GIHSN ANNUAL MEETING 17-19 JUNE 2026

18 June 2026 PM

Foundation for Influenza Epidemiology

Sous l'égide de Fondation de France

Coordination IMPACT Healthcare

GIHSN ANNUAL MEETING, 18 JUNE 2026

LEVERAGING AI TO BETTER PREDICT INFLUENZA EPIDEMIOLOGY EVOLUTION

Joël BELAFA, Biolevate

Foundation for Influenza Epidemiology

Sous l'égide de Fondation de France

Leveraging AI to better predict Influenza Epidemiology Evolution

From viral surveillance to useful anticipation for vaccine decision-making

The challenge: Deciding before Knowing

Biolevate

Vaccine composition is an anticipatory decision made under uncertainty.

Evolving virus

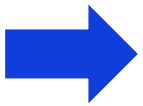
Dominant strains can change from one season to the next through antigenic drift, reassortment or growth advantage.

Decision calendar

The vaccine has to be selected, produced and deployed before all signals from the coming season are observable.

Imperfect data

Genomic, antigenic and clinical surveillance arrive with delays, sampling bias and geographic gaps.



Which signals are reliable enough to guide decision under time-constraints?

Mapping support for vaccine decisions

Biolevate

Through an ai-TLR scoped around the full decision pathway.

Combined analysis in one ai-TLR

1. Anticipate circulation

Which variants, strains, clades or lineages may emerge, replace others or become dominant?

2. Understand impact

Which mutations actually change immune recognition or antigenic distance?

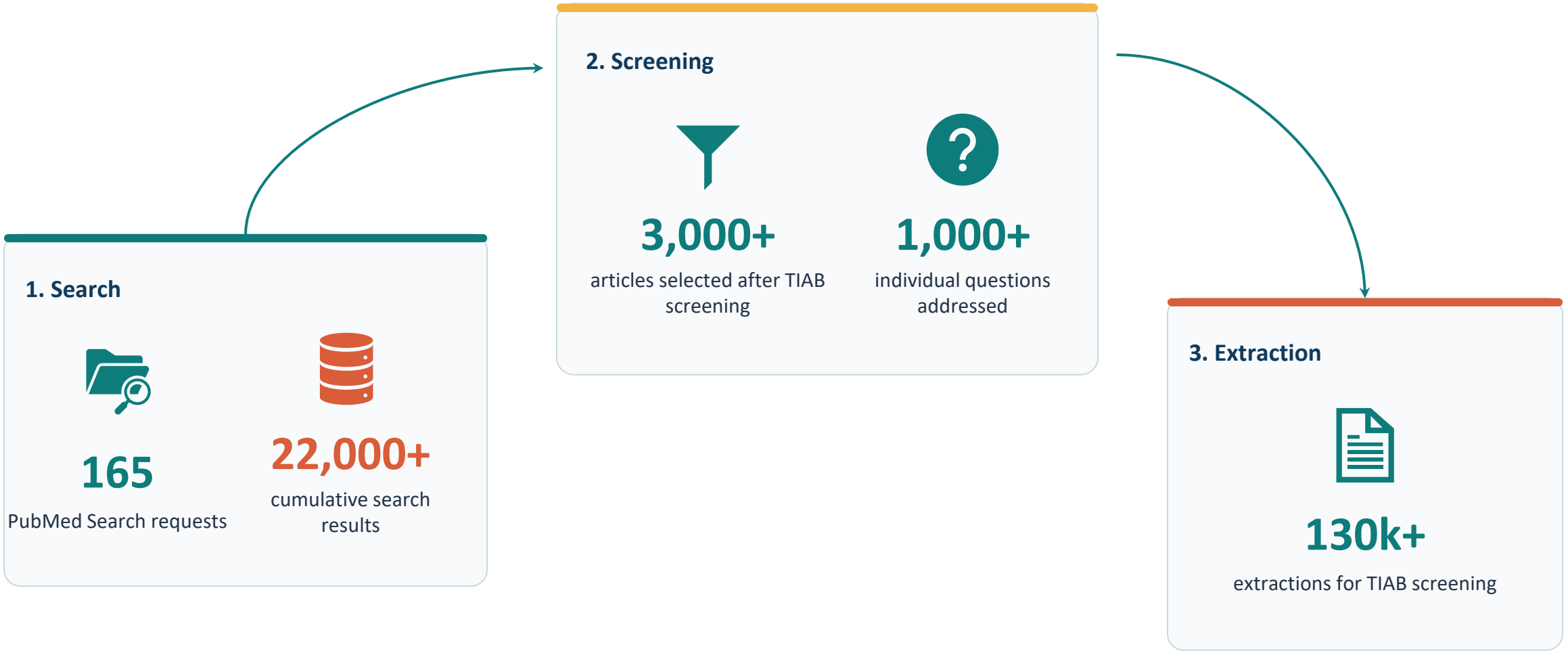
3. Vaccine performance

How do these changes translate into immunogenicity, efficacy or real-world effectiveness?

Designed at scale for full auditability

Biolevate

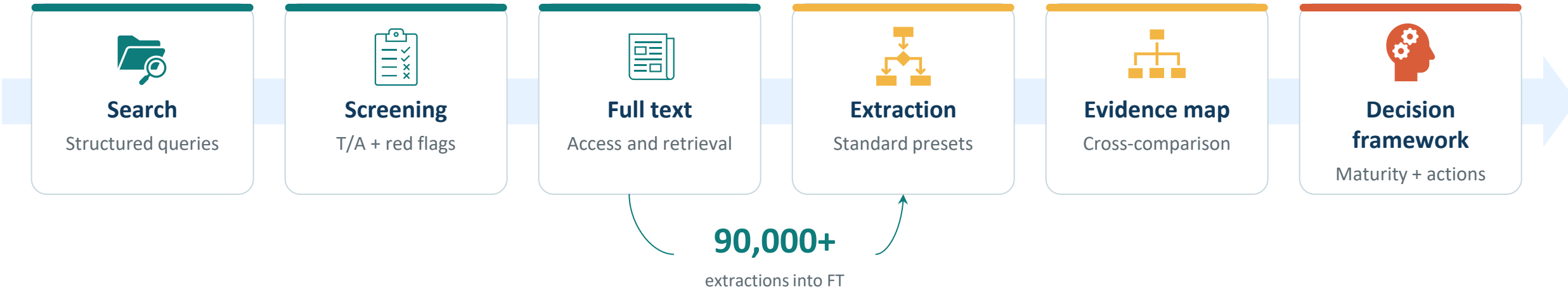
A structured approach enabling systematic cross-comparisons across methods, data sources, validation strategies, and decision relevance.



From raw corpus to decision-oriented synthesis

Biolevate

One collection per research axis analyzed in an auditable workflow.



Analyze thousands of heterogeneous records into comparable evidence categories

Preview of our aiTLR output

Biolevate

A field full of potential… but still fragmented

The building blocks exist; operational integration remains a challenge.

1. Many model families

Lineage frequency, phylodynamics, fitness, phylogeography, machine learning and deep learning.

2. Uneven validation

Many studies are retrospective; fewer are prospectively tested or validated across seasons.

3. Data is the bottleneck

Sampling bias, delays, missing metadata, sparse antigenic data and hard-to-link VE data.

4. Expertise remains central

AI is useful when it makes uncertainty visible, interpretable and discussable by experts.

AI is promising for prioritization and early warning; not yet for direct vaccine-composition.

AI tools must be validated, interpretable and actionable

Biolevate

4 maturity levels:

1. Exploratory

Proof of concept; limited validation.

2. Retrospectively informative

Useful for explanation and backtesting.

3. Feasibility-ready

Ready for a controlled pilot.

4. Decision-support ready

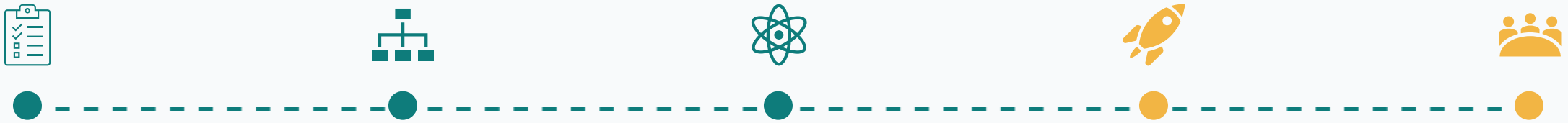
Validated, interpretable and usable in expert review.

A simple, well-validated and explainable tool may be more useful than a complex model that cannot be interpreted.

From mapping evidence to building a decision framework

Biolevate

Prioritizing, validating and testing the most actionable hypotheses.



1. Finalize extraction

Complete priority full texts and harmonize key fields.

2. Rank maturity

Exploratory, retrospective, feasibility-ready, decision-ready.

3. Data model

Sequences, dates, locations, antigenicity, immunity, VE.

4. Pilot use cases

H3N2 dominance, mutation impact, and vaccine performance.

5. Workshop

Turn map into practical WHO criteria.

Start small, but make it decision-oriented

Biolevate

Building a pilot to test real-world efficiency, not only algorithmic performance.

Pilot 1: Early warning for dominance

Which influenza lineages are rising, where, and with what uncertainty?

Pilot 2: Antigenic impact

Which mutations deserve priority characterization or closer monitoring?

Pilot 3: Mismatch and performance

Which signals connect antigenic distance with lower vaccine performance?

Success criterion: an earlier, more interpretable and robust signal that can guide expert review.

From surveillance to anticipation

Biolevate

Which signals, early enough and reliable enough, can improve the decision?

Connect

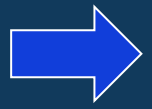
viral evolution, antigenicity and vaccine performance

Prioritize

signals and data that can change action

Decide better

with human expertise, not instead of it



Use AI to help experts see viral evolution earlier, not decide blindly faster.

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LEVERAGING AI TO BETTER PREDICT INFLUENZA EPIDEMIOLOGY EVOLUTION

ROUNDTABLE

Foundation for Influenza Epidemiology

Sous l'égide de Fondation de France

ROUNDTABLE

- **John McCauley**, Foundation Scientific Committee, London, UK
- **Bruno Lina**, Lyon University and NIC, Lyon, France
- **Wenqing Zhang**, WHO, Geneva, Switzerland
- **Sebastian Maurer-Stroh**, GISAID

Global Influenza Hospital Surveillance Network

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GIHSN EUROPEAN PILOT: MONITORING THE DRIVERS OF VACCINE PROTECTION

Mendel HAAG, Seqirus

Foundation for Influenza Epidemiology

Sous l'égide de Fondation de France

GIHSN European Pilot

CSL Seqirus

sanofi

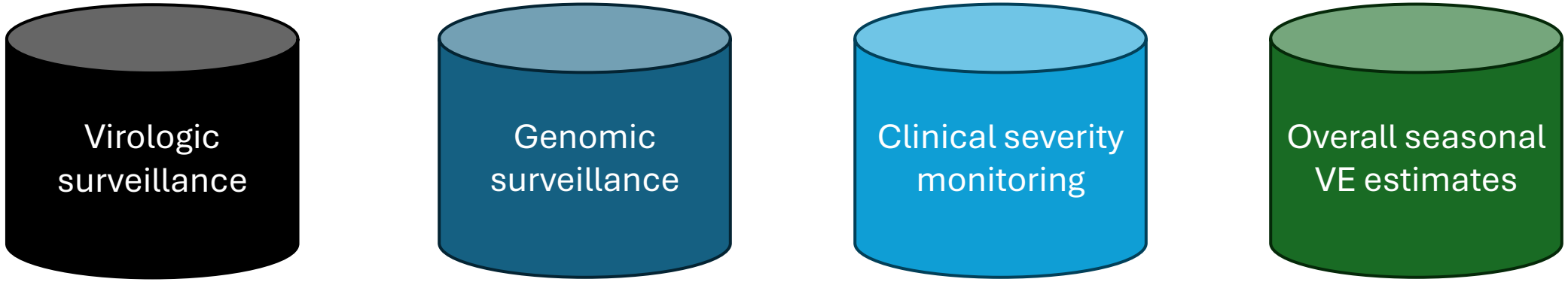
Monitoring Drivers of Vaccine Protection

GENESIS OF THE INITIATIVE

- Builds on lessons learned from the DRIVE project and subsequent discussions on influenza vaccine effectiveness monitoring.
- Need for a sustainable surveillance capability that delivers ongoing public health value while strengthening preparedness and readiness for future public health emergencies.
- Interest in understanding the drivers of vaccine protection (host, vaccine, and viral factors).
- Recognition that existing surveillance systems collect many relevant data streams but rarely integrate them.

LEVERAGE EXISTING SURVEILLANCE SYSTEMS

Current capabilities



Current opportunities

- Data streams often operate independently
- Limited linkage between vaccination status, viral evolution, and clinical outcomes
- Few systems capable of monitoring changes in vaccine protection during the season
- Limited ability to understand why vaccine performance varies across seasons

PILOT OVERVIEW

Approach

- Expand the European GIHSN footprint through 3 additional sites
- Enhance collection of vaccination history and severity data
- Scale whole genome sequencing of influenza-positive cases
- Link epidemiologic, clinical, and genomic information

Key Analyses

- Monitoring severe disease among vaccinated and unvaccinated individuals
- Assessment of vaccine protection across host, vaccine, and viral factors
- Evaluation of associations between viral evolution and clinical outcomes

Expected Outputs

- Early detection of unexpected patterns in vaccine protection
- Improved understanding of drivers of vaccine performance (host, vaccine, & viral factors)
- Enhanced contextualization of seasonal vaccine effectiveness findings

WHAT DOES THIS MEAN FOR GIHSN?

- Opportunity to expand the scientific scope and utility of the network and its data
- Increased visibility with European public health and regulatory stakeholders
- Enhanced genomic surveillance capabilities
- Additional opportunities for collaboration across sites
- Potential expansion of funding and partnerships
- Development of new analytical approaches using existing GIHSN infrastructure

PROPOSED DEVELOPMENT PLAN

Year 1: Feasibility & Proof of Concept	Years 2-3: Expansion & Validation*
Establish pilot activities across participating GIHSN EU sites	Refine and validate monitoring methods across multiple seasons
Assess data availability, sample size, sequencing capacity, and timeliness	Expand participating sites and sequencing capacity as feasible
Conduct descriptive analyses to evaluate potential signal detection approaches	Enhance data timeliness and connectivity
Deliver interim analyses and end-of-season feasibility assessment	Evaluate scalability and long-term value of the framework

*Subject to Year 1 findings and stakeholder feedback.

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GIHSN EUROPEAN PILOT: MONITORING THE DRIVERS OF VACCINE PROTECTION

ROUNDTABLE

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ROUNDTABLE

- **Marco Cavaleri**, EMA, Netherlands (*remote*)
- **Marc-Alain Widdowson**, WHO Euro, Danemark
- **Bruno Lina**, Lyon University and NIC, France
- **Jonathan Ewbank**, ERINHA and BE READY, Belgium

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WORKSHOP 1 - COMBINATION OF VIRUS WGS & CLINICAL DATA

Laurence TORCEL-PAGNON & Laurence JOSSET, NIC Lyon

Foundation for Influenza Epidemiology

Sous l'égide de Fondation de France

WHY WE COLLECT INFLUENZA VIRUS WHOLE-GENOME SEQUENCING (WGS) DATA

The Scientific rationale

Mechanistic insight: WGS links genotype → phenotype → clinical outcome, providing a complete picture of viral behavior

Current influenza surveillance focuses primarily on the hemagglutinin (HA) gene. However, WGS enables tracking of mutations across all influenza segments, delivering:

- Deeper understanding of epidemiological effects of intra- and inter-seasonal evolutionary dynamics
- Exploration of potential associations between viral mutations and patient clinical outcomes

GIHSN Strategic Objectives

WGS Objective 1. Continue leveraging GIHSN data to support WHO recommendations for influenza vaccine composition (Feb and Sep)

Support vaccines optimization (identify immune escape variants and improve antigenic match) and enhance forecasting models used for WHO strains selection

WGS Objective 2. Scale up the number of WGS viruses in the network to enhance:

- Comprehensive signal detection: WGS combined with host metadata reveals clinically relevant mutations that HA-only analyses miss
- Better attribution of severity: Distinguishes viral virulence factors from host susceptibility (age, comorbidities, immune status)
- Population-aware evolution: Understand how immune landscapes (age, vaccination) shape viral evolution
- Global relevance: Contribute to data-rich, standardized surveillance systems

WORKSHOP 1 – CURRENT SITUATION (2025-26 SEASON)

Analysis of whole genome sequencing (WGS) data assessing **oxygen requirement** as a proxy for disease severity among hospitalized patients to determine whether specific lineages or clades are associated with a higher frequency of severe clinical presentation. A **binomial logistic regression** model is applied with limited adjustment for confounders.

From the most recent report (Feb 2026), **1,013 WGS** were analyzed from hospitalized patients across 21 sites in 19 countries. **Adjustment was limited to geographic region.**

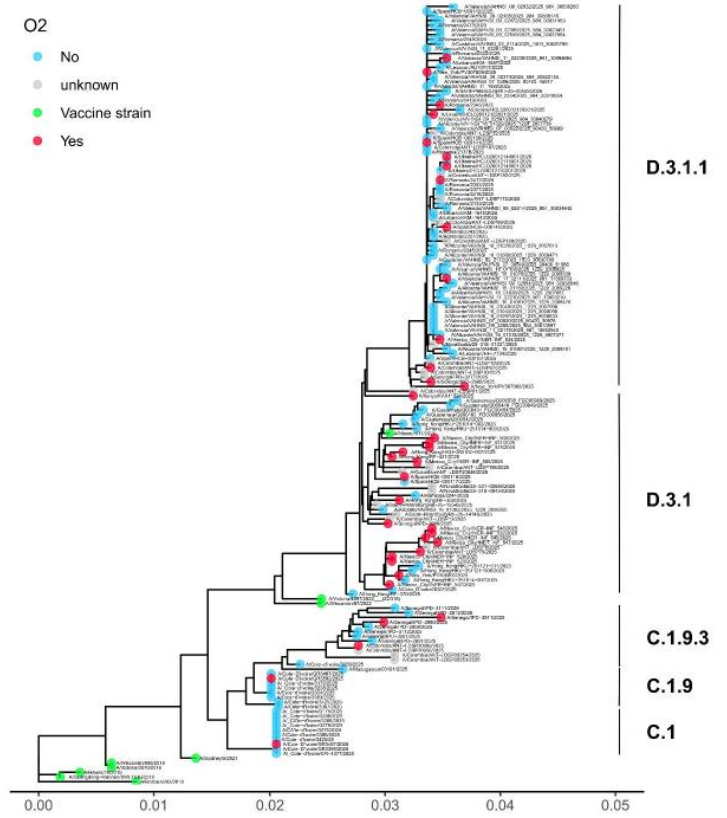


Fig 2: Phylogenetic tree of the A(H1N1) viruses analyzed between September 2025 and February 2026. The phylogeny has been inferred using a Neighbor Joining approach (Seaview). Visualization was displayed using ggtree in R. Tips (samples) colors correspond to Oxygen supplementation (yes: red; no:blue) with vaccine reference strains displayed in green.

GIHSN report - Feb 2026

WORKSHOP 1 – COMPLETED RESEARCH PROJECT

Published in Jan 2026

- Objective: Assess the association between influenza viral subtype/clade and disease severity in hospitalized patients.
- Severity assessment:
  - 3- variable definition: at least one of mechanical ventilation, ICU admission or in-hospital death
  - 4- variable definition: 3- variable definition or oxygen supplementation
- Analysis: mixed-effects logistic regression models, adjusting for age group, sex, underlying medical conditions, influenza vaccination status, antiviral use, country income level and epidemic period, while study site was included as a random effect -> 745 WGS analyzed from 15 sites across 14 countries
- Key limitations: selected specimens, missing covariate data, one single flu season, site-specific variations in clinical practice

BMJ Open

Association of influenza viral genetic information with severity markers in patients hospitalised with influenza: multicentre retrospective cohort study

Aung Pone Myint [1,2] George Shirreff,[2] Vicky Baillie,[3] Antonin Bal,[4] Celina F Boutros,[5] Elena Burtseva,[6] Daouda Coulibaly,[7] Daria Danilenko,[8] Ghassan Dbaibo,[9] Gregory Destras,[4] Ndongo Dia,[10] Anca Cristina Drăgănescu,[11] Heloisa I G Giamberardino,[12] Andrey B Komissarov,[8] Parvaiz A Koul,[13] Victor Alberto Laguna-Torres,[14] Jason J LeBlanc,[15] Ainara Mira-Iglesias,[16,17] Alla Mironenko,[18] Alejandro Orrico-Sánchez,[16,17] Nancy A Otieno,[19] Oana Săndulescu [20] Viviana Simon,[21] Anna Sominina,[8] Emilia Sordillo,[21] Mine Durusu Tanriover,[22] Nataliia Teteriuk,[18] Serhat Unal,[23] Harm Van Bakel,[21] Melissa K Andrew,[15] Joseph Bresee,[24] Bruno Lina,[4] F Xavier López-Labrador,[16,25] Justin R Ortiz,[26] Sonia M Raboni [27] Wenqing Zhang,[28] Sandra S Chaves,[29] Giacomo Cacciapaglia,[30] Laurence Josset,[4] Cécile Chauvel,[2] Marta C Nunes [2,3]

e111643.full.pdf

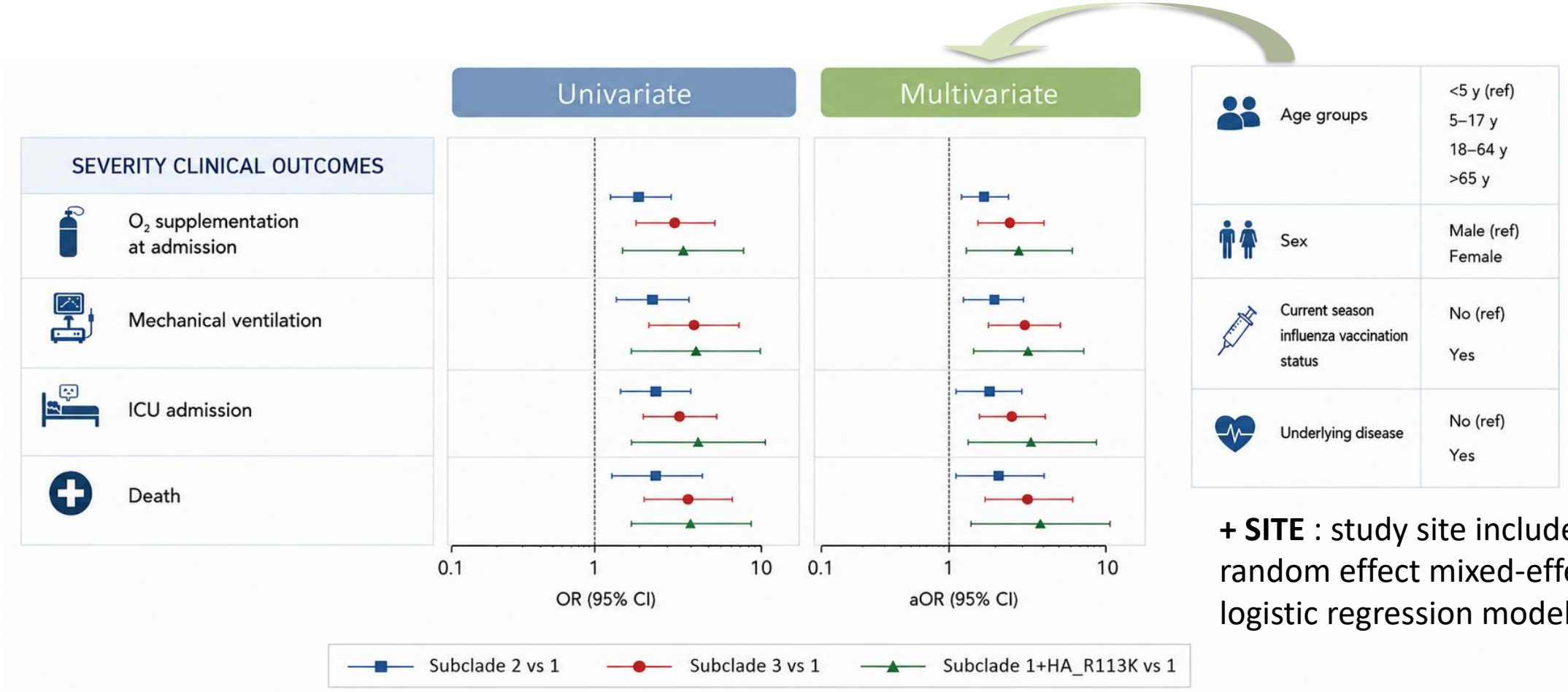
WORKSHOP 1 - MOVING FORWARD (2026-27 SEASON AND BEYOND)

Identify ways to strengthen the WGS analysis included in WHO"s biannual report by incorporating additional severity indicators and leveraging clinical data collected by sites

- Question to sites: which **range of severity outcomes** we could consider?
- Rediscuss **analytical approach** (look at last year analytical report to reconsider variables, model and adjustments)

Ensure that any proposed enhancements are feasible within the VCM timelines (Feb and Sep each year)

WORKSHOP 1 – NIC LYON DRAFT PROPOSAL (2026-27 SEASON)



+ SITE : study site included as a random effect mixed-effects logistic regression models

Univariate analysis could be included in the next report, with multivariate models and constellations analysis automated ideally for Feb 2027.

WORKSHOP 1 – QUESTIONS

Overall question: Do you agree with the proposed analysis framework for 2026–27? If not, what specific changes would you recommend (e.g. outcomes, variables, or modelling approach)?

1. Which **severity outcomes** should be prioritized for analysis (beyond *oxygen supplementation at admission*)?
Should they be tiered (level 1 etc) or listed separately (Y/N)?

2. Should the **site questionnaire** be updated to reflect additional needs? And how?
Example: oxygen supplementation throughout admission (various levels)

- Level 1: Basic oxygen delivery with minimal invasion [low flow nasal cannula, Hudson prongs, face tents]
- Level 2: Enhanced oxygen delivery requiring more monitoring [high flow nasal cannula, RAM cannula, various masks]
- Level 3: Mechanical assistance without direct airway invasion [CPAP, BiPAP, NSIMV (Nasal Synchronized Intermittent Mandatory Ventilation) – often used in neonates via nasal prongs or cannula]
- Level 4: Direct airway access requiring highest level of care [Endotracheal tube (ETT), tracheostomies, ECMO]

3. What additional variables are essential for **adjustment** to improve comparability across sites (beyond age, sex, vaccination status and comorbidities)?

4. Which **analytical approach** is most appropriate and feasible for routine reporting (e.g. logistic regression vs. alternatives)?
Should we prioritize simplicity for timeliness, or more complex models for accuracy?

For mid/long term perspectives: How can we enrich WGS analysis with additional strains specific data (e.g. WHO CC cross reactivity data for current vaccines, other GISAID data: emerging variants, clade fitness, mutation annotation, antigenic change prediction)?

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THANK YOU!

CLOSING DAY 1

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