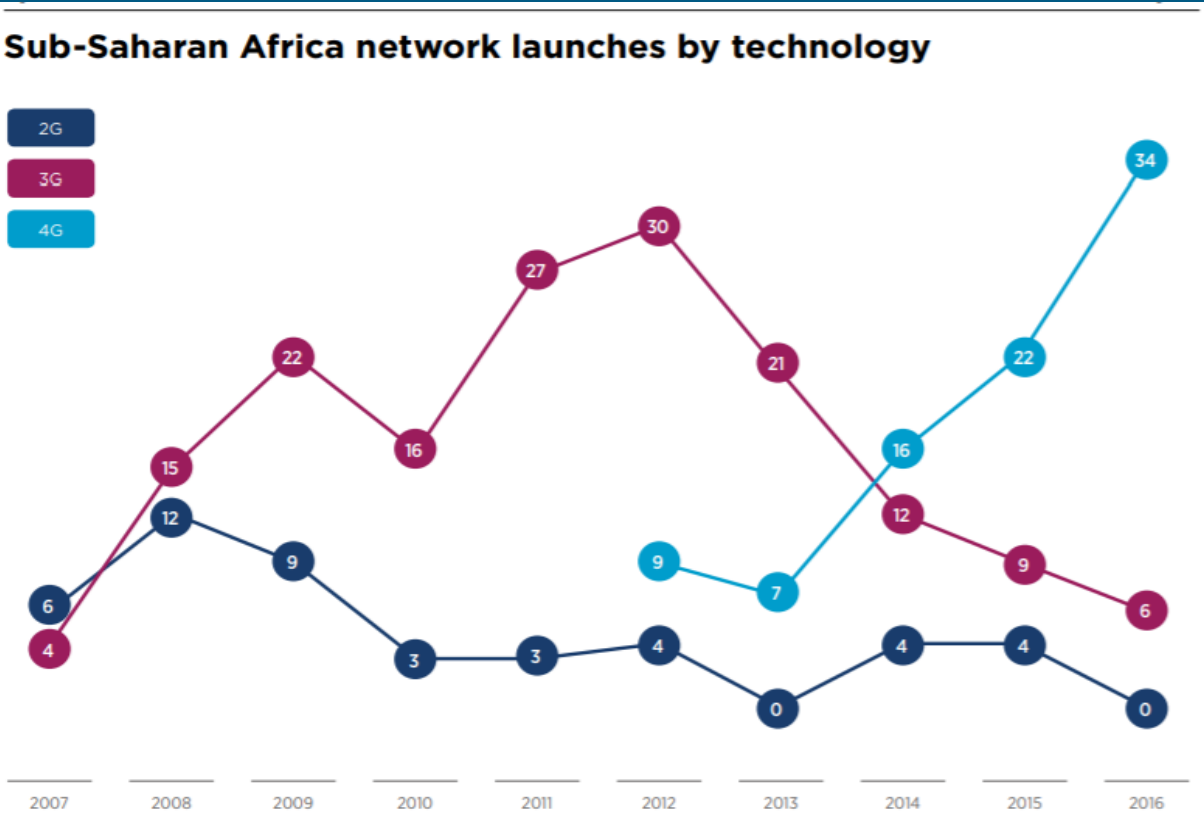
Laksanasopin et al. *Science Transl Med* 2015:7:273



Priye, A. et al. A smartphone-based diagnostic platform for rapid detection of Zika, chikungunya, and dengue viruses. Sci Rep 2017;7:44778

Africa CDC: Can we leapfrog public health practice by building connected health systems?





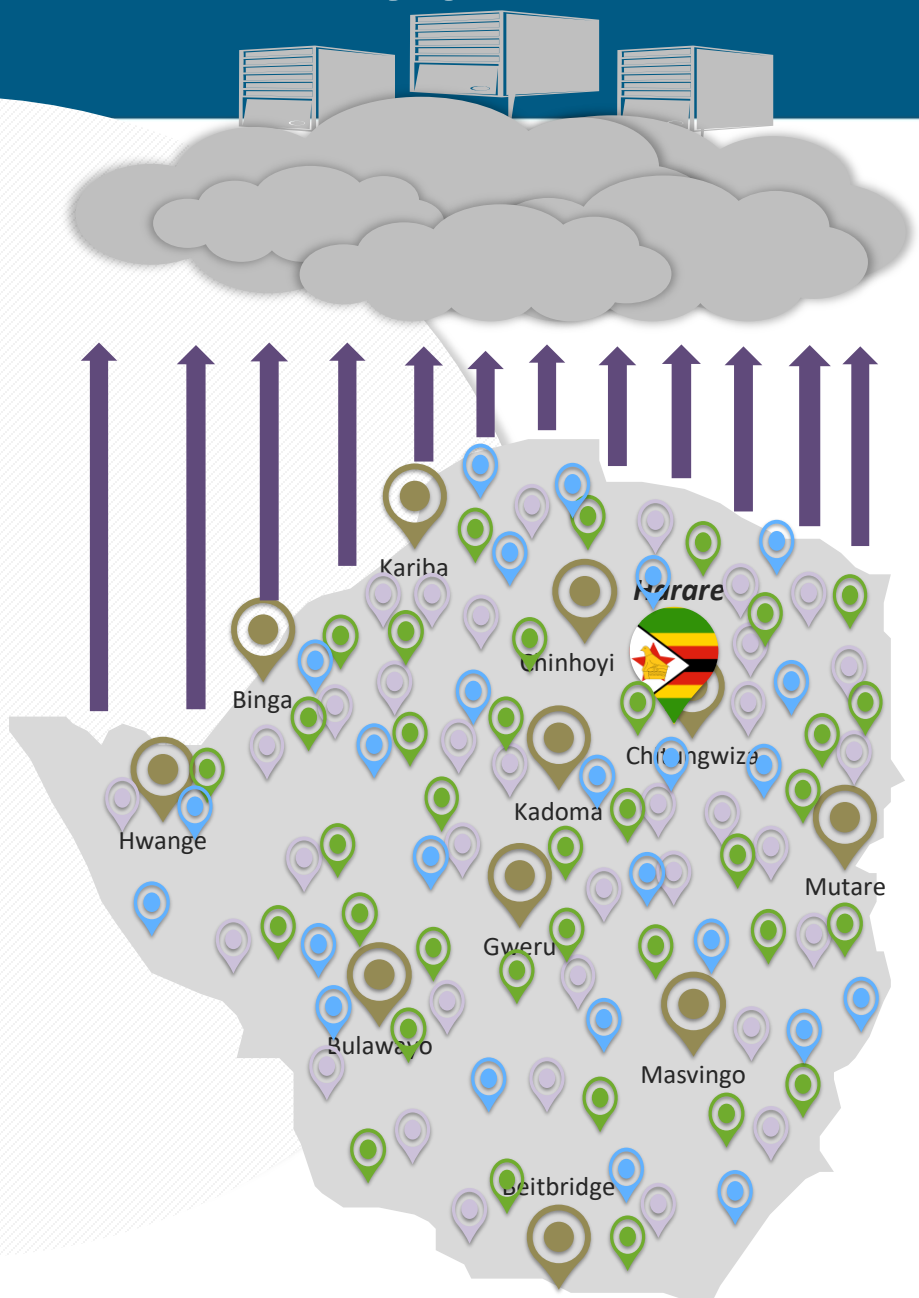
- At the end of 2016, there were 420 million unique mobile subscribers in Sub-Saharan Africa, equivalent to a penetration rate of 43%.
- Phone adoption in Africa continues to grow faster than any other region of the world

Convergence of digital technology & POC diagnostics: Strengthening Health Systems

Connectivity allows data to be turned into real-time intelligence to provide alerts of outbreaks, improve quality of testing, strengthen efficiency of health systems in terms of stock management 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

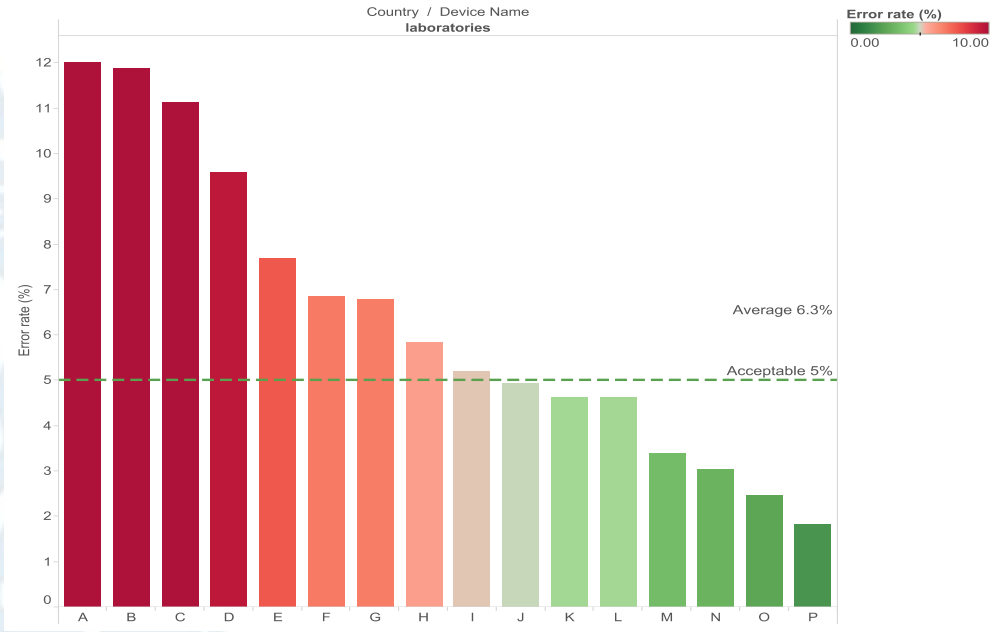
Connectivity pilot in Zimbabwe



Testing data and proficiency panels results from 3 POC devices (Alere CD4, Cepheid GeneXpert TB and Rif resistance, and Hemocue) were sent real time to MOH central database in the office of the Chief of Lab Services

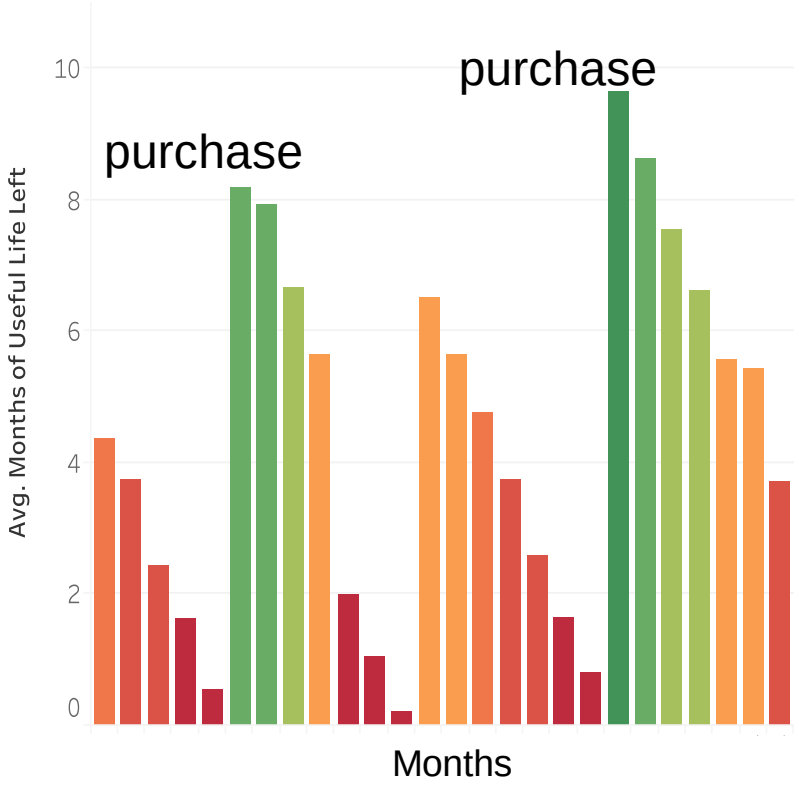
Dashboards for trends and alerts

Monitoring Error Rates:



Laboratories or POC Testing sites

Monitoring stock/supplies:



Gous N, Boeras DI, Cheng B, Takle J, Cunningham B, **Peeling RW**. The impact of digital technologies on point-of-care diagnostics in resource-limited settings. Expert Rev Mol Diagn. 2018 Apr;18(4):385-397.

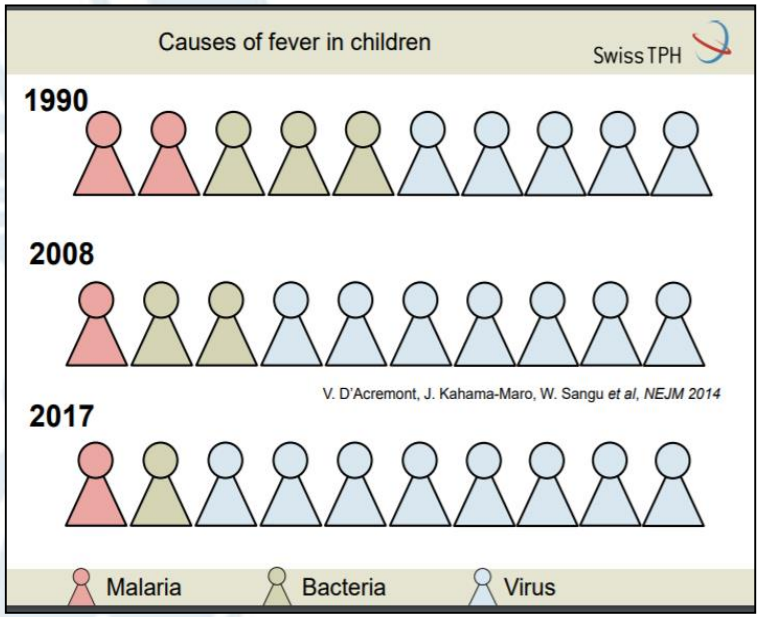
Technology Convergence

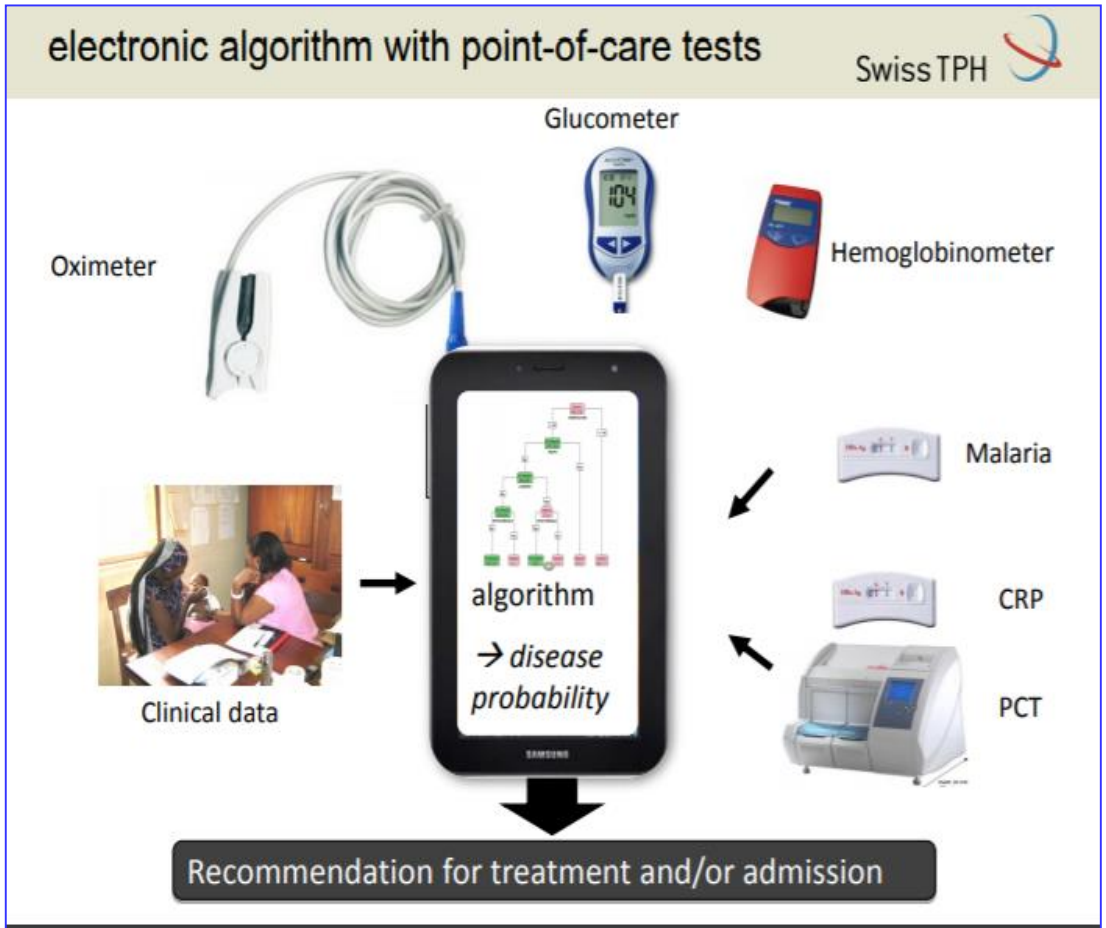
Connected diagnostics can form the backbone of a health care system

Area	Novel Technologies	Web-enabled functions
Outbreak Identification	Social media alerts of possible outbreaks Syndromic surveillance	Electronic capture of epidemiological and clinical data Multi source data capture for alerts
Global health security and disease control	- Real time reporting to public health agencies through data transmission from POC devices - Transform data into intelligence to inform control strategies - Portable genetic sequencing of samples to map resistance and transmission patterns	Cluster 'hot spot' identification Data visualisation based on geospatial and phylogenetic mapping for disease control and contact management Real time monitoring of the effectiveness of interventions
Health System Strengthening	More efficient and effective use of clinics/patient /staff time	Automated report generation with reduced transcription errors; quality of testing validated through linking results with proficiency panel testing; automated supply chain management

Future Directions: convergence of digital diagnostic technology and artificial intelligence

Rapid Test results can be incorporated into electronic clinical decision support systems with decades of data on epidemiology of fever to improve patient management and reduce inappropriate antibiotic use:



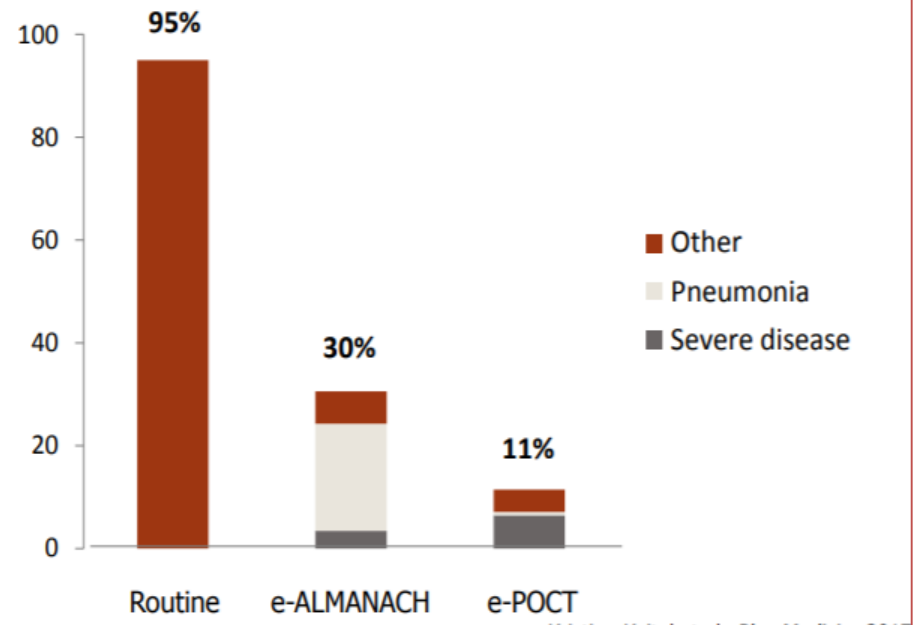


Future Directions: convergence of digital diagnostic technology and artificial intelligence

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

% children with antibiotics

Swiss TPH



Kristina Keitel et al, *Plos Medicine* 2017

Major findings of the e-POCT trial

Swiss TPH

e-POCT, a novel electronic algorithm based on:

- key clinical signs
- host biomarker POCTs

was better than the current reference IMCI-based e-algorithm:

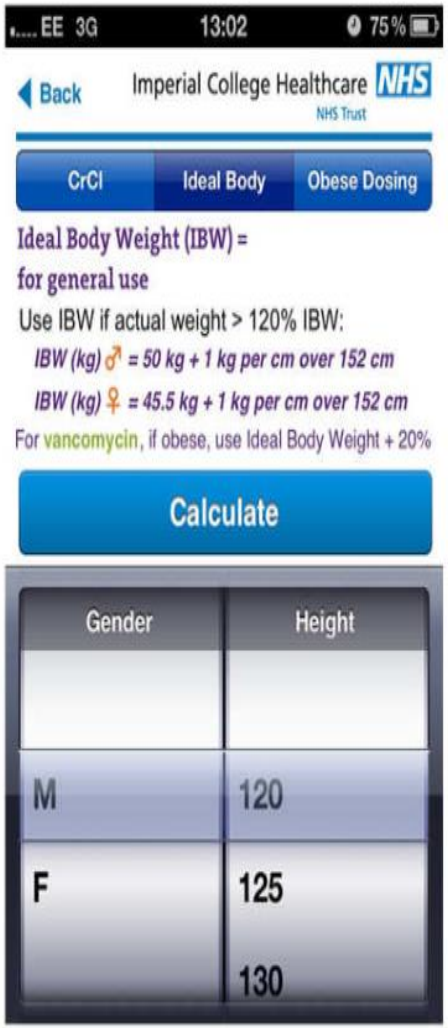
- Reduced relative risk of clinical failure by 50%
- Reduced antibiotic prescription from 95% to 11%
- Improved targeting on children in need for antibiotic prescription
- Better identified children with severe disease

Kristina Keitel et al, *Plos Medicine* 2017

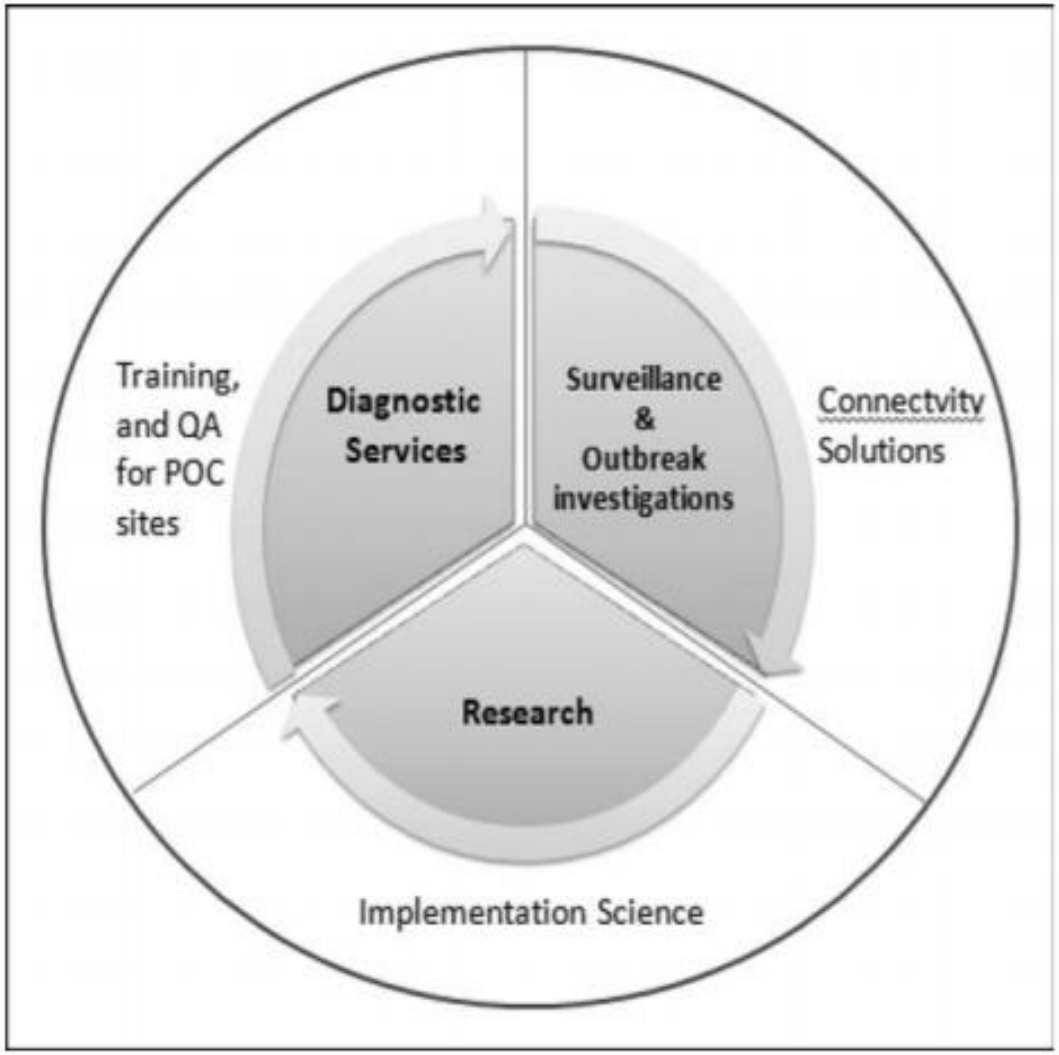
Improving Patient Management through Electronic Decision Support

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

The Imperial Antibiotic Prescribing Policy (IAPP) smart phone app provides clinical decision support at the point of care to improve antimicrobial stewardship and appropriate prescribing:



The Lab as a Command Centre



The lab serves as the Command Centre that can provide:

- Quality diagnostic services
- Training and proficiency testing at point-of-care testing sites

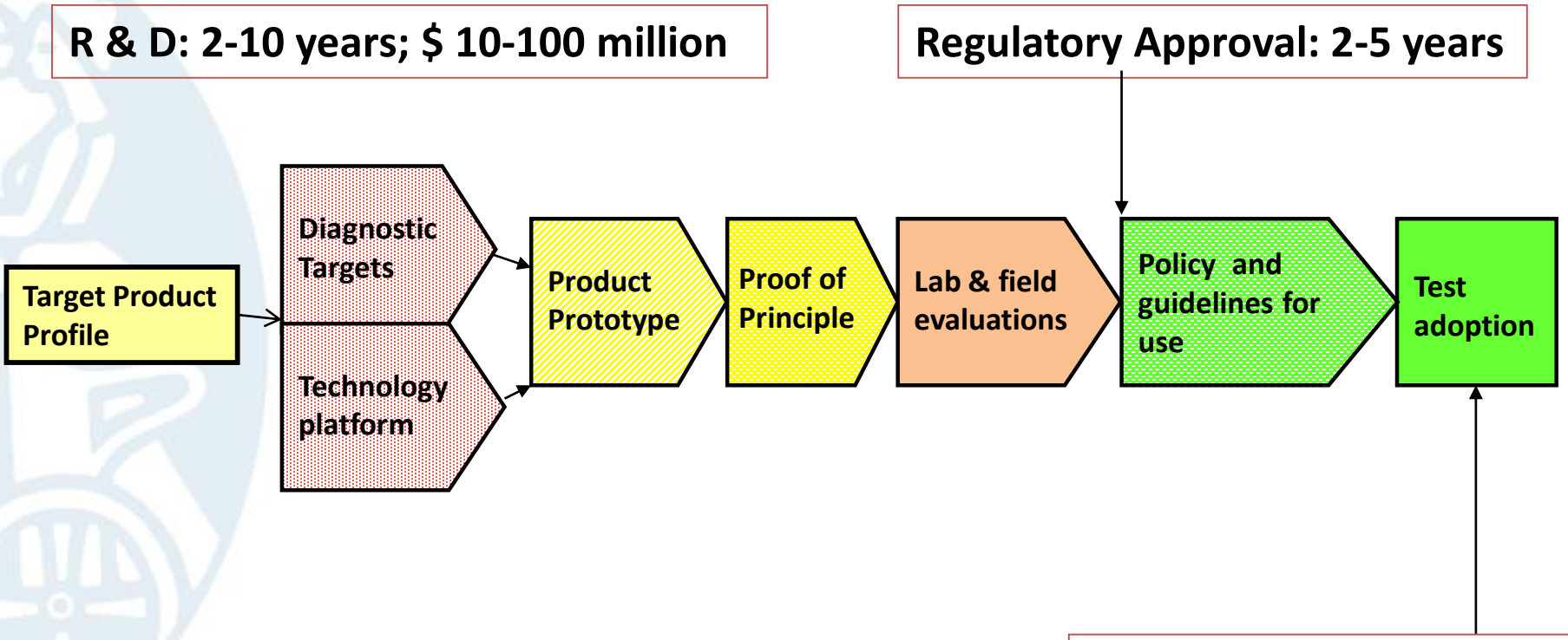
- surveillance and outbreak investigations
- Epidemiologic data for clinical decision support

- Research
- Implementation science for introducing novel technologies and interventions

Ref: Boeras DI, Nkengasong JN, Peeling RW. Implementation science: the laboratory as a command centre. Curr Opin HIV AIDS 2017: 12:171–174.

Urgent Need to Accelerate the Bench-to-Bedside Pathway

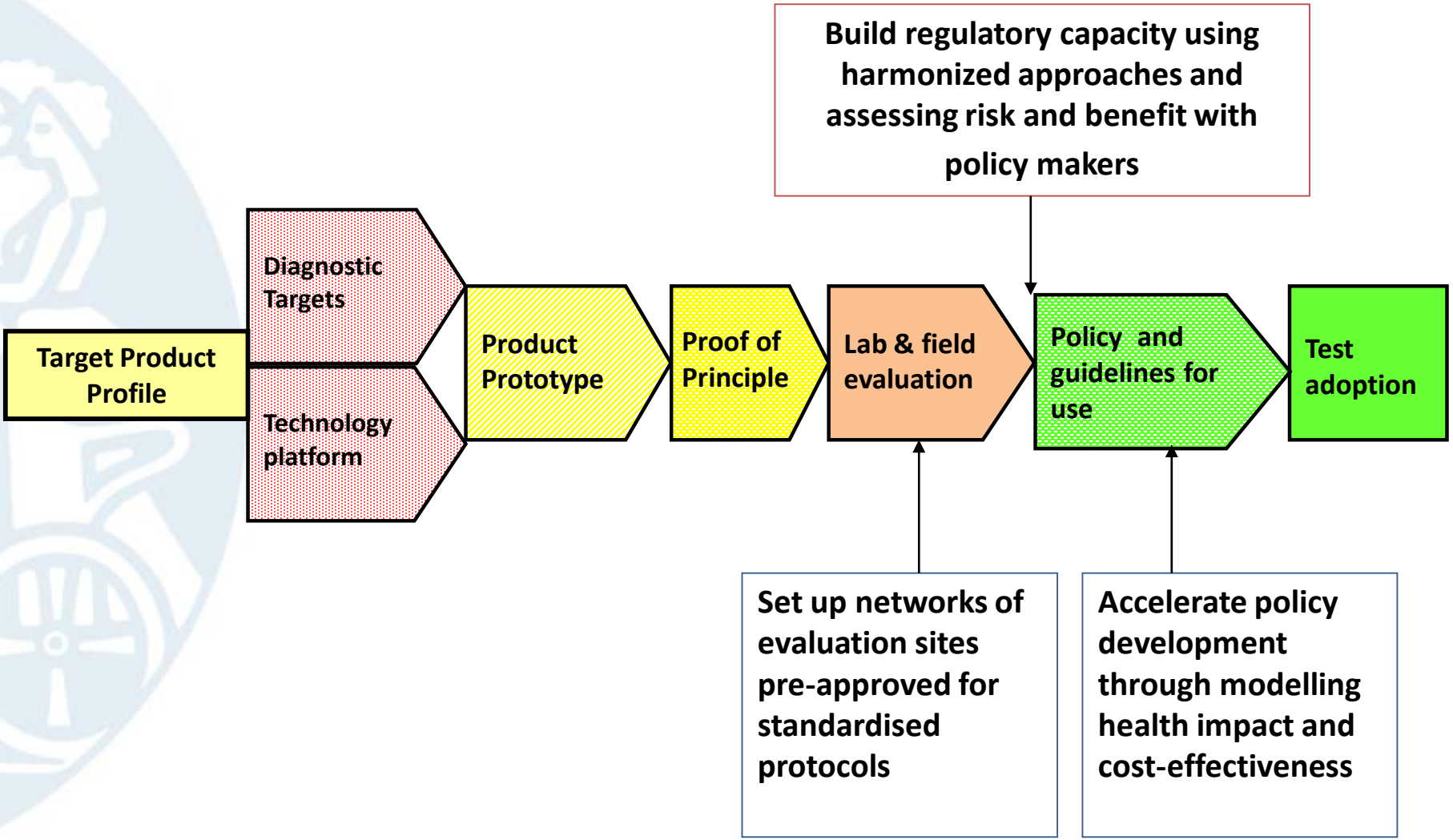
LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE



Regulatory science needs to keep pace with technological innovations to accelerate access to diagnostics

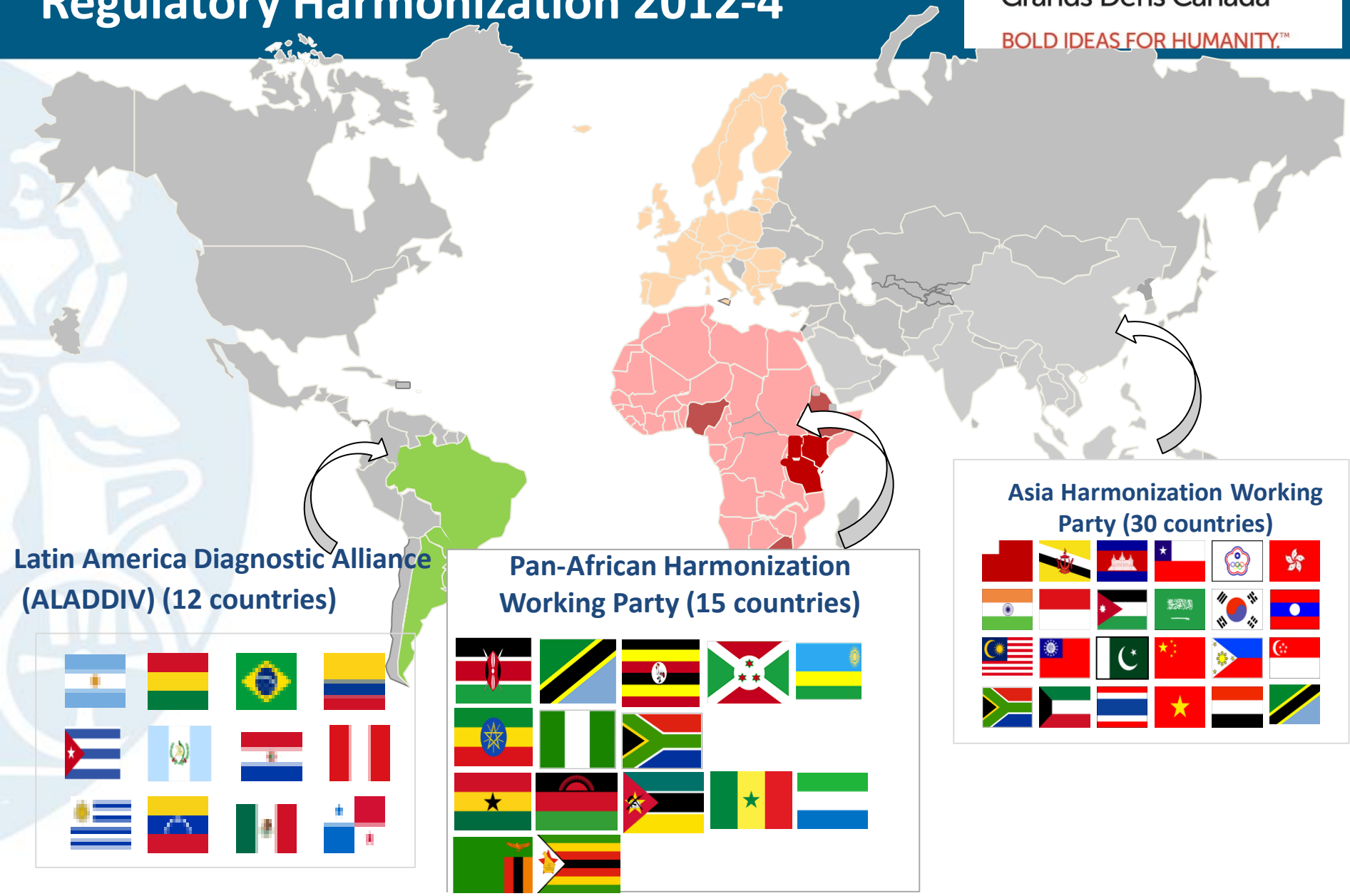
Urgent Need to Accelerate the Bench-to-Bedside Pathway for Novel Rapid test to be Put into Use

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE



Progress towards IVD Regulatory Harmonization 2012-4

Grand Challenges Canada™
Grands Défis Canada™
BOLD IDEAS FOR HUMANITY.™



Latin America Diagnostic Alliance (ALADDIV) (12 countries)

Pan-African Harmonization Working Party (15 countries)

Asia Harmonization Working Party (30 countries)

The Future is in Our Hands (1)

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

Promise of Rapid Diagnostics:

- **Rapid tests that leverage digital technology with artificial intelligence and machine learning can:**
  - **provide clinical decision support at the point-of-care, improve patient management and have the potential to reduce inappropriate use of antibiotics**
  - **turn real-time surveillance and sequencing data into intelligence enabling:**
    - **earlier warning of infectious disease outbreaks**
    - **more evidence-based disease control strategies**
    - **assessment of the impact of interventions**
  - **catalyse health system efficiencies, reducing number of patient visits, optimising supply chain management and improving patient outcomes**

The Future is in Our Hands (2)

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

Challenges:

- When the decision to adopt new rapid diagnostics is made, it is important to understand the necessary infrastructure and skilled human resource needed to maintain these new diagnostic systems and ensure data quality and optimal usage

- Outbreaks cannot be prevented, but rapid diagnostics can facilitate a faster, smarter response leading to earlier quarantine and a dramatic reduction in the cost of each outbreak as well as impact on morbidity and mortality, but data quality, governance and security are critical in building stronger disease surveillance and intelligence networks

- Accelerating the Bench-to-Bedside pathway through regulatory harmonization and joint assessment of risk and benefit is critical for simple rapid tests to be available for epidemic preparedness, combating AMR and health system strengthening

Acknowledgement

LSHTM/IDC:
Noah Fongwen, Debra Boeras, Robert Luo, Joe Tucker, Priyanka Shrestha, Helen Kelly, Catherine Wedderburn, Ben Cheng, Philomena Raftery, Jack Butterworth, Hannah Miyanji, Adriana Goncalves, David Mabey

SystemOne: Brad Cunningham, Natasha Gous

Funding: Bill & Melinda Gates Foundation, Grand Challenges Canada, UNITAID, WHO, EU, UK EPSRC