Use of genomic sequencing for AMR surveillance an introduction

David Aanensen
University of Oxford

RADAAR
Regional AMR Data Analysis for Advocacy, Response, and Policy

Centre for Genomic Pathogen Surveillance
BRIGHAM AND WOMEN'S HOSPITAL
PUBLIC HEALTH SURVEILLANCE GROUP
The Fleming Fund Regional Grants
UKaid from the British people

Centre for Genomic Pathogen Surveillance

Machine Learning | CS & AI

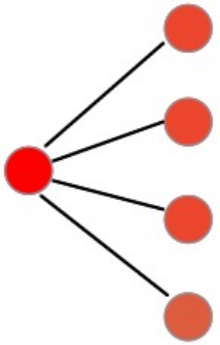
Sequencing / lab / bioinformatics

Analysis of large, complex heterogeneous datasets for research into the causes and consequences, prevention and treatment of disease

Translational big data and genomics for public health

Genomic Pathogen Surveillance

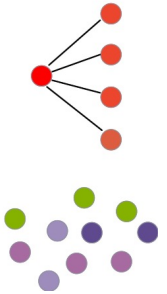
Where, what, when, who



Related Cases / clone

Unrelated Isolates

Whole Genome Sequencing



illumina®

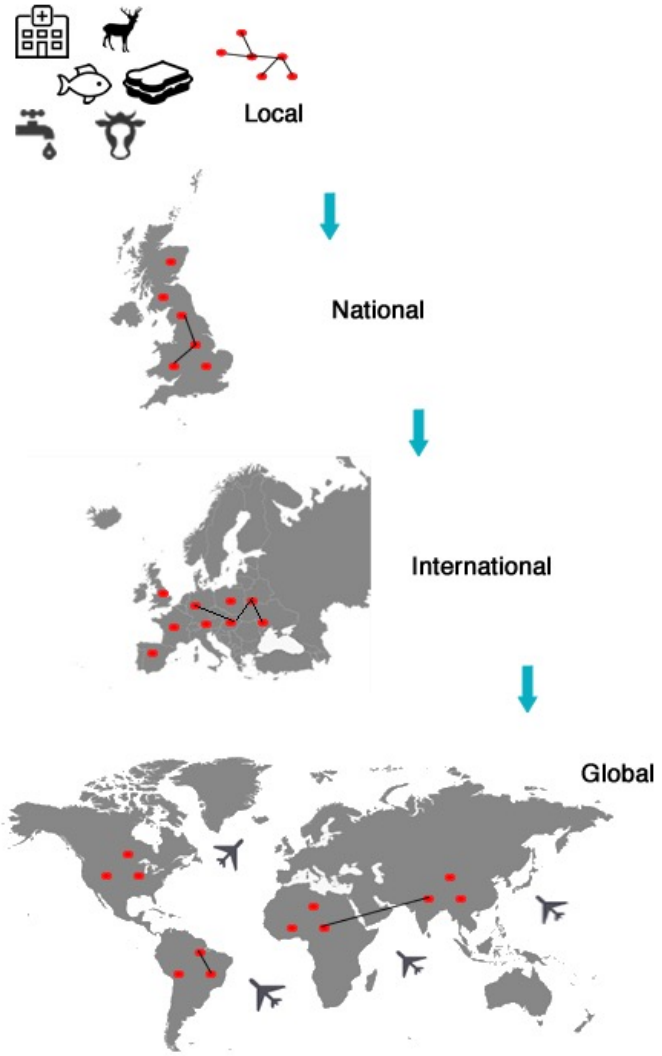
PACBIO®

华大基因 BGI

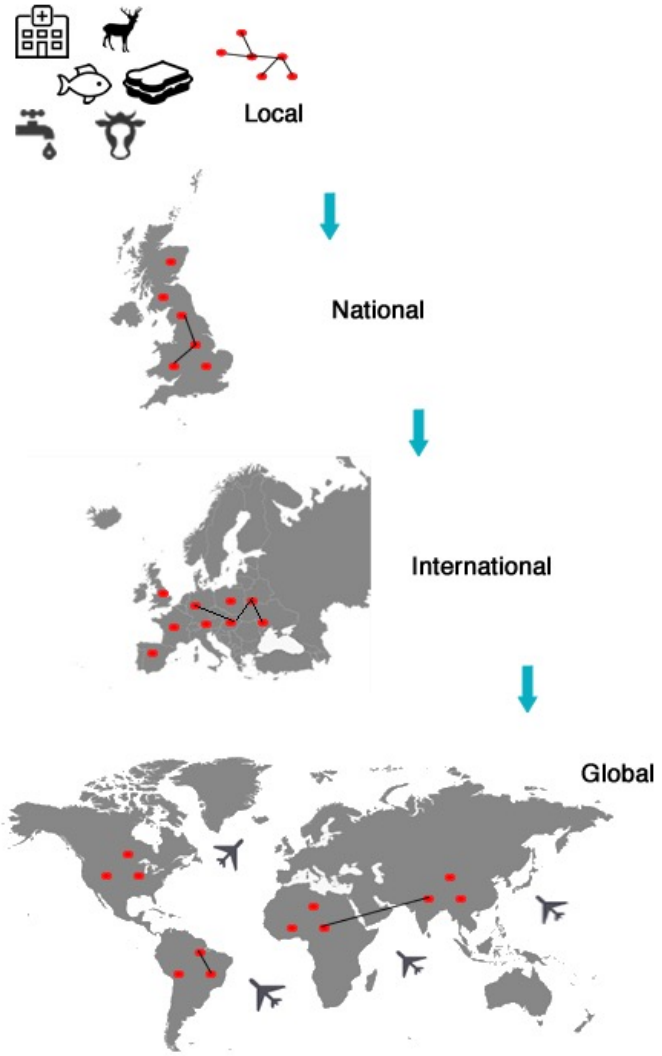
Short or long read

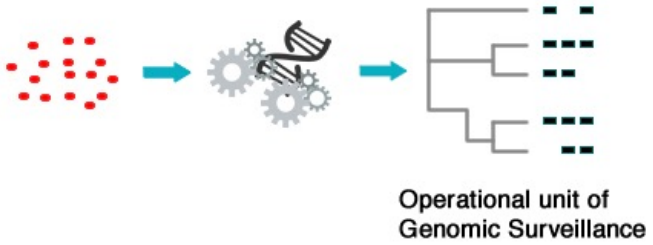
Oxford NANOPORE Technologies®

Data Scales

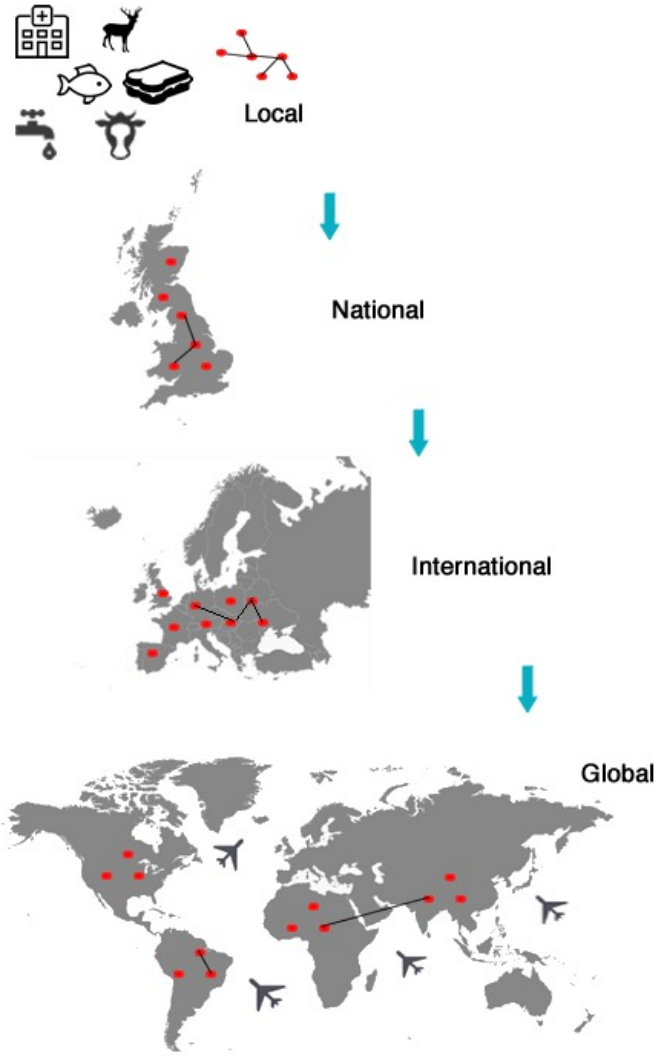


Data Scales


Local
National
International
Global


Operational unit of
Genomic Surveillance

Data Scales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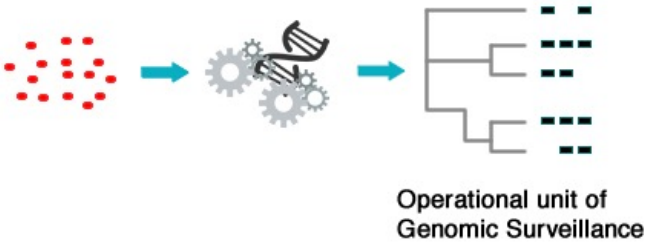
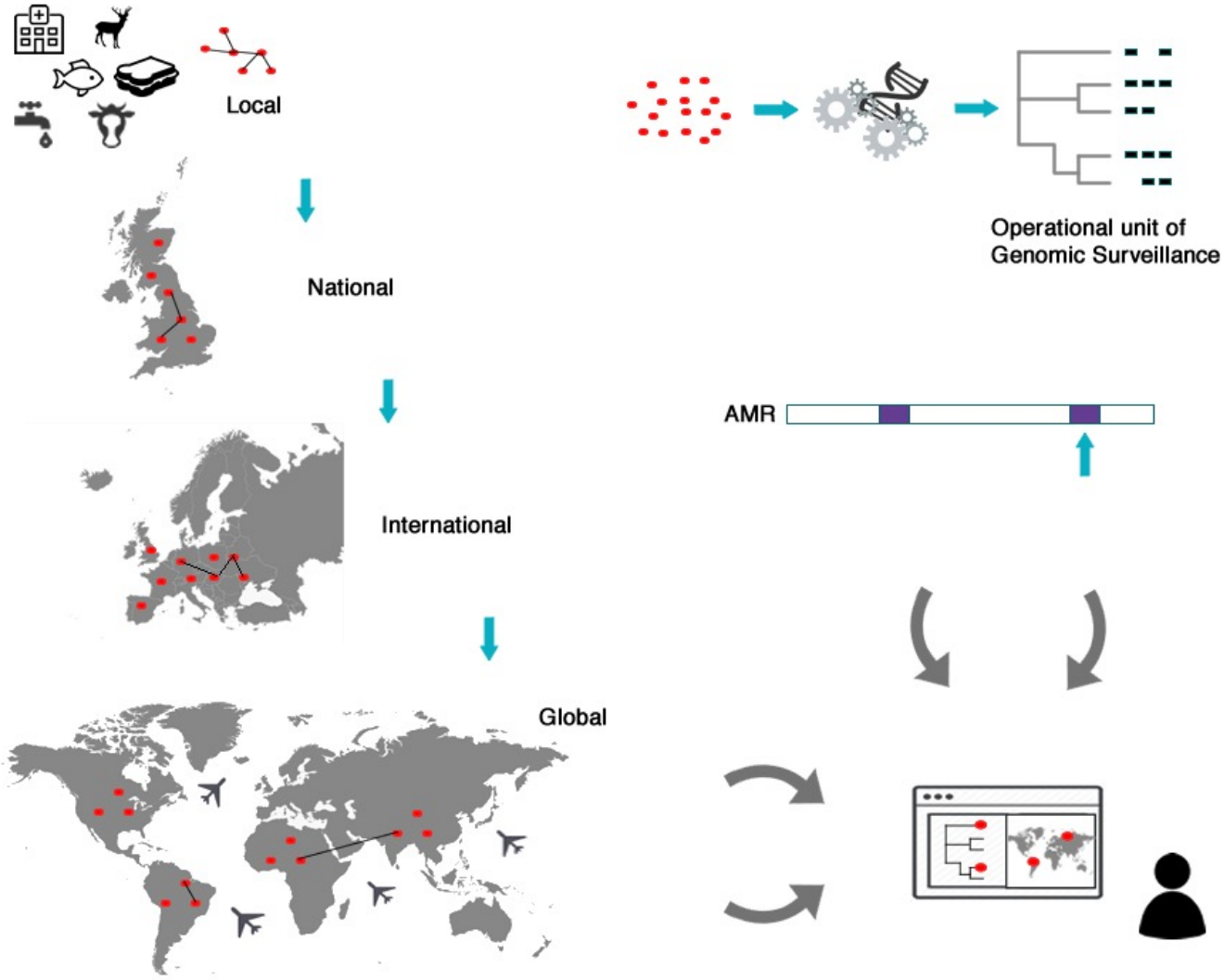

Operational unit of
Genomic Surveillance

AMR

Data Scales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National
International
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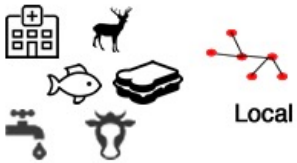
Operational unit of
Genomic Surveillance
AMR

Data Scales



Local

National

International

Global

Operational unit of
Genomic Surveillance

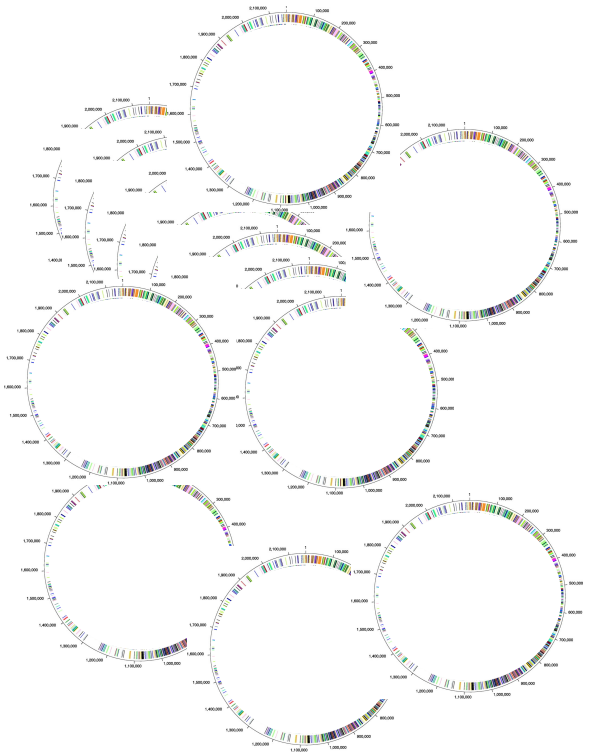
AMR

Public Health
England

ecdc
EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

AFRICA CDC
Centres for Disease Control and Prevention
Safeguarding Africa's Health

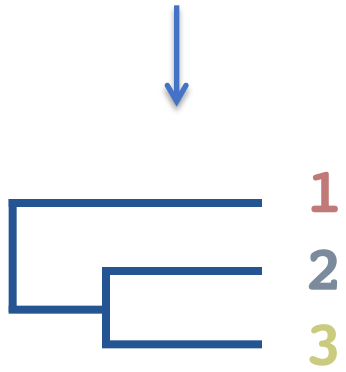
World Health
Organization

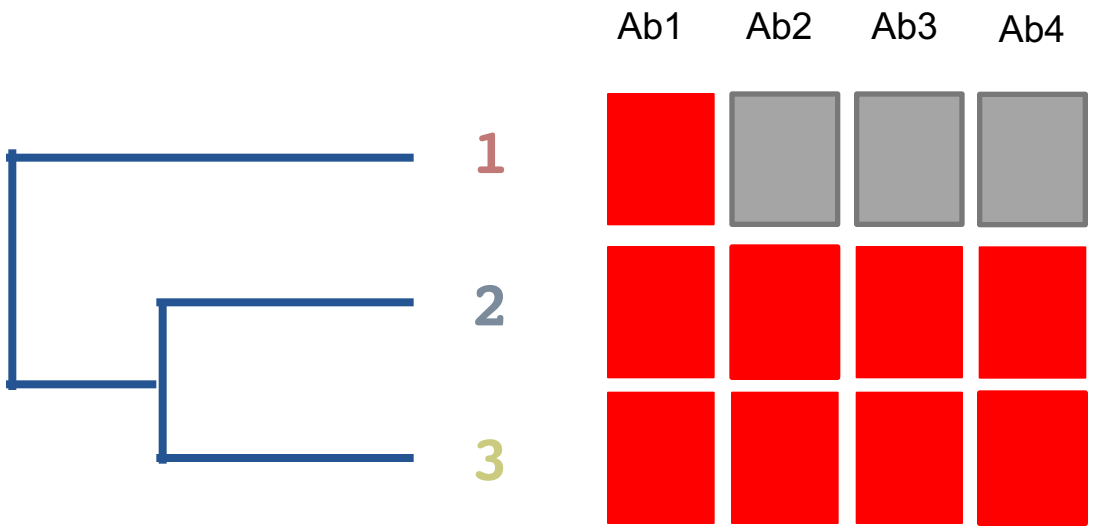


Centre for **Genomic**
Pathogen Surveillance

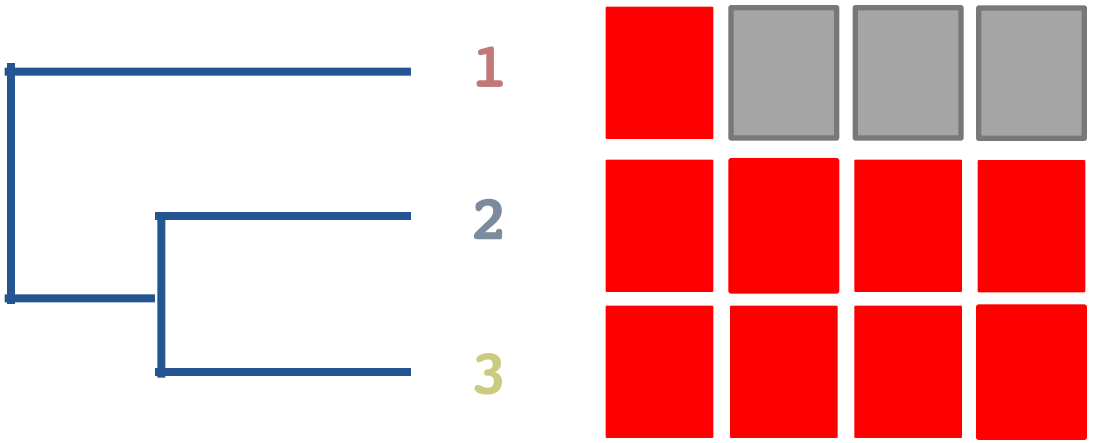
Sequence Comparison

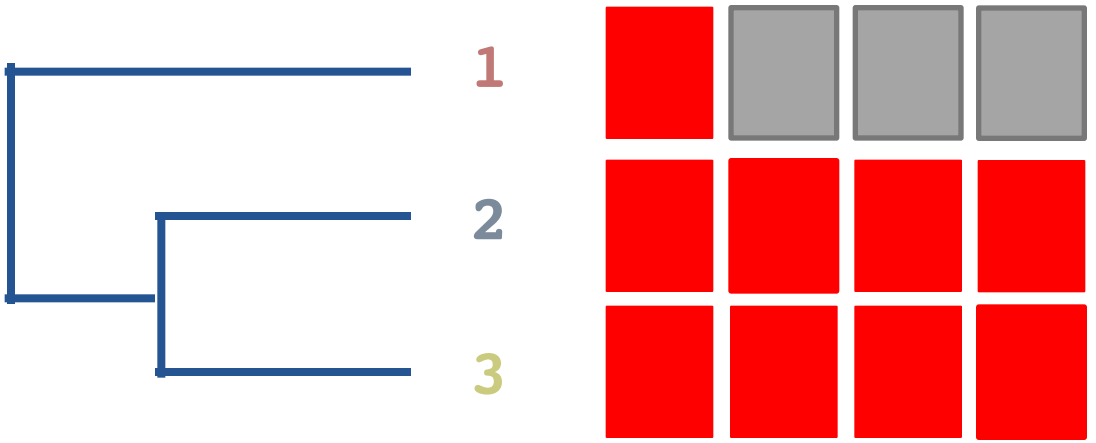
```
1    AATCGCTTTACGACCAG...
2    AATGGCTTTATGACAAG...
3    AATCGCTTTATGACAAG...
        *       *   *
```




Ab1
Ab2
Ab3
Ab4
1
2
3

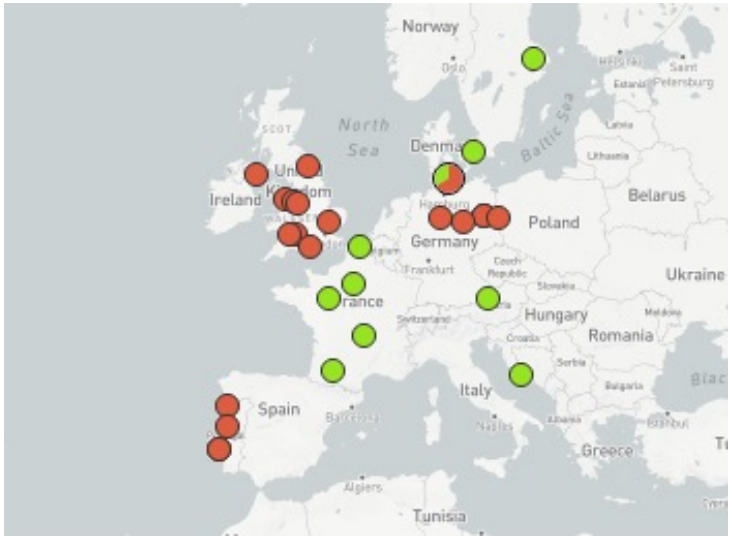
1
2
3

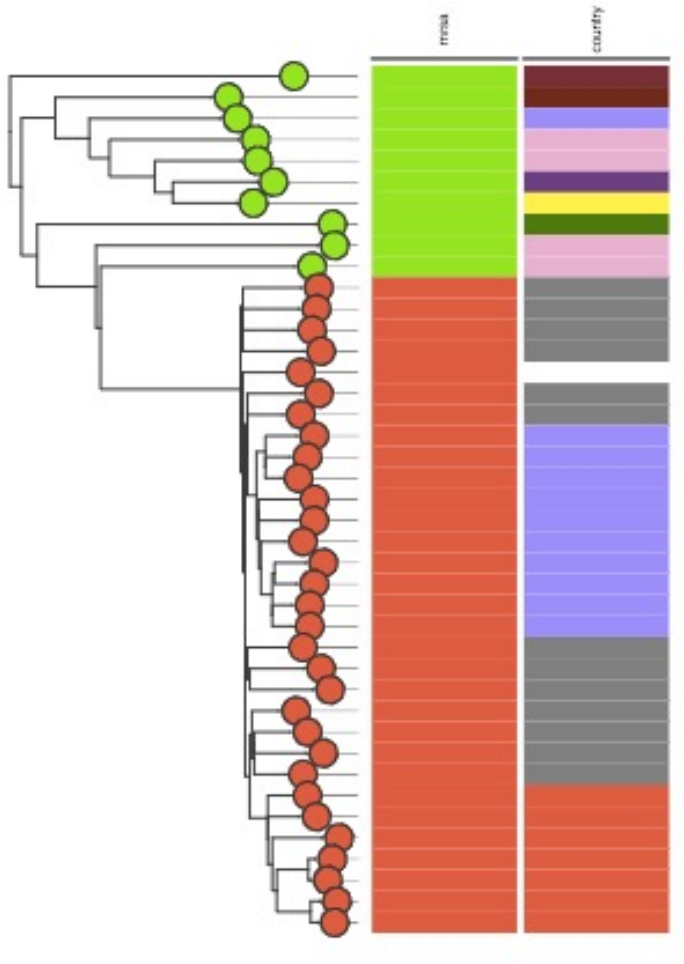

1
2
3



Risk

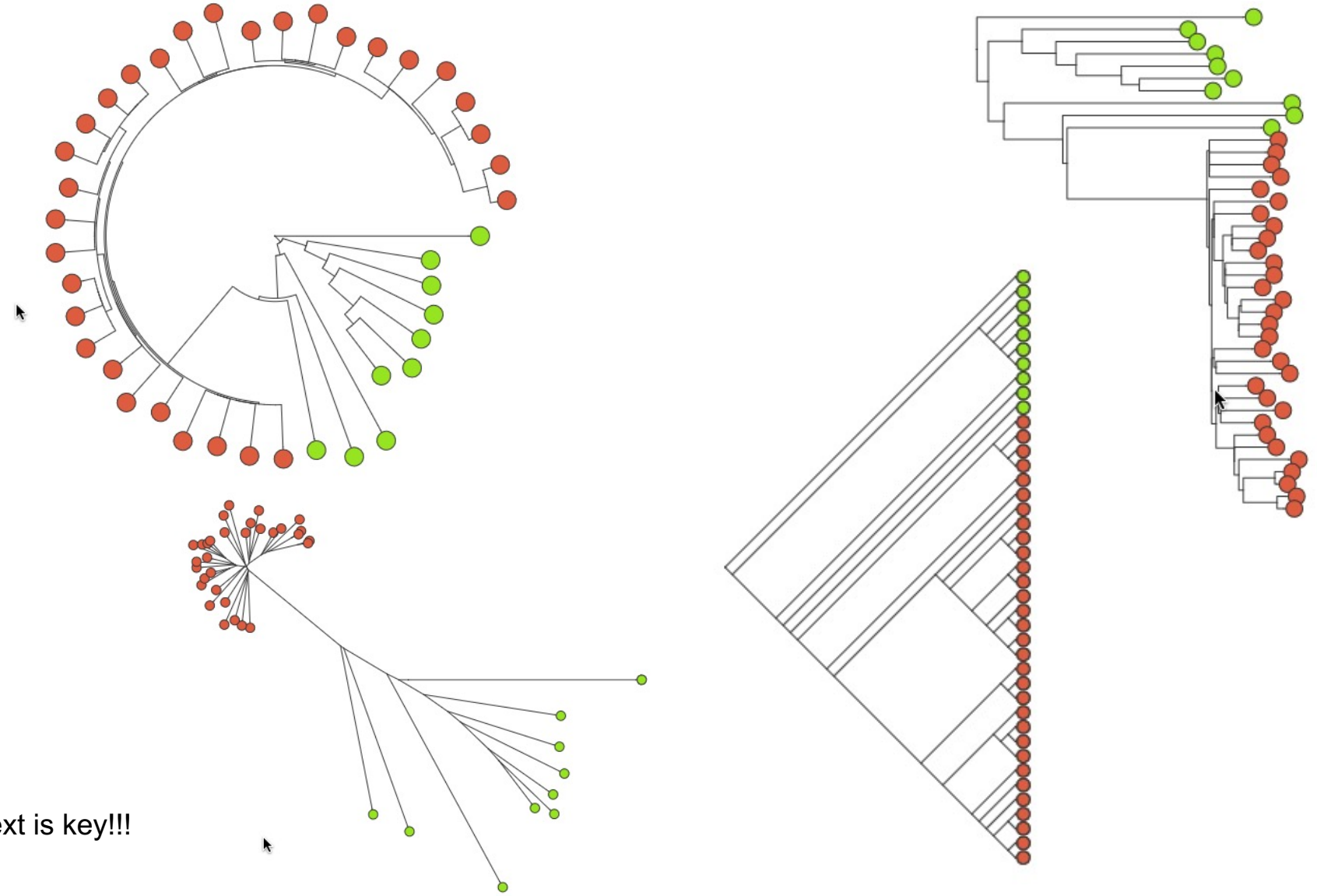
Genomic Epidemiology. Delivering assessment of risk





Microreact

Different views of same tree

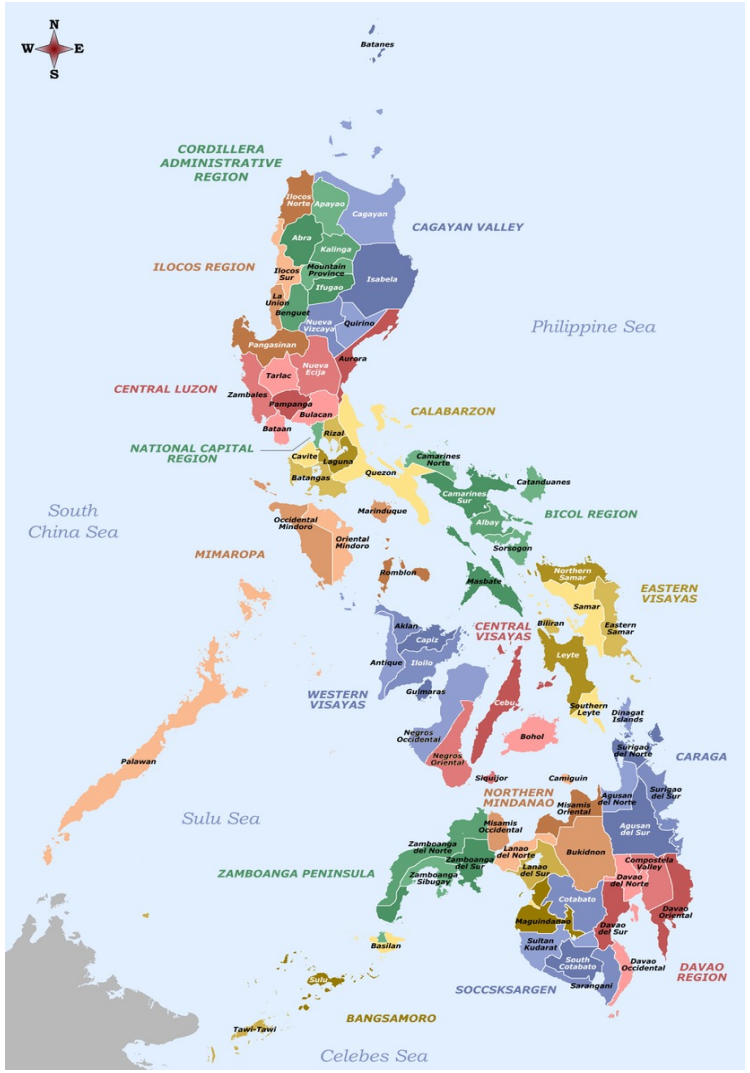


Context is key!!!

Two Applications:

1) Antimicrobial Resistance
2) COVID-19

Philippines AMR Surveillance Programme



Phillipines
Celia Carlos

30 year AMR surveillance

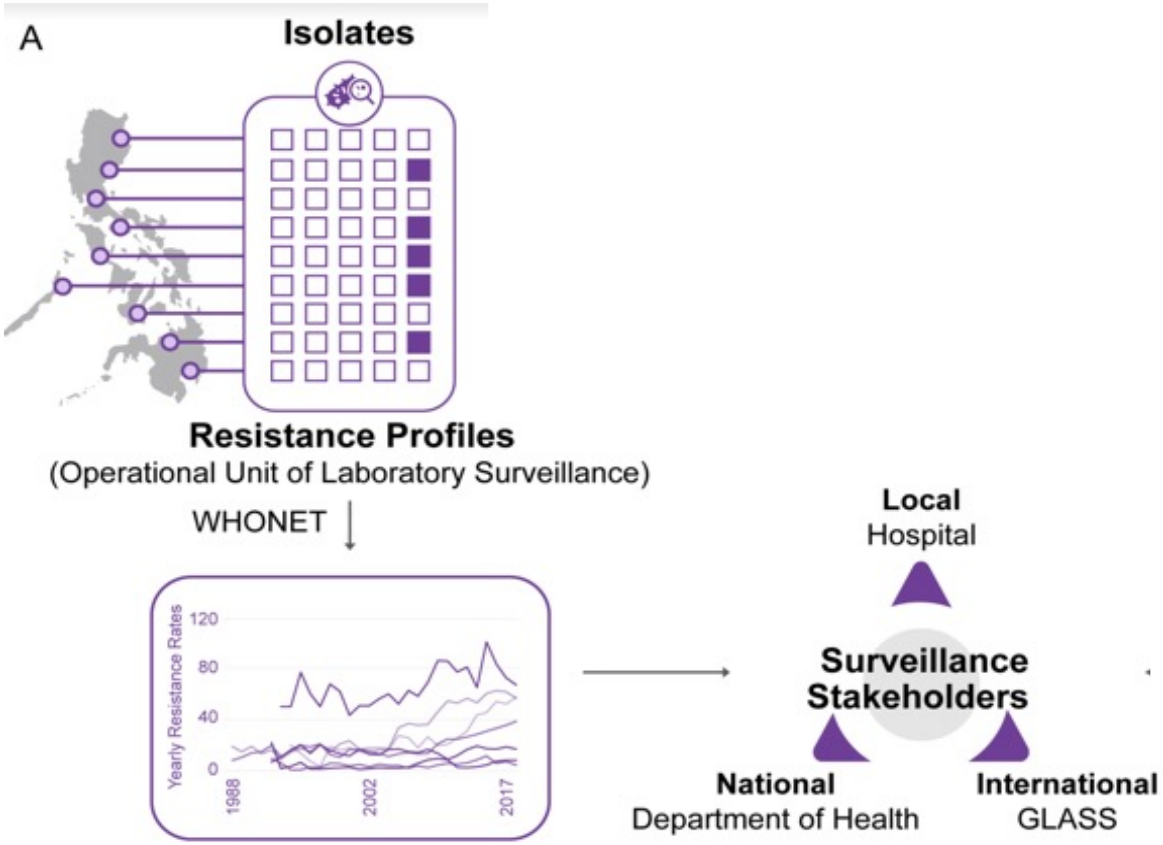
Phenotypic

Sentinel hospitals

WHO Priority pathogens

Annual report for bug-drug combinations

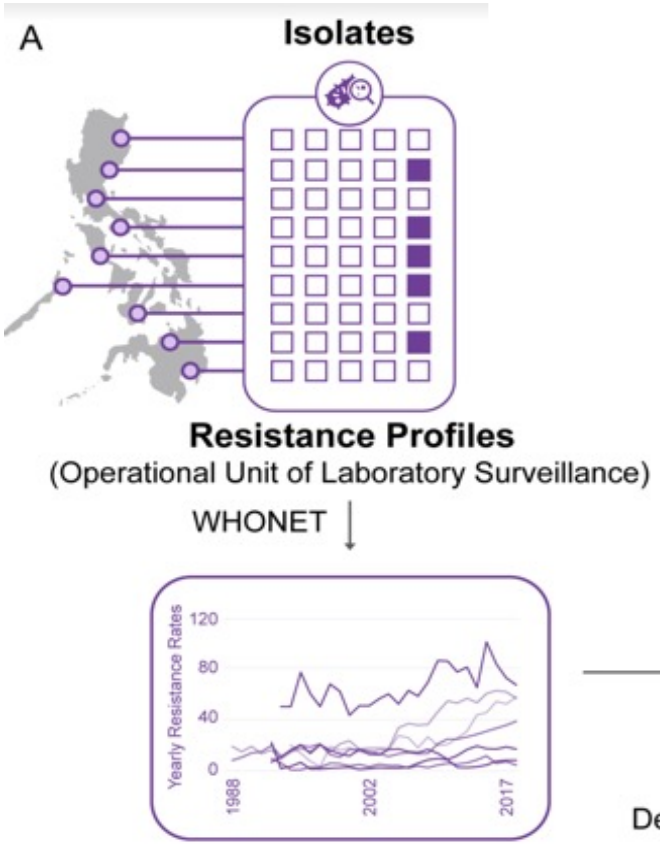
Enhancing National AMR Programmes through Genomics : See and Sequence



Phillipines
Celia Carlos

Argimon S *et al* (2019) Biorxiv

Enhancing National AMR Programmes through Genomics : See and Sequence



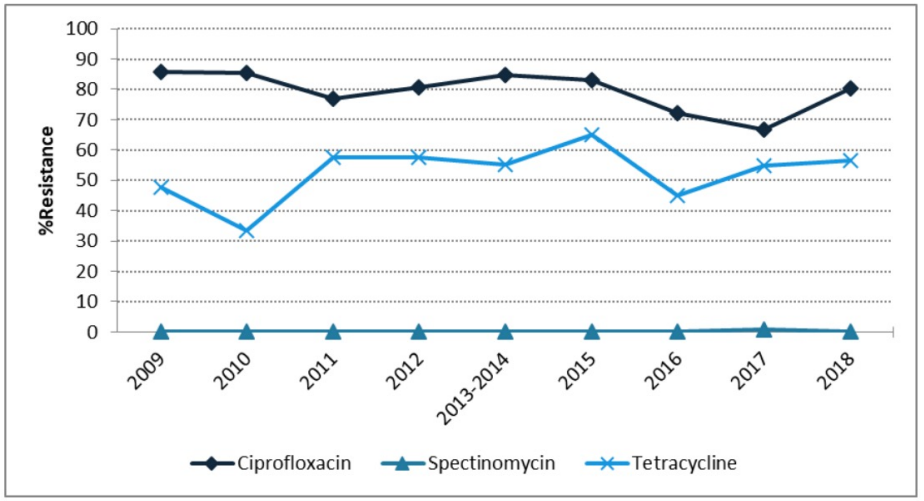
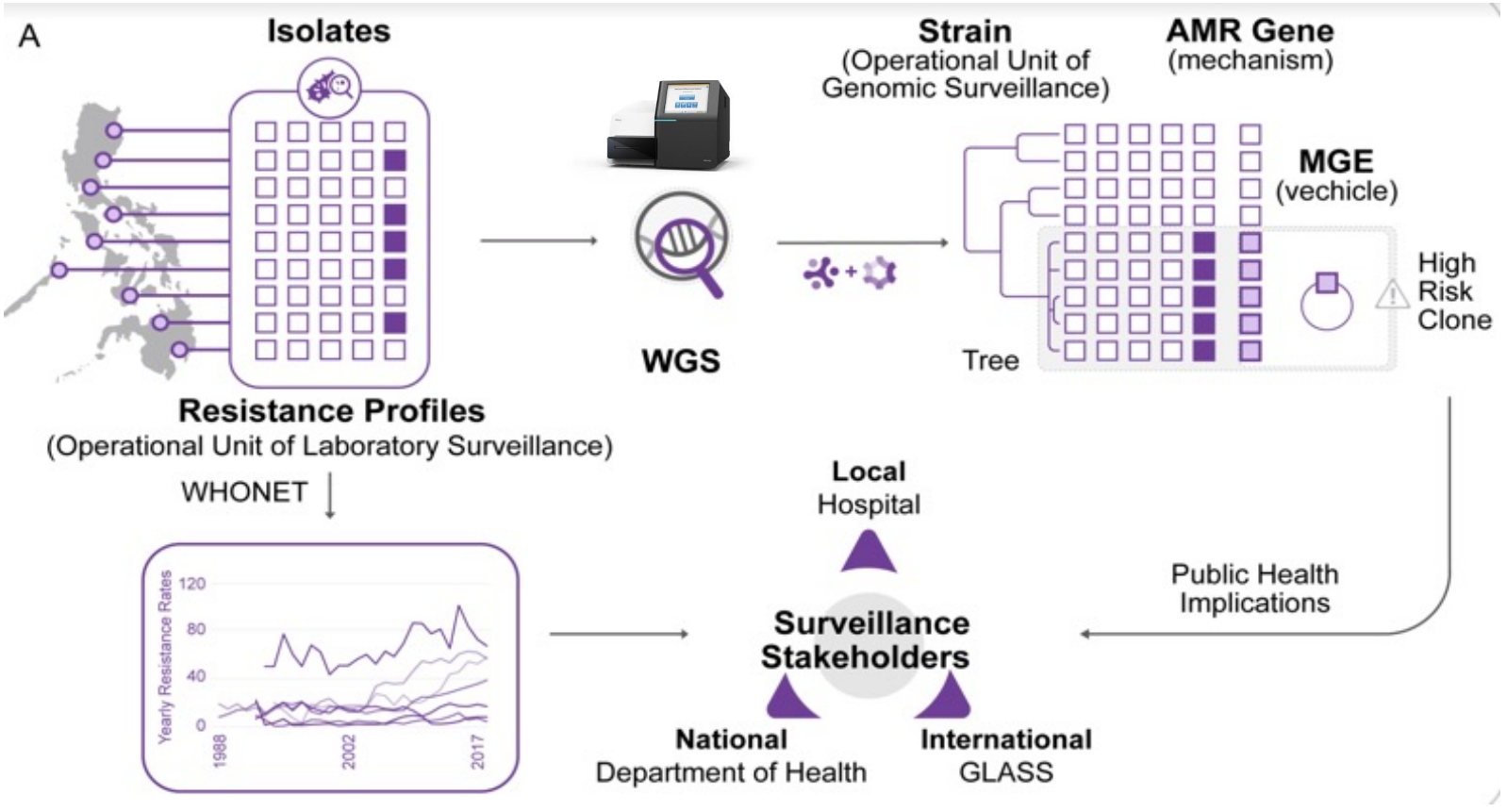


Figure 26. Yearly resistance rates of *Neisseria gonorrhoeae*, DOH ARSP, 2009-2018

Phillipines
Celia Carlos

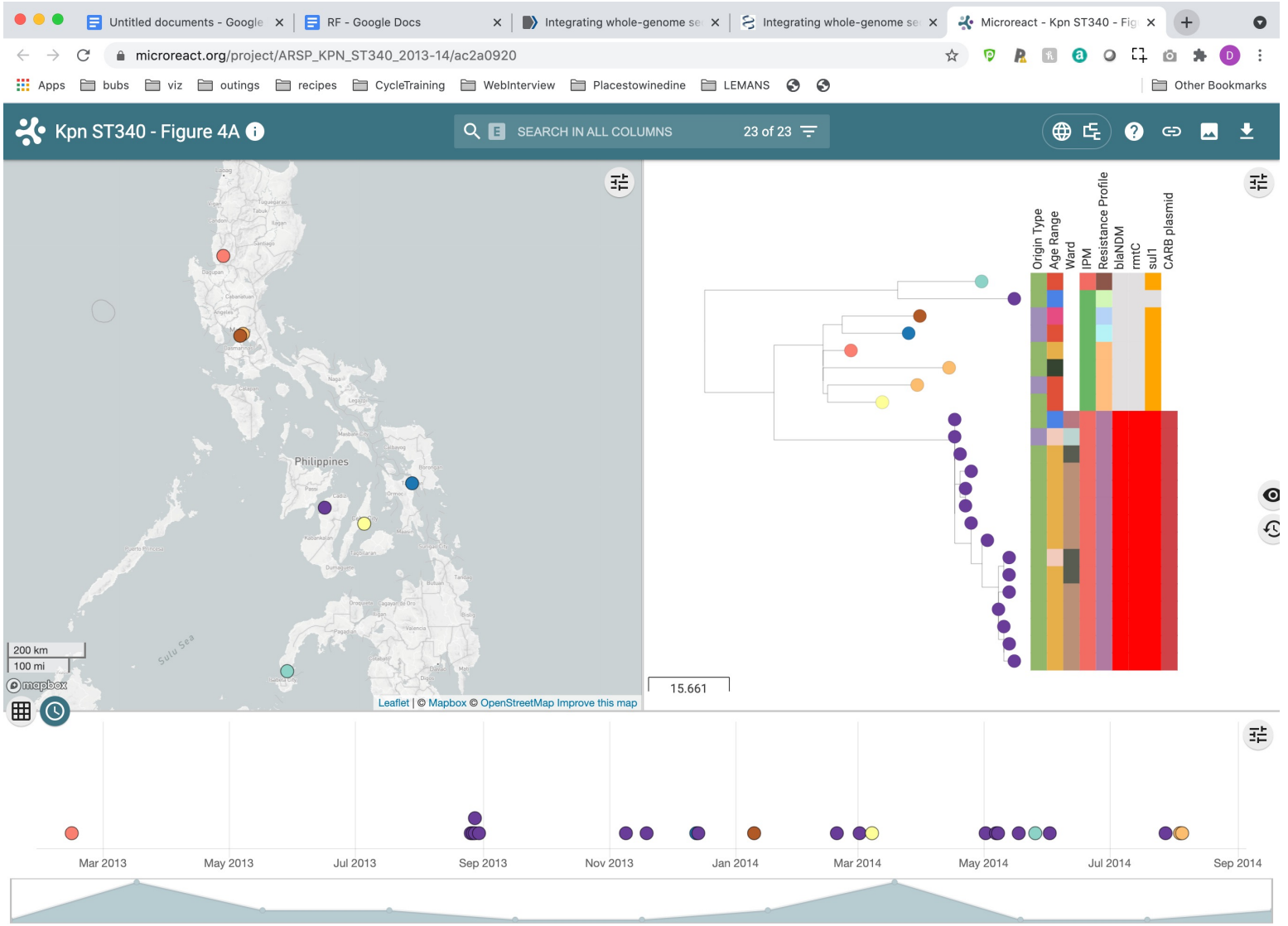
Argimon S *et al* (2020) Nature comms

Enhancing National AMR Programmes through Genomics : See and Sequence



Phillipines
Celia Carlos

Argimon S *et al* (2020) Nature comms



Argimon S *et al* (2020) Nature comms

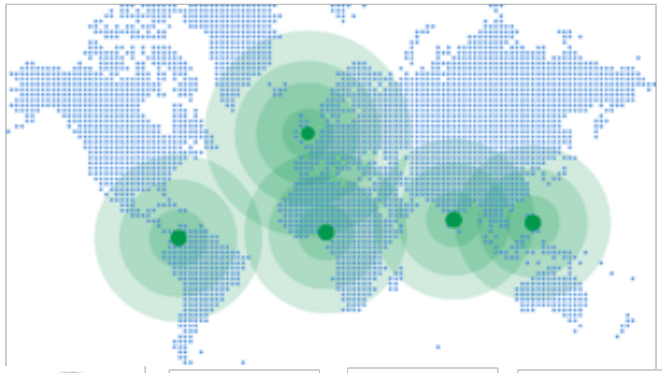
National Surveillance Labs - AMR - LMICs

Technical Support Modules - Reproducible

1. Laboratory
2. Bioinformatics
3. Data-Flow
4. Financial
5. Quality Assessment

ADVANCED COURSES+
SCIENTIFIC CONFERENCES

Microreact



Pathogenwatch

Colombia Pilar Godoy

Nigeria Iruka Okeke

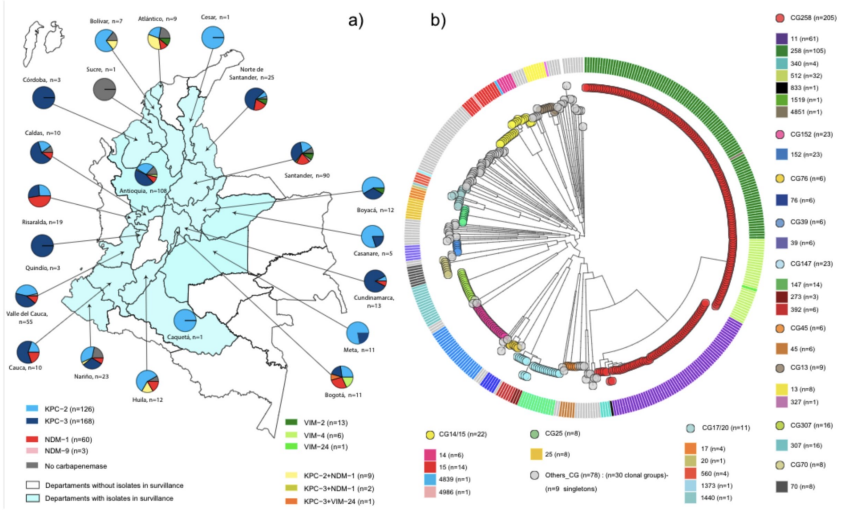
India Ravi Kumar

Phillipines Celia Carlos

Global Health Research Unit
Genomic Surveillance of AMR

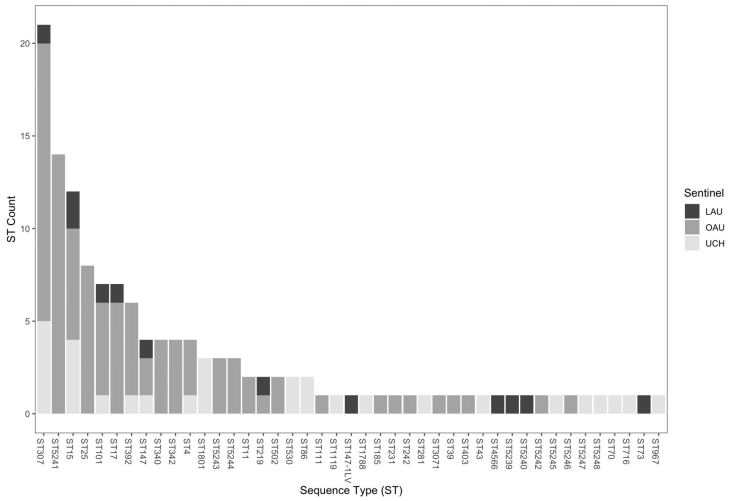
NIHR | National Institute for Health Research

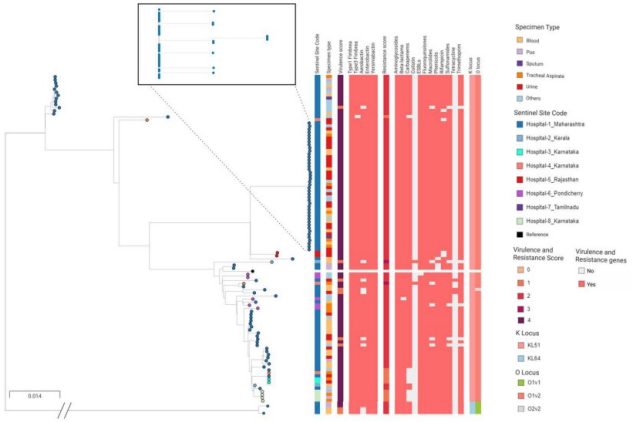
National Surveillance Labs - AMR



Colombia

Nigeria





India

Risk assessment / lineages / AMR

Common data platforms for local utility

Open data for international comparison

Bottlenecks

Data and data tools

Linking genomics to epidemiology

Rapid Interpretation

As well as political / supply chains expense etc..

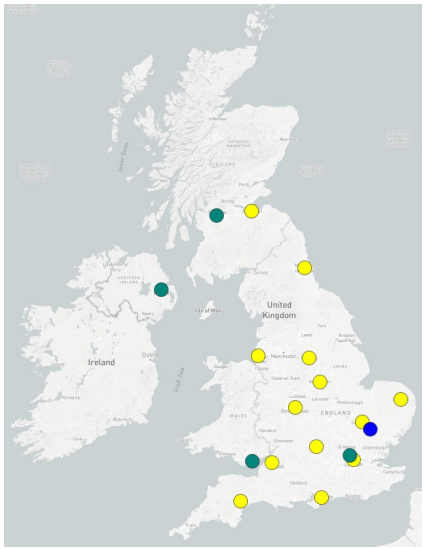
COVID-19

COVID-19 GENOMICS UK CONSORTIUM

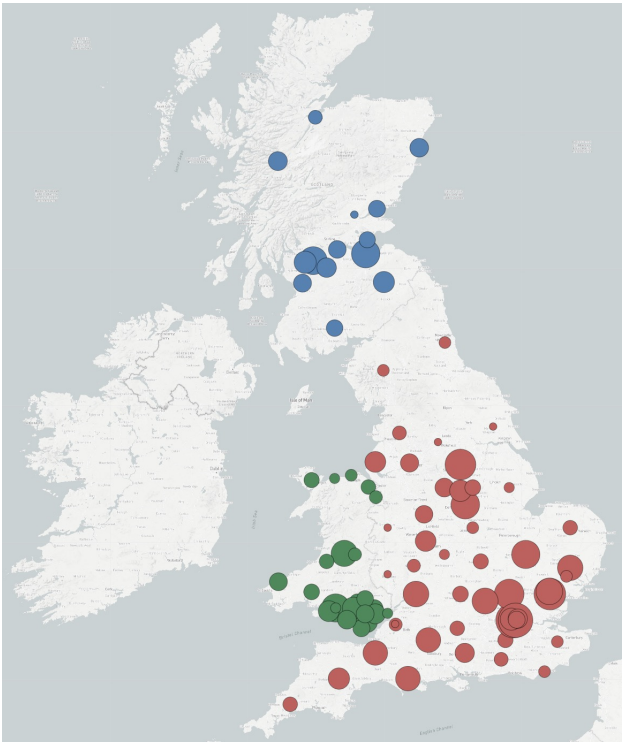
https://www.cogconsortium.uk/

The current COVID-19 pandemic, caused by the SARS-CoV-2 virus, represents a major threat to health.

The COVID-19 Genomics UK (COG-UK) consortium was created to deliver large-scale and rapid whole-genome virus sequencing to local NHS centres and the UK government.



GISAID – Global Repository



Department of Health & Social Care

wellcome

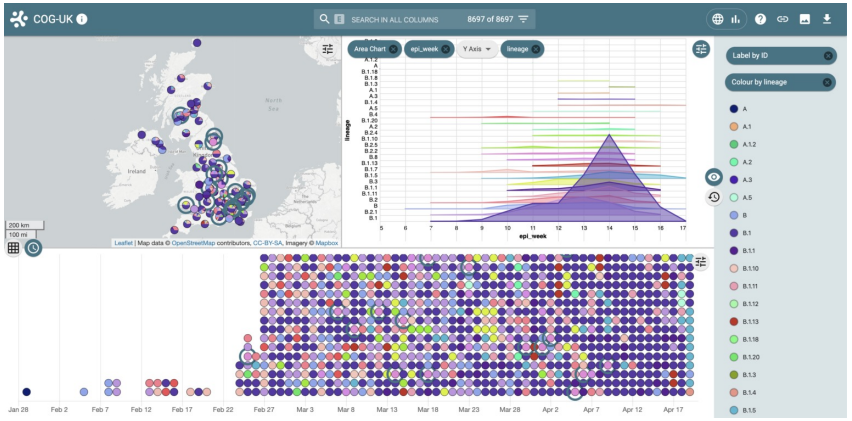
UKRI

UK Research and Innovation

Centre for Genomic Pathogen Surveillance

COG-UK

COVID-19
GENOMICS
UK CONSORTIUM



Open access and data sharing

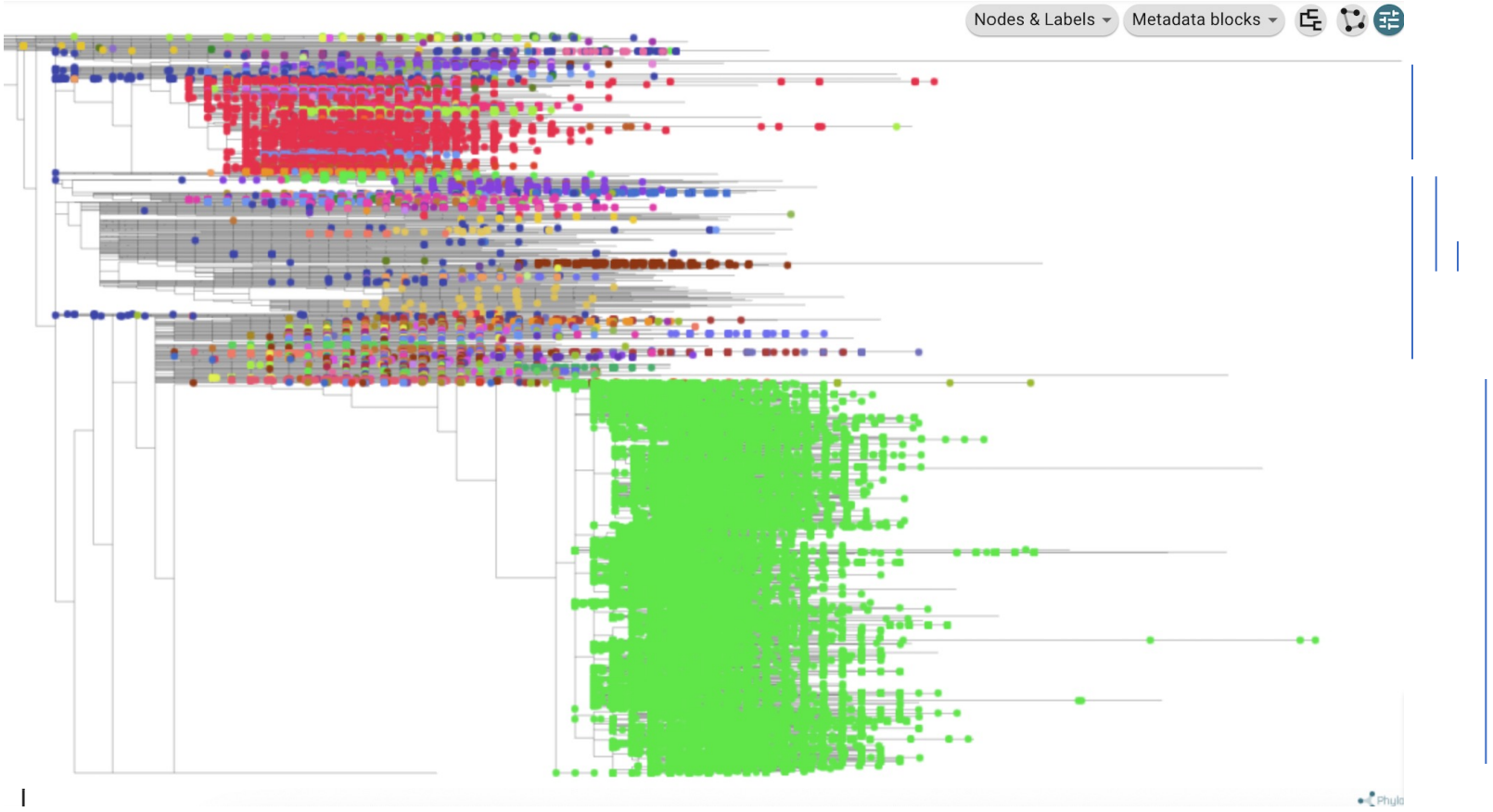
Data Linkage within NHS and PHX
Decentralised sequencing
Linkage to mobile data
Linkage to contact tracing etc.

Identification and monitoring of lineages - Pangolin
- monitor removal of interventions

COG-UK

COVID-19
GENOMICS
UK CONSORTIUM

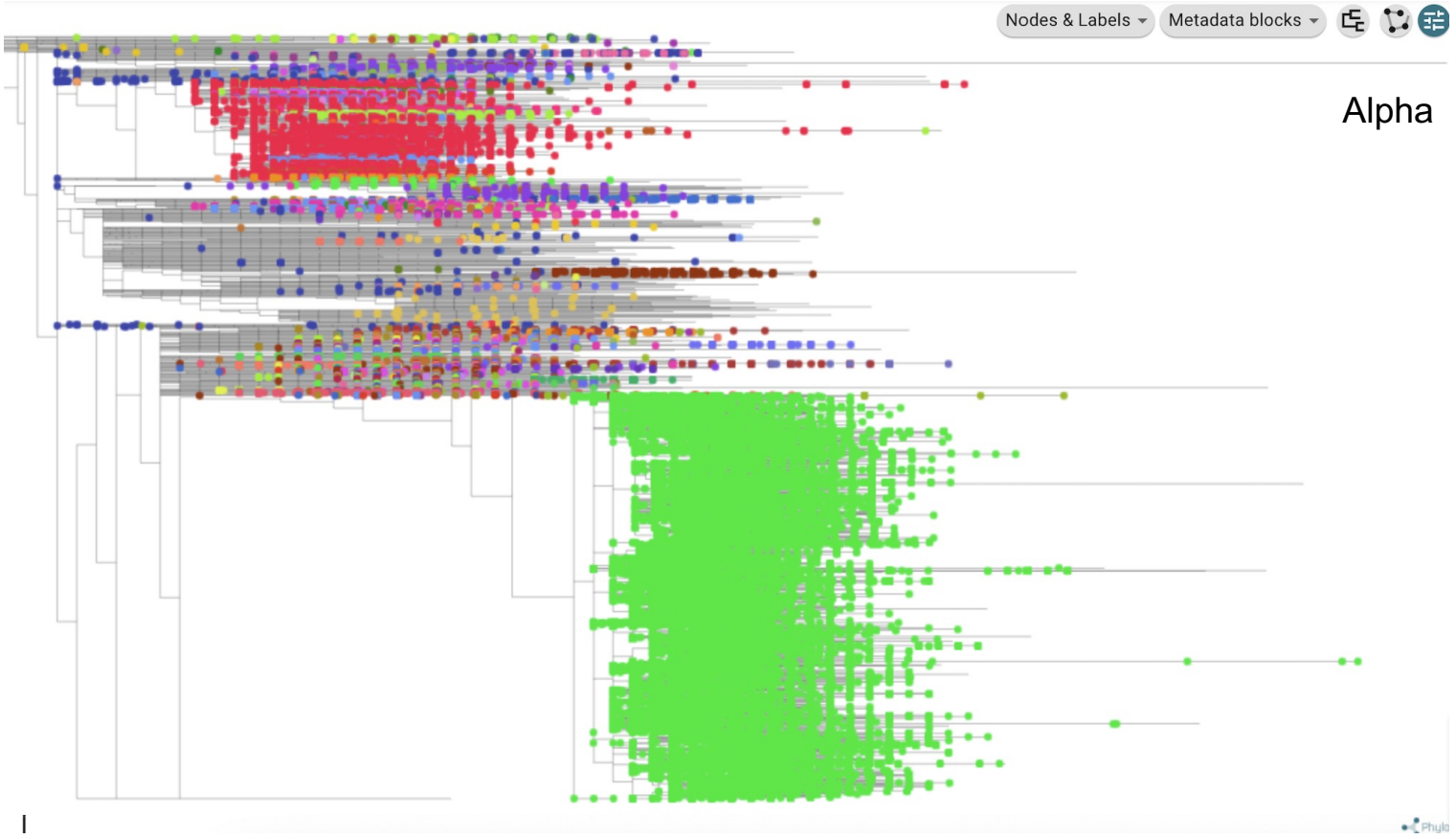
Tree of 532957 genomes



COG-UK

COVID-19
GENOMICS
UK CONSORTIUM

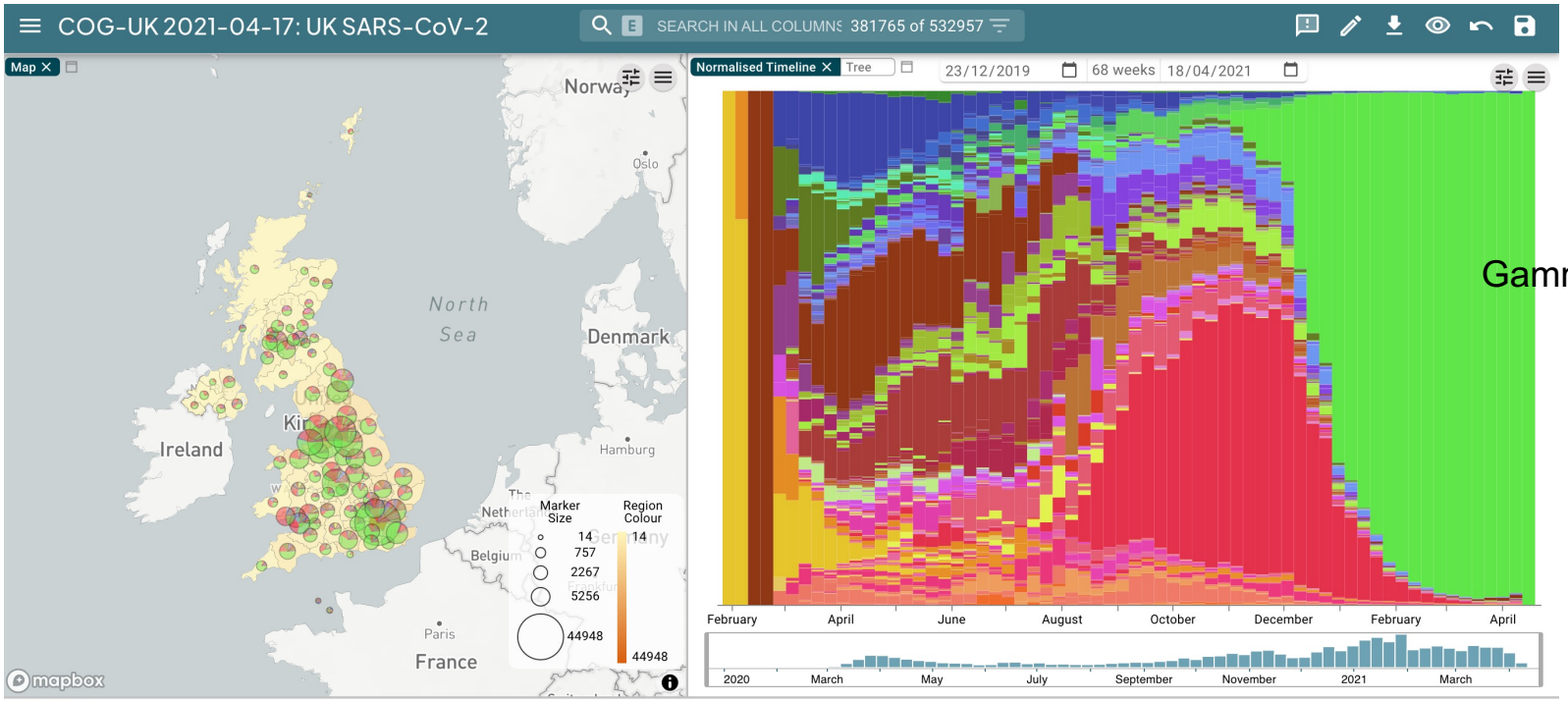
Tree of genomes



COG-UK

COVID-19 GENOMICS UK CONSORTIUM

https://microreact.org/project/cogconsortium



Gamma

Metadata

	sequence_n...	sample_date	epi_week	country	adm1	submission...	pillar_2	lineage	lineage_sup...	uk_lineage	primary_uk_...	d614g	n439k	p3
☐	COG613463	09/04/2021	67	UK	UK-ENG	SANG	True	B.1.1.7	1	UK1534	UK1534	G	N	L
☐	COG543180	09/04/2021	67	UK	UK-ENG	SANG	True	B.1.1.7	1	UK1534	UK1534	G	N	L
☐	COG928498	09/04/2021	67	UK	UK-ENG	SANG	True	B.1.1.7	1	UK1534	UK1534	G	N	L
☐	COG981659	09/04/2021	67	UK	UK-ENG	SANG	True	B.1.1.7	1	UK1534	UK1534	G	N	L
☐	COG586921	10/04/2021	67	UK	UK-ENG	SANG	True	B.1.1.7	1	UK1534	UK1534	G	N	L
☐	COG765797	09/04/2021	67	UK	UK-ENG	SANG	True	B.1.1.7	1	UK1534	UK1534	G	N	L

Bottlenecks

Data and data tools

Linking genomics to epidemiology

Rapid Interpretation

As well as political / supply chains expense etc..

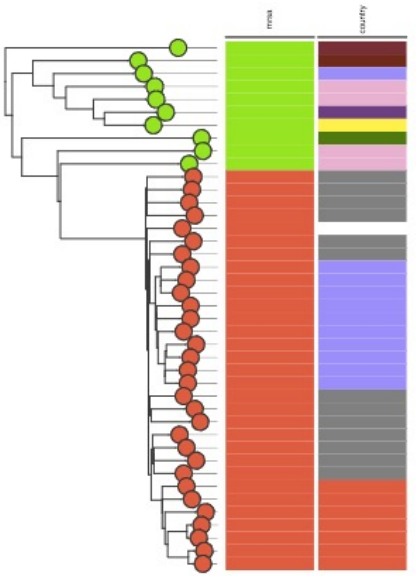
Pivotting Learnings

Horizontal data processes

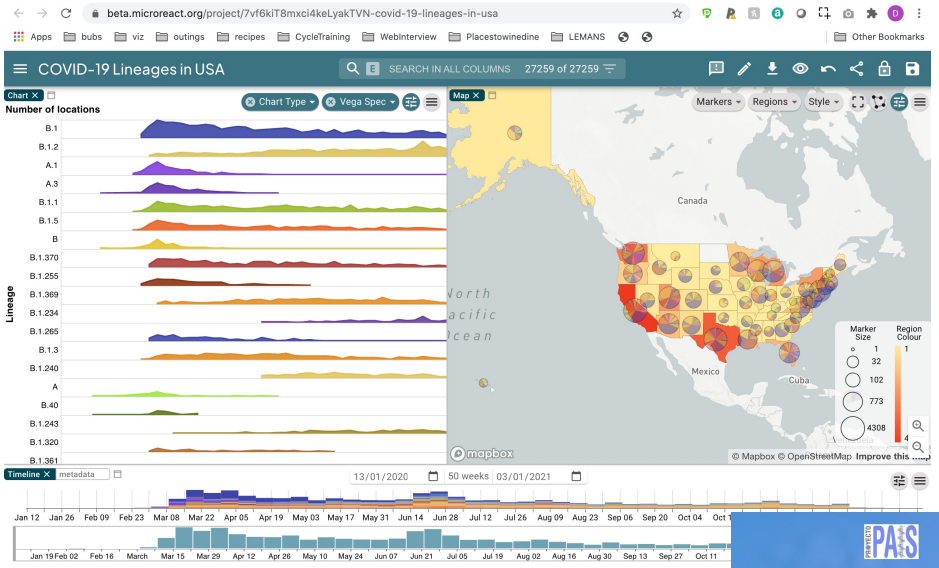
- Trees
- Maps
- Time
- Epi Variables

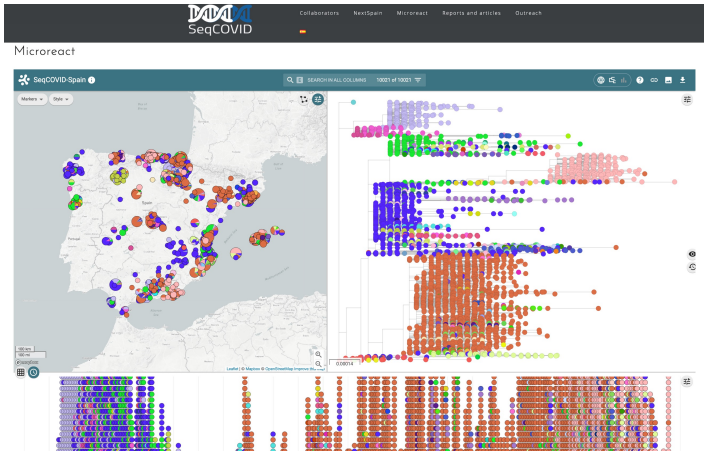
Vertical application

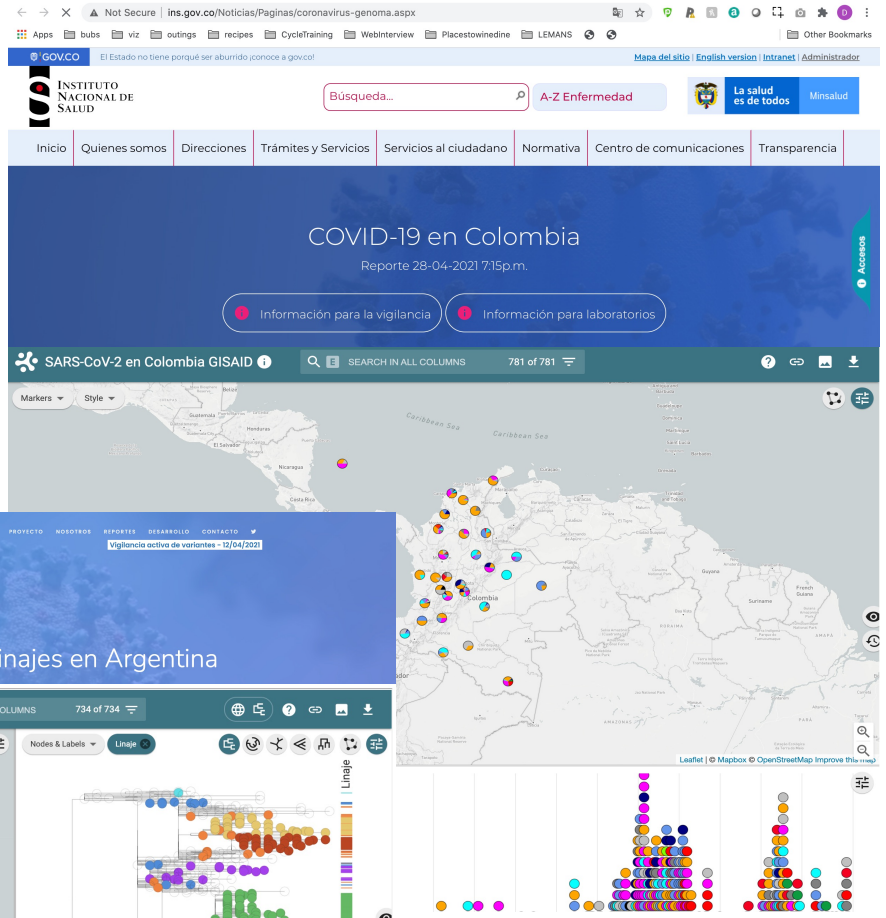
- SARS-CoV-2
- AMR



Global Health Research Unit
Genomic Surveillance of AMR

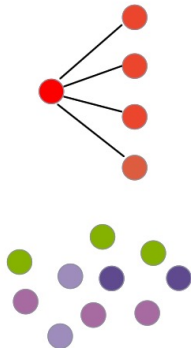






Centre for Genomic Pathogen Surveillance

Genomic Data Landscape



	COVID	ABR
Type	Viral (SARS-CoV-2)	Bacterial
Clone / lineage	Pangolin (b.1.1.7 etc)	MLST / cgMLST / Genotyphi etc etc..
Risk markers	mutations of note	AMR determinants / genes / SNP. Many more – serotype etc..

Process is conceptually the same - horizontal data processes delivered for vertical organisms

World Health Organization

Priority 1: CRITICAL#

Acinetobacter baumannii, carbapenem-resistant

Pseudomonas aeruginosa, carbapenem-resistant

Enterobacteriaceae*, carbapenem-resistant, 3rd generation cephalosporin-resistant

Priority 2: HIGH

Enterococcus faecium, vancomycin-resistant

Staphylococcus aureus, methicillin-resistant, vancomycin intermediate and resistant

Helicobacter pylori, clarithromycin-resistant

Campylobacter, fluoroquinolone-resistant

Salmonella *spp.*, fluoroquinolone-resistant

Neisseria gonorrhoeae, 3rd generation cephalosporin-resistant, fluoroquinolone-resistant

Priority 3: MEDIUM

Streptococcus pneumoniae, penicillin-non-susceptible

Haemophilus influenzae, ampicillin-resistant

Shigella *spp.*, fluoroquinolone-resistant

*Mycobacteria* (including *Mycobacterium tuberculosis*, the cause of human tuberculosis), was not subjected to review for inclusion in this prioritization exercise as it is already a globally established priority for which innovative new treatments are urgently needed.

***** Enterobacteriaceae include: *Klebsiella pneumonia*, *Escherichia coli*, *Enterobacter* spp., *Serratia* spp., *Proteus* spp., and *Providencia* spp, *Morganella* spp.

Pathways to Implementation

Global Health Research Unit
Genomic Surveillance of AMR

Global Action Plan
|
National Action Plans
|
Local delivery of value

Technical Support Modules - Reproducible

1 Laboratory | 2 Bioinformatics | 3 Data-Flow | 4 Financial

5 Quality Assessment — ADVANCED COURSES+ SCIENTIFIC CONFERENCES

Shared data Infrastructure

Data tools for local value

Aggregating data stores for national / regional action

Global understanding / trends / surveillance

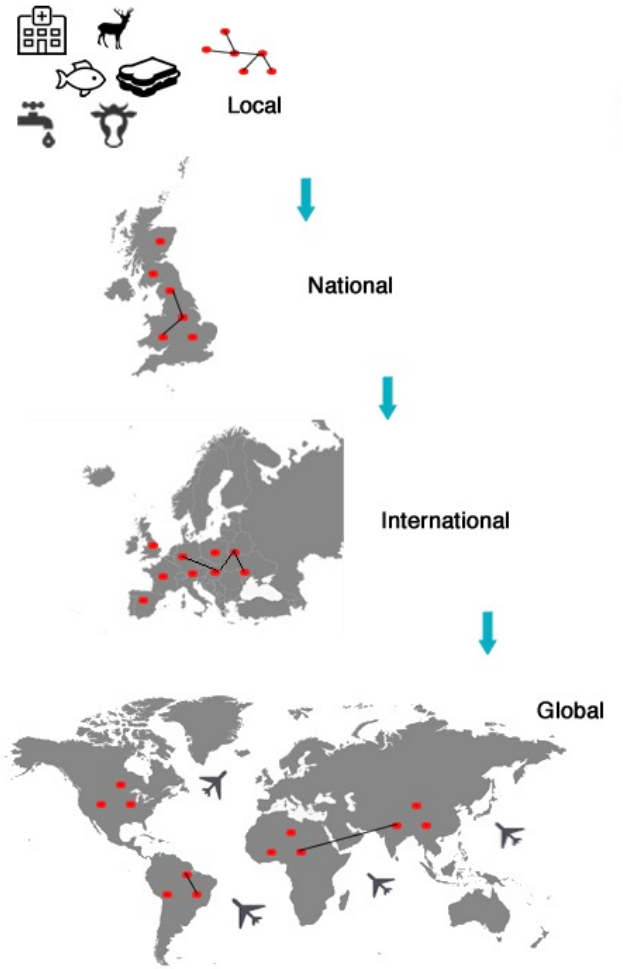
Shared data Infrastructure

Data tools for local value

Aggregating data stores for national / regional action

Global understanding / trends / surveillance

Shared data Infrastructure – value up/down info chain



Data tools for local value
Rapidly return risk

Aggregating data stores for national / regional action

Global understanding / trends / surveillance
eg GLASS / INSDC databases

Use Cases - Translational Tools

1) Local

Markers for local decision making

Genome Report
Yes / No

E.g. AMR / virulence

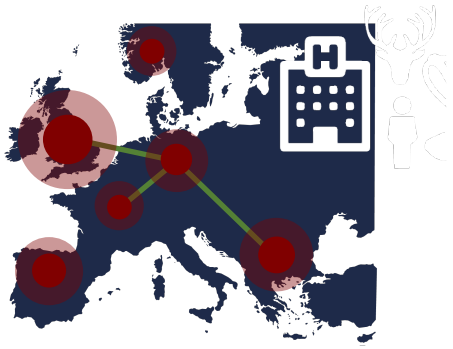
Use Cases - Translational Tools

1) Local

Markers for local decision making

Genome Report
Yes / No

2) Regional



Outbreaks, transmission Within location / cross-border

Clustering and rapid reporting

E.g. AMR / virulence

TIME AND DATA FLOW

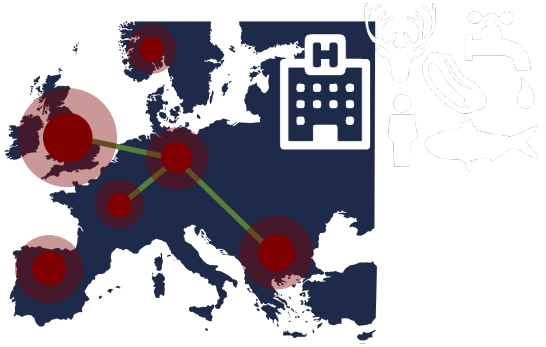
Use Cases - Translational Tools

1) Local

Markers for local decision making

Genome Report
Yes / No

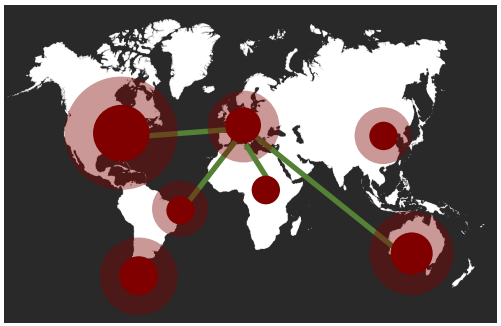
2) Regional



Outbreaks, transmission Within Hospital / cross-border

Clustering and rapid reporting

3) Global



Emergence and spread of new lineages of risk

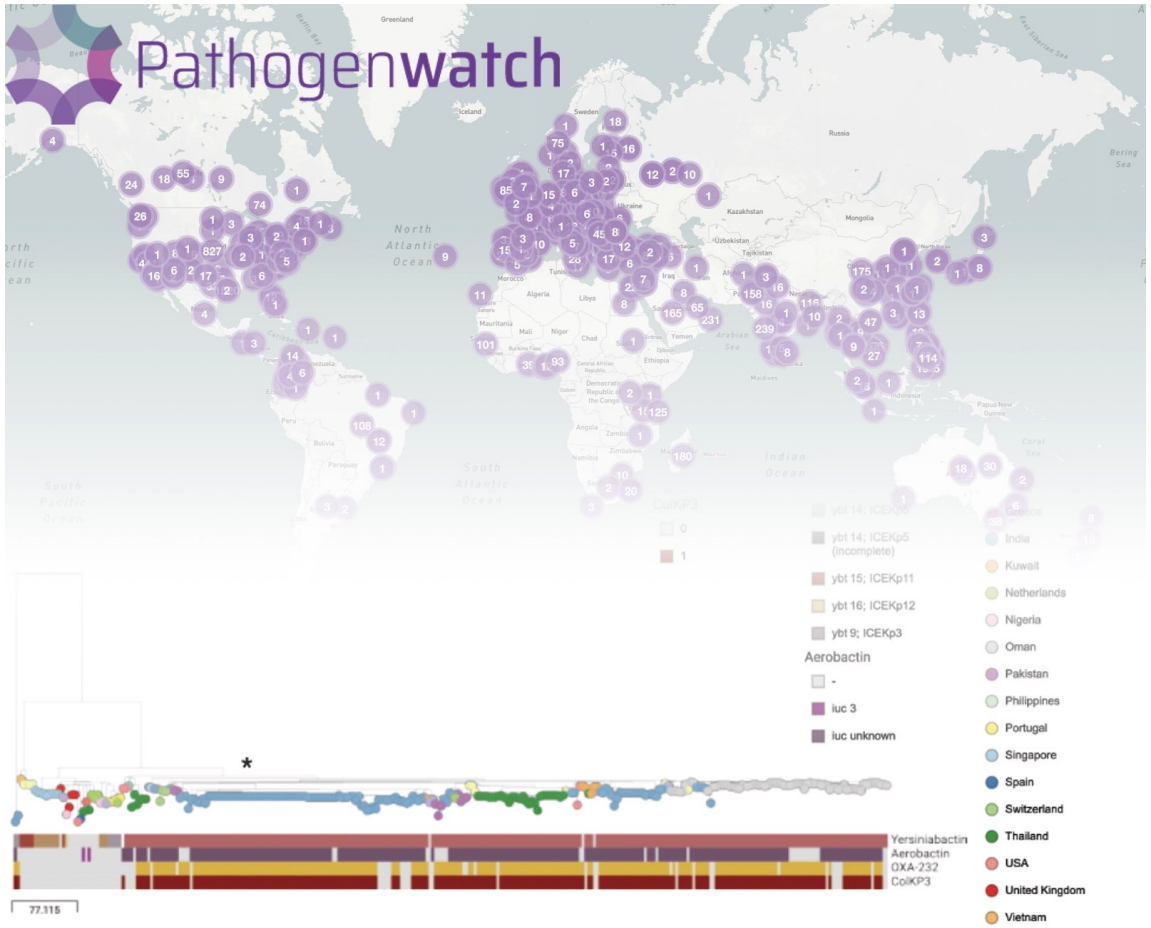
Monitoring & Reporting Learning and Alerting

E.g. AMR / virulence

TIME AND DATA FLOW

Vaccine design / intervention / impact

https://Pathogen.Watch – process genomic / epi data



Upload raw genome data – risk assessment

Local and regional context

Global monitoring

Pathways to Implementation

Global Action Plan
|
National Action Plans
|
Local delivery of value

Enhanced momentum around COVID-19 MUST be harnessed

Team

SUPPORTED BY NIHR | National Institute for Health Research

Global Health Research Unit
Genomic Surveillance of AMR

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https://pathogensurveillance.net