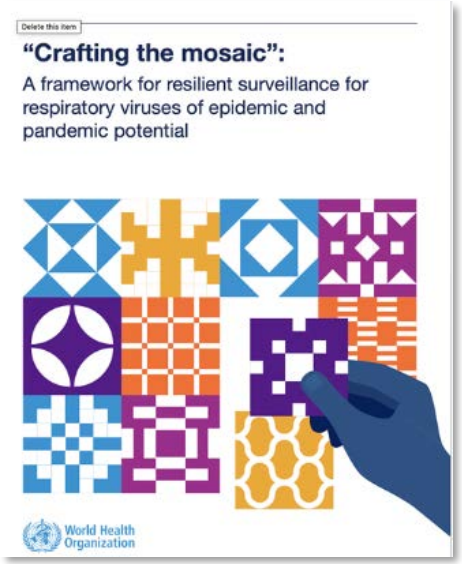
UK Health Security Agency

The vision of respiratory surveillance in the post-pandemic era

GIHSN Annual Meeting
25 – 26 November 2024

Prof. Maria Zambon

Collaborative Surveillance: data collection, analysis and sharing



Across Diseases & Threats, Sectors, Event Lifecycle, Geographies

1.1 Strengthened integrated disease, threat & vulnerability surveillance

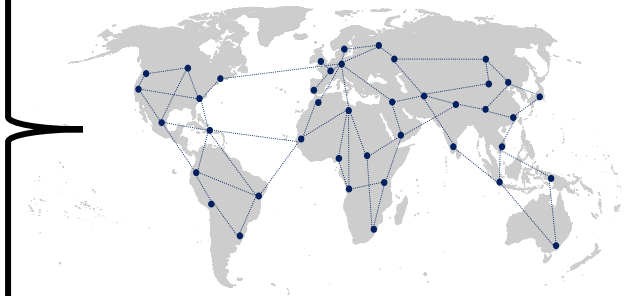
Integrated public health, health system, One Health, contextual and community surveillance, with collaborative governance and integration

1.2 Diagnostic and laboratory capacity for pathogen & genomic surveillance

Expanded laboratory capacity including genomics, decentralized testing, risk-based biosafety and biosecurity with integrated lab networks

1.3 Collaborative approaches for risk assessment, event detection & response monitoring

Scalable architecture for integration, tools for analysis and sharing, integrated data visualization and enhanced networks for collaboration

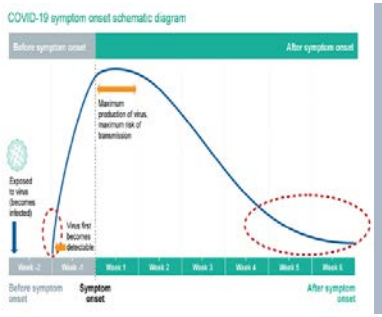


Better decisions

Lessons from Pandemic 1

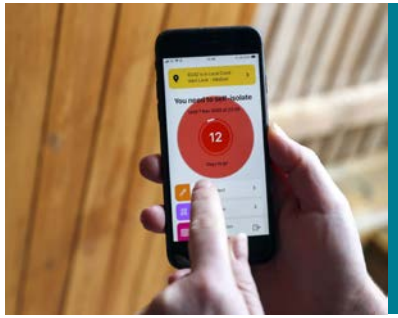
Societal Expectations about testing arrangements

Public engagement & awareness



Understanding scientific basis of testing

Access to testing (Location & purchase)

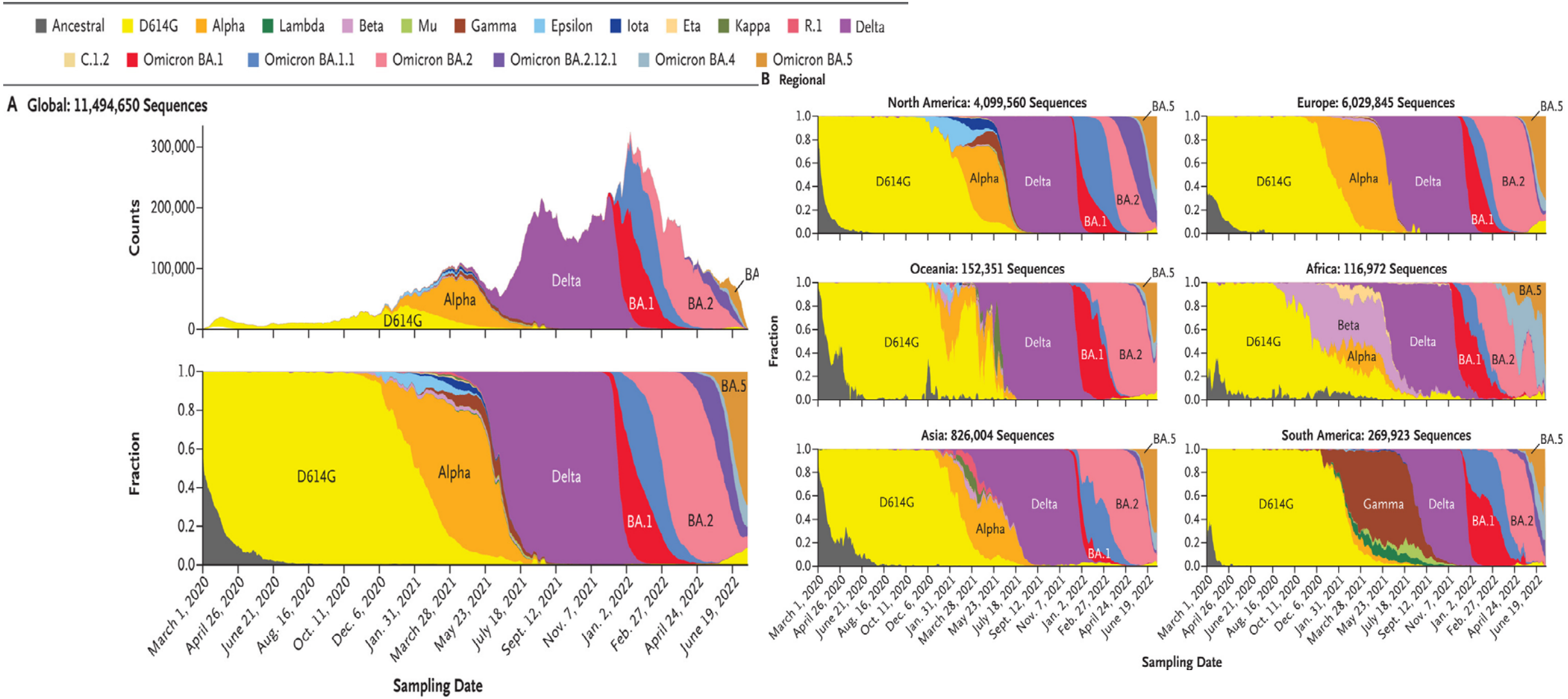


Results going directly to patient

Different types of tests
Home tests

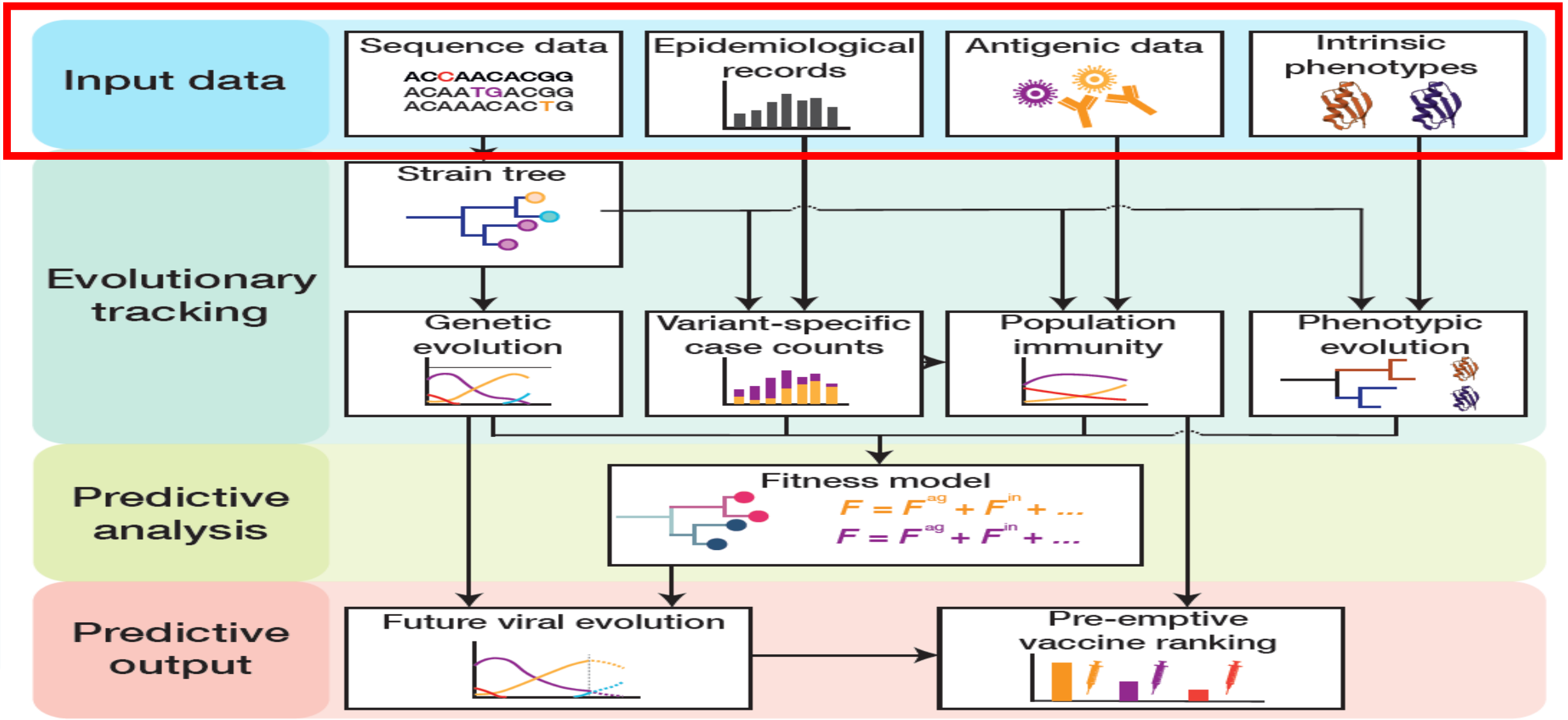
Explanations of limitations of testing

Massive expansion of sequence data
SARS-CoV-2 variants - tracking viral diversity



Barouch. *Covid-19 Vaccines — Immunity, Variants, Boosters*. New England Journal of Medicine. 2022. DOI: 10.1056/NEJMra2206573

Moving towards prediction of virus evolution



Meijers et al, 2024 Concepts and methods for predicting viral evolution arXiv:2403.12684

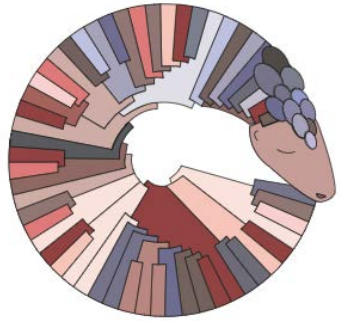
Lessons of pandemic 2: sharing, consensus, pooling, linkage

Affordability, sizing

GISAID – Sequence Sharing

Over 20,000,366 sequences shared via GISAID since 10 January 2020.

Agreement on information handling
PANGOLIN lineage assignment



Multinational Studies: Pooled analysis
RECOVERY Trial

Randomised Evaluation of COVID-19 Therapy

Data Linkage / Hospital Informatics

The Sunday Telegraph

Vaccines effective against Indian variant

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 12, 2021 VOL. 385 NO. 7

Effectiveness of Covid-19 Vaccines against the B.1.617.2 (Delta) Variant

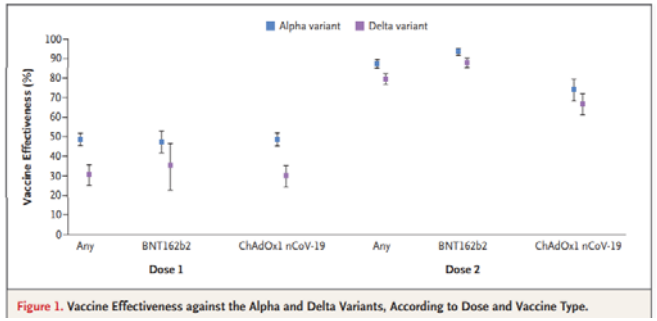
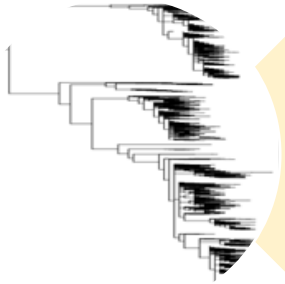


Figure 1. Vaccine Effectiveness against the Alpha and Delta Variants, According to Dose and Vaccine Type.

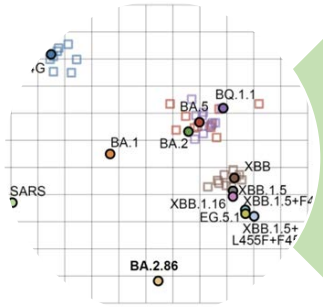
Era of genomic surveillance : Influenza, SARS, RSV
Genotype to phenotype – predict & confirm



Virus (sub)type, lineage, signatures

Relevant to disease burden

https://www.gisaid.org | https://nextstrain.org/flu/seasonal/ | https://flusurver.bii.a-star.edu.sg

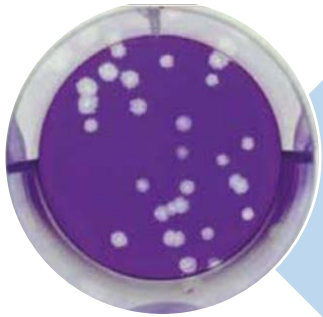


Antigenic properties

Relevant to vaccines

Substitutions near the receptor binding site determine major antigenic change during influenza virus evolution

Koel et al., Science 342:976-9. 2013.



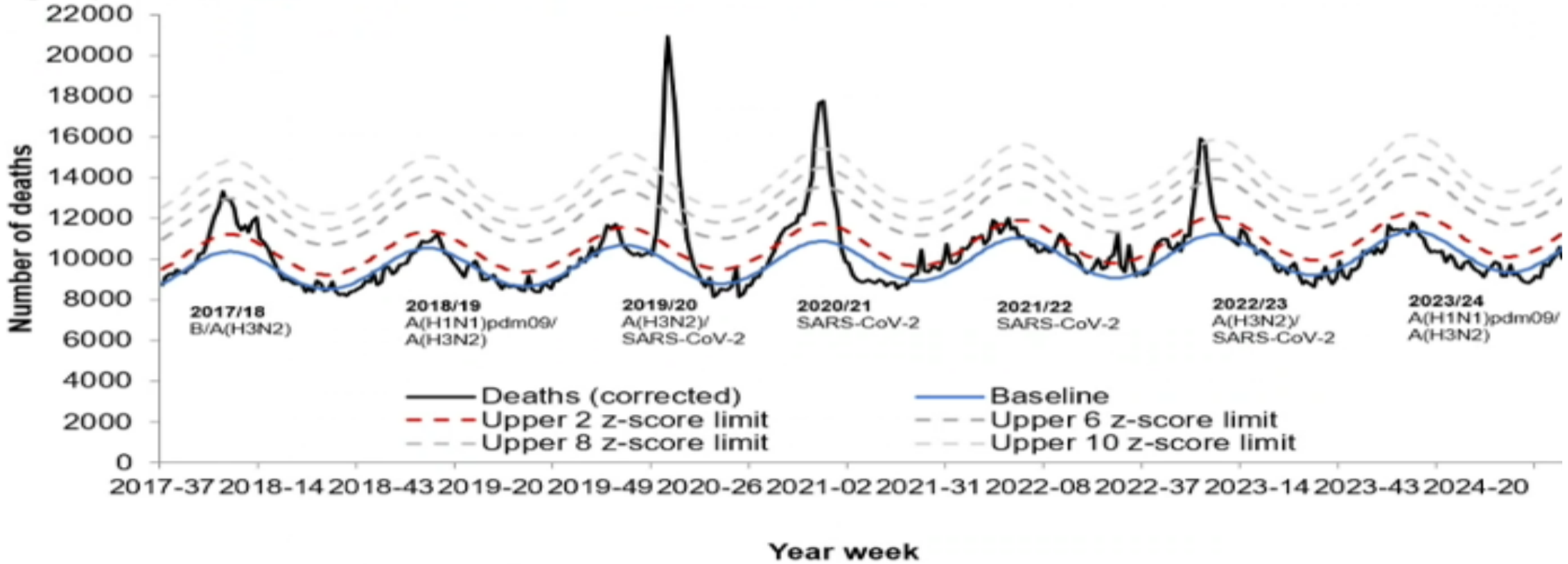
Drug resistance (M2, NA, polymerase inhibitors)

Relevant to antiviral usage

Susceptibilities of human influenza viruses to licensed antivirals
Takashita et al., Antiviral Res 175:104718. 2020.

Why ? Prevent premature deaths

Figure 1. Weekly observed and expected number of all-cause deaths in all ages, with the dominant circulating respiratory virus, England, 2017 to week 43 of 2024



Note: the recent weeks' data are estimates which may be subject to registration delay corrections and therefore should be interpreted with caution. These estimates may differ in future reports as more deaths are registered.

https://www.euromomo.eu/

Trends that impact surveillance capabilities
Divergence between testing & surveillance

- Prioritisation: Best use of funding
- Sustainability…building durable systems
- Affordability….right size of surveillance
- Technology changes.
- Information sharing capability

Evolutionary pressure
Local health care systems
Affected by trends

Healthcare Efficiency

- Changes post pandemic
- Syndromic approach for testing
- Bundle testing key infections together
- Commercial test provision with multiple parallel testing

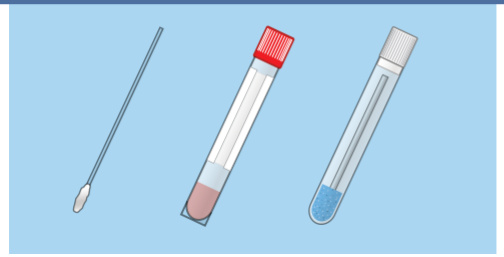
Secondary care

- Test at point of admission
- Test and treat options
- Simple equipment
- Automated read outs
- Non lab staff
- Infection control improvements

SARS, Influenza, RSV

Innovation in diagnostic testing pathways

Sampling from patient



- Smart swab materials
- New media for transport
- Different biological samples
- Self-sampling

Environmental Detection

- Wearable detectors
- Smart watches/clothing
- Smart swab materials

Detection near the patient

- Portable instrumentation
- Mobile testing units
- Combination with mobile phones
- Biosensor Development
- Signal transduction improvement
- Microfluidic devices
- Individual sample sequence analysis

Complex laboratory testing capability

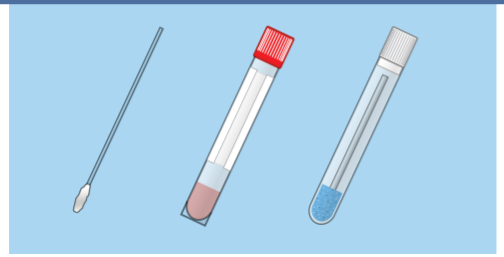
- Newer technologies (LAMP)
- Increasing use of sequencing technologies
- Multiplex (multi-analyte testing)
- Use of biomarkers to predict infection

Data and analytics pathways

- Creation of data linkages
- Cloud uploads
- Global databases
- Real time tracking

Health care efficiency:impact on surveillance

Sampling from patient



Lack of virus culture
Loss of biological information

Environmental Detection

Relationship to infection and cases
Which signals to act upon

Detection near the patient

Loss of data capture for surveillance

Complex laboratory testing capability

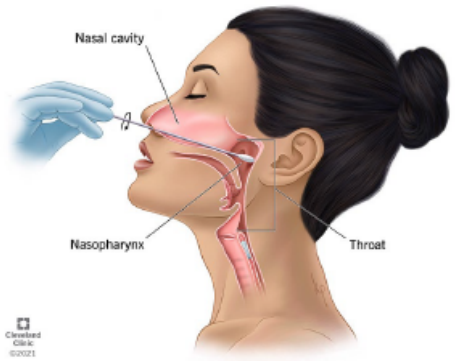
Parallel testing
Understanding Co-infections

Data and analytics pathways

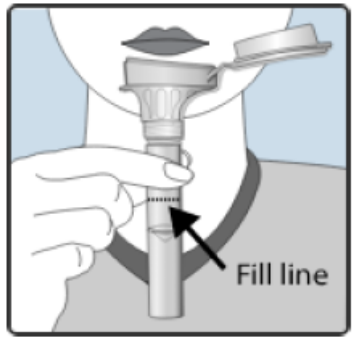
Complex data flows
Information governance

Swab materials

Preferred sample type
- Nasal swab
- Nasopharyngeal swab
- +/- throat swab



Non-Preferred sample type
- Saliva
- Throat swab alone



Standard transport medium
- Good for virus culture
- Good for RT-PCR
- Good for sequencing

UTM/VTM

Molecular/Inactivation medium
- NO Good for virus culture
- Good for RT-PCR
- Good for sequencing

Eg. Thermo Fisher InhibiSURE Viral Inactivation Medium

Dry flocked swabs
- Poor for virus culture
- Good for RT-PCR
- Good for sequencing

Use of host biomarkers : FebriDx

- Lateral flow technology, disposable device
- FDA approved and CE marked
- 10 minutes. £11-12 per test
- Test for CRP (20mg/L) and MxA (40ng/ml)
- Studies suggest good accuracy for bacterial and viral infection across a range of settings
- No sampling for microorganism detection

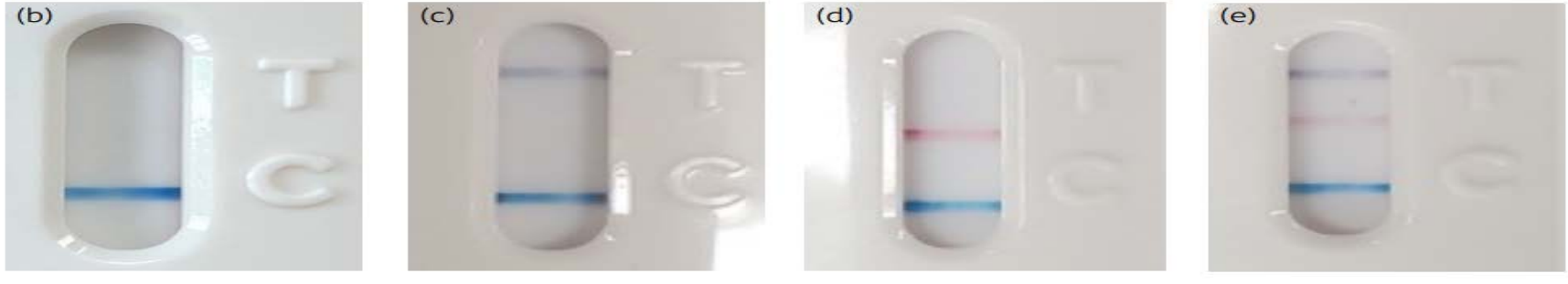


Figure 1. The FebriDx® device and its possible results. (a) The FebriDx® device. (b) Negative result with control line. (c) CRP-only positive. (d) MxA-only positive. (e) CRP and MxA positive. Figures 1b–e supplied by Lumos Diagnostics, USA. This figure appears in colour in the online version of *IAC* and in black

ED triage. March 2022-2023. n=5426

Co-circulation of SARS-CoV-2, Influenza, and RSV

All three viruses combined

Sensitivity	1481/1675	88.4	86.8–89.9
Specificity	2507/3751	66.8	65.3–68.3
PPV	1481/2725	54.3	52.5–56.2
NPV	**2507/2701**	**92.8**	**91.8–93.7**
Prevalence	1675/5426	30.9	29.6–32.1

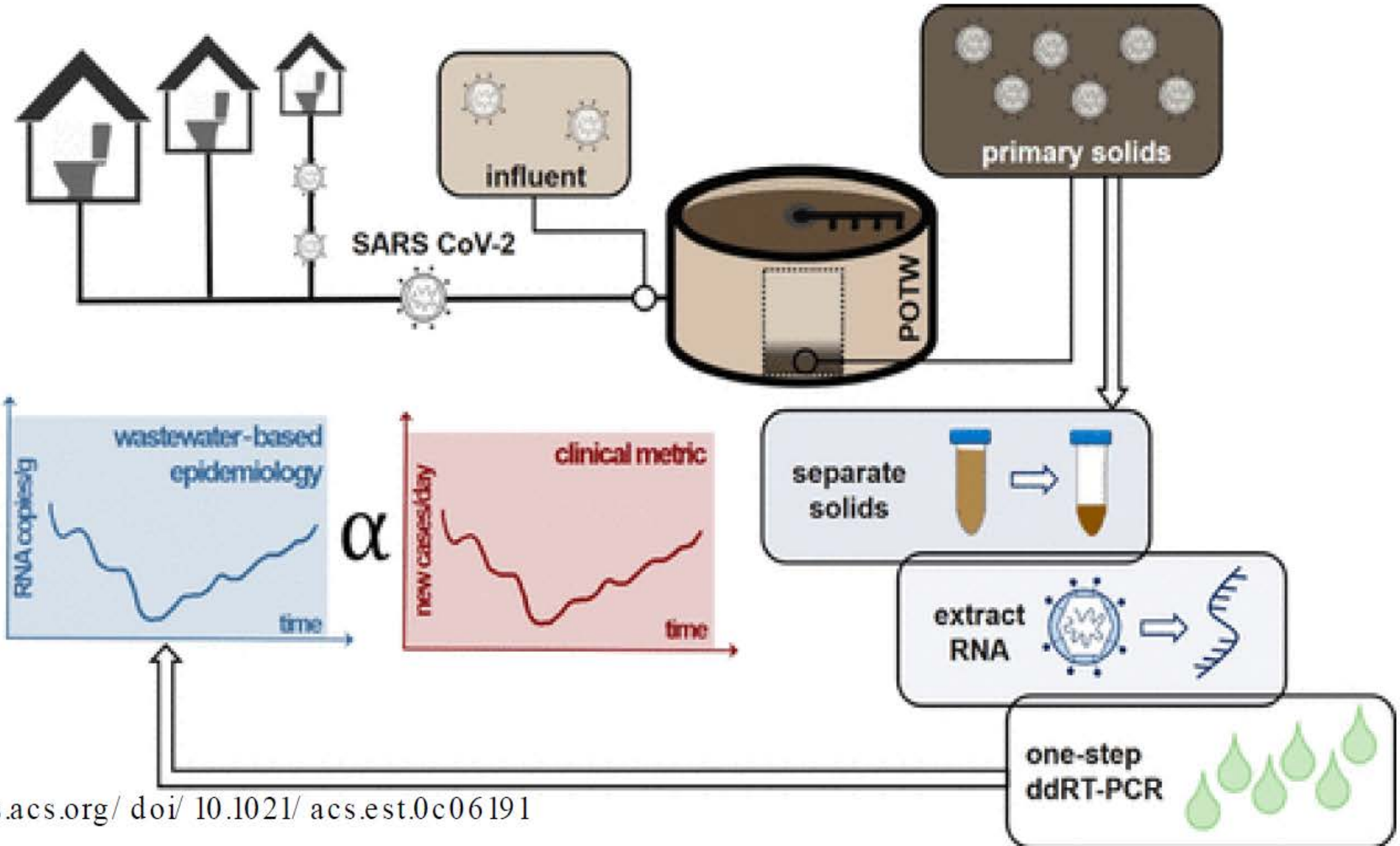
Brendish N, *Journal of infection* 2024

Influenza

Sensitivity	932/999	93.3	91.6–94.7
Specificity	2634/4427	59.5	58.0–60.9
PPV	932/2725	34.2	32.4–36.0
NPV	**2634/2701**	**97.5**	**96.9–98.0**
Prevalence	999/5426	18.4	17.4–19.5

‘FebriDx MxA continues to be valuable as a ‘rule out’ triage tool in patients with acute respiratory illness in the Emergency Department and could be scaled to provide a national triage tool in future viral pandemics.’

Wastewater surveillance

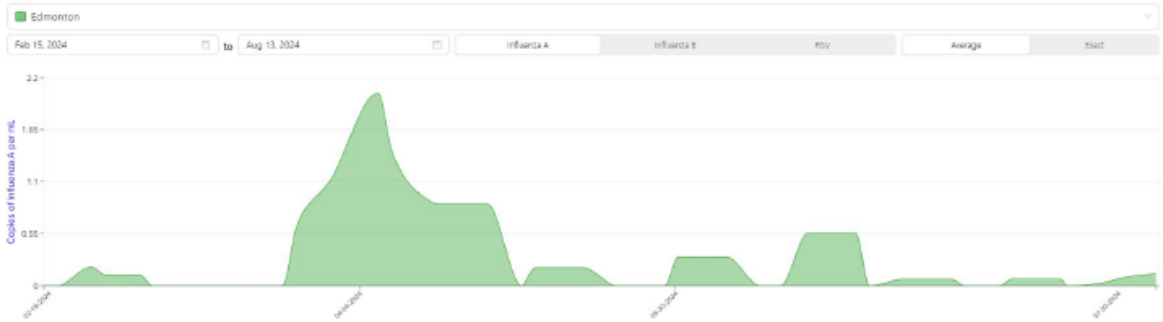


https://pubs.acs.org/doi/10.1021/acs.est.0c06191

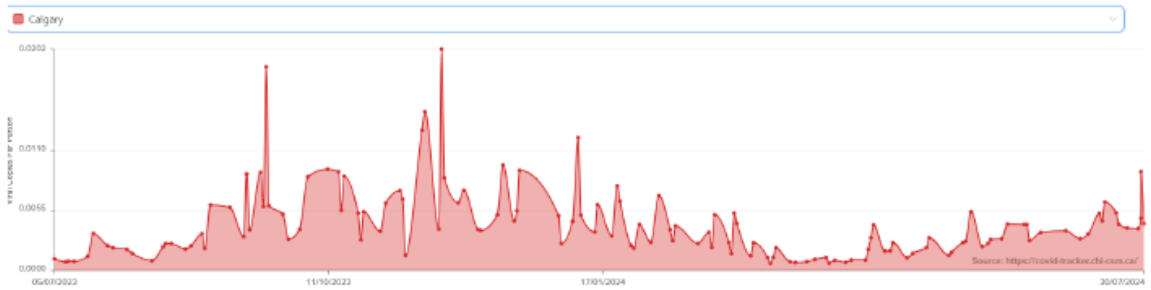
Relationship to traditional infection case counting

Real Time PCR detections in waste water samples in cities in Alberta Canada

Influenza A

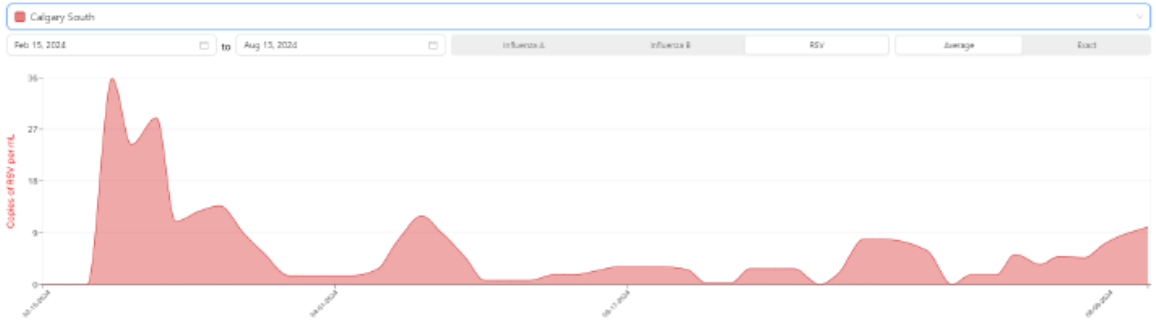


COVID-19



Influenza B

RSV



https://covid-tracker.chi-csm.ca/

Application of technologies

Intensive Care
Deaths

.
Metagenomic methodologies ?
Rapid sequence analysis

Secondary Care
Hospitalised cases

Multiple parallel analysis
Cost Effective diagnosis within hours of admission.
Prognostic factors to guide severity assessments

Primary Care
Seen by medical services

Rapid PoC/Biomarkers
Target specific risk groups

Community
Cases not seen by medical services

- Home testing Behaviour
- Wastewater surveillance

Multiple parallel analyses : Number of positive samples by pathogen, England 2023 to week 24, 2024

Figure 2. Number of samples tested for SARS-CoV-2, influenza, and other respiratory viruses in England by week, GP sentinel swabbing [note 1]

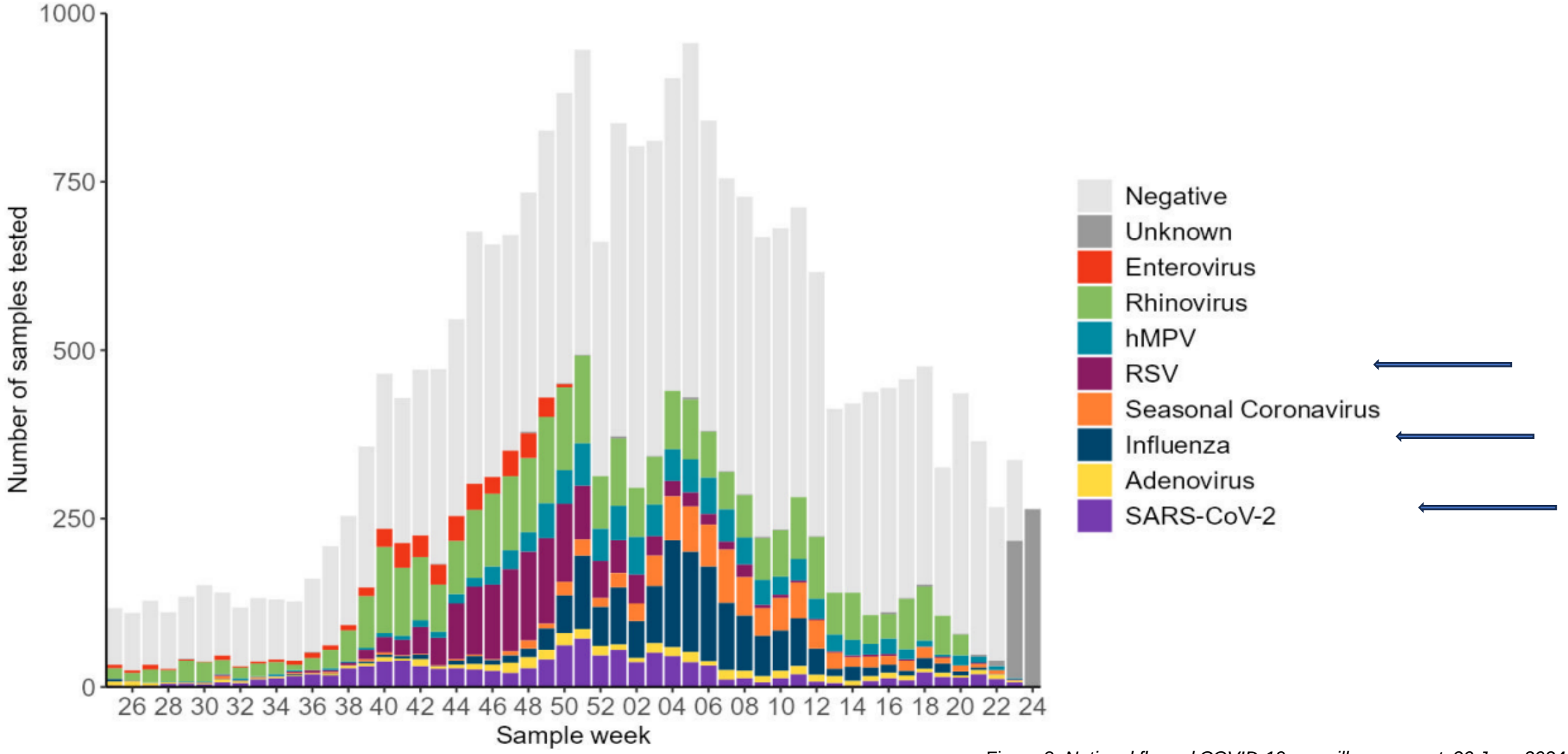
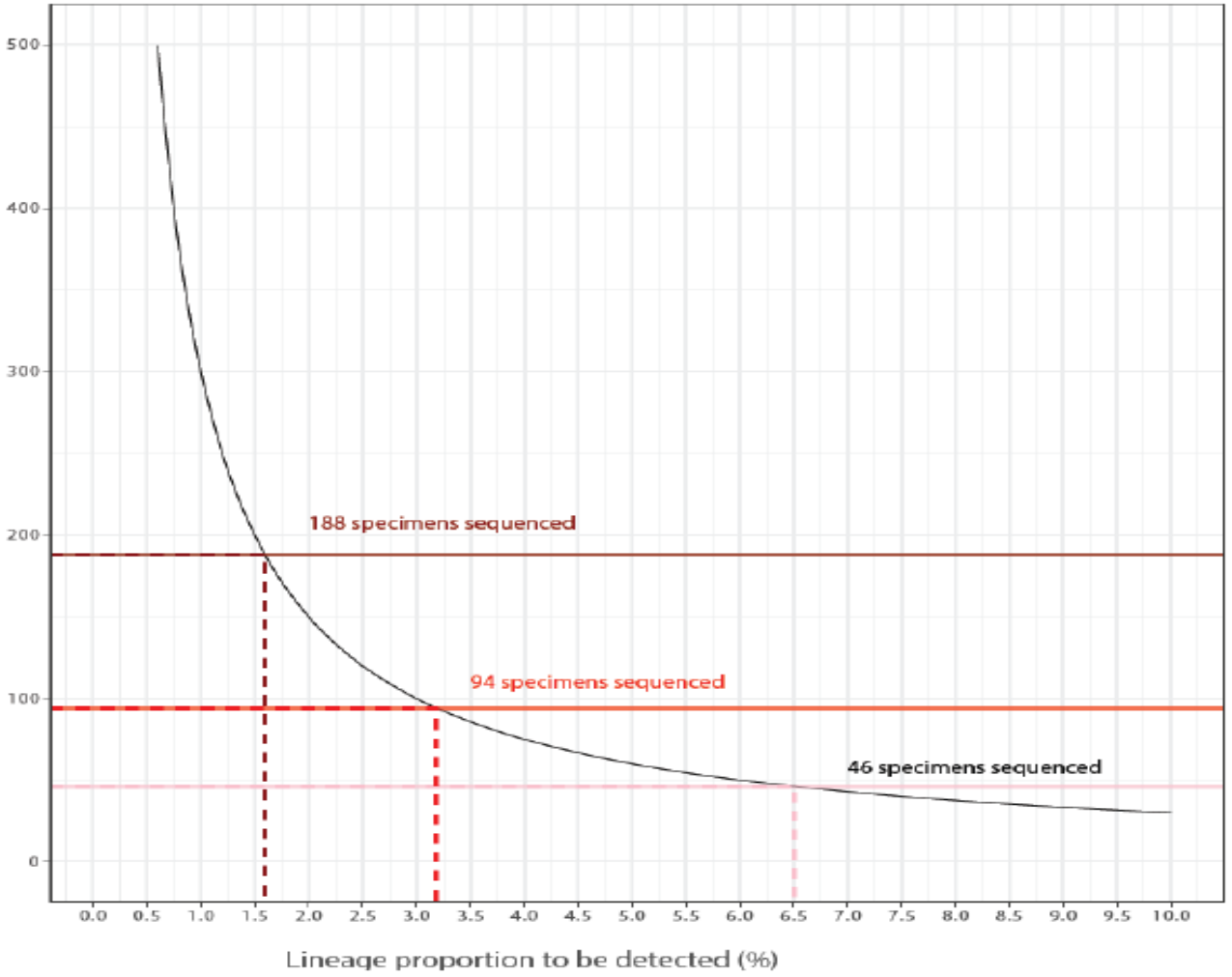


Figure 2. *National flu and COVID-19 surveillance report: 20 June 2024 (week 25).* https://assets.publishing.service.gov.uk/media/66740b2fd427ab249955cecf/weekly-flu-and-COVID-19-report-2024-week-25.pdf. [Accessed 02/07/2024]

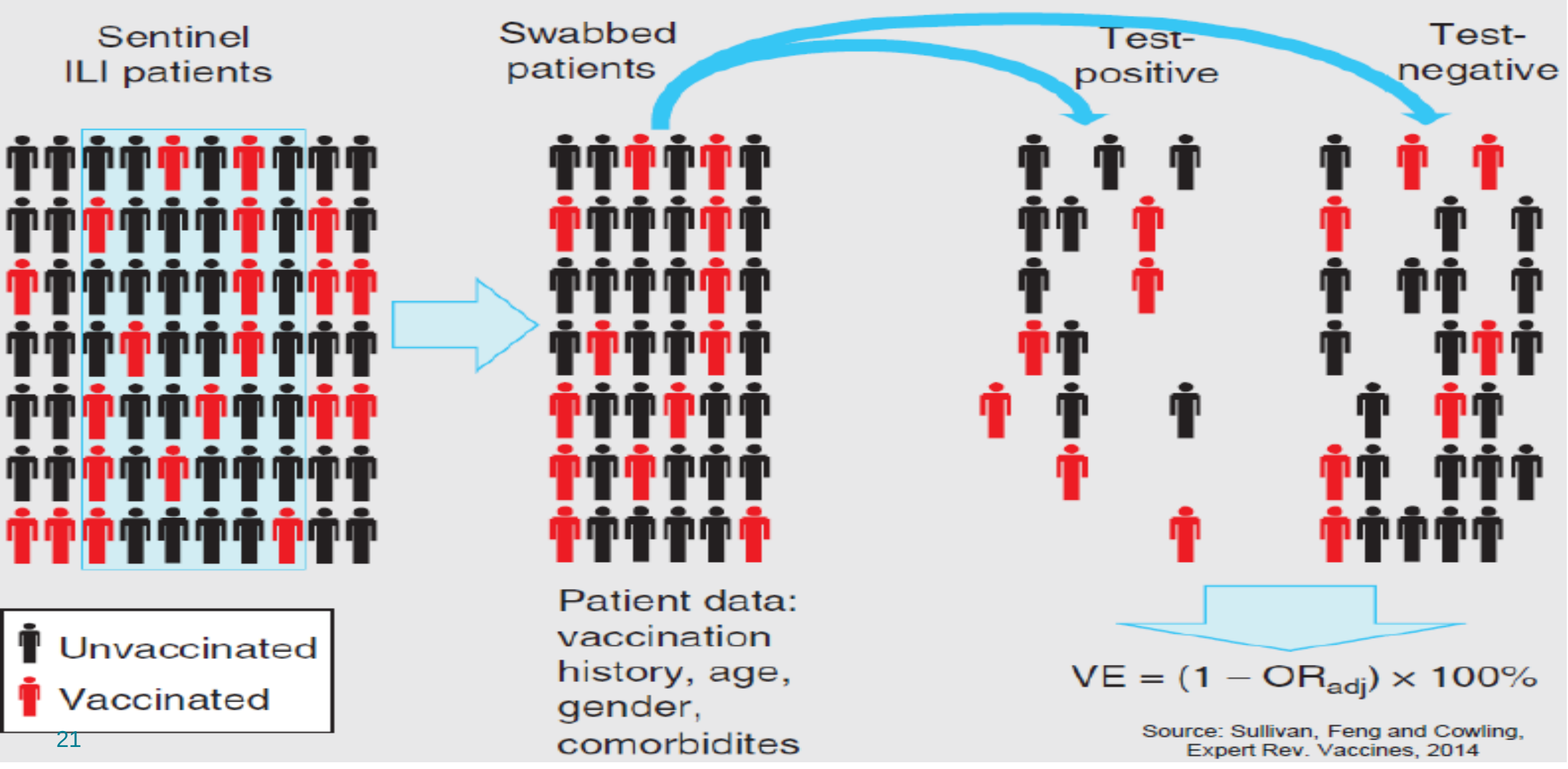
Affordability :What are the surveillance objectives ?



Sample size to detect lineages at different prevalences

- Recommend **46 sequences per country per year**
  - Identify lineages circulating at a prevalence of 10% (95% CI 4.2-22.0%)
  - Permit identification of a lineage circulating to a prevalence of **6.6% nationally**, and **0.27% globally**
- Choose proportion of RSV-A to RSV-B samples based on the circulating distribution

Test-negative design for estimating VE



Monitoring the Success of Interventions
Rapidity & precision

The Sunday Telegraph

Vaccines effective against Indian variant

By Steve Bird, Christopher Hope and Patrick Sawer

BRITAIN'S vaccines are "highly effective" against the Indian coronavirus variant, government scientists said last night, putting the country back on course for a full reopening by June 21.

In a marked change in tone, Public Health England scientists said the first real-world data showed double doses of Pfizer BioNTech or AstraZeneca are nearly as effective against the new emerging strain as they are against the Kent variant.

The findings, from a study which included more than 1,000 people who had contracted the Indian variant, were described as "groundbreaking" by a buoyant Matt Hancock, the Health Secretary, and "astounding" by Nadhim Zahawi, the vaccines minister.

Dr Mary Ramsay, head of immunisation at PHE, urged people last night to get their "vital" second vaccine as soon as it is offered, saying it provides "maximum protection against all existing and emerging variants".

Scientists found the Pfizer vaccine was 88 per cent effective against symptomatic disease from the Indian variant from two weeks after the second dose, compared with 93 per cent effective against the Kent strain.

The AstraZeneca vaccine was found to be 60 per cent effective against the Indian strain, compared with 66 per cent against the Kent variant, over the same period.

Scientists also insisted two jabs of either vaccine were expected to offer even greater protection against being admitted to hospital and death.

No 10 was said last night to be "fairly confident" that June 21's reopening was on track but cautioned that it was necessary to wait to check that admissions to hospital have not gone up later this week before knowing if "we are out of the woods". Last night Sir Iain Duncan Smith, the former Conservative Party leader, said that the results meant "it is time the scientists were put back in their laboratories again and told 'leave the Government to us'".

It comes as:

◆ Dominic Cummings, the Prime Minister's former chief adviser, criticised the Government, scientists and PHE for failing to properly plan for a pandemic which would have prevented every single lockdown;

◆ The NHS declared the number of vaccinations delivered in England alone had exceeded the 50million "milestone";

◆ *The Sunday Telegraph* learnt millions of Britons had their mobile phones "unwittingly tracked" to establish whether people travel further from home after their jabs.

Mr Hancock welcomed the PHE's latest research, saying it "proves our Covid-19 vaccination programme is protecting people".

He added: "We can now be confident that over 20million people – more than

Continued on Page 8

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Comment: Page 17

37,726,924 VACCINE FIRST DOSE +208,310

22,071,497 VACCINE SECOND DOSE +411,714

2,694 DAILY CORONAVIRUS CASES

-8.68% CHANGE IN 7-DAY AVERAGE

127,716 DEATHS +6

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 12, 2021 VOL. 385 NO. 7

Effectiveness of Covid-19 Vaccines against the B.1.617.2 (Delta) Variant

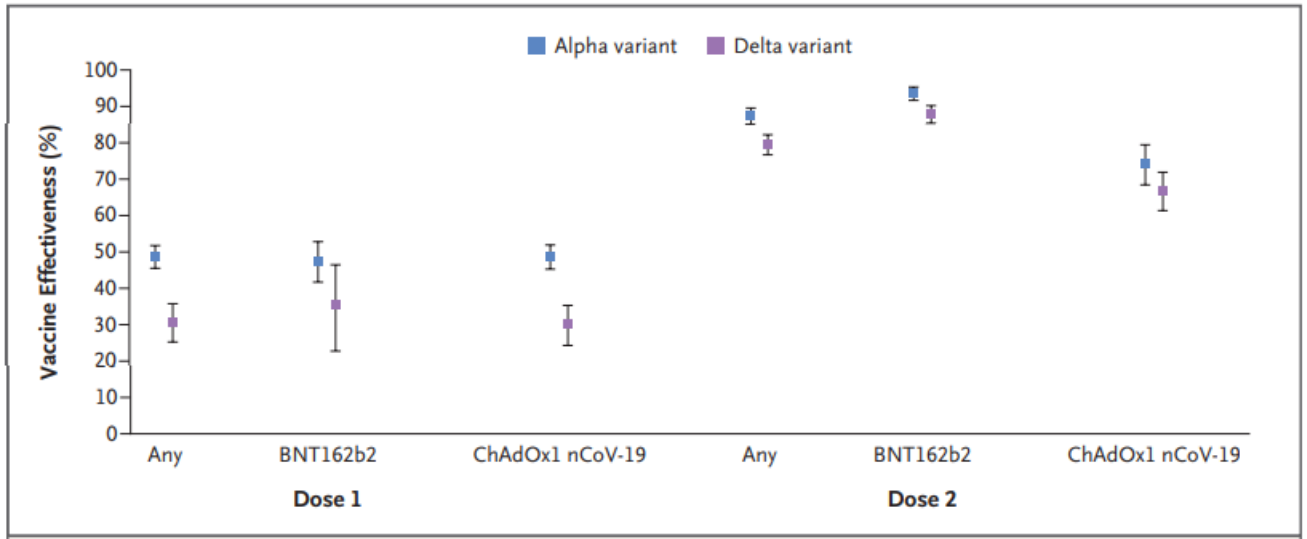
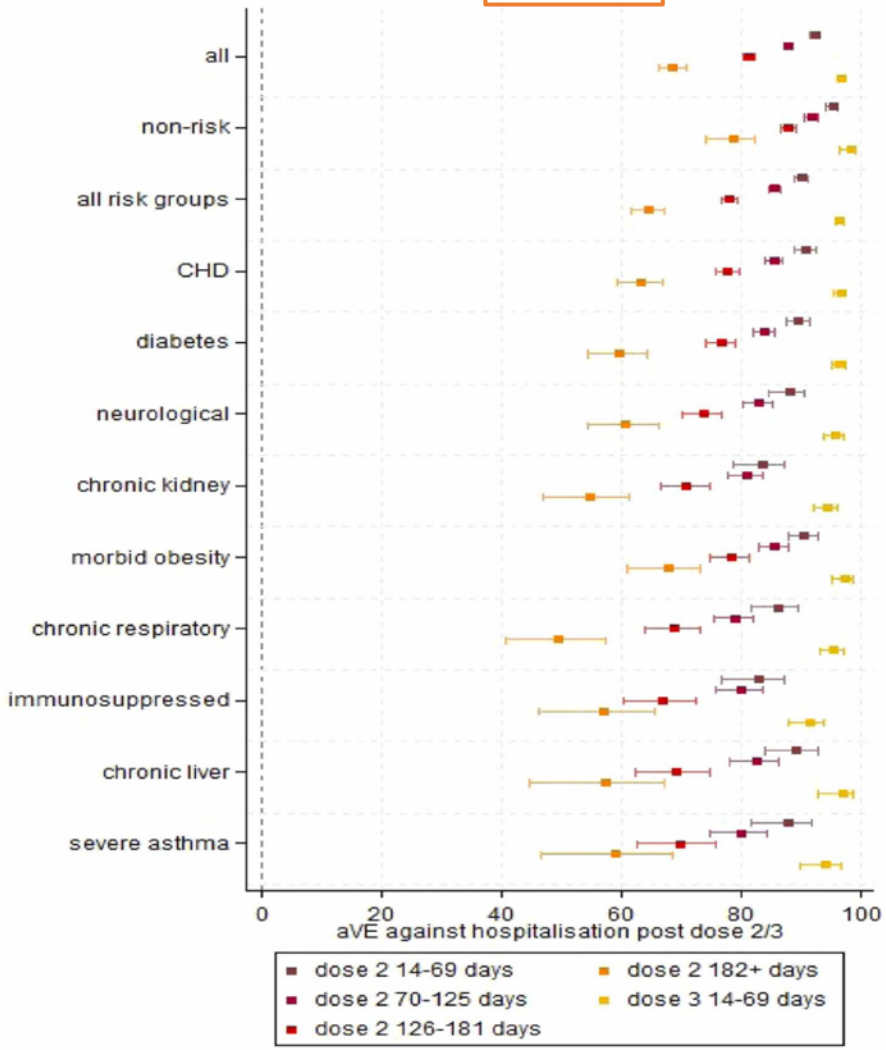


Figure 1. Vaccine Effectiveness against the Alpha and Delta Variants, According to Dose and Vaccine Type.

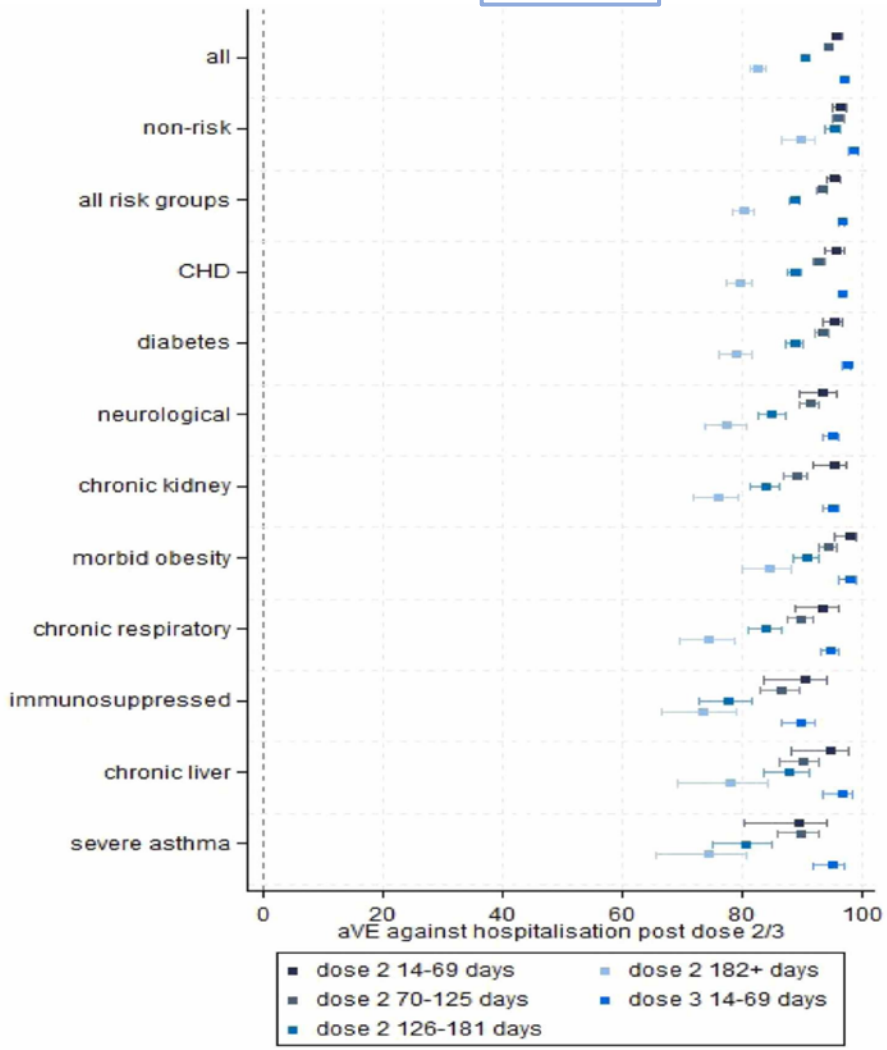
Bernal JL, *et al. N Eng J Med.* 2021;385(7):585-94.

SARS VE in different clinical risk groups

AZ



Pfizer

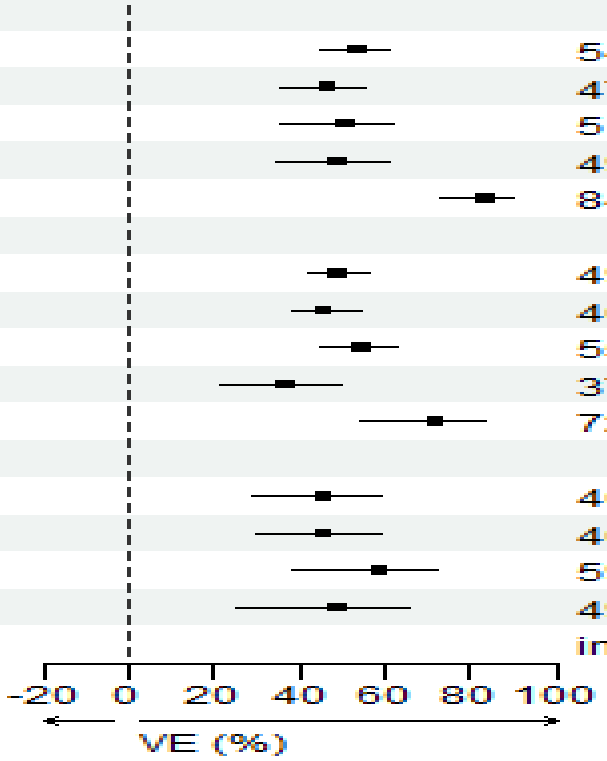


Whitaker HJ, et al. COVID-19 vaccine effectiveness against hospitalisation and death of people in clinical risk groups during the Delta variant period: English primary care network cohort study. Journal of Infection. 2023;87(4):315-27.

UK 2023/2024 A/H1 flu VE main estimates by age

Primary care

	controls		cases		
cohort / flu type	unvacc	vacc	unvacc	vacc	VE (95% CI)
kids 2-17					
all influenza	3929	3420	522	304	54% (45 to 61%)
all influenza A	3929	3420	422	282	47% (36 to 55%)
influenza A/H1	3929	3420	189	107	51% (36 to 62%)
influenza A/H3	3929	3420	200	126	49% (35 to 61%)
influenza B	3929	3420	103	22	84% (73 to 90%)
adults 18-64					
all influenza	11736	4065	2338	412	49% (42 to 56%)
all influenza A	11736	4049	1968	389	46% (38 to 54%)
influenza A/H1	11736	4065	949	173	55% (45 to 63%)
influenza A/H3	11736	4065	801	158	37% (22 to 50%)
influenza B	11736	4065	380	23	72% (54 to 83%)
adults 65+					
all influenza	1194	3982	109	325	46% (29 to 59%)
all influenza A	1194	3976	107	316	46% (30 to 59%)
influenza A/H1	1194	3982	50	121	59% (38 to 72%)
influenza A/H3	1194	3982	47	131	49% (25 to 66%)
influenza B	1194	3982	2	10	insufficient



Adjusted for week, age group, scheme, risk status, sex

https://www.gov.uk/government/statistics/surveillance-of-influenza-and-other-seasonal-respiratory-viruses-in-the-uk-winter-2023-to-2024

SWOT analysis laboratory based surveillance

Opportunities

- New sampling methods
- Point of Care testing
- Integration of syndromic surveillance
- Upscaling genomics work
- Innovation in detection capabilities
- New biomarkers
- Data linkage
- Wastewater
- Tools for virus discovery

Threats

- Loss of traditional sampling arrangements
- Supply chains for reagents/equipment
- Workforce
- Lack of culture based work
- Deprioritisation

SWOT, Strengths, Weaknesses, Opportunities and Threats.

Surveillance considerations

- Clinical care developments feed into national surveillance
- Multiplex respiratory virus testing is the general direction of travel
- Expansion of testing capability using near patient applications
- Data linkage from field locations is becoming easier
- Data linkages are critical to support increasing complexity
- Necessity to monitor interventions efficiently

- **Exciting times for diagnostic technologies.**
- **Improving operational workflows may be as important as technology developments.**
- **Flow of information is as important as technology. Much more to gain.**

Concluding remarks

- Move away from traditional single pathogen laboratory detection approaches
- Move towards syndromic surveillance (multi analyte)
- Driven by health care innovation & economic pressure

- Efficiency means doing more with less……
- Protocols which can be applied to many different pathogens
- >150 countries undertaking WGS for SARS CoV 2…agnostic technology
- Harness innovation to assist surveillance & preparedness
- Enhanced capacity, but needs attention to quality, data analysis, visualisation

- Moving towards monitoring viral evolution in real time…better tools for interpretation
- Agnostic and parallel investigation strategies & techniques
- Invest in data platforms which facilitate information sharing, e.g. GISAID