



UK Health
Security
Agency

Pathogen genomics in health security

The next five years

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Disclosures and Conflict of Interests

- Employed by government, NHS and university
- Research grants from NIHR, UKRI, MRC etc
- No commercial sponsorships



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Pathogen Genomics Services since 2012

Ten years of public health working productively with academic partners:



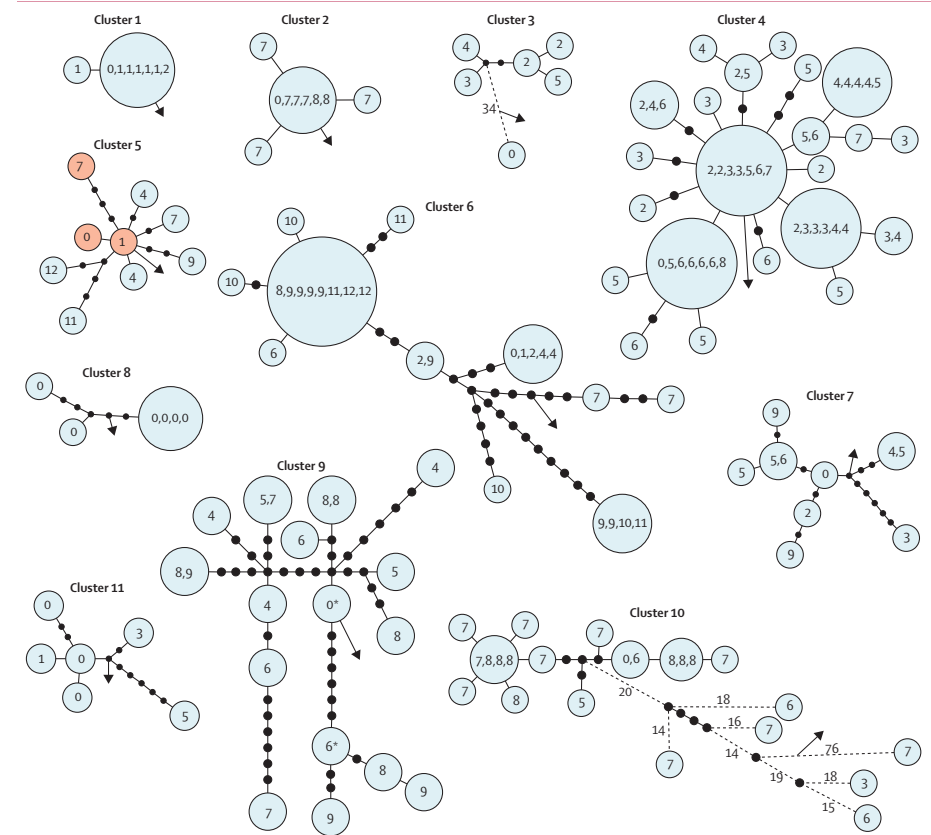
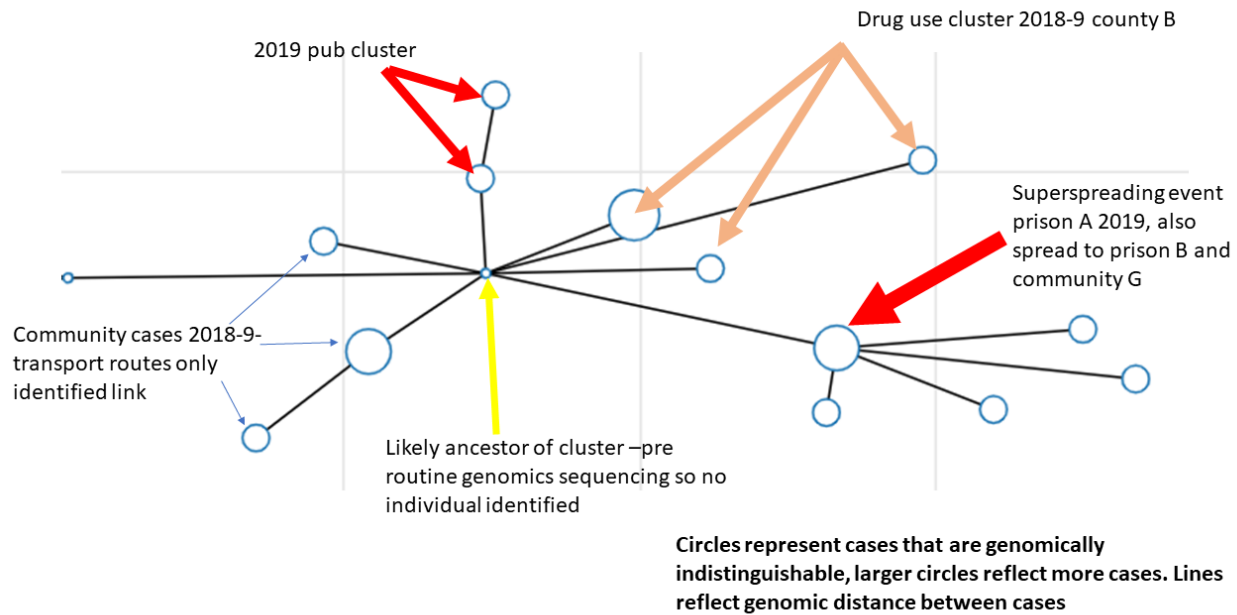
- Delivering **genomics end-to-end solutions** exemplified by **first-in-world service** for tuberculosis
- Delivering **national surveillance and food chain and environmental investigation** of gastrointestinal/food poisoning and hospitalised patients and imported fever cases
- Delivering **targeted outbreak investigation** of serious illnesses
- **Responded** to global threats - Ebola and Zika



Ground breaking analyses of combined genomics and epidemiological:

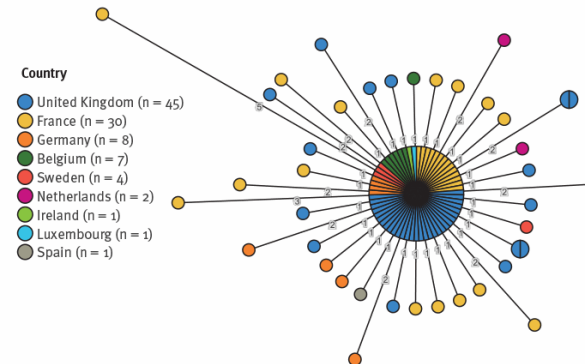
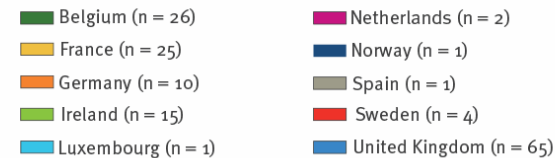
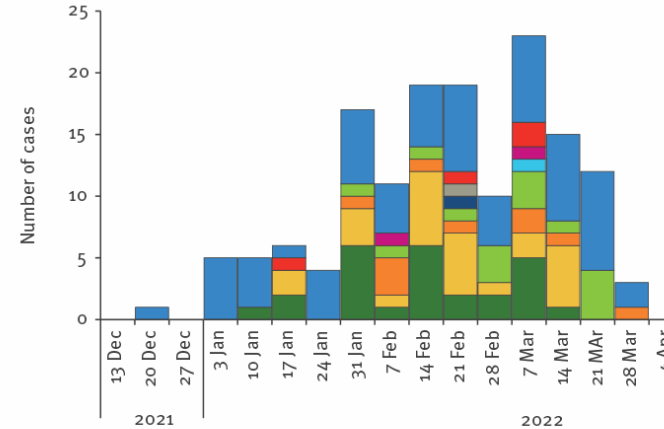
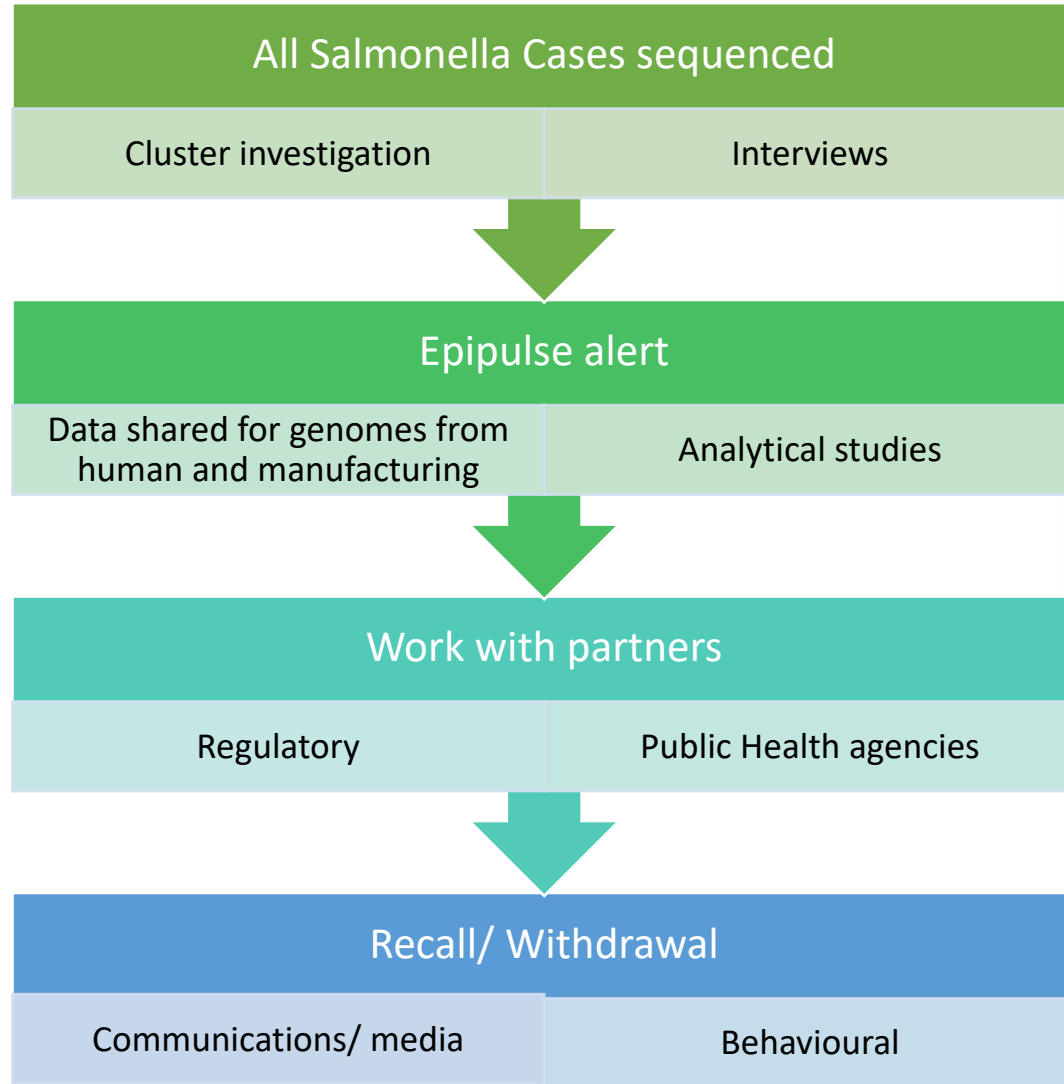
- **Reservoirs** - Mycobacterium chimera in heater cooler units leading to surgery linked mortalities
- **Control** of national epidemics - *Clostridium difficile* a
- **Outbreak control** - carbapenem resistant enteric bacteria, interrupting transmission from reusable devices
- Generating **evidence from winter surveillance of Flu** for annual **vaccine formulation**
- Supporting successful introduction of **new antivirals for Hepatitis C infections**
- **Sequenced the first SARS-CoV-19 genome in the UK** and delivered real time genomes from hospitalised patients and healthcare workers

Surveillance of Mycobacterium tuberculosis



Cost of MDR/patient £100k/year
WGS shortens time to drug susceptibility results from 42-84 days to 10-14 days

Find source, Communicate effectively



INFOSAN Global Alert: Multi-country outbreak of *Salmonella* Typhimurium possibly linked to chocolate products



RAPPEL DE PRODUIT

Version imprimable | Dernière mise à jour le 14/04/2022

08/04/2022 (Mise à jour du rappel de produit du 05/04/2022)

Rappel de Ferrero (version allemande en pdf)

Produits : Plusieurs chocolats Kinder.

Problématique : Présence possible de Salmonelle.

FERRERO ANNONCE LA SUSPENSION TEMPORAIRE DE SES ACTIVITÉS À ARLON, EN BELGIQUE, ET ÉTEND LE RAPPEL DES PRODUITS KINDER FABRIQUÉS DANS LA MÊME USINE

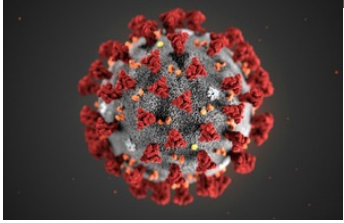


FOOD ALERT

Ferrero recalls Kinder Surprise because of the possible presence of Salmonella



COVID-19: scale of the challenge



Source: <https://www.gov.uk/government/news/uk-to-support-rest-of-the-world-to-find-covid-19-virus-variants>

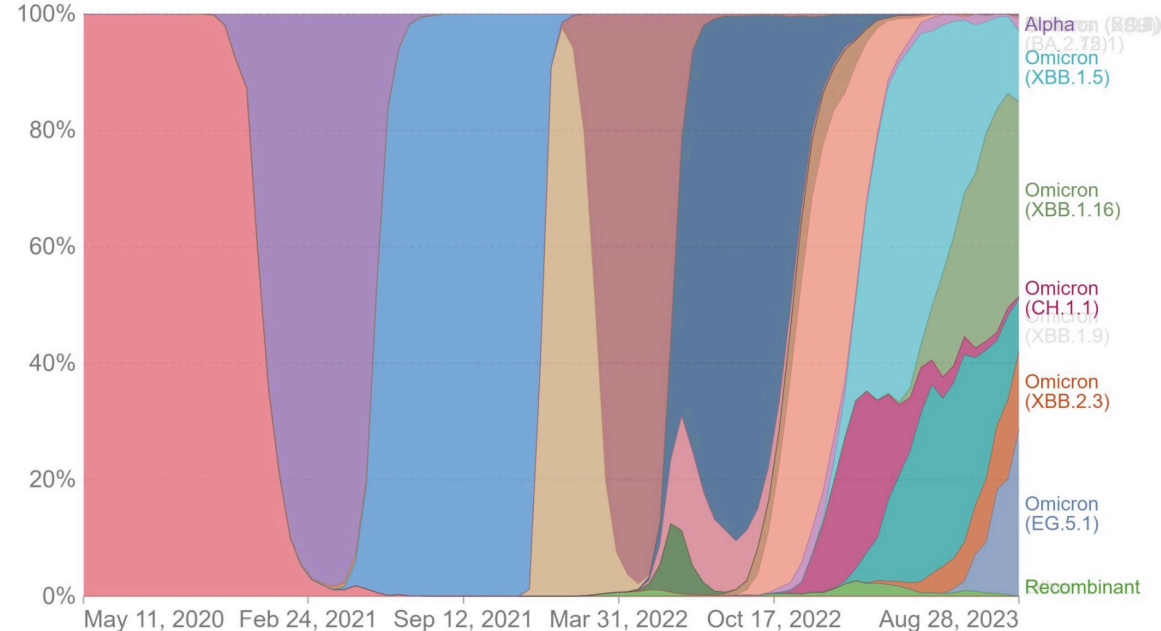
- Feedback loop through structural models, laboratory and clinical studies
- Data linkage and integration; investment in analysis and products
- Free and rapid sharing of data and analysis
 - Validation of lab and point of care assays
 - Morbidity, mortality and vaccine effectiveness for each variant

2,820,245m
SARS-CoV-2 positive
cases sequenced

SARS-CoV-2 variants in analyzed sequences, United Kingdom

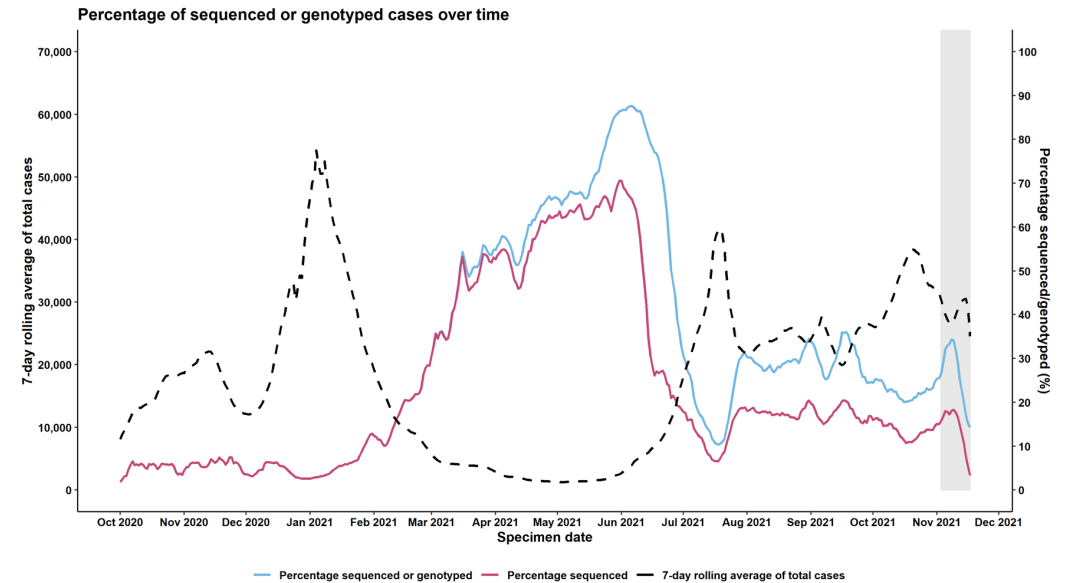
The number of analyzed sequences in the preceding two weeks that correspond to each variant group. This number may not reflect the complete breakdown of cases since only a fraction of all cases are sequenced.

Our World
in Data



Source: GISAID, via CoVariants.org – Last updated 6 September 2023

OurWorldInData.org/coronavirus • CC BY



Data extract from 18 November 2021; data from 01 October 2020 to 17 November 2021. Grey shading was applied to the previous 14 days to account for reporting delays in sequencing data.

The next five years:

**Pathogen genomics
integration is possible
across the breadth of
infectious diseases**



Aims of the Pathogen Genomic Strategy

SEVEN STRATEGIC AIMS



Use genomics data to optimise decision-making from local to global



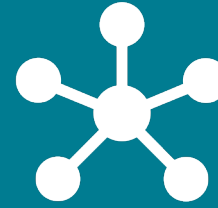
Use genomic data to drive improvements in diagnostics, vaccines & therapeutics



Provide a coordinated, high-throughput pathogen genomics service



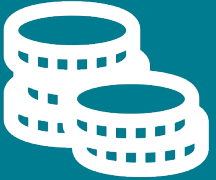
Undertake a genomics workforce transformation within and beyond UKHSA



Commit to pathogen genomics data sharing and global collaboration

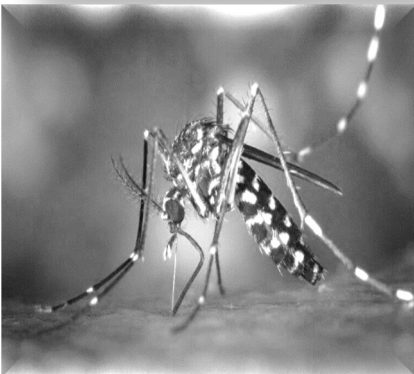


Drive innovation in pathogen genomics



Build high-impact services that are good value for money

Priority areas



Antimicrobial resistance (AMR)

- Understand **resistance mechanisms** including for our drugs of last resort
- Understand **transmission and control outbreaks**
- Detect new mechanisms of resistance and **inform the therapeutics pipeline**
- Understand drivers and target interventions

Vaccine & elimination programmes

- Inform **vaccine selection**
- Provide data for new **vaccine development**
- Support **elimination programmes** through detecting transmission

Emerging infections and biosecurity

- Deploy metagenomic surveillance as an **early warning system**
- Detect **new and variant** pathogens
- Guide timely public health responses
- Strengthen biosecurity and mitigate the impact of global threats.

Strategic enablers



Develop ethical guidelines

We will create frameworks for the ethical use of pathogen genomic and metagenomic data.



Address data privacy concerns

We will implement measures to protect the privacy of individuals from whom genomic epidemiological data is derived.



Promote equitable access to pathogen genomic data

We will ensure that the benefits of pathogen genomics are shared broadly and help to reduce health inequalities.



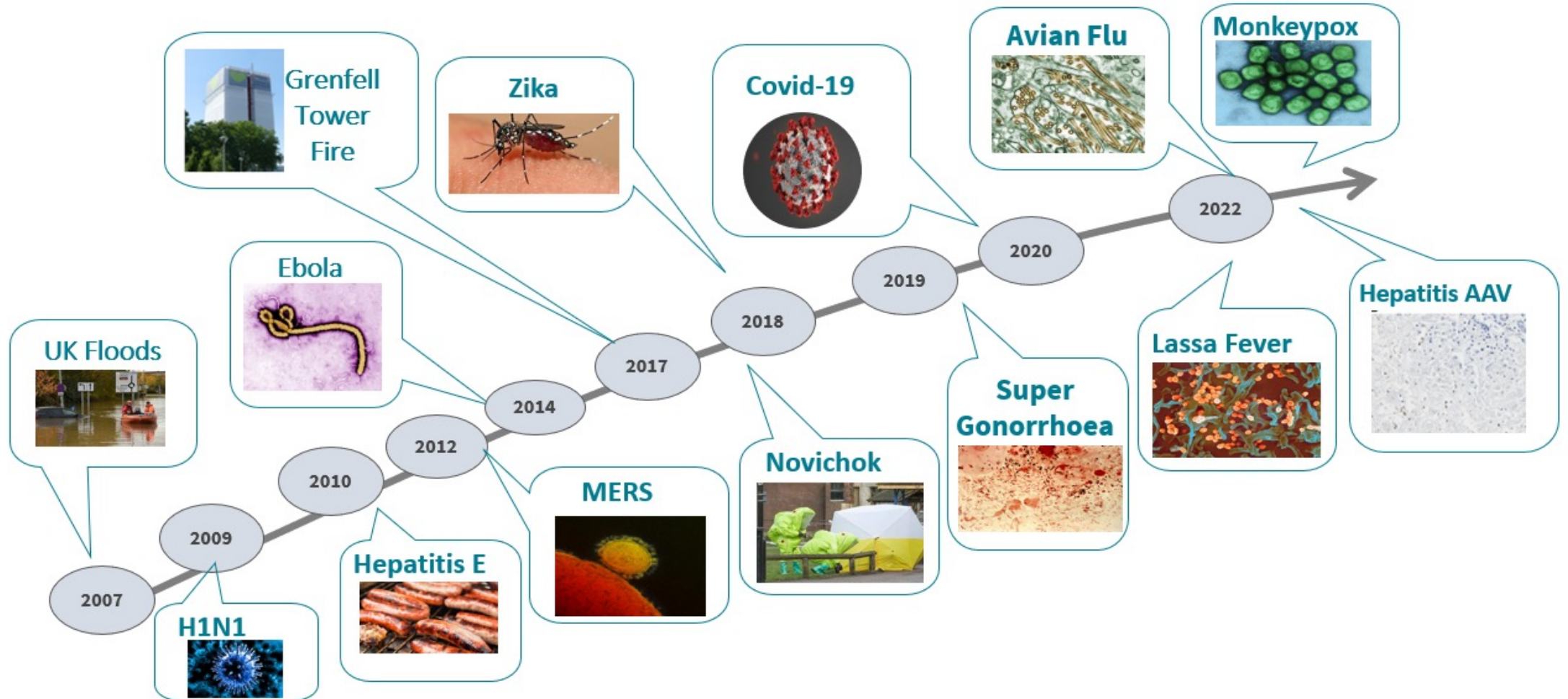
Deliver public communication

We will create educational resources and communication plans to explain the role and benefits of pathogen genomics to the public.

Focusing the question: our target is the pathogen we weren't looking for

UK health security landscape 2007 – 2022

We deal with around 10,000 incidents a year



Focusing the question (2):

Our priority aim is to detect emergence or very early community transmission in the UK

Pre-UK Emergence

Long-term threat assessments

Reviews of different health hazards and risk these may cause a pandemic. E.g. SGSS

Epidemiological Intelligence

Monitoring of health events globally to identify

Border Health / Returning Worker Scheme

Assessment of actual importations or risk of importations from high-risk exposures

OneHealth Surveillance (non-UKHSA)

Animal surveillance (APHA), Human Animal Infections and Risk Surveillance (HAIRS) group

Risks/Gaps:

Global: data (cases, genomics) transparency, International data sharing, Immaturity of surveillance systems in some countries

UK: lack of traveller data

Emergence in UK

Testing of people categorised as high risk (for example, occupational exposure)

Person infected (prior to testing)

Sero-epidemiology

Symptomatic persons (without testing)

Google Flu trends, FluSurvey, Syndromic surveillance

Symptomatic persons (test confirmed) in the community

Laboratory surveillance systems, FFX protocol (first few hundred), Household contact study for Influenza pandemics, Swabbing of community

Risks/Gaps: Dependency on NHS recognition, 24/7 testing [vast majority of new pathogen testing occurs in UKHSA] and reporting

Community Transmission

Respiratory syndromes [ONS]

- **Primary care** - RCGP/ UKHSA surveillance
- **Hospitalisation** – SARI-watch
- **Critical Care** – SARI-watch, enhanced surveillance
- **Healthcare worker** - SIREN

Transmission studies – scalability critical for trace, data linkage, studies

Genomics – requires capacity to be enhanced, E2E pipeline development with academia

Mortality

Excess mortality monitoring

Risks/Gaps: Dependency on NHS testing and reporting, funding for surveillance studies

Are we ready for metagenomic surveillance and how exactly is it going to help us?

The options for deployment

Global epidemic intelligence	Outbreaks (pathogens or syndromes) reported by other countries
Behavioural indicators	People googling 'flu'
Syndromic	People presenting to GPs or calling NHS111 with respiratory illness
Pathogen: designed surveillance samples (clinical and environmental)	<div>GP and Hospital sentinel surveillance</div> <div>Designed metagenomic surveillance</div>
Pathogen: 'clinician suspects'	<div>Directed testing of unexplained disease cluster</div> <div>Investigation of unexplained outbreaks and cases</div>
Pathogen: routine clinical testing	<div>Standard panel of tests for respiratory admissions</div> <div>Routine clinical metagenomics</div>

Are we ready for metagenomic surveillance and how exactly is it going to help us?

TARGET: Respiratory and Emerging infections

AIM: Detect UK transmission

'Clinician suspects' – investigate unusual outbreaks

Emerging infections breadth of syndromes. Low cost. **NOW**

Designed metagenomic surveillance

Respiratory syndromes (big threats). Moderate cost
Targeted cohorts - ICU Environment - wastewater **THIS YEAR**

Routine clinical metagenomics and data centralisation

System transformation
Value for money?

ETHICS

- The clinician should know the type of testing that is being performed and should have counselled the patient appropriately
- There must be a way to report findings which may impact the management of the person's health (e.g. HIV, blood borne viruses even if found at a delay)
- There must be a way to act on findings where there is a severe risk to population health (high consequence infectious diseases)

Sequencing partners

- Clinical services
- Research studies

MRC CLIMB

- Restricted area for use by named mSCAPE collaborators

UKHSA

Secure repository limited to UKHSA surveillance team

Phase 1: To establish data sharing platform, test analytic approaches, establish readiness of wet lab methods and establish network of sequencing centres

Phase 2: To evaluate timeliness, quality and sufficiency of existing sample flows, and to establish and evaluate any new sample flows, to establish data ingest to UKHSA and pilot aggregate surveillance analyses, comparing this analysis with conventional surveillance outputs

Metagenomic sequence data generated

Removal of human DNA sequence

Link to basic metadata*

Upload to CLIMB

Genomic analytic output accessible for method development across collaborators**

UKHSA ingest (in Phase 2)

Significant pathogen genome assembly where appropriate

Identify microbes present and relative abundance in sample

QC check on removal of human sequence, and metadata

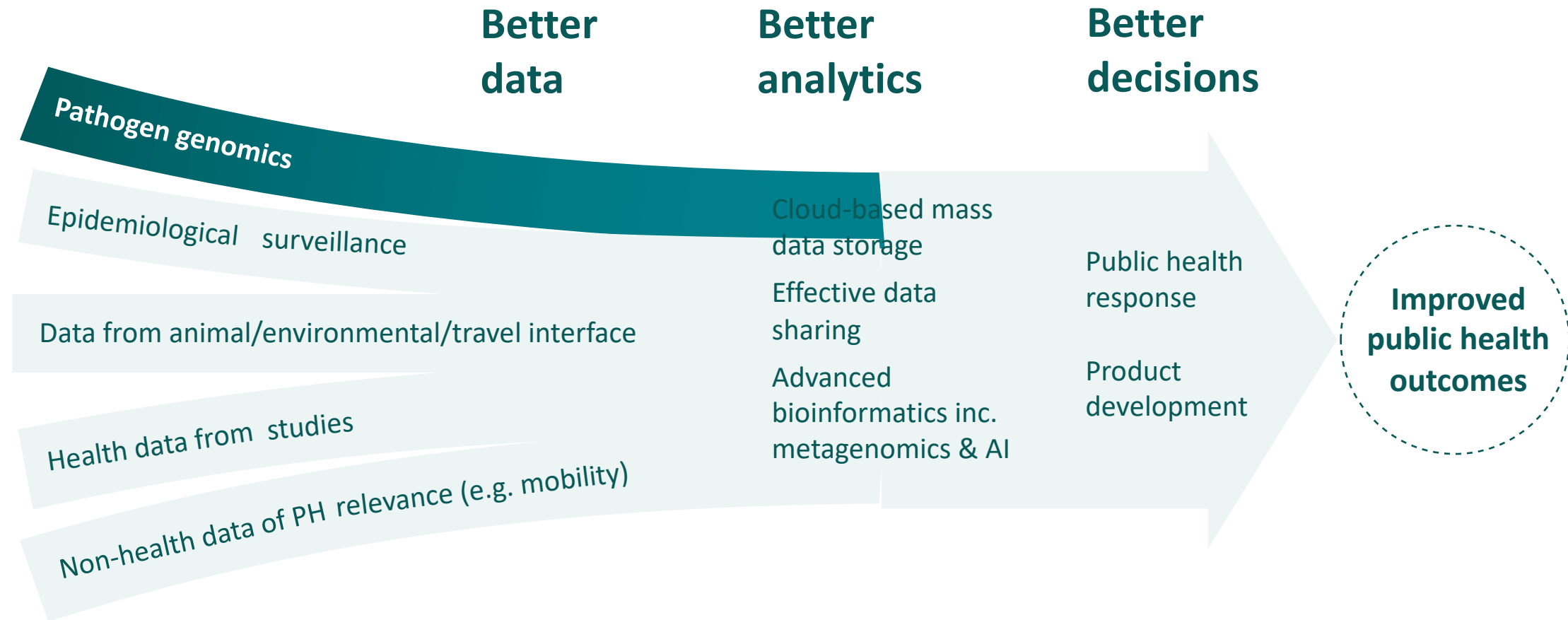
Genomic analytic output accessible for UKHSA surveillance team**

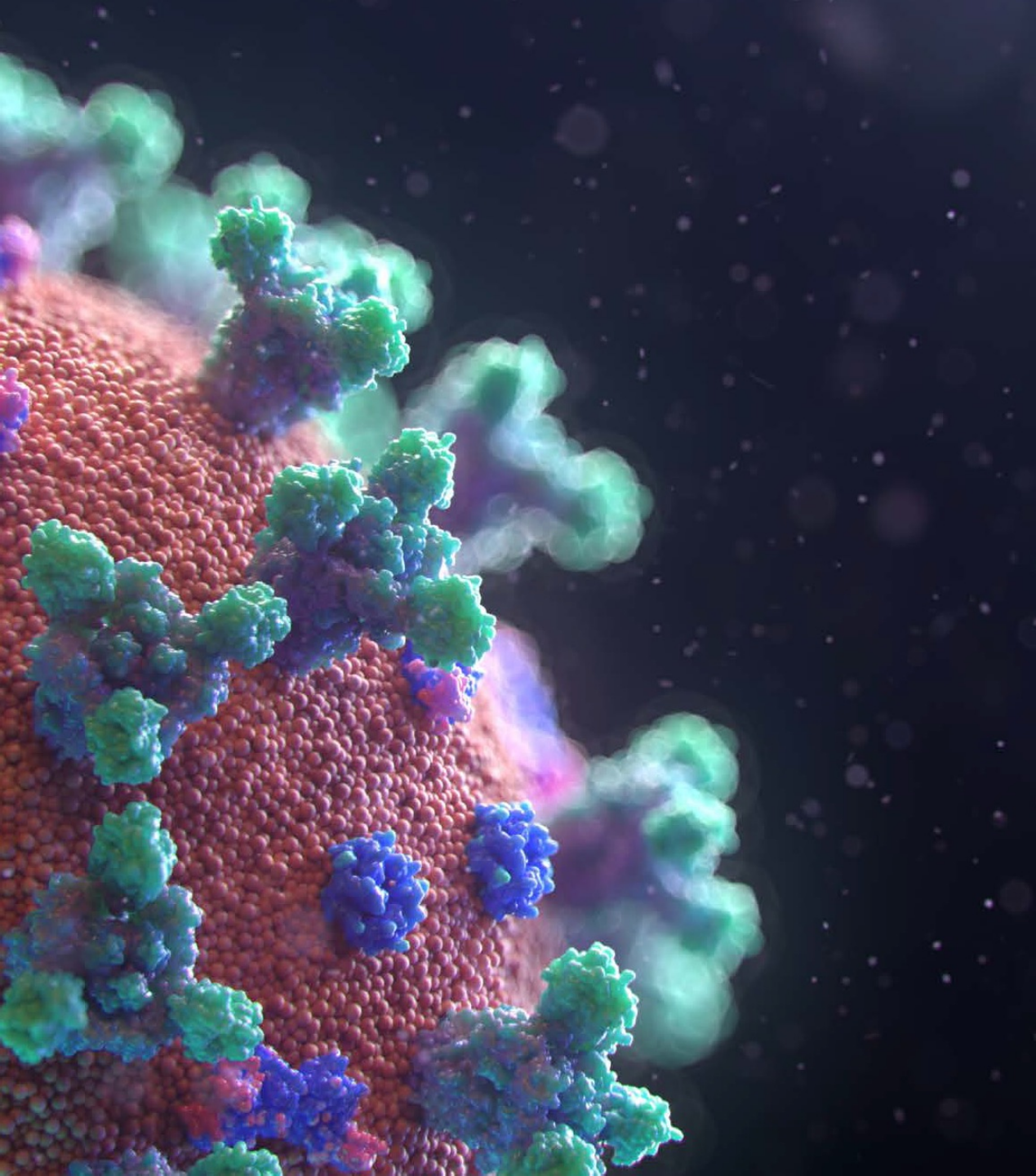
Onwards analysis by comparison (no linkage) to surveillance datasets

Clinical service
reports back to users under local clinical governance

Research studies
Reporting as per local ethics approved study protocol

Pathogen genomics is one strand of infectious disease surveillance





...to rising associated with climate change,
biological threats and other dangers.