FIND

# Understanding the Introduction of Pathogens into Humans- Preventing Patient Zero:

DIAGNOSTIC CONSIDERATIONS FOR EPIDEMIC PREPAREDNESS AND RESPONSE

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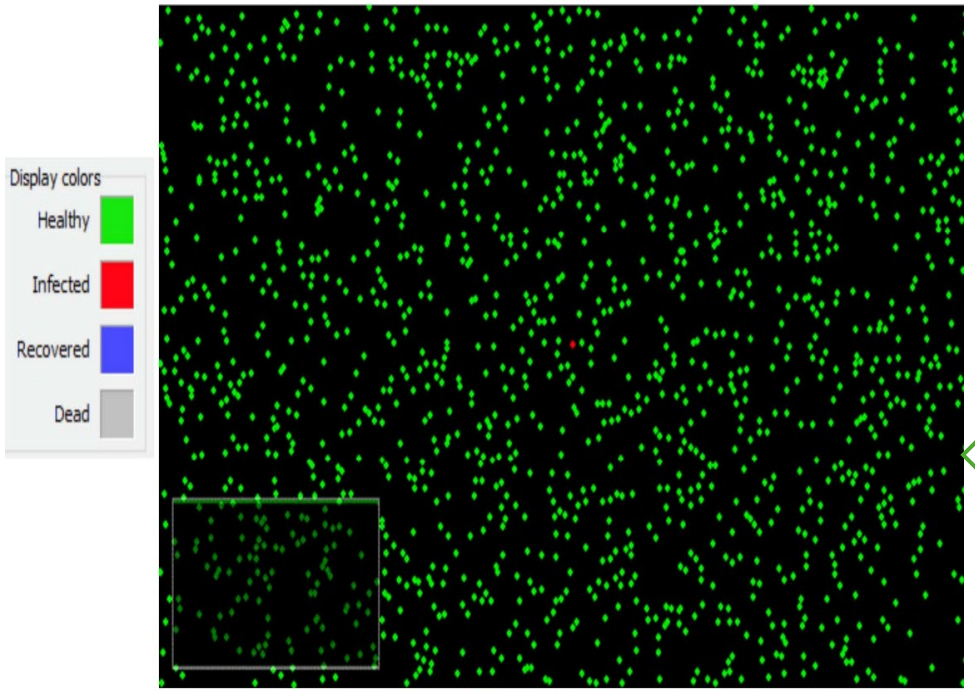
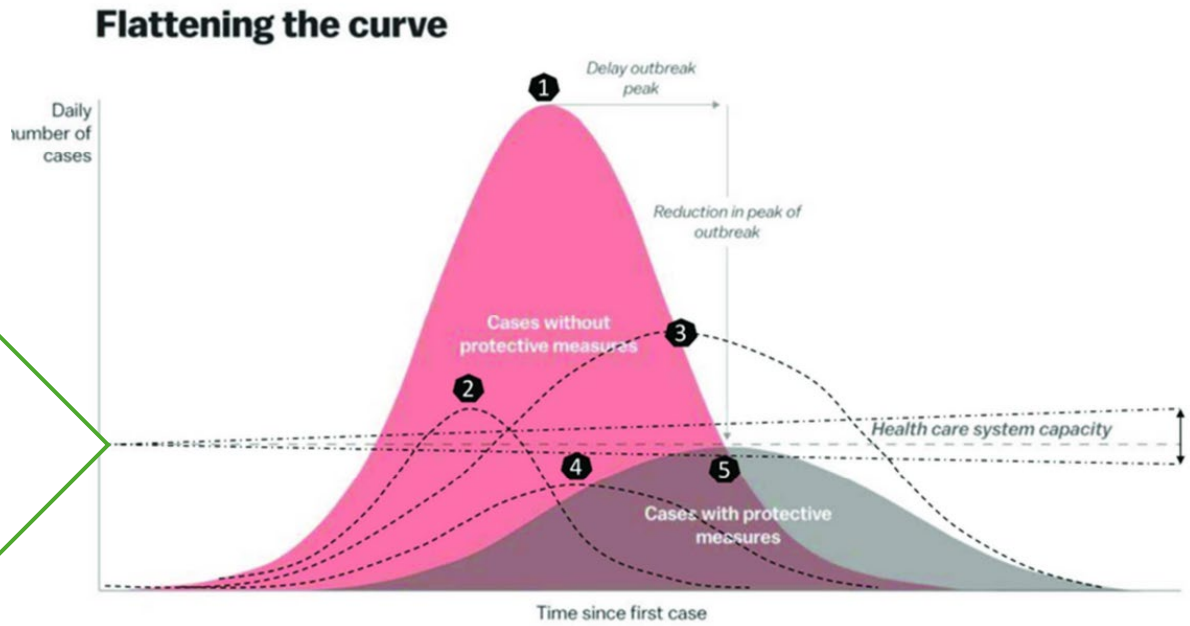
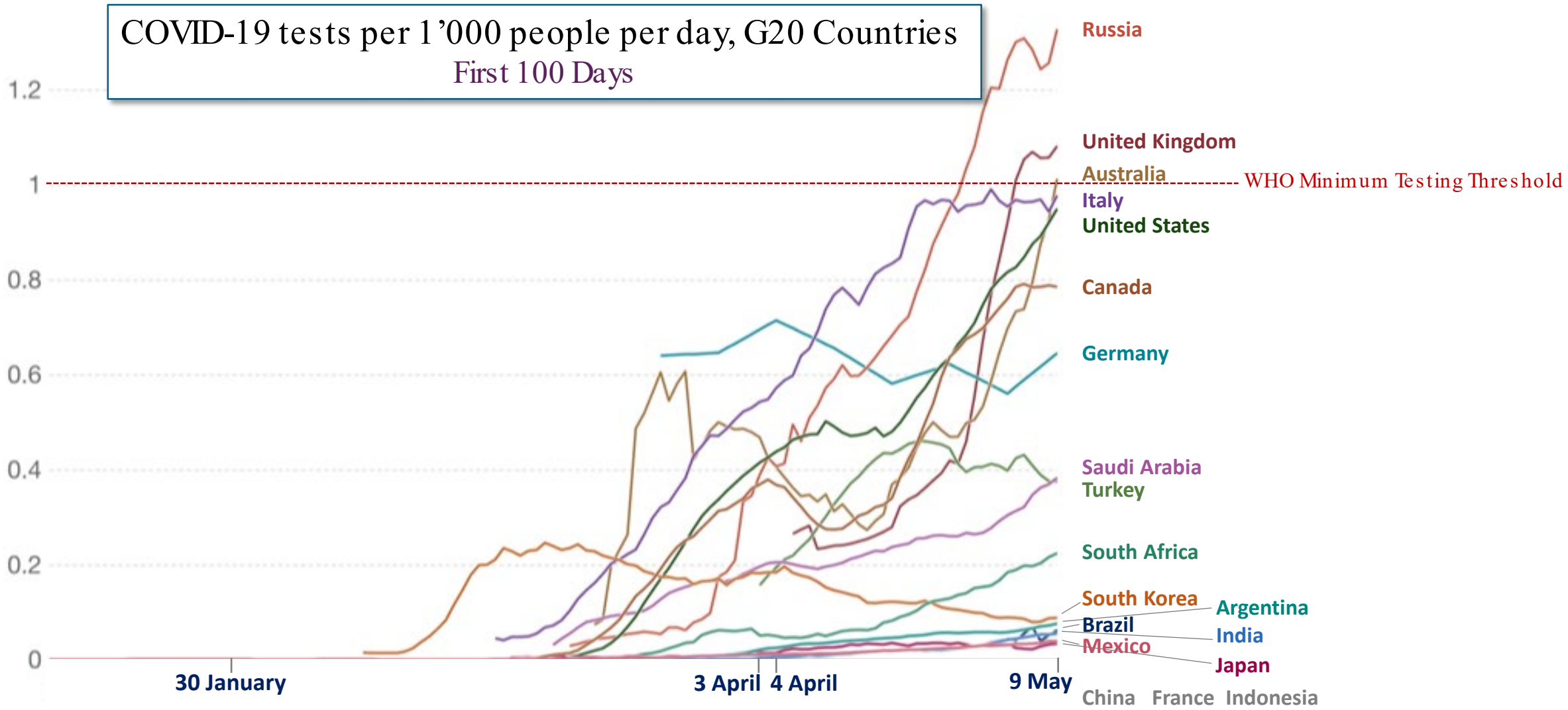
# From Patient Zero- to containing the outbreak…




Health system and other factors



# • CRITICAL NEED FOR A QUICKER DIAGNOSTIC RESPONSE




*Sources:* Our World in Data and FIND Test Tracker

# • POST COVID-19 - WHAT EXPERIENCE TAUGHT US

## CHALLENGES

**Developers initially hindered due to:**

- Slow access to samples / reference material
- Lack of clear product requirements
- Insufficient regulatory harmonisation

**Lack of demand and supportive policy** for affordable, fast and accurate diagnostics prior to COVID-191

- Limited evidence to inform policy
- Limited manufacturing capacity
- Market underprepared

**Access to accurate tests in LMICs and integration of with surveillance networks remain fundamental issues**[2,3]

## SUCCESSES

**Collaboration between academia and industry**[3,4]

- Automated PCR tests available in 64 days from PHEIC
- Rapid diagnostic tests approved in 236 days

**Increase demand from Governments, increasing manufacturing capacity and capabilities**[5,6]

- Reduced costs for diagnostics
- Increased access for LMICs

*LMICs, lower- and middle-income countries.*

*1. Venkatesan, P. (2020). COVID-19 diagnostics—not at the expense of other diseases. The Lancet Microbe, [online] 1(2), p.e64; 2. Ondoa, P., et al. (2021). Transforming access to diagnostics: how to turn good intentions into action? The Lancet, [online] 0(0). Available at: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02182-6/fulltext; 3. Vandenberg, O., et al. (2020). Considerations for diagnostic COVID-19 tests. Nature Reviews Microbiology, 19(171–183); 4. G7 Pandemic Preparedness Partnership (2021). 100 Days Mission to respond to future pandemic threats. [online] gov.uk. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/992762/100_Days_Mission_to_respond_to_future_pandemic_threats__3_.pdf; 5. WHO (n.d.). Global partnership to make available 120 million affordable, quality COVID-19 rapid tests for low- and middle-income countries. [online] www.who.int; 6. ACT now, ACT together 2020-2021 Impact Report", World Health Organization, April 2021.*

# • CRITICAL NEED FOR A QUICKER DIAGNOSTIC RESPONSE

2020

30 January — WHO declares PHEIC

3 April — **64 days**: First real-time **PCR** test granted WHO EUL


4 April — **65 days: WHO reports 1 million confirmed COVID-19 cases**

9 May — **100 days**

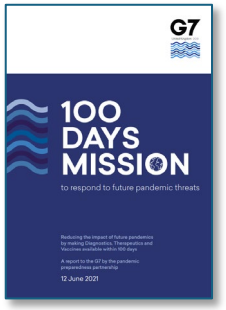
2 September — **216 days:** WHO approves dexamethasone as the **first COVID-19 therapeutic**

22 September — **236 days**: First **rapid diagnostic test** granted WHO EUL

25 November — **300 days**

31 December — **336 days** WHO issued its **first EUL for a COVID-19 vaccine**

WHO declares Public Health Emergency of International Concern (PHEIC)



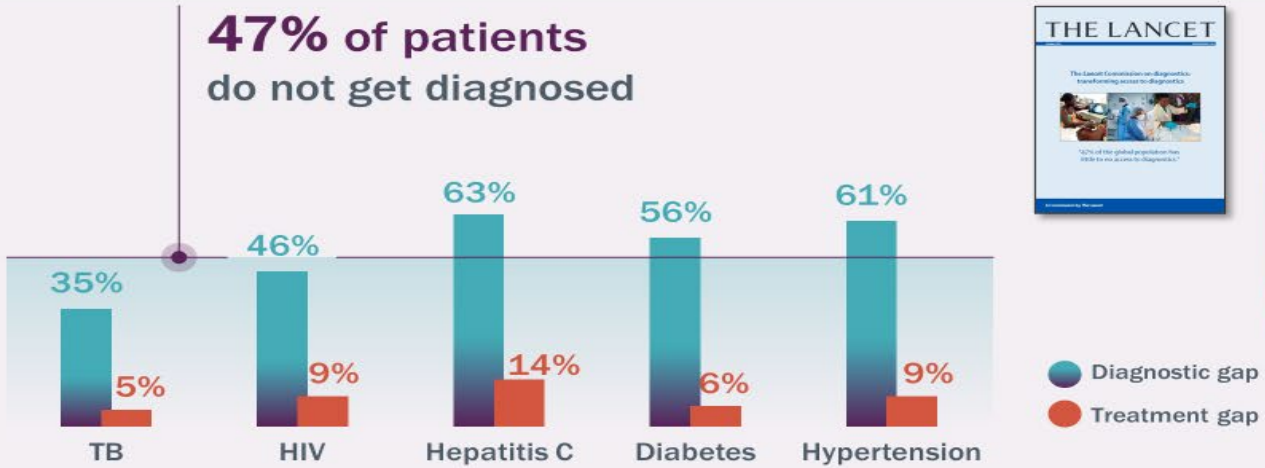

Accurate and approved **molecular tests and RDTs**

An initial regimen of **therapeutics**

**Vaccines** ready to be produced at scale

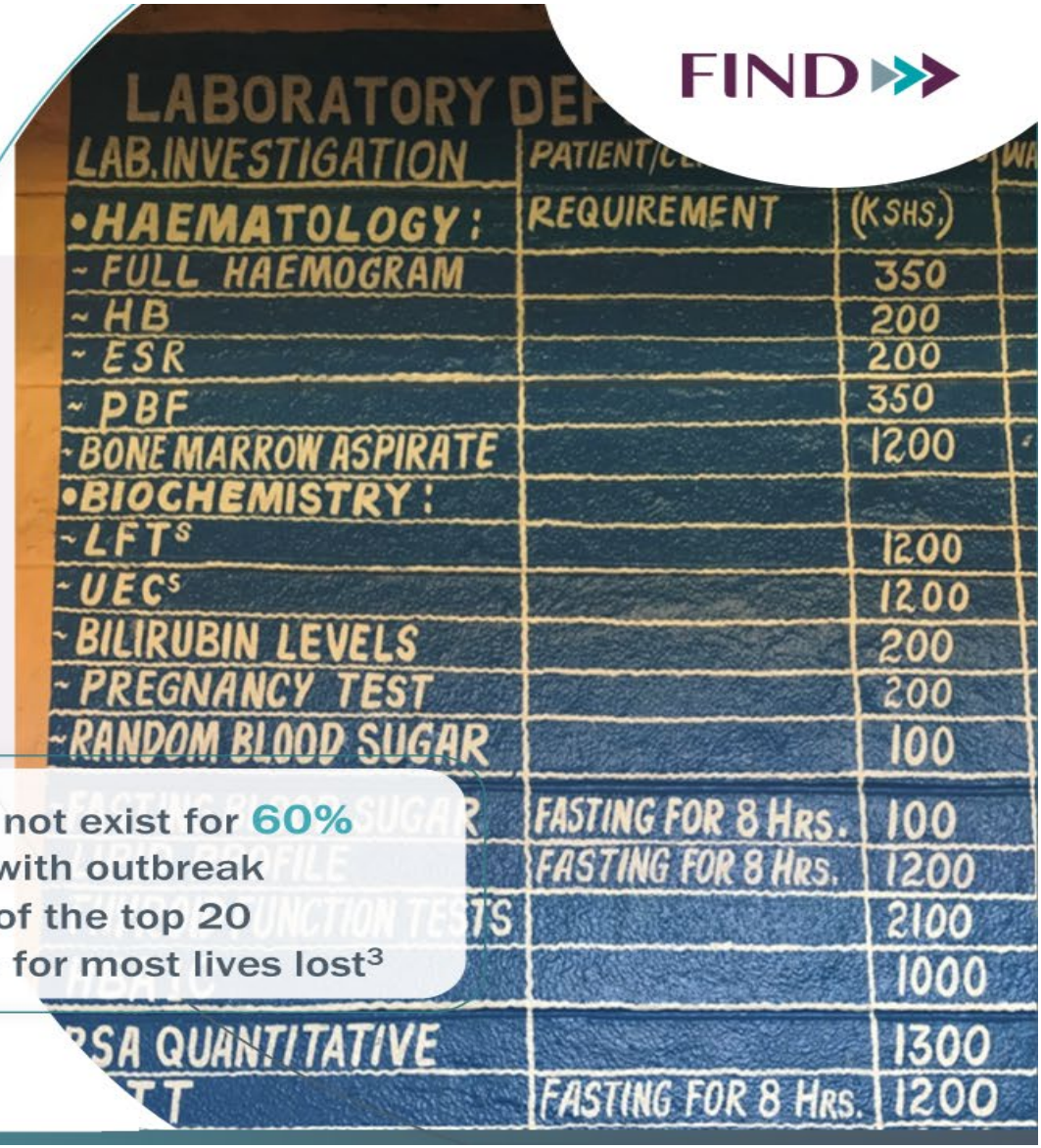
## MASSIVE DIAGNOSTIC GAPS

# HALF THE WORLD LACKS ACCESS TO ESSENTIAL DIAGNOSTICS










Basic diagnostic capacity is available in only **1%** of primary care clinics and **14%** of hospitals in some LMICs[1]

Appropriate tests do not exist for **60%** of infectious agents with outbreak potential[2] and **50%** of the top 20 diseases responsible for most lives lost[3]

[1] Leslie et al. *Bull World Health Organ* 2017;95:738–748, http://dx.doi.org/10.2471/BLT.17.191916.
[2] Kelly-Cirino et al. *BMJ Glob Health* 2019;4:e001179. doi:10.1136/bmjgh-2018-001179
[3] Pai et al. Analysis from Global Burden of Disease Report 2020

# Health System Impact of Rapid Diagnostic Tests

## LMIC Use Setting/Capacity: L0-L4

| | Self-Testing | Level 0 (L0) - Community | Level 1 (L1) - Primary Care | Level 2 (L2) - District Hospital Lab | Level 3 (L3) - Regional/Provincial Lab | Level 4 (L4) – Reference/National Lab |
|---|---|---|---|---|---|---|
| **Use setting** | • Home testing | • Community outreach<br>• Home testing | • Primary care facility | • Near-patient laboratory<br>• Referral hospital laboratory<br>• Emergency Department testing | • Near-patient laboratory<br>• Referral hospital laboratory<br>• Emergency Department testing | • Reference laboratory |
| **Lab infrastructure** | • No mains power<br>• No water<br>• No lab equipment<br>• No environmental control (e.g., temp, dust, humidity) | • No mains power<br>• No water<br>• No lab equipment<br>• No environmental control (e.g., temp, dust, humidity) | • No mains power (unreliable)<br>• Minimal lab equipment (may not support cold chain)<br>• BSL-1 containment<br>• No environmental control (e.g., temp, dust, humidity) | • Mains power (may be intermittent)<br>• Basic lab equipment (biosafety cabinet, centrifuge, calibrated pipets, fridge)<br>• -20 freezers (some)<br>• BSL-2/1 containment (some)<br>• Environmental control (e.g., temp, dust, humidity) (some) | • Mains power (may be intermittent)<br>• Basic lab equipment (biosafety cabinet, centrifuge, calibrated pipets, fridge)<br>• -20 freezers<br>• BSL-2/1 containment<br>• Environmental control (e.g., temp, dust, humidity) | • Mains power (reliable)<br>• High infrastructure facility<br>• -20 freezers<br>• -80 freezers (some)<br>• BSL-2/3 containment<br>• Environmental control (e.g., temp, dust, humidity) |
| **Operator skill** | • Self-testing<br>➢ Simple reagent/sample transfer | • Nurse/pharmacist<br>• Community health workers<br>➢ Simple reagent/sample transfer | • Nurse<br>• Trained laboratory worker<br>➢ Minimal sample processing (≤ 3 steps) | • Laboratory technician (1-2 year certif)<br>➢ Sample processing with calibrated volumes (≤ 3 steps) | • Laboratory technician (1-2 year certif)<br>➢ Sample processing with calibrated volumes (≤ 3 steps) | • Science research specialists<br>• Laboratory technician (1-2 year certif) |
| **Specimen capacity** | • Can process minimally invasive samples: fingerstick blood, nasal swabs, saliva, urine | • Can process minimally invasive samples: fingerstick blood, nasal swabs, saliva, urine | • Can process upper respiratory specimens; clinic may not have capacity for lower respiratory, venipuncture, plasma | • Can process most BSL-2 specimens; depends on clinic sample capacity | • Can process most BSL-2 specimens; depends on clinic sample capacity | • Can process most BSL2/3 specimens |
| **Test capacity** | • True-POC MDx (some)<br>• RDT | • True-POC MDx (some)<br>• RDT | • True-POC MDx<br>• Basic microscopy<br>• RDT | • Near-POC MDx<br>• ELISA with simple reader<br>• Microscopy<br>• RDT<br>• Clinical chemistry (some) | • Blood culture and microbiology capacity (some)<br>• Near-POC MDx<br>• ELISA with simple reader<br>• Microscopy<br>• RDT<br>• Clinical chemistry | • Blood culture and microbiology capacity<br>• Lab MDx / PCR / LDT<br>• ELISA/EIA/CLIA/PRNT<br>• Fluorescence microscopy<br>• Clinical chemistry<br>• Sequencing (some)<br>• Mass spectrometry (some) |

Souche plus mortelle

# «Les risques d'explosion sont réels» - La variole du singe inquiète

Une nouvelle souche de la variole du singe, aussi appelée Mpox, identifiée en République démocratique du Congo (RDC) puis signalée dans plusieurs pays voisins fait craindre une propagation de ce virus, deux ans après la précédente épidémie mondiale.

Science & technology | Viruses

## A deadly new strain of mpox is raising alarm

Health officials warn it could rapidly spread beyond the Democratic Republic of Congo

Monde Publié le 13 août 2024 à 17:48 Partager

## La rapide propagation en Afrique d'une nouvelle souche plus mortelle du mpox inquiète

NEWS | HEALTH

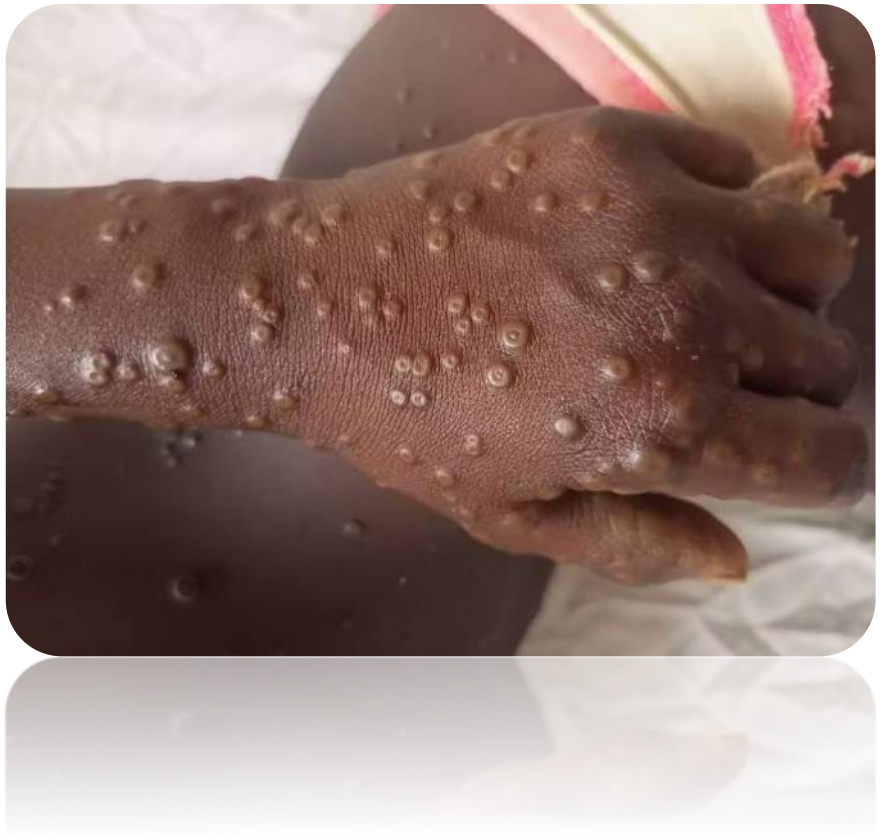
## Amid Congo's deadliest mpox outbreak, a new worry: virus has become sexually transmissible

A related viral strain caused a global mpox outbreak in men who have sex with men

Case Study: Mpox

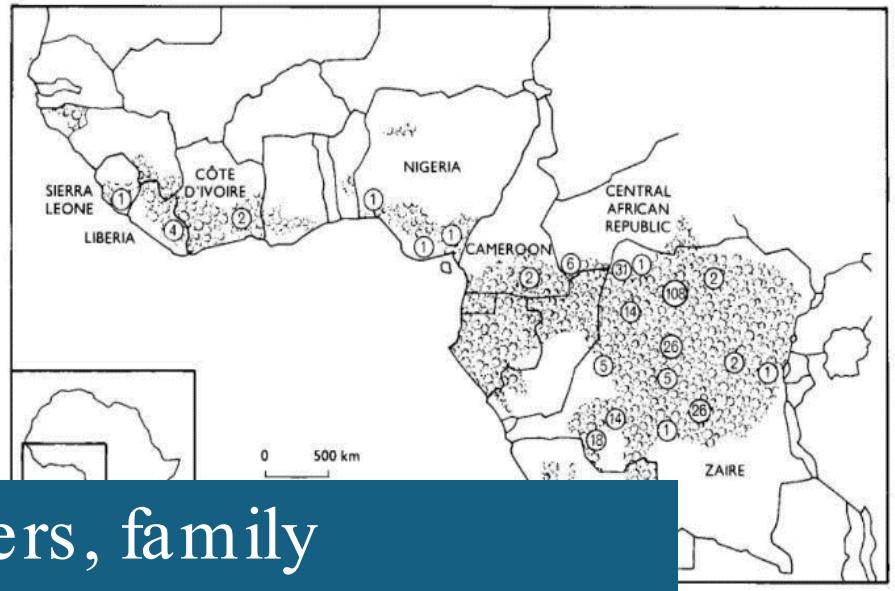
# Mpox

- Virus monkeypox (MPXV), genus *Orthopoxvirus,* family *Poxviridae*
- Same family as variola virus, the cause of smallpox
- Historically:
  - Classic zoonosis endemic in Africa
  - First isolated from a monkey imported to Denmark in 1958, but monkeys are not a natural reservoir
  - The name “monkeypox” is a misnomer and has now been changed to mpox
  - Thought maintained in small mammals, such as forest squirrels, Gambian pouched rats, dormice and others
  - Classically 2 clades distinguished by geography and virulence:
    - Clade I in Central Africa (CFR ~10%)
    - Clade II in West Africa (CFR 1-3%)



# Mpox Modes of Transmission

- From animals to humans
  - Bites or scratches from infected animals? Hunting and food preparation?
- Between humans
  - Close physical contact (sexual or non-sexual) with a symptomatic person
    - Cutaneous and mucosal lesions, body fluids (e.g. serous fluid, pus, or blood from lesions) and lesions crusts are particularly infectious.
    - Mouth ulcers, saliva
  - Fomites: Contact with contaminated clothes, bed linens, or kitchen utensils
  - Vertical transmission during pregnancy

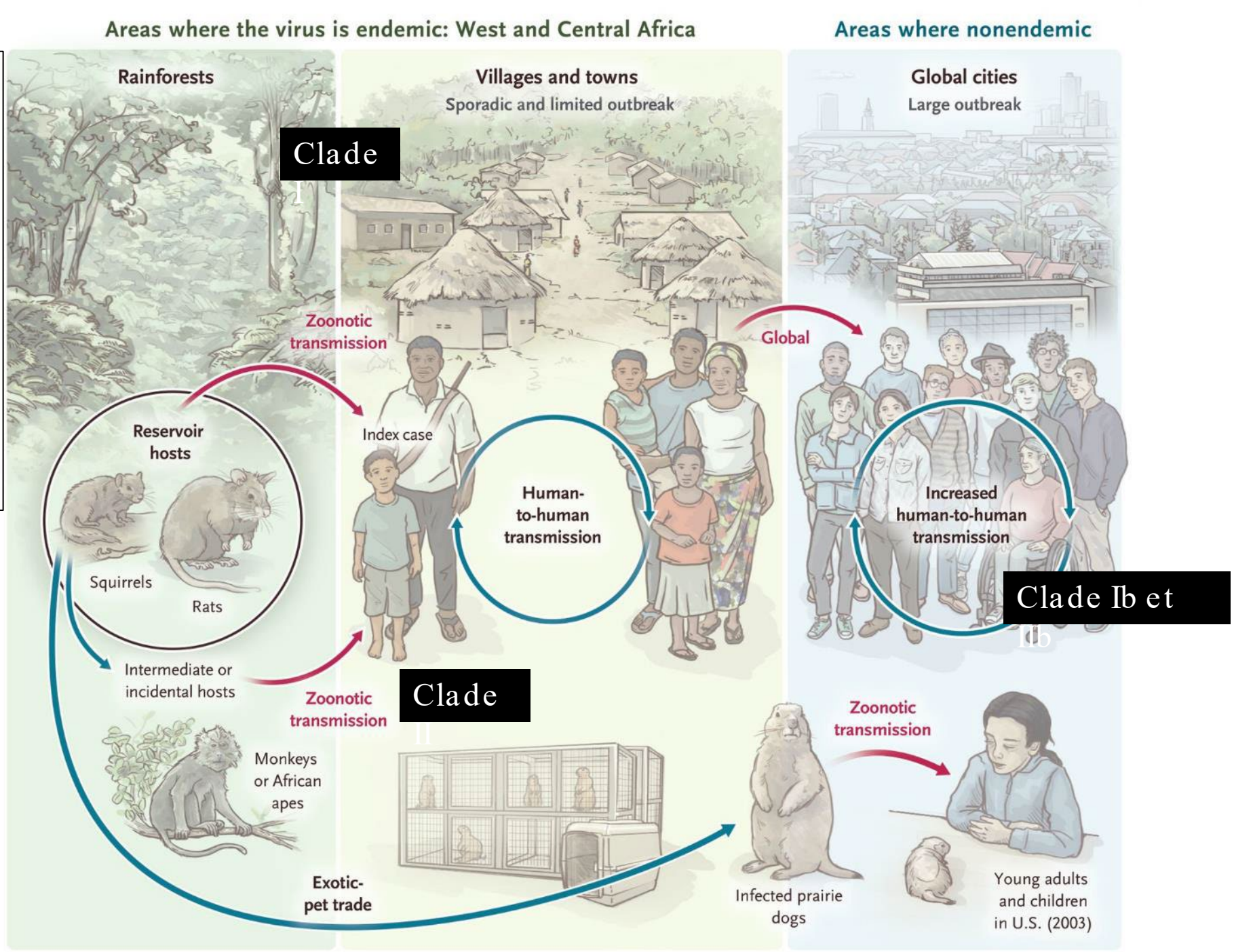



the locations where cases

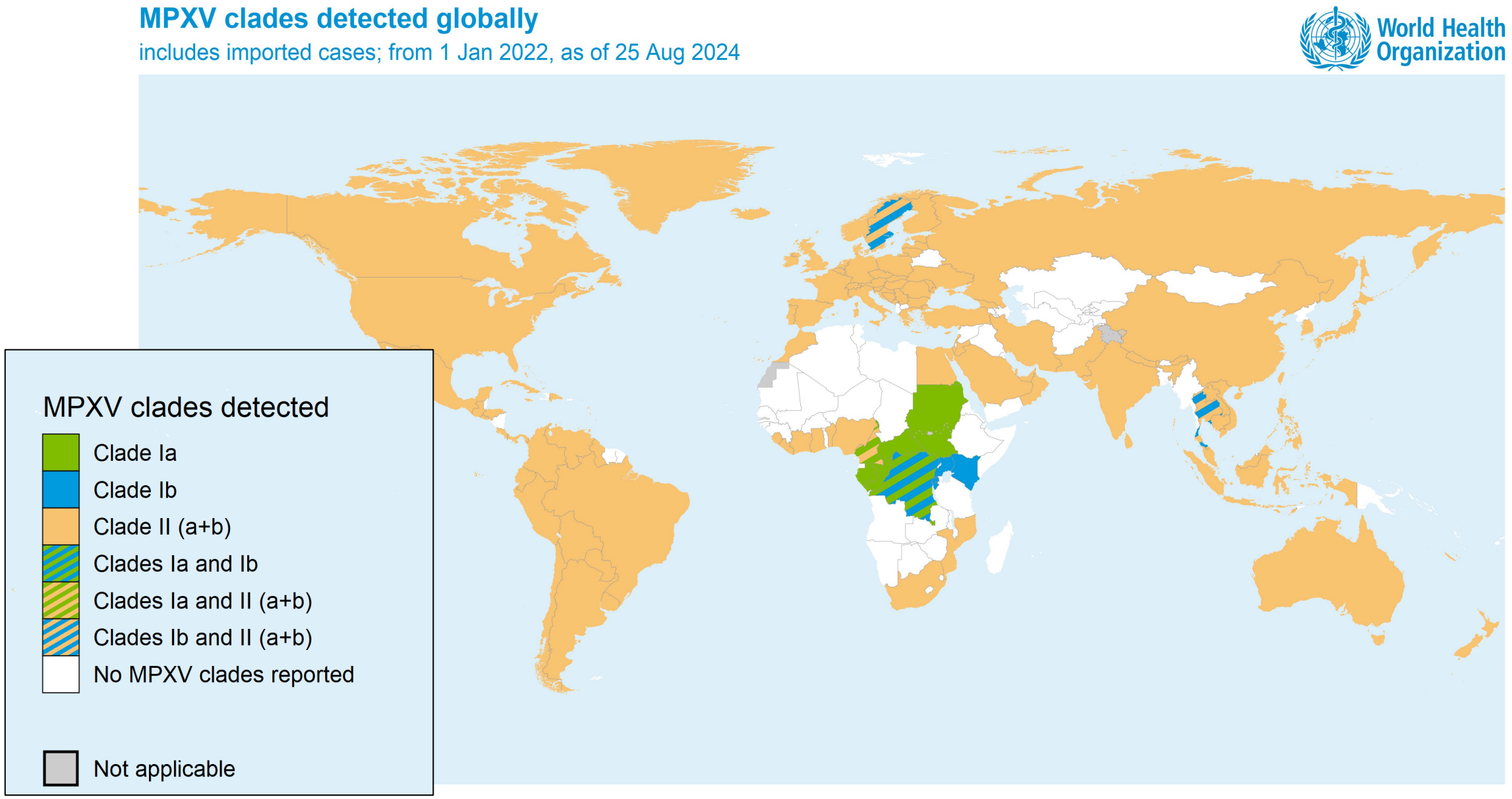
Persons at elevated risk: household members, family caregivers and sexual partners, health workers without adequate personal protection

## Simultaneous epidemics

- Distinct clades
- Various modes of transmission
- Varied risks

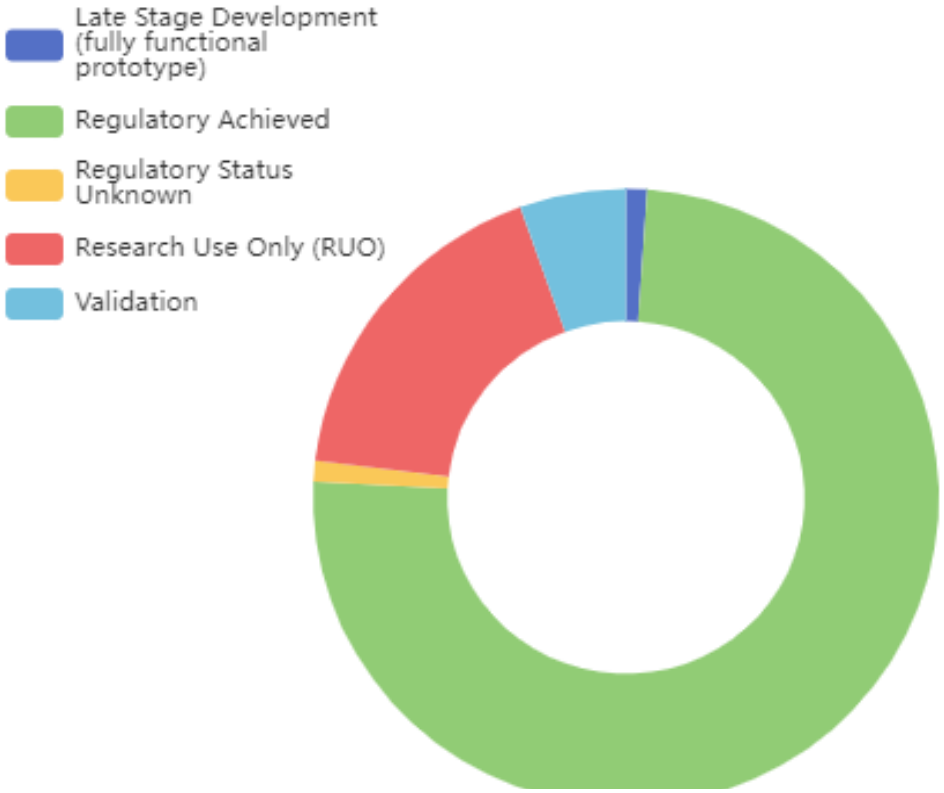


# Current Global Situation



• 91 LAB-BASED MOLECULAR TESTS (2022-2023 DATA)

# Mpox Diagnostic Landscape




- No sequencing kits available (only protocols)

69 regulatory achieved tests

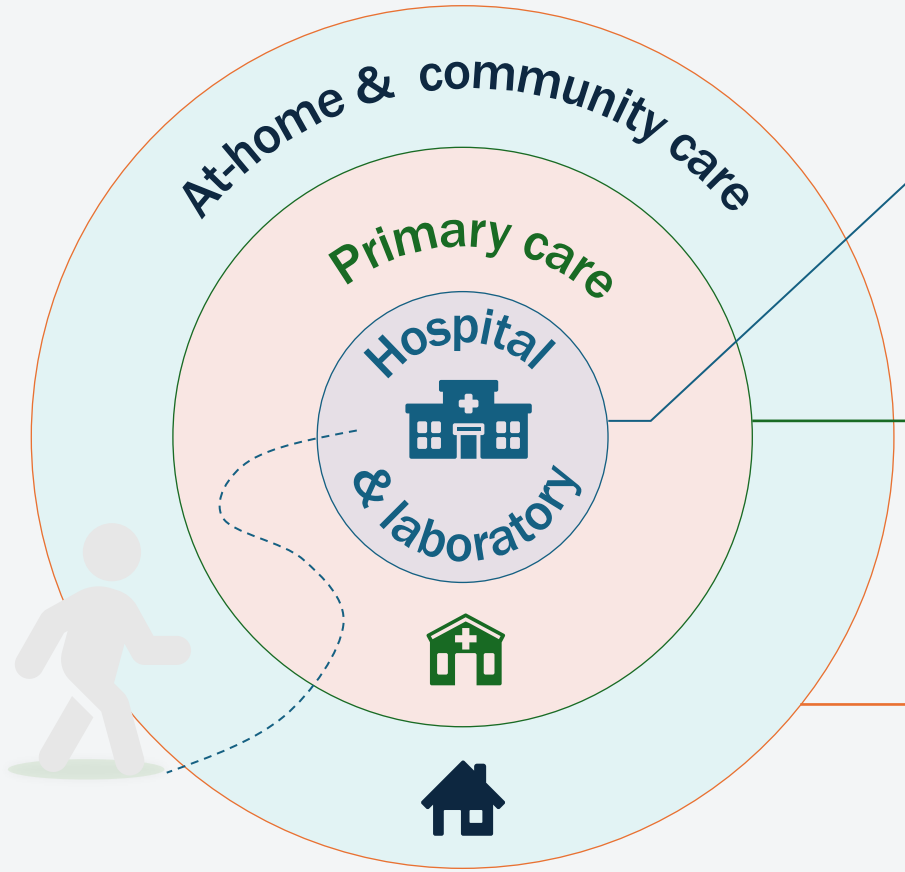
5 US FDA EUA | 60 CE-IVDD | Others

| | Clade(s) detected | Sensitivity (IFU) | Specificity (IFU) |
|---|---|---|---|
| Alinity m MPXV (Abbott) | MPX Clade I / MPX Clade II | 100% | 100% |
| QuantiVirus MPXV Test Kit (Dicarta) | MPX Clade I / MPX Clade II | 100% | 100% |
| Monkeypox Virus Qualitative Real-Time PCR (Quest Diagnostics) | MPX Clade II | n/a | n/a |
| cobas MPXV (Roche) | MPX Clade I / MPX Clade II | 100% | 100% |
| Non-variola Orthopoxvirus Real-time PCR Primer and Probe Set (US CDC) | OPX | 100% | 100% |

Source: https://www.finddx.org/test-directory/

# MOLECULAR DIAGNOSTICS AT the point of care COULD

- **FILL CRITICAL GAPS ACROSS DIFFERENT HEALTHCARE SETTINGS**




## Technologies suitable to testing infrastructures

**Near POC**
- Basic lab equipment requirements
- Benchtop/desktop units, mains power
- Semi-automated testing processes

**True POC**
- No laboratory equipment requirements
- Portable, battery-operated devices
- Kits including disposable sample materials
- Fully automated testing process

**Instrument free POC**
- No instrument or power requirements
- Kits including disposable sample materials
- Fully automated testing processes

Increasing accessibility

# Key requirements for new INNOVATIVE diagnostic tools

- **TO CLOSE THE GAP AT POC**

Improved performance

## POINT-OF-CARE (POC)

**Usable where people live and seek care**
(incl. communities and primary care settings)

## MULTI-PATHOGEN

**Able to identify multiple diseases in one sample**
(incl. outbreak-prone pathogens)

Progress towards universal health coverage and global health security

## AFFORDABLE

**Pricing structures adapted to LMICs**

## ACCURATE

**Robust and highly sensitive results**

Improved access

# 30% of 7-1-7 bottlenecks identified were laboratory related

- Laboratory Confirmation
- Human Resources gaps for Health
- Delayed Specimen Collection
- Specimen Transportation
- Data entry delay
- New or Unexpected pathogen
- Logistics and shipment delays
- Scarcity of Diagnostic commodities (Lab reagents, Rap. Diagnostic tests, or specimen collection kits)

| | | | | |
|---|---|---|---|---|
| | 1 (2%) | 7 (22%) | 1 (2%) | 9 (7%) |
| ed in remote, fragile, or conflict settings) | 2 (5%) | 1 (3%) | 5 (9%) | 8 (6%) |
| orities (including COVID-19) | 3 (7%) | 0 | 5 (9%) | 8 (6%) |
| resources gaps for public health | 1 (2%) | 3 (9%) | 3 (5%) | 7 (5%) |
| lity of countermeasures or personal protective equipment | 0 | 0 | 7 (13%) | 7 (5%) |
| ination | 0 | 2 (6%) | 4 (7%) | 6 (5%) |
| nge for electronic surveillance or reporting systems (eg, network coverage) | 1 (2%) | 4 (13%) | 0 | 5 (4%) |
| point or capacity | 1 (2%) | 2 (6%) | 1 (2%) | 4 (3%) |
| | 3 (7%) | 1 (3%) | 0 | 4 (3%) |
| trust | 2 (5%) | 0 | 2 (4%) | 4 (3%) |
| collaboration (eg, between human health and animal health) | 2 (5%) | 1 (3%) | 1 (2%) | 4 (3%) |
| ortation | 0 | 1 (3%) | 3 (5%) | 4 (3%) |
| dination, including incident management and rapid response team capacity | 0 | 1 (3%) | 3 (5%) | 4 (3%) |
| delay | 2 (5%) | 1 (3%) | 0 | 3 (2%) |
| o conduct early risk assessment or event verification | 1 (2%) | 2 (6%) | 0 | 3 (2%) |
| New or unexpected pathogen | 1 (2%) | 2 (6%) | 0 | 3 (2%) |
| nsitivity of community detection | 3 (7%) | 0 | 0 | 3 (2%) |
| re seeking by patients | 2 (5%) | 0 | 0 | 2 (2%) |
| fficient clinical case management capacity | 0 | 0 | 2 (4%) | 2 (2%) |
| uate risk assessments or preparedness plans | 0 | 0 | 1 (2%) | 1 (1%) |

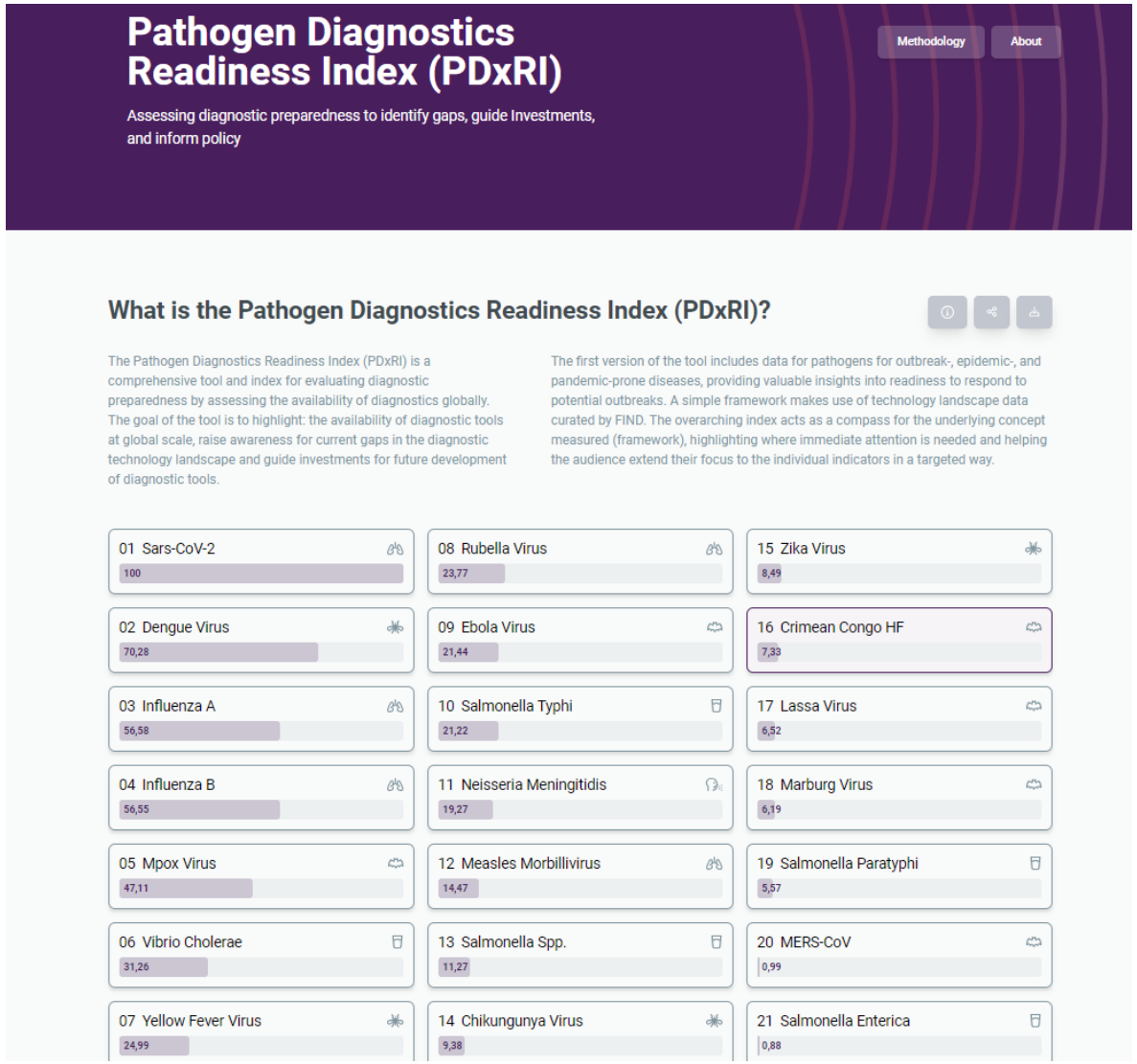
## ementation of the 7-1-7 target for detection, tification, and response to public health threats in ive countries: a retrospective, observational study

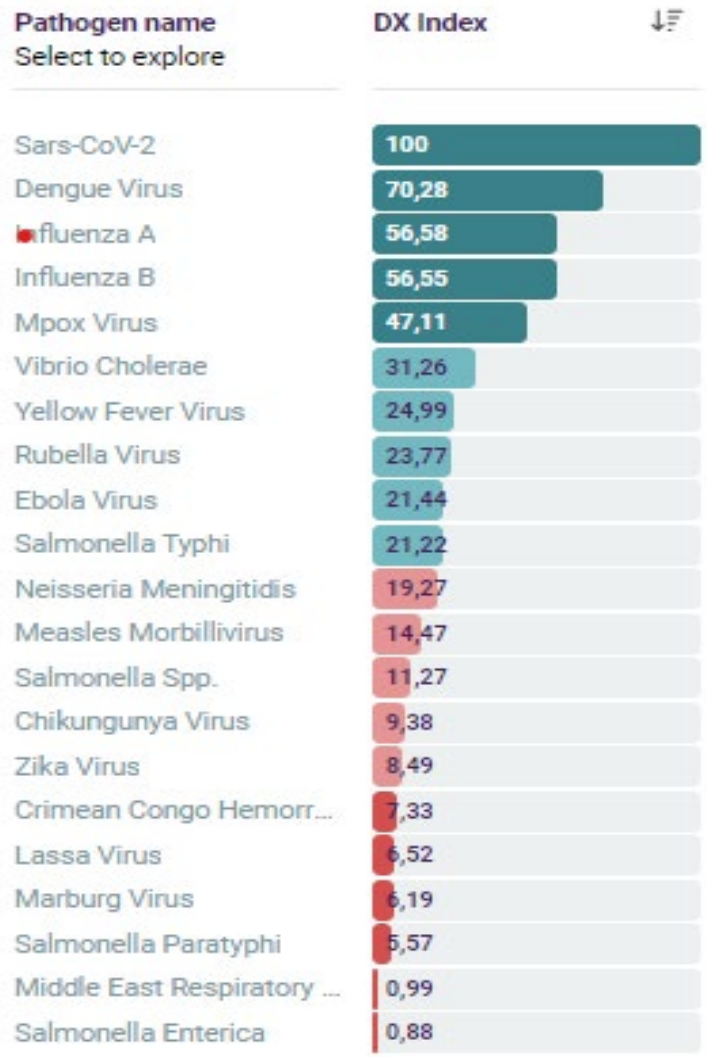
chner, Issa Makumbi, Olaolu Aderinola, Aschalew Abayneh, Ralph Jetoh, Rahel L Yemanaberhan, Jenom S Danjuma, Francis T Lazaro, Mahmoud, Trokon O Yeabah, Lydia Nakiire, Aperki K Yahaya, Renato A Teixeira, Mohammed Lamorde, Immaculate Nabukenya, Ifedayo M O Adetifa, Wanderson Oliveira, Amanda McClelland, Christopher T Lee

otimal detection and response to recent outbreaks, including COVID-19 and mpox (formerly known have shown that the world is insufficiently prepared for public health threats. Routine monitoring of se performance of health emergency systems through timeliness metrics has been proposed to rove outbreak preparedness and contain health threats early. We implemented 7-1-7 to measure the tion (target of ≤7 days from emergence), notification (target of ≤1 day from detection), and ly response actions (target of ≤7 days from notification), and we identified bottlenecks to and mance.

*Lancet Glob Health* 2023; 11: e871–79
Published Online April 12, 2023 https://doi.org/10.1016/S2214-109X(23)00133-X
See Comment page e805
Resolve to Save Lives, New York, NY, USA

# • SNAPSHOT OF THE STATE OF DIAGNOSTICS FOR WHO R & D PATHOGENS



- **PARAMETERS MEASURED**

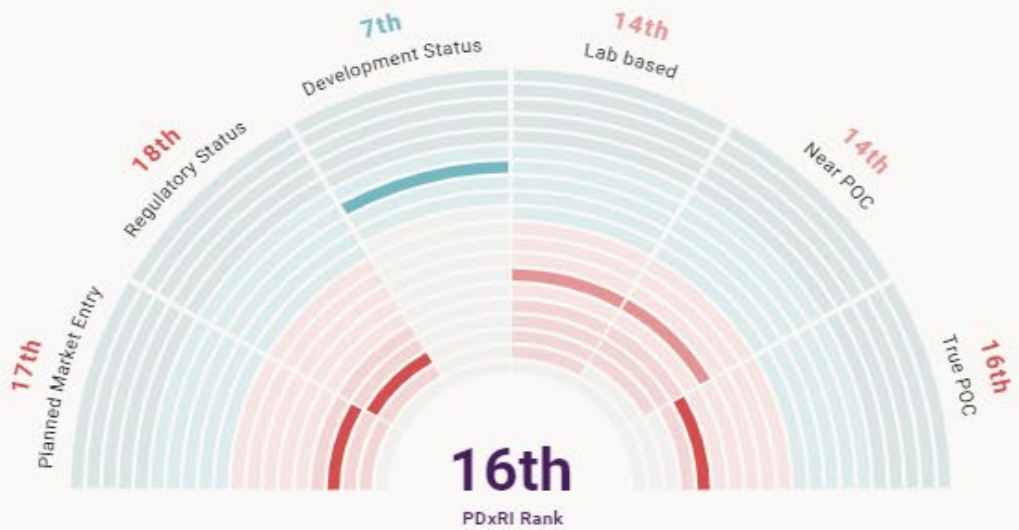
| | Definition |
|---|---|
| Planned market entry | Is the test commercially available? |
| Development status | Is the test under development? |
| Regulatory status | Is the test approved by any international medical device regulatory Forum (IMDRF) agency? |
| Laboratory-based | Is there a test available for a Reference laboratory? |
| Near POC | Is the test available for near Point of Care setting? |
| True POC | Is the test available for True Point of Care setting (e.g., RDT for PHC? |
| *TPP available<br>*TPP development is a WHO responsibility | Is there a diagnostic target product profile available? |

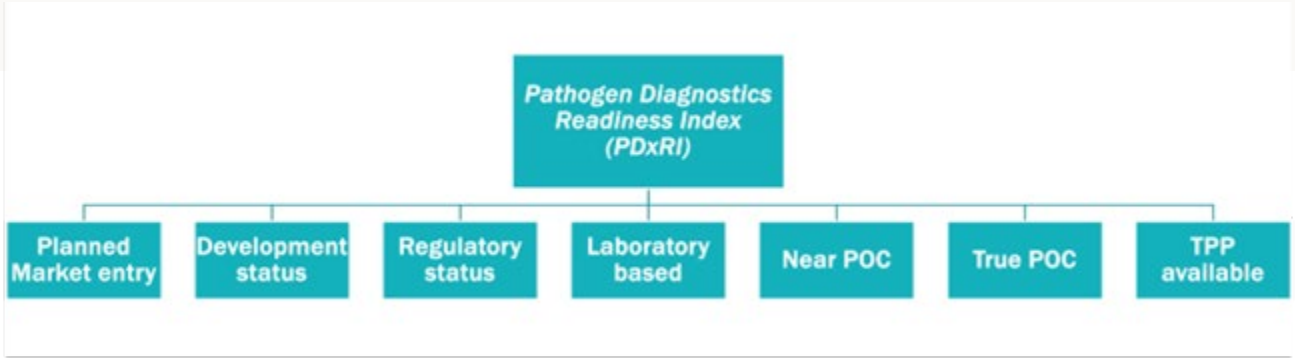
# PDxRI and indicator ranks for Lassa Virus

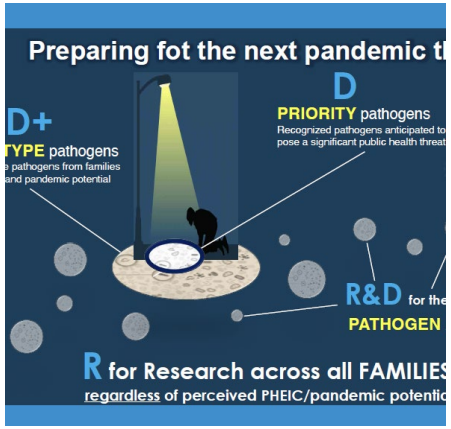
Lassa Virus is ranked 16 out of 20. It scores highest in Lab based and lowest in True POC.

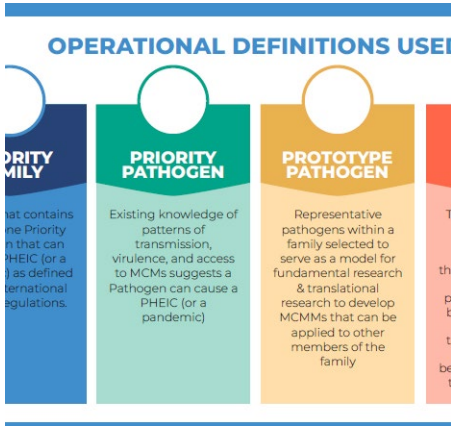
Contact zoonotic | TPP

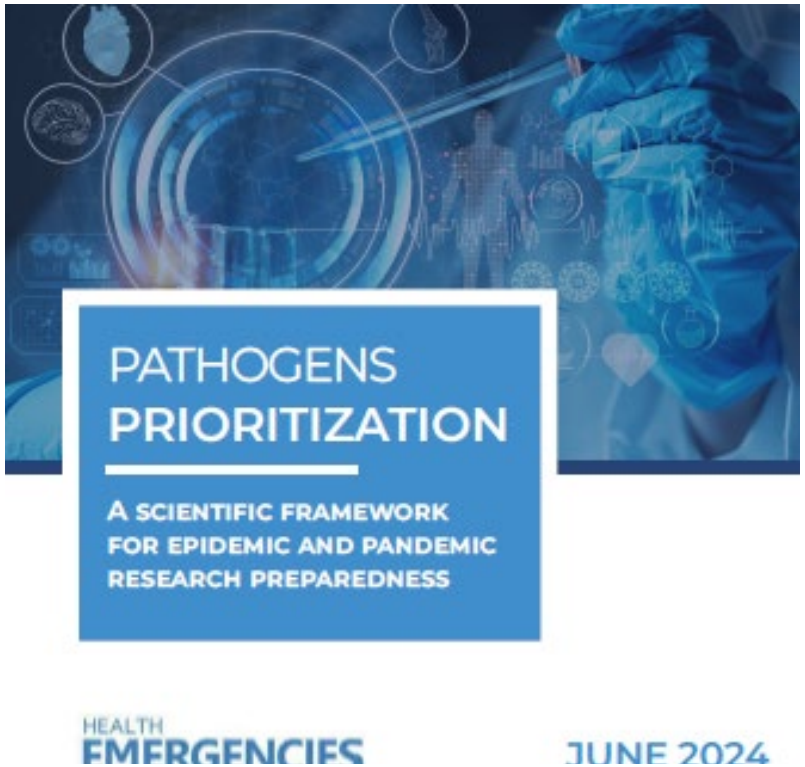
Include Sars-CoV-2

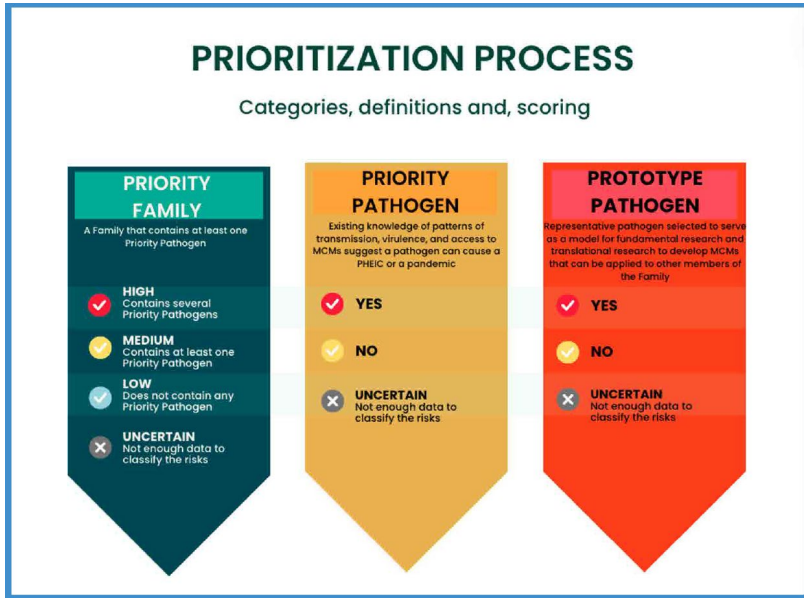


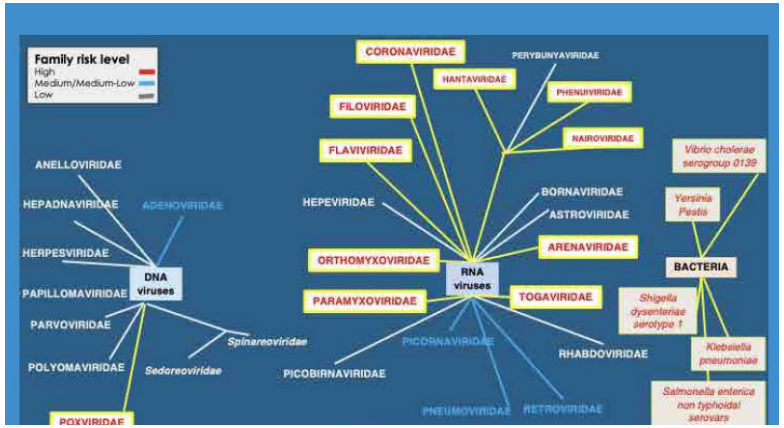





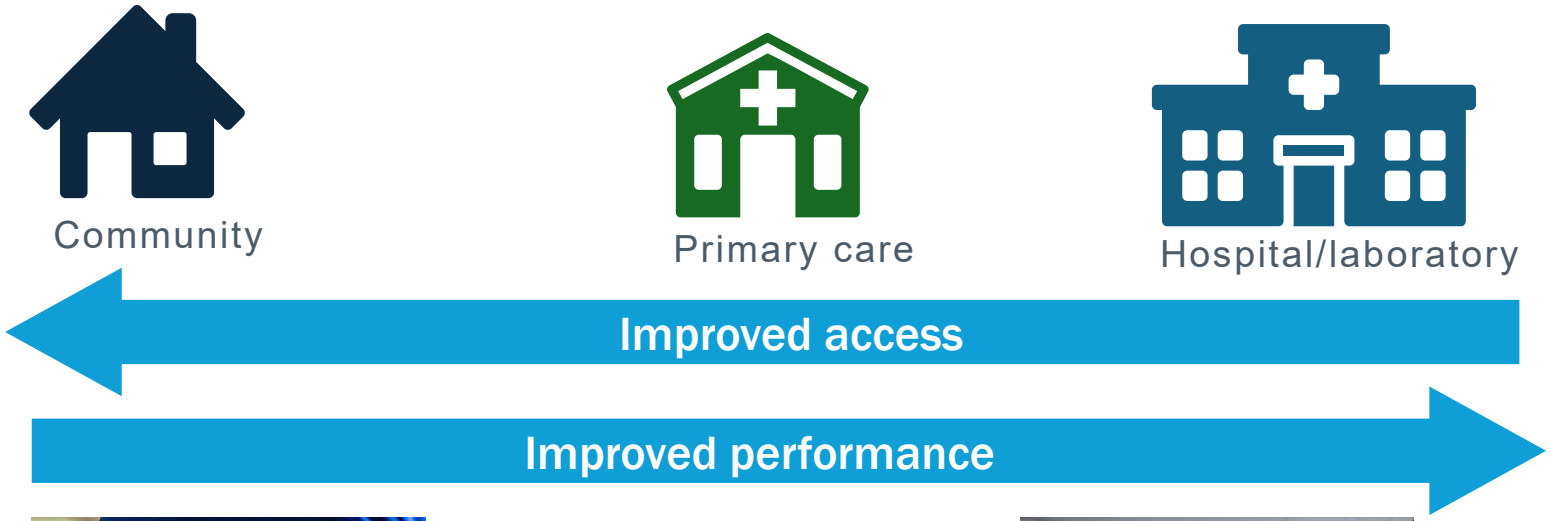



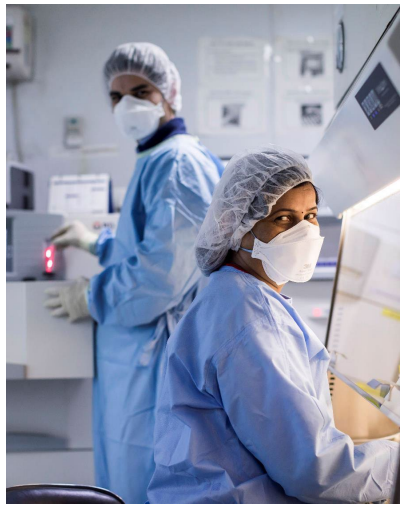




# WHO R and D Approach 2024: Start with the Viral families

# DISRUPTING THE TRADITIONAL TRADE-OFF BETWEEN PERFORMANCE AND ACCESSIBILITY



Today, new innovations mean high-quality testing is getting closer and closer to the point-of-care where people can most readily access it

# THE DIAGNOSTIC PREPAREDNESS ROADMAP TO ENABLE THE 100 DAYS MISSION

## Accelerate product Research & Development

1. Develop novel diagnostic platforms
2. Build prototype diagnostic library for 10 pathogens
3. Establish clinical reference standards

## Streamline evidence generation and regulatory approval

4. Integrated global biobanking network
5. Establish global clinical trial and product evaluation network
6. Formalize pathway to enable collaborative product registration

## Strengthen surveillance and community-based testing infrastructure

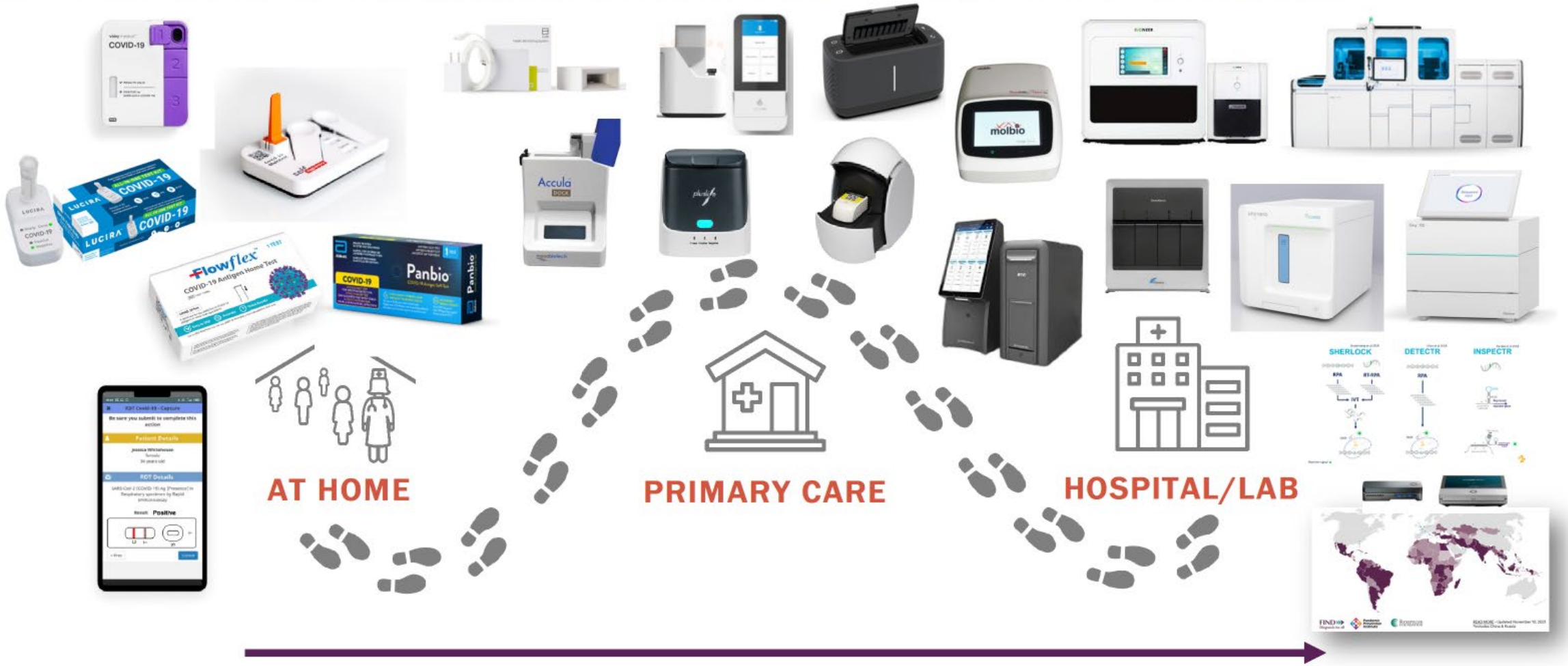
7. Strengthen global disease surveillance
8. Normalize point-of-care testing programmes
9. Support digital connectivity and diagnostic network optimization

## Establish warm base for manufacturing and reliable pull mechanism

10. Support development of regional manufacturing hubs
11. Institute reliable pull mechanism

Advocacy for evidence-based policy, equitable access and universal health coverage

# THE COMING EXPLOSION IN NEW POC MOLECULAR PLATFORMS




Connected diagnostics and interoperable systems for data management, data aggregation and data sharing for surveillance

- TO ACCELERATE DEVELOPMENT AND ACCESS OF INNOVATIVE MOLPOC FOR RESOURCE LIMITED SETTINGS

## Priority actions

| | | |
|---|---|---|
| 1 | Build the business case for Resource limited setting | Working with TGF, Medaccess, WHO, companies and countries to pave the way for market introduction |
| 2 | De-risk investment | Investing to develop fit for purpose tests for resource limited settings |
| 3 | Partner Matchmaking | Introducing companies each others to build innovative solutions |
| 4 | Open cartridge system | Collaborating with manufacturers to explore the open cartridge model for Decentralized Molecular testing |

# Regulatory Innovation is necessary for access!

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## Proposal for a national diagnostics action plan for the United States

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ABSTRACT

Providing a definitive diagnostic test in a disease emergency is critical to limit pathogen spread, develop and deploy medical countermeasures, and mitigate the social and economic harms of a serious epidemic. While major accomplishments have accelerated test development, expanded laboratory testing capacity, and established widespread point-of-care testing, the United States does not have a plan to rapidly respond, to develop, manufacture, deploy, and sustain diagnostic testing at a national scale. To address this gap, we are proposing a **National Diagnostics Action Plan** that describes the steps that are urgently needed to prepare for future infectious disease emergencies, as well as the actions we must take at the first signs of such' events. These recommendations require substantial collaboration between the US government (USG) and the private sector to solve a series of challenges now, as well as to prepare for the massive and rapid scale-up of laboratory and point-of-care test development and testing capacity in future emergencies. The recommendations include establishing pre-event contracts; ensuring rapid access to clinical samples; creating a permanent public–private testing coordinating body to allow for rapid information sharing and improved cooperation among the USG, test developers, and clinical laboratories; and accelerating testing rollout at the beginning of an event—and thus, the effective public health management of a disease crisis.

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## Manufacturers' considerations for in vitro diagnostic medical devices in a public health emergency

*Aspects à prendre en compte par les fabricants de dispositifs médicaux de diagnostic in vitro en situation d'urgence de santé publique*

# Key Messages

- Access to diagnostics is an equity issue; the global diagnostic gaps are significant
- Surveillance cannot be effective without access to diagnostics
- Regulatory bottlenecks have become exacerbated post-COVID-19 and can potentially stifle the introduction of innovative solutions
- Modelling has demonstrated the potential impact of introducing diagnostics in early detection and control (flattening the curve)
- More integrated diagnostic approaches are needed: including collaboration between human, animal and wildlife
- Access to biostocks, biobanks are critical for development of new diagnostics; global considerations need to be addressed

# THANK YOU FOR LISTENING

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