Developing accessible mpox tests

Dr Jennifer Heaney
Senior Research Fellow
Clinical Immunology Services
University of Birmingham

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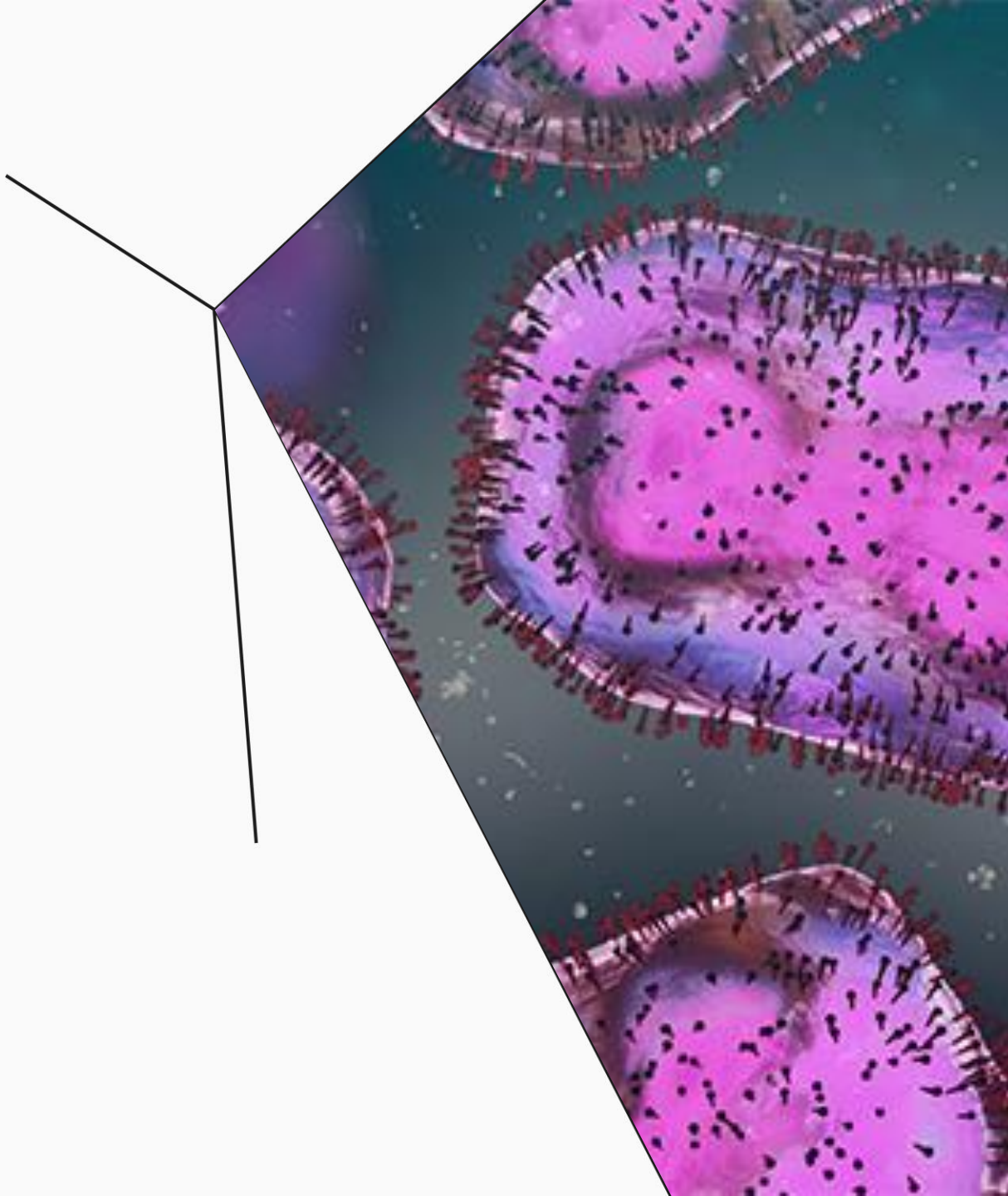
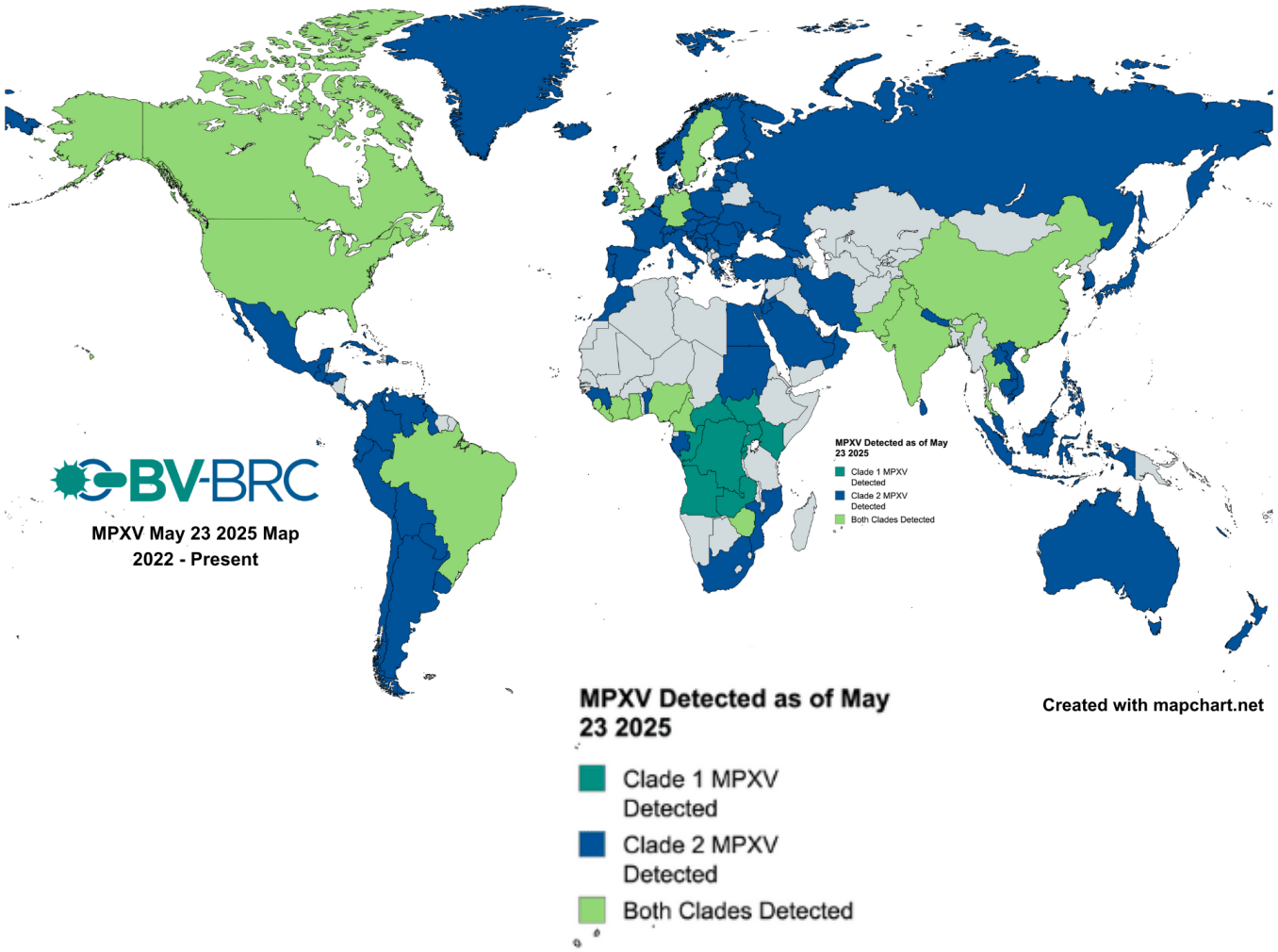


Mpox: a global threat to public health

Different types of Mpox virus (Clade I and Clade II): both have caused WHO Public Health Emergencies of International Concern

Mpox clade II was mainly found in Western Africa until the **2022 outbreak** where it spread worldwide with 102,000 cases. Cases still ongoing……..

Mpox clade I endemic in Central Africa and evolution of novel subclade Ib caused **2024 outbreak** to neighbouring countries and other continents
Transmission ongoing in Africa……



Mpox: diagnostics gap

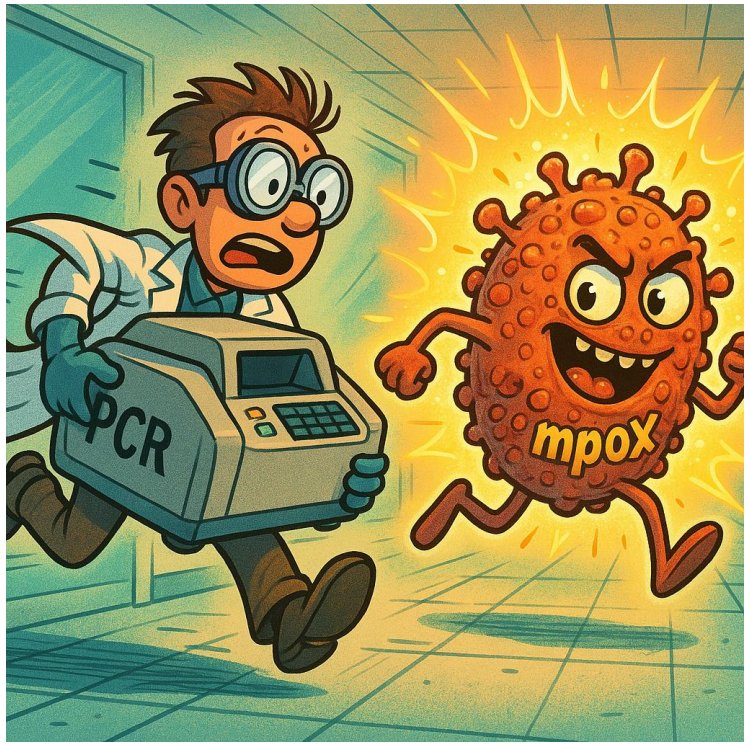
Evolution of the virus and geographical spread has outpaced development and availability of suitable diagnostic assays

Assay challenges for case detection/acute infection

1) case differentiation (Clade I vs II): severity and fatality differences

2) Platform and training: centralised reference laboratories

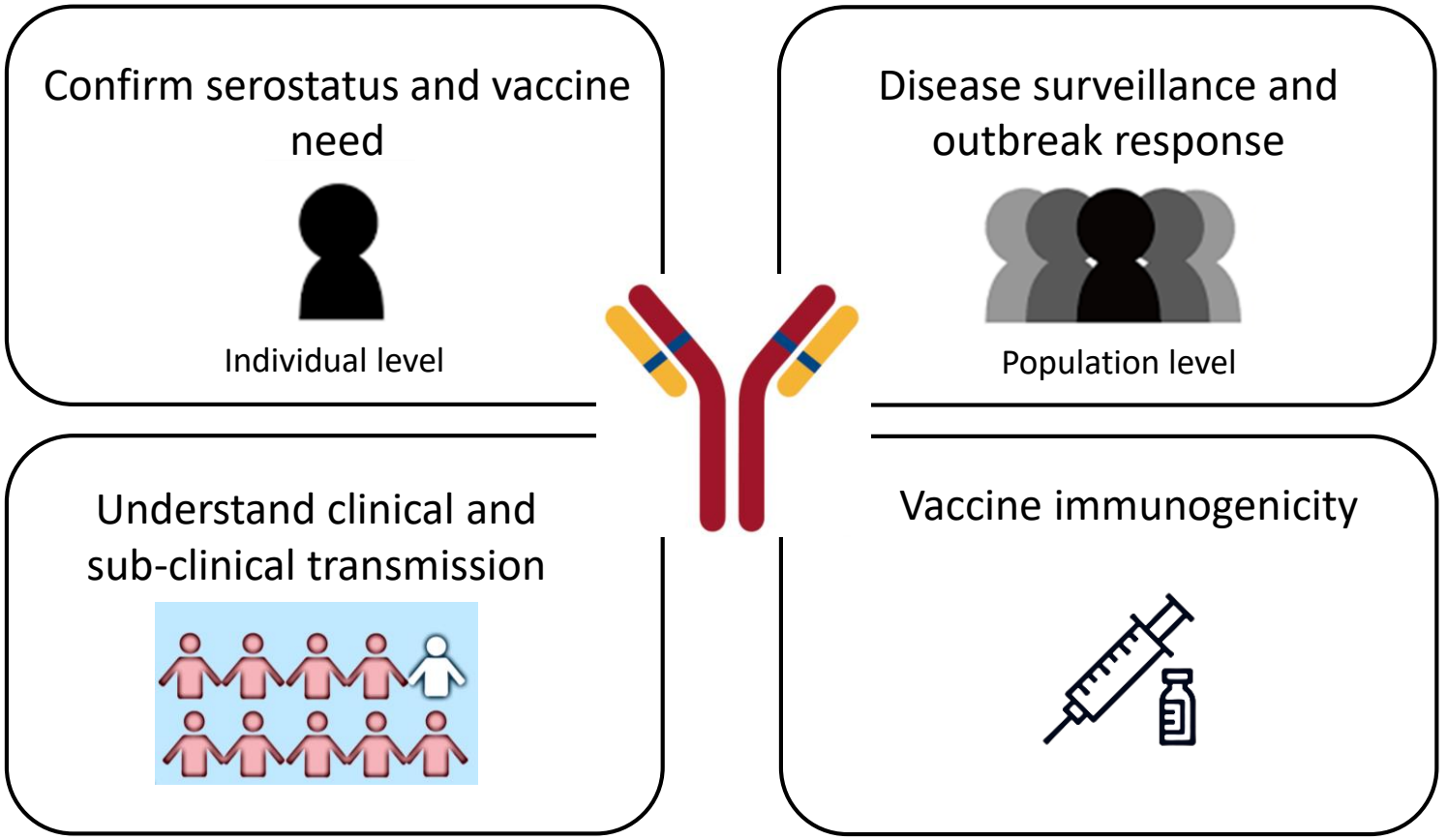
3) Lack of rapid diagnostic tests: limited molecular POC tests (PCR) and no suitable rapid antigen (viral protein) POC tests



Diagnostics gap global problem

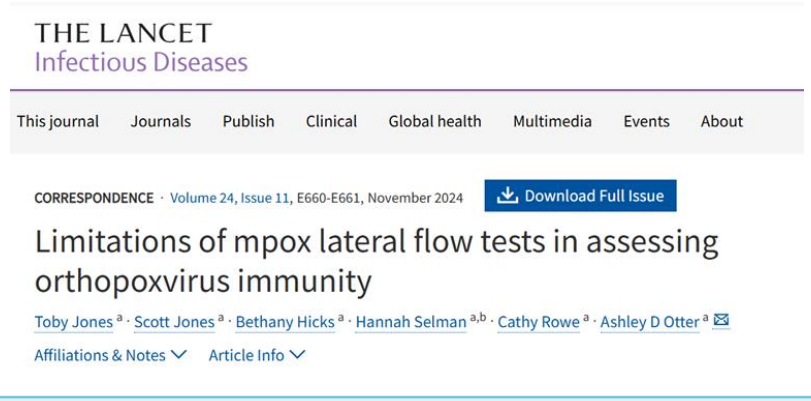
Mpox: immunodiagnostics gap

We have the issue of not only detection of acute infection but surveillance and monitoring, requiring **antibody detection**



We need affordable and accessible tools that permit antibody detection and quantitation across locations and populations

Immunodiagnostic landscape: **PoC tests**



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Limitations of mpox lateral flow tests in assessing orthopoxvirus immunity

Toby Jones [a] · Scott Jones [a] · Bethany Hicks [a] · Hannah Selman [a,b] · Cathy Rowe [a] · Ashley D Otter [a]

Affiliations & Notes Article Info

	Lateral flow device for IgG					Lateral flow device for IgM				
	1	2	3	4	5	1	2	3	4	5
Lateral flow device characteristics										
Specificity (%; 95% CI)	100 (69·15–100)	100 (80·49–100)	100 (66·37–100)	100 (79·41–100)	100 (79·41–100)	100 (69·15–100)	100 (82·35–100)	100 (66·37–100)	100 (80·49–100)	93·75 (69·77–99·84)
Sensitivity (%; 95% CI; infection or vaccine)	0 (0–10·89)	5·26 (1·10–14·62)	2·78 (0·07–14·53)	0 (0–6·16)	26·32 (15·54–39·66)	0 (0–10·89)	3·51 (0·43–12·11)	0 (0–9·74)	1·72 (0·04–9·24)	35·09 (22·91–48·87)
Sensitivity (%; 95% CI; infection only)	0 (0–28·49)	3·57 (0·09–18·35)	7·69 (0·19–36·03)	0 (0–12·34)	44·44 (25·48–64·67)	0 (0–28·49)	0 (0–12·34)	0 (0–24·71)	3·57 (0·09–18·35)	55·56 (35·33–74·52)

Sensitivity ≤ 56% on commercially available lateral flow tests

Problem 1: Lack of point of care immunodiagnostics with acceptable performance characteristics

Immunodiagnostic landscape: **lab tests**

Luminex multiplex

MpoxPlex

UK Health Security Agency

12 antigens

Electrochemiluminescence immunoassay

MSD Orthopoxvirus assay

10 antigens

Commercial ELISA kits

Typically single antigen

Problem 2: Real-world application of laboratory testing → requires specialised technology platforms and/or the need to measure multiple antigens, with associated cost, time and expertise

Assay translation for resource limited settings

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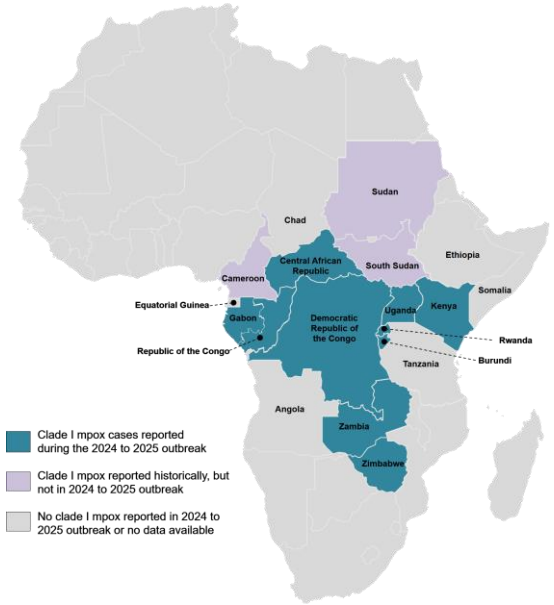


End user needs

Sensitive/ specific

Infrastructure

Equipment

User friendly

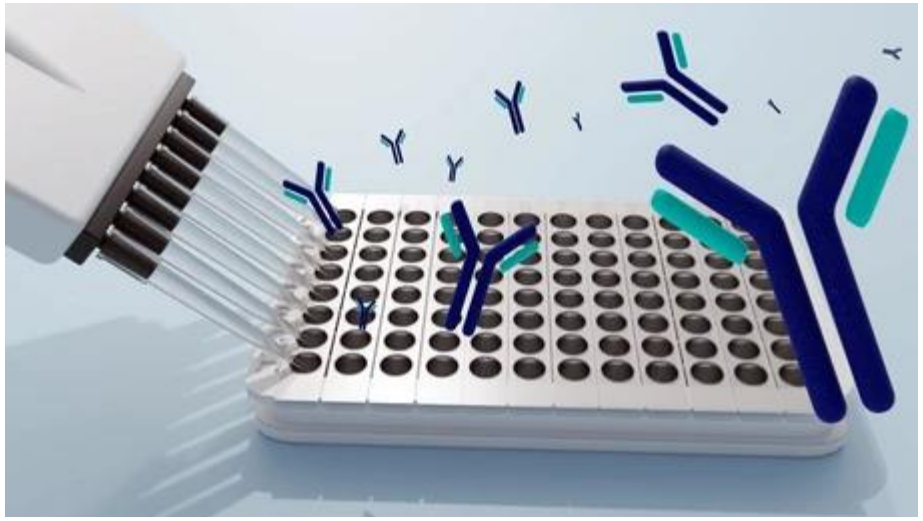
Time

Cost

Assay design for end user needs

1. Available and sustainable platform

ELISA



> Routinely used in clinical laboratories worldwide

> Allow multiple patient samples to be screened simultaneously

> Low cost to manufacture

> No specialised technology platforms (maintenance, reagent, costs, training)

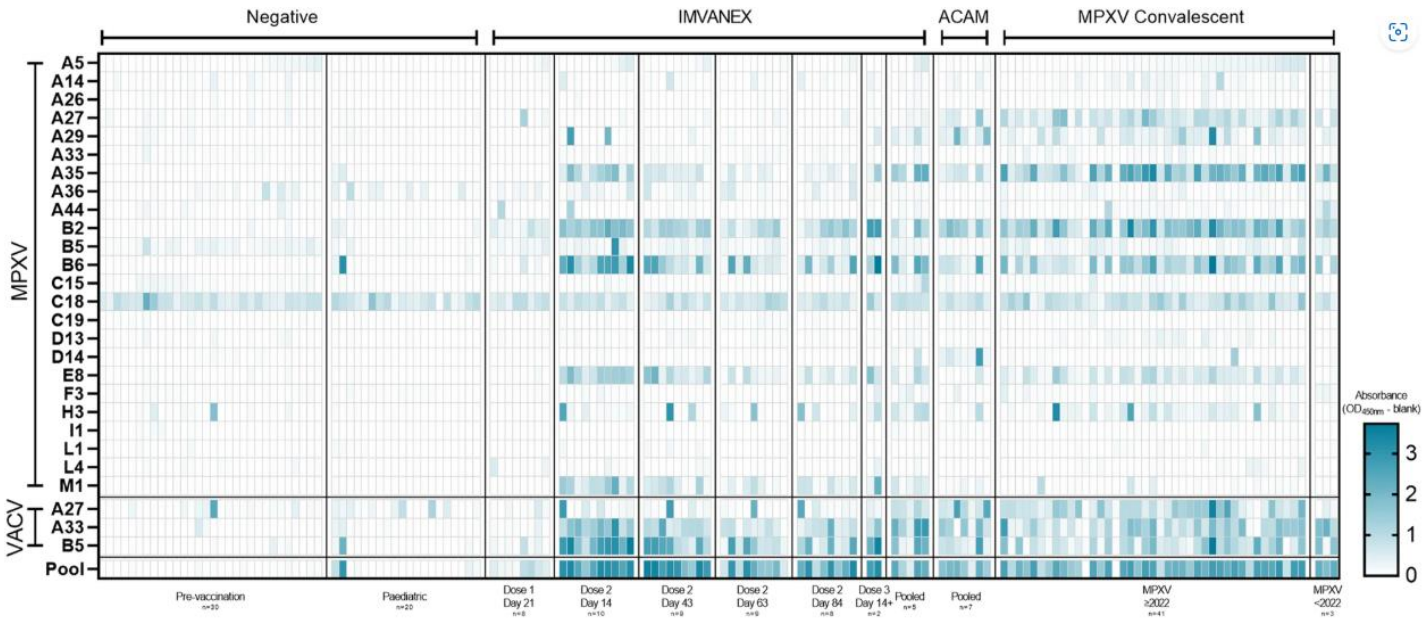
Assay design for end user needs

UK Health Security Agency

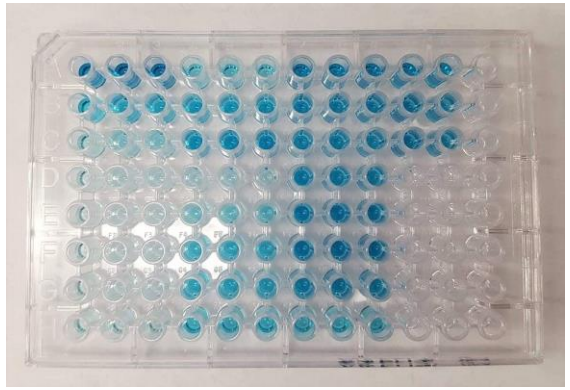
2. Accurately identify and quantify antibodies from infection and/or vaccination

3. Lowest number of antigens

4. Single readout to minimise complexity and determine serostatus



Combined 4-antigen ELISA



Combination of four immunodominant mpox proteins to enable parallel detection of mpox-specific IgG antibodies derived from both infection and vaccination

Nature Communications **volume 14**, 5948 (2023)

Assay format for end user needs

Ship to Rwanda or other laboratories

Ease of use within and between laboratories

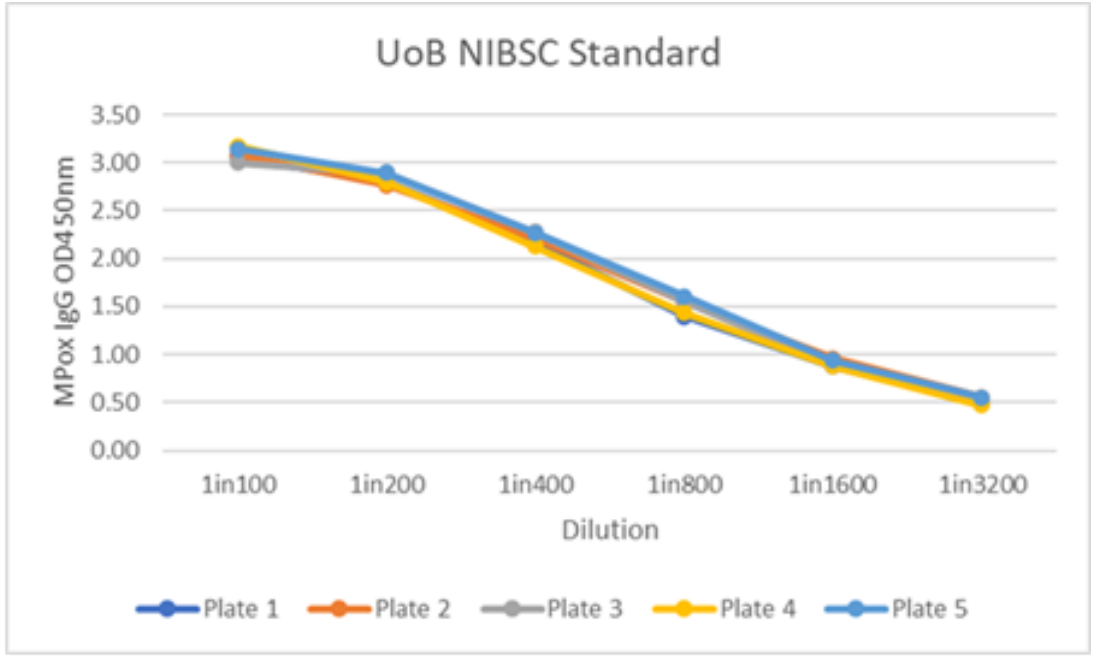
Simple kit format with recombinant antigen mix dried into plates and pre-dispensed reagents

Development into kit format

Assay readout for end user needs

There is currently no international reference sera for Mpox with assigned units

However, NIBSC do have a working reagent for anti-mpox antibodies



For each serum sample measured, the assay provides a single data point (OD), which is then adjusted using the NIBSC reagent to provide **an IgG antibody ratio**

Performance validation UK

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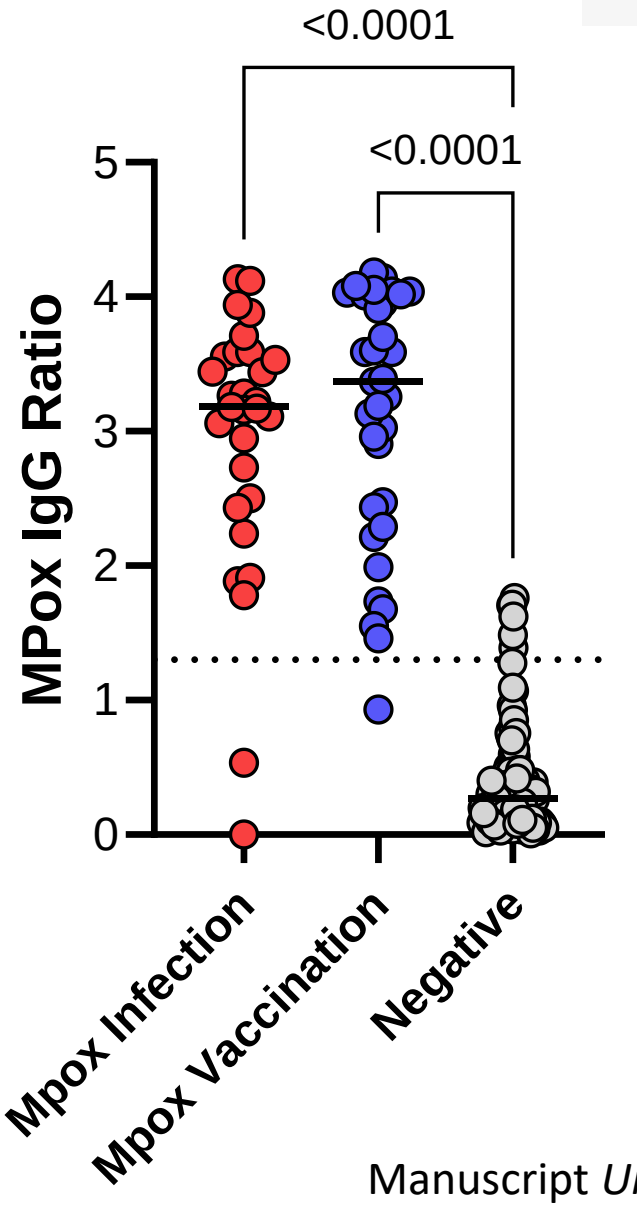
UK Health Security Agency

Mpox infection: n = 29 (24-113 days post infection, Clade II)

Mpox vaccinated IMVANEX-vaccinated: (24-77 days post 1st dose [n =8], 14-84 days post 2nd dose [n = 24], 14 days post 3rd dose [n = 1])

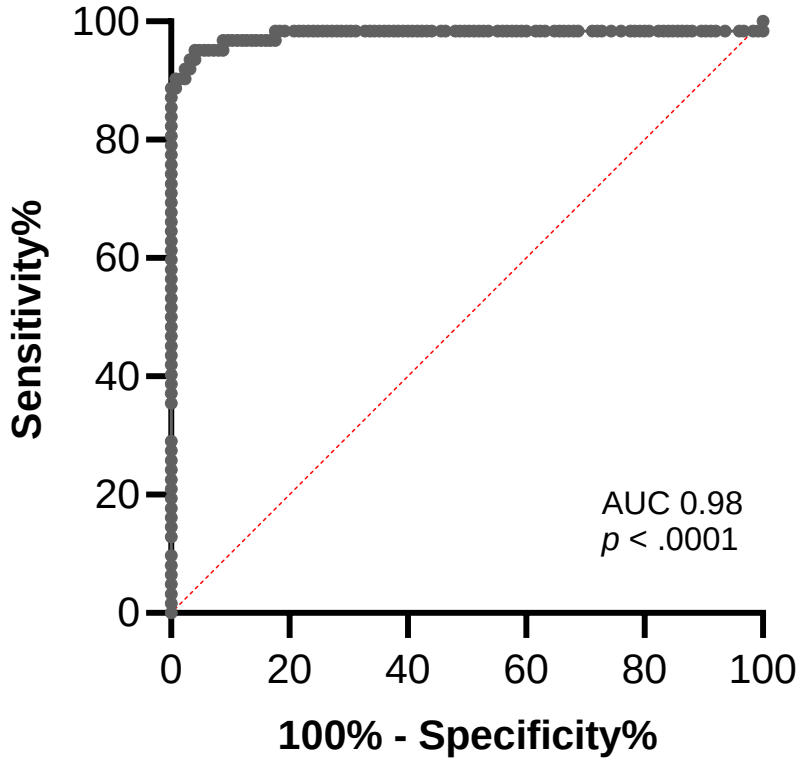
Negative (healthy donors with no known history of mpox infection or IMVANEX vaccination): n = 125

The combined four-antigen ELISA detected significantly higher mpox serum IgG antibodies in both infection and vaccination cohorts compared with negative donors.



Manuscript *Under Review*

Performance validation UK



The ELISA effectively discriminated individuals with prior infection or vaccination from those without

An IgG ratio cut off ≥ 1.33

Sensitivity 95% (95% CI 86·71–98·68%)

Specificity 95% (95% CI 89·92–97·78%)

IgG ratio offers an effective quantitative method to distinguish past exposure and/or vaccination, and assess antibody kinetics and change over time

Manuscript *Under Review*

Performance validation Rwanda

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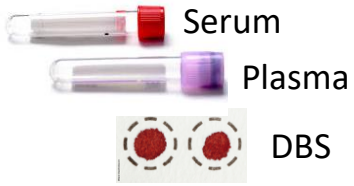
Assay validation (n = 150) in Rwandan population and Clade I

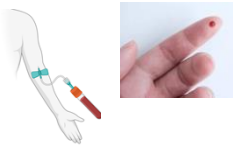
Groups: past infection/vaccinated, controls



Sampling method

Logistics

Acceptability



Mpox CARE (N = 500)

Comprehensive **A**ssessment for **R**esponsive Immunisation in **E**mergency Outbreaks

Groups: past infection/vaccinated, controls, at risk

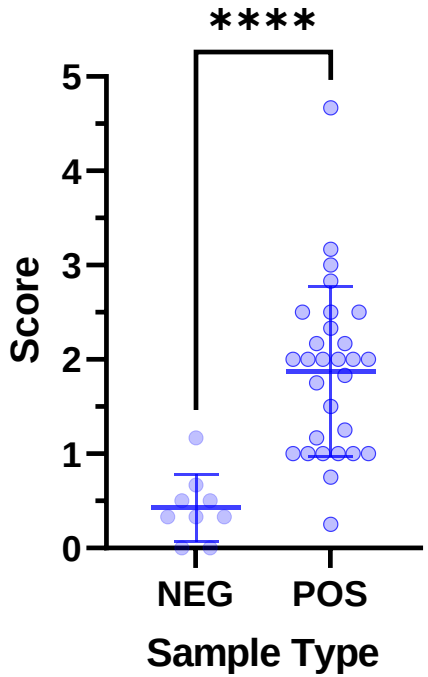
Aim: Evaluate immunodiagnostics to estimate Mpox's sero-prevalence as a tool to monitor disease burden and prioritise future vaccine utilisation

Immunosurveillance platform established within National Reference Laboratory

Next steps

- Pending successful validation in Rwanda, explore interest from other laboratories, offer as research tool
- Funding or partnerships to progress (assay optimisation and regulatory approval)
- Address lack of community and PoC antibody tests

Proof of concept for mpox IgG lateral flow test as part of this collaborative project



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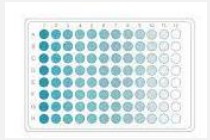
MEDTECH TO MARKET

UKRI Medical Research Council

Training and capacity building

- PhD Scholars
- Laboratory placements

R&D programme to improve access & equity of testing



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Diagnostic areas

Infectious disease and vaccination immunity
- Measles, Tetanus

Pandemic preparedness
- Mpox, Influenza, H5N1

Screening non-communicable disease
- Autoimmunity – T1D and lupus
- Blood cancer – myeloma

Partner locations

- Rwanda
- South Africa
- Ghana

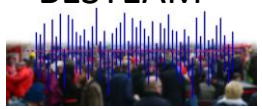


Evaluation in UK and Africa

UK Health Security Agency

MHRA

BESTEAM



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Partnerships with industry

GLOBAL ACCESS ga DIAGNOSTICS

MEDTECH TO MARKET

UnifAI Technology

Project Team

UNIVERSITY OF BIRMINGHAM | Clinical Immunology Services

Dr Jennifer Heaney
Dr Sian Faustini
Prof Alex Richter
Chloe Tanner
Frank Hai Kwok

UK Health Security Agency

Dr Ash Otter
Dr Scott Jones

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Dr Christopher Green
Herve Semukunzi
Professor Claude Mambo Muvunyi

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Dr Matt Pearce
Jake Hodgson
Rebecca Newman
Dr Andrea Murray

Funders

UKRI Medical Research Council

UKRI Research England

UoB Infrastructure

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