

The vision of respiratory surveillance in the postpandemic era

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Organization

Collaborative Surveillance: data collection, analysis and sharing

"Crafting the mosaic":

A framework for resilient surveillance for respiratory viruses of epidemic and pandemic potential







1.2

1.3

Strengthened integrated disease, threat & vulnerability surveillance

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



Across Diseases & Threats, Sectors, Event Lifecycle, Geographies

Diagnostic and laboratory capacity for pathogen & genomic surveillance

Expanded laboratory capacity including genomics, decentralized testing, riskbased biosafety and biosecurity with integrated lab networks

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





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.

Multinational Studies: Pooled analysis RECOVERY Trial

RECXVERY

Randomised Evaluation of COVID-19 Therapy

Agreement on information handling PANGOLIN lineage assignment





Data Linkage / Hospital Informatics

The Sunday Telegraph Vaccines

effective against Indian variant





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.astar.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



Year week

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



Non-Preferred sample type

- Saliva
- Throat swab alone



Standard transport medium

- Good for virus culture
- Good for RT-PCR
- Good for sequencing

Molecular/Inactivation medium

- NO Good for virus culture
- Good for RT-PCR
- Good for sequencing

UTM/VTM



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





ED triage. March 2022-2023. n=5426

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

All three viruses combine

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



Relationship to traditional infection case counting

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



Influenza B





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

Application of technologies



• Wa ste wa te r surve illa nc e



Community Cases not seen by medical services

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]



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	Smith, the former leader, said that th	Conservative Party e results meant "it is in more out back in	
and Patrick Suove BIRTIAN'S sectors are "highly effec- tive" against the Indian commavirus vivint, government desensits and its course for a full respensing by June 3 In a marcle charge in toose, Politic Headh England a scientists and the first Fiber Hilder and the sector of the sec- tor and the sector of the sector of the respective signal and the sector of the Piber Hilder Check explainst the new emerging strain as effective signals the new emerging strain as effective signals the new emerging strain as a field of the sector of the The findings, from a study which included more thank 1000 people who had contracted the Indian variant, were bouyout Matt Illucco, the Fieldshove retary, and "actionating" by Nublin Edward, the sector insider. Dr Mary Emmay, head of Immunita- gether "Unit" sector variants and the sector of the sector sector variant sector variant sector variants and perfective sector variants and the sector variant sec- tor sector variant sector variants and the sec- tor sector variant sector variants and the sec- tor sector variant sector variants and the sector variant perfector variant sector variants and the sector variant sec- tor sector variant sector variants and the sector variant sec- tor sector variant sector variants and the sector variant sec- tor sector variant sector variants and sector variants and the sector variant sector variant sector variants and the sector varian	 Ireader, said that the results mean "(is the lack is the back is		
as it is offered, saying it provides "max- imum protection against all existing	that over 20million people - more the Continued on Page 8		
Scientists found the Pfarer vaccine was 88 per cent effective against symp- tomatic disease from the Indian variant	Reports: Pages 8 &: Comment: Page 17	9	
compared with 93 per cent effective	37.726,924	22,071,497	
The AstraZeneea vaccine was found to be 60 per cent effective against the Indian strain, compared with 66 per	VACCINE FIRST DOSE +208,310	VACCINE SECOND DOSE +411,714	
cross against the nerit variant, over the same period. Scientists also insisted two jabs of either vaccine were expected to offer even grouter notection against being	2,694 DAILY CORONAVIRUS CASES		
admitted to hospital and death. No 30 was said last night to be "fairly confident" that June 21's reopening was on track but cautioned that it was nec-	+8.68% CHANGE IN 7-DAY AVERAGE		
essary 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 lain Duncan	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



SARS VE in different clinical risk groups



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

	cont	rols	cas	es		
cohort / flu type	unvacc	vacc	unvacc	vacc		VE (95% CI)
kids 2-17					1	
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
				-20 (20 40 60 80 1	00
				÷		-
					VE (%)	

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

https://www.gov.uk/government/statistics/surveillance-of-influenzaand-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

erformance

Continuously improv

People

Improve management Respect people and suppliers

> Process Create process flow and pull Level out workload Standardize tasks

> > Purpose Long-term philosophy Core values Mission and vision

Test and evaluate Make decisions

N

- Lack of culture based work
- Deprioritisation Grow and empower leaders

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