CERP
CENTRE of EXCELLENCE in RESPIRATORY PATHOGENS

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Center of Excellence in Respiratory Pathogens

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VIRESP

Program Workpackages

	Title	Lead partner	Other partners
WP 1	**Burden of respiratory viruses**	UCBL-CIRI	HCL, National Influenza Center, GIHSN, Nivel, NIH, Sanofi
WP 2	**Evolution of respiratory viruses**	UCBL-CIRI	IP2I, HCL, National Influenza Center, GISAID, Nivel, AIOLOS, Sanofi
WP 3	**Vaccine performance**	UCBL-CIRI	Sanofi
WP 4	Post-graduate training program	UCBL-CIRI	IP2I, York University, University of Witwatersrand, Sanofi
WP 5	Coordination	UCBL-CIRI	HCL, Sanofi

UCBL-CIRI: Université Claude Bernard Lyon 1 - Centre International de Recherche en Infectiologie
HCL: Hospices Civils de Lyon
GIHSN: Global Influenza Hospitalization Surveillance Network
NIH: National Institutes of Health
IP2I: Institut de Physique des deux Infinis
GISAID: Global Initiative on Sharing All Influenza Data

VIRESP Main Data Sources

Hospices Civils de Lyon

~9,000 patients / year respiratory disease

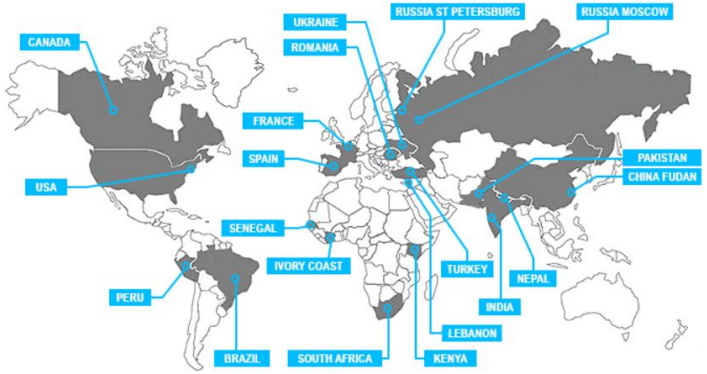
HEALTH DATA HUB

Liberté • Égalité • Fraternité
RÉPUBLIQUE FRANÇAISE

SNDS
Système national des données de santé

- health insurance
- hospitalizations
- medical causes of death
- disability-related
- sample of data from complementary health insurance organisations

Global Influenza Hospital Surveillance Network



- 143,200 patients enrolled
- 24,488 influenza cases
- 42,342 patients with other respiratory viruses

GENomique EPIdémiologique des maladies Infectieuses
genEPII

GISAID

FluNet

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Access to the HCL data

- FIRESP - Fardeau des infections respiratoires aigües aux Hospices Civils de Lyon pour les saisons épidémiques 2016-2017 à 2022-2023

- Submission to the CNIL to obtain a dispensation to inform the +50 000 patients

- Objectives: study the evolution of numbers of incident cases, the severity of infections, the risk of readmission and viral and bacterial coinfections

- Data: demographics, comorbidities, biological and care data

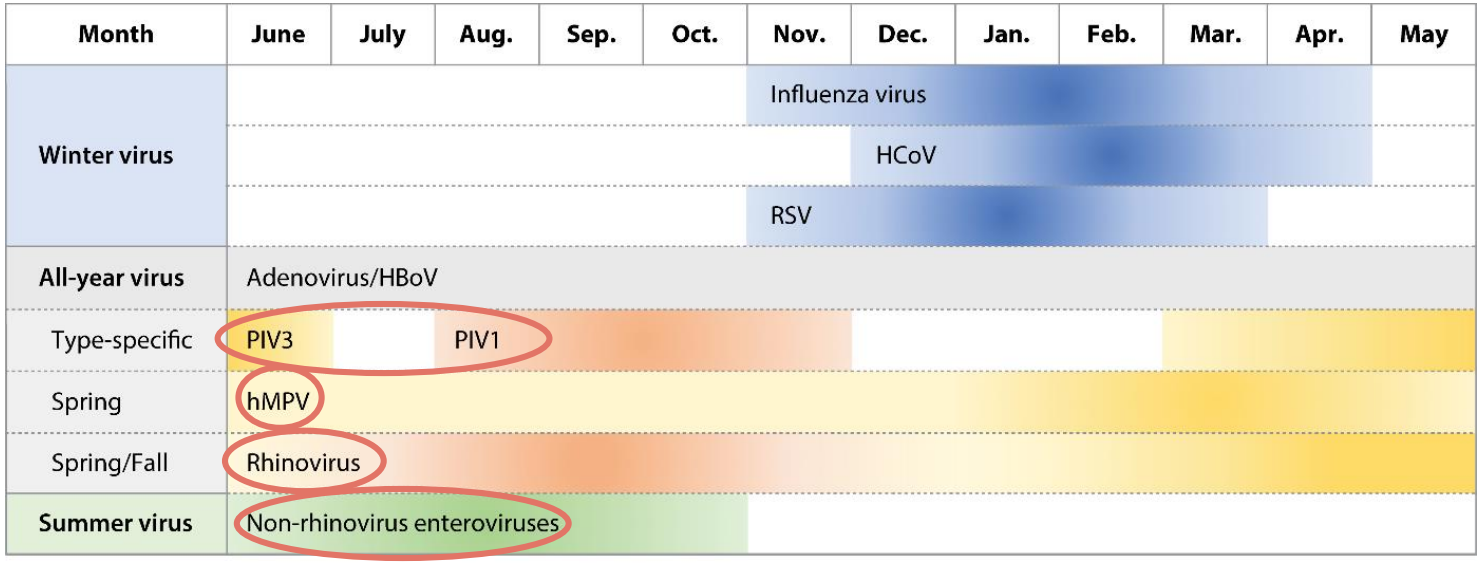
I. Burden of Respiratory Viruses

4 AIMS

- Assess the burden in the pediatric population
- Assess the burden in the adult population
- Develop algorithms to identify the more severe patients
- Define hospital-based catchment areas

External partners

Major Respiratory Viruses (non SARS-CoV-2)



Moriyama M, et al. 2020.
Annu. Rev. Virol. 7:83–101

HCoV: human coronavirus (such as strains OC43, HKU1, 229E, and NL63)
RSV: human respiratory syncytial virus
HBoV: human bocavirus
PIV: parainfluenza virus
hMPV: human metapneumovirus

Burden of Respiratory Viruses

Take advantage of the highly valuable data from the HCL and GIHSN combined with up-to-date data science:

Project	What's new	Goal
Evolution of the number of infected patients with respiratory viruses and their outcomes at HCL overtime	Statistical inference to detect seasonality, trends, changes and compare infection intensities over the years	• Detect sudden epidemiological changes • Evaluate the true impact of the COVID-19 pandemic • Evaluate the burden of less described viruses to identify the need of vaccines against them
Clinical impact of viral co-infections among hospitalized children	• Statistical longitudinal analysis to detect evolution of co-infections over time (yearly seasonality, discrepancies between weeks) • Determination of risk factors for viral co-infections applying machine learning	Comprehensive view of viral infections to identify the need for new interventions (e.g. combo vaccine) and adapt the care of patients
Predict respiratory disease outcome and decipher risk factors in children and older adults	Machine learning models applied to big data → better predictive performances	Identify more accurately populations most vulnerable to infection for optimal vaccine deployment
Define features triggering severe respiratory infections and deliver a age-specific severity scale	Machine learning models applied to big data → better predictive performances	Categorize patients by severity of disease to: • inform patient care and maximize healthcare resources • with supplement genome sequencing data

HCL: Hospices Civils de Lyon; GIHSN: Global Influenza Hospitalization Surveillance Network
RSV: human respiratory syncytial virus; HCoV: human coronavirus; PIV: parainfluenza virus; hMPV: human metapneumovirus

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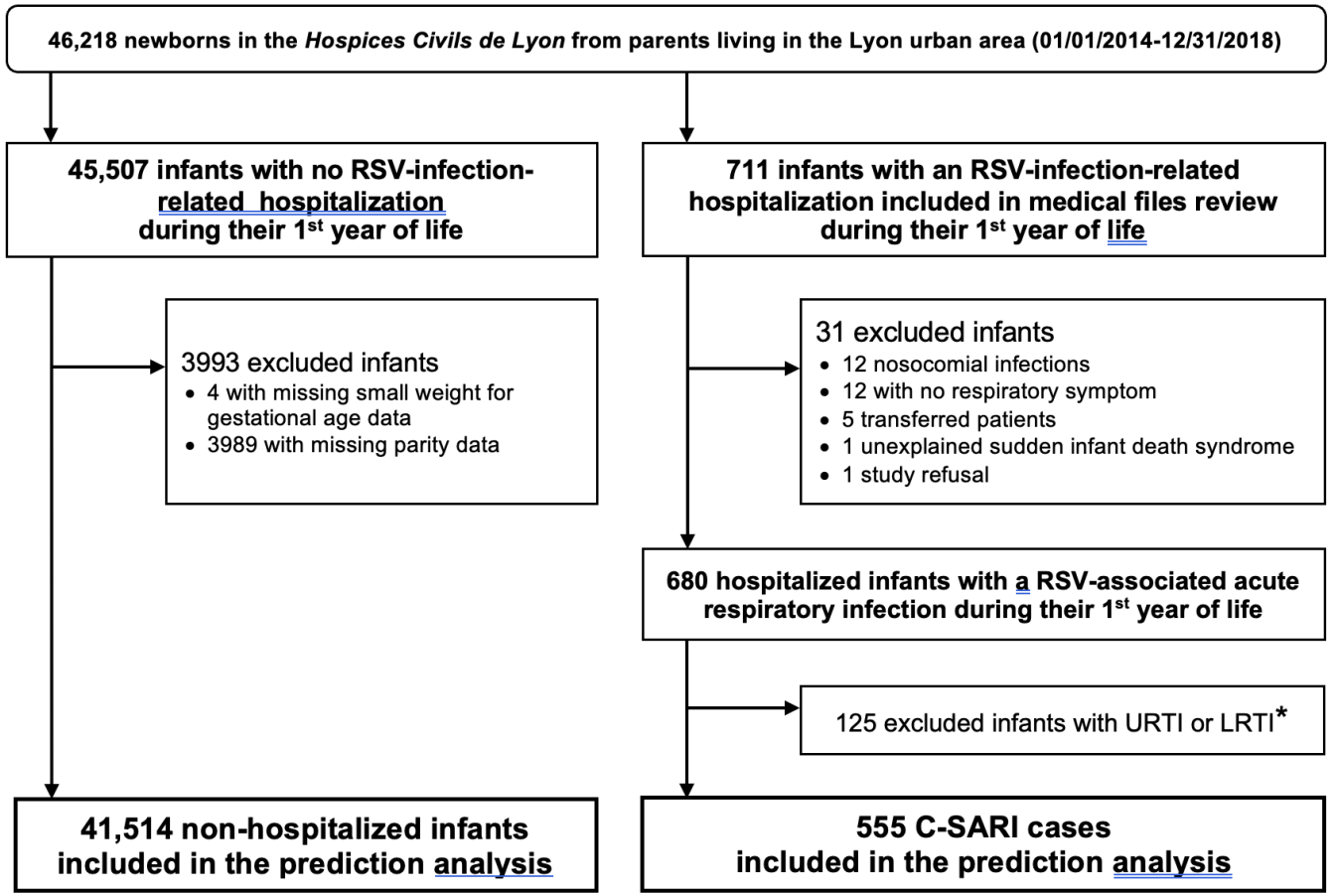
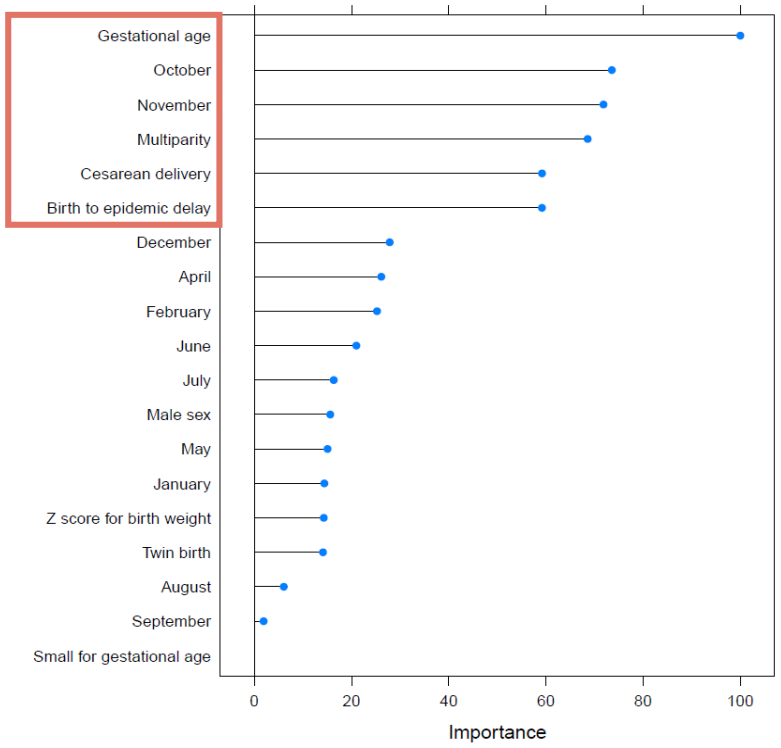
RSV severe infection risk stratification in a French 5 -year birth cohort using machine learning

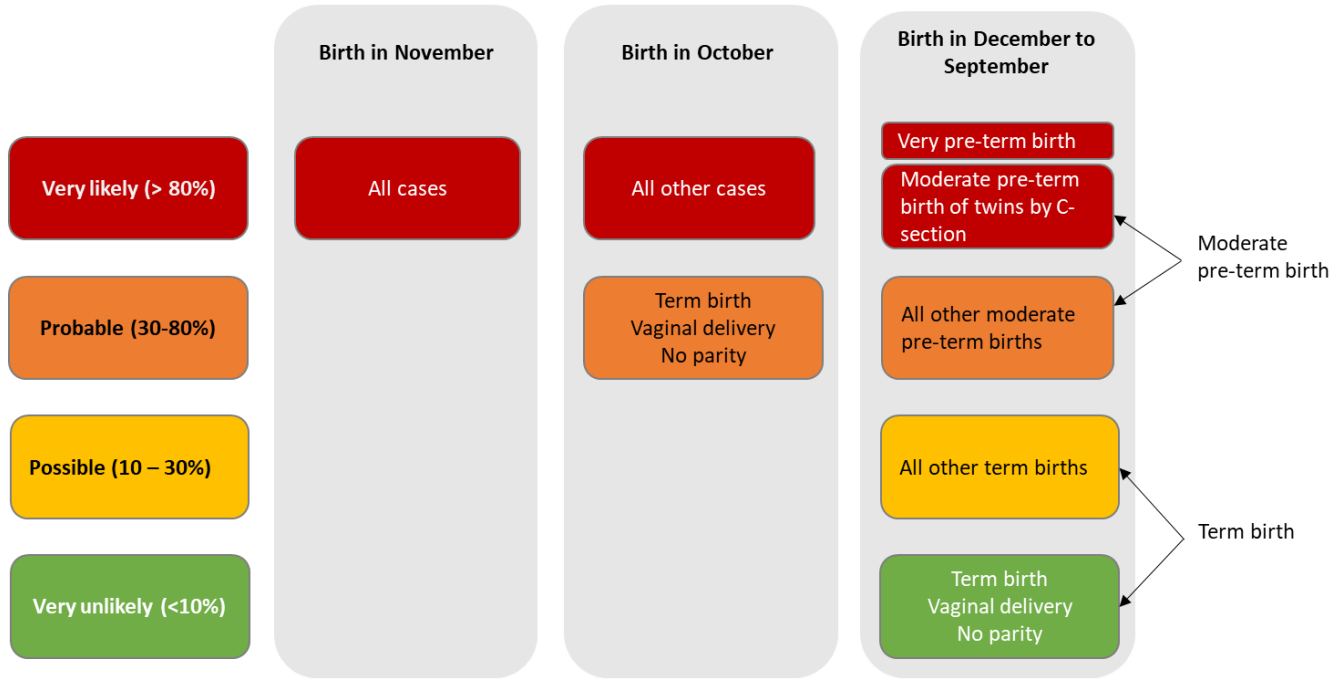


Stratification of infants for the risk of developing severe RSV infection within the 1st year of life

Most important variables



Classes of frequencies of C-SARI predictions using the ML model



HCL Older Adults

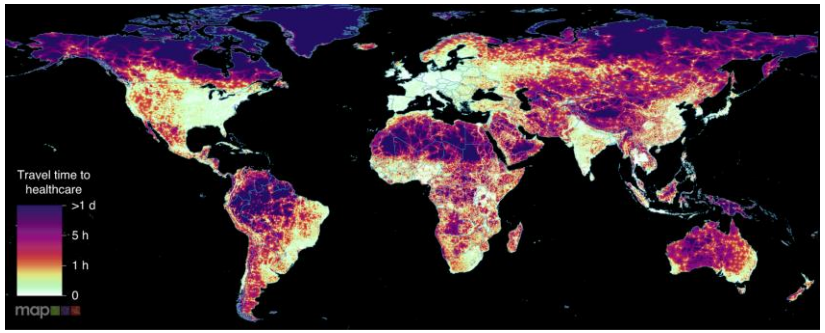
Prospective study among the adult population with viral-associated hospitalizations.

- In-hospital outcomes
- Prospectively follow-up post-discharge

Mathematical-Statistical Framework to Delineate Catchment Areas

- Distance to healthcare facilities is an important determinant of care-seeking behaviour, with implications both for **health outcomes and infectious disease surveillance.**
- The lack of denominators is a challenge in most hospital-based surveillance systems.
- We will explore several **candidate spatial-statistical models** (Poisson, negative-binomial) to estimate admission rates for administrative units within the catchment area.
- Population denominators local sources and WorldPop dataset.
- Distance and travel-time to study hospitals will be estimated using the WHO's AccessMod software.
- **Separate models** will be run for each hospital and stratified by timing, severity at admission, influenza subtype, and patient age, to identify determinants of care-seeking.

Optimal travel time to healthcare with access to motorized transport



Weiss DJ, et al. Global maps of travel time to healthcare facilities. Nat Med. 2020;26(12).

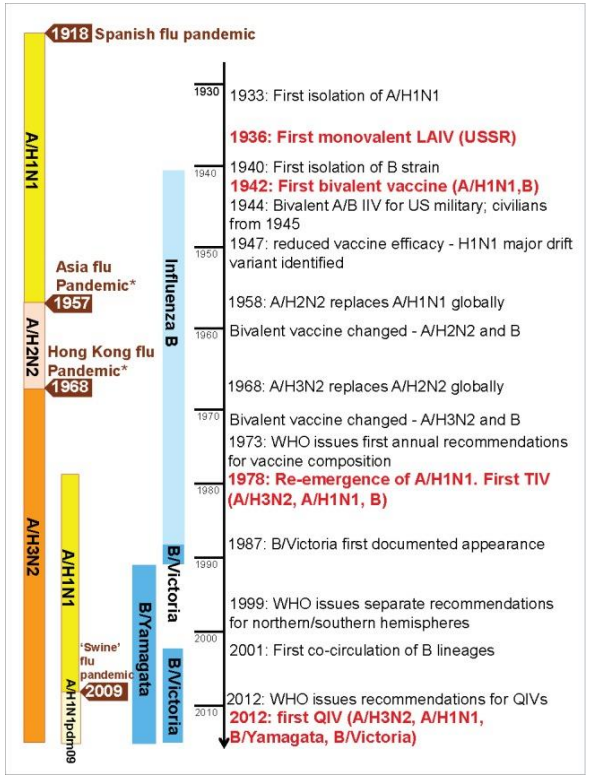
II. Evolution of Respiratory Viruses

2 AIMS

- Describe influenza B circulation
- Develop a variant-driven early warning system

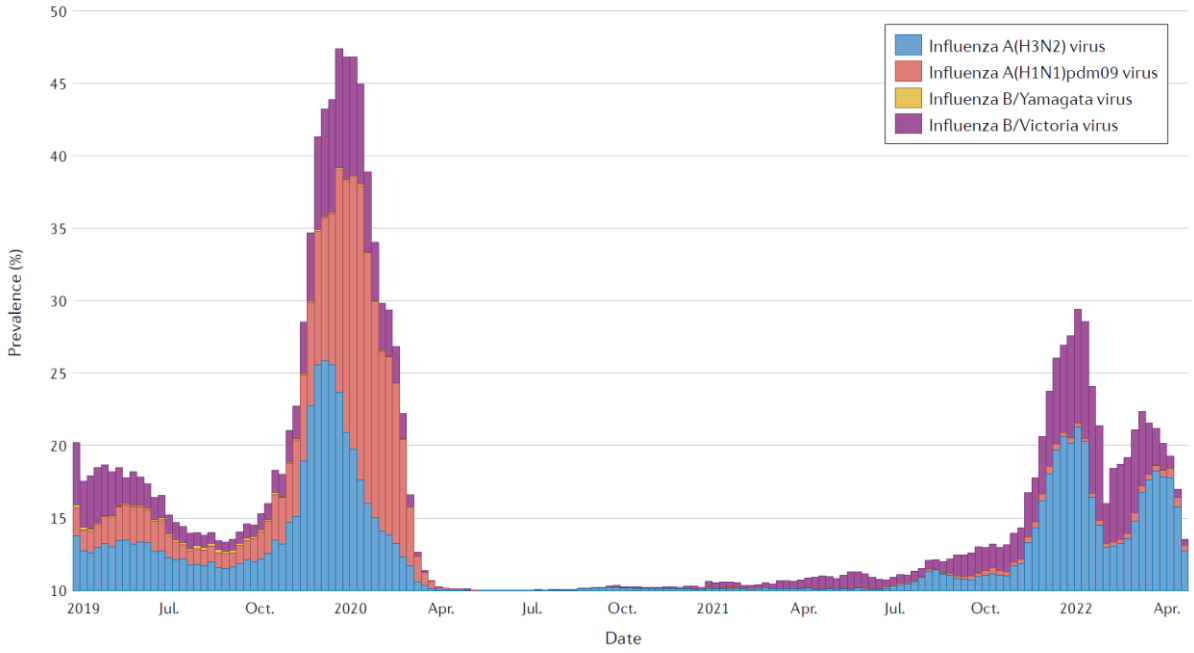
External partners

Evolution of Influenza Viruses and Vaccine Development



LAIV: live-attenuated trivalent influenza vaccine
TIV: trivalent influenza vaccine
QIV: quadrivalent influenza vaccine

Surveillance of influenza viruses by the World Health Organization Global Influenza Surveillance and Response System 2019–2022



Ray R, et al. A review of the value of quadrivalent influenza vaccines and their potential contribution to influenza control. Human Vaccines and Immunotherapeutics. 2017;13(7).
Chow EJ, Uyeki TM, Chu HY. The effects of the COVID-19 pandemic on community respiratory virus activity. Nature Reviews Microbiology. 2023;21(3).

NIVEL Kennis voor betere zorg

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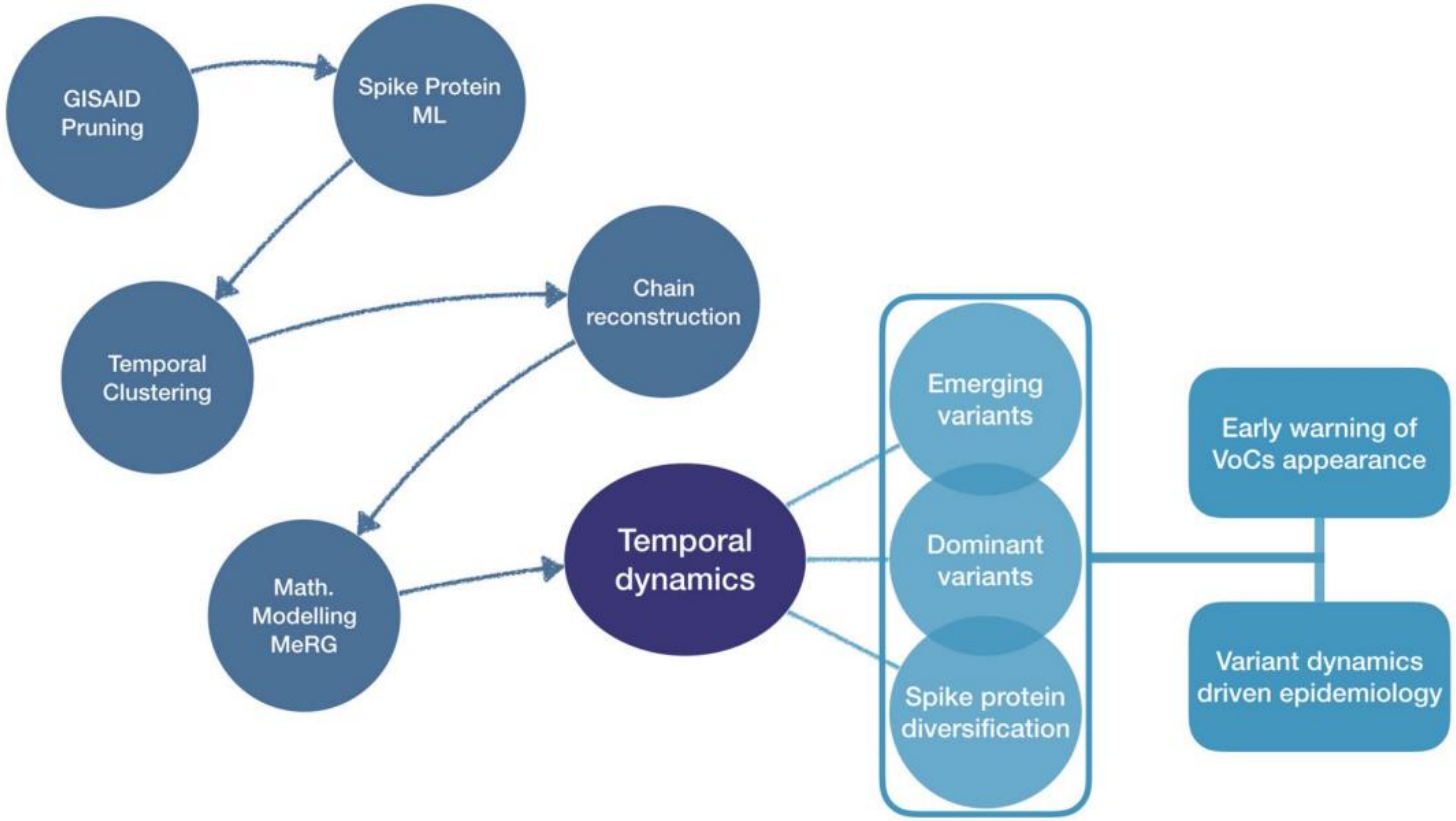
Assessing Viral Genetic Evolution



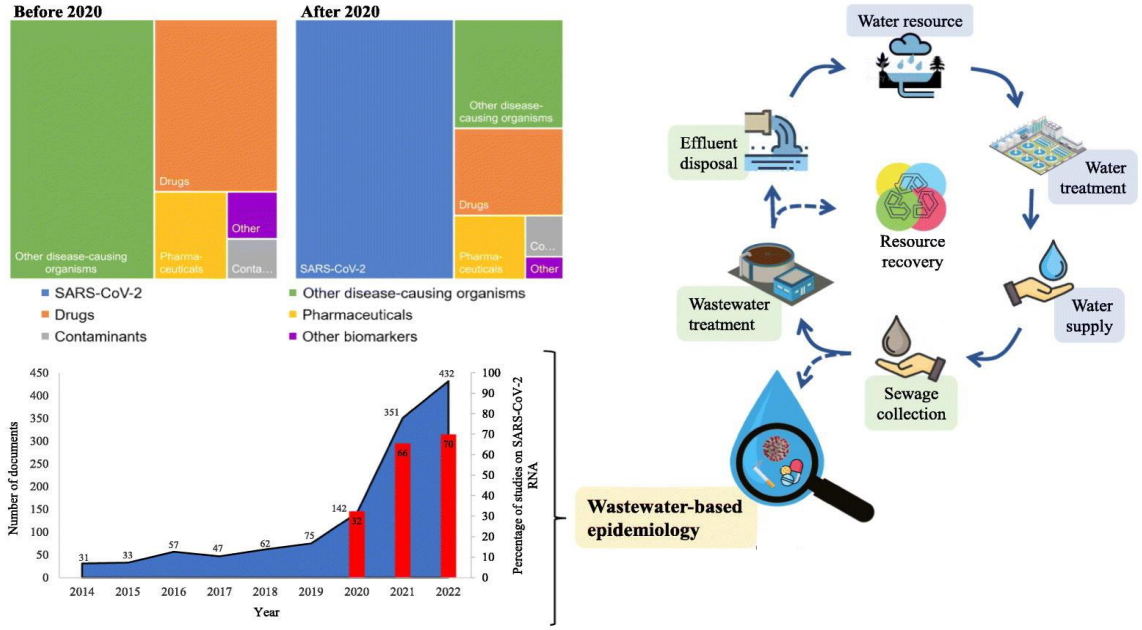
ML: Machine Learning
MeRG: Epidemic Renormalisation Group framework including mutations
VoCs: Variants of concern

de Hoffer, A., Vatani, S., Cot, C. et al. Variant-driven early warning via unsupervised machine learning analysis of spike protein mutations for COVID-19. Sci Rep. 2022;12(1).

Assessing Viral Genetic Evolution

- Clinical information
- Wastewater-based surveillance

The Impact of COVID-19 on wastewater-based epidemiology



Barcellos DS, et. Al. Sci Total Environ. 2023 May 30;892.

III. Vaccine Performance

2 AIMS

- Develop new ways to evaluate influenza vaccines
- Assess the impact of RSV preventive strategies

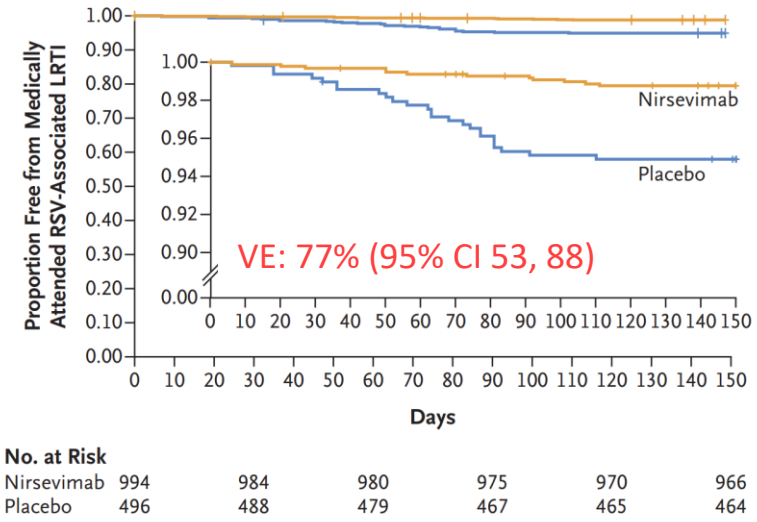
Real-World Data

- Data collected through routine care
- More inclusive making results more generalizable
- Less costly vs. new data collection
- Prospective: can be combined with clinical trials (e.g. pragmatic trials) or pharmaco-epidemiological studies (e.g. EPI-PHARE)
- Retrospectively studies interrogating administrative health registries

- We will use the SNDS platform to investigate the impact of influenza vaccination

Prevention of RSV in Randomized Clinical Trials

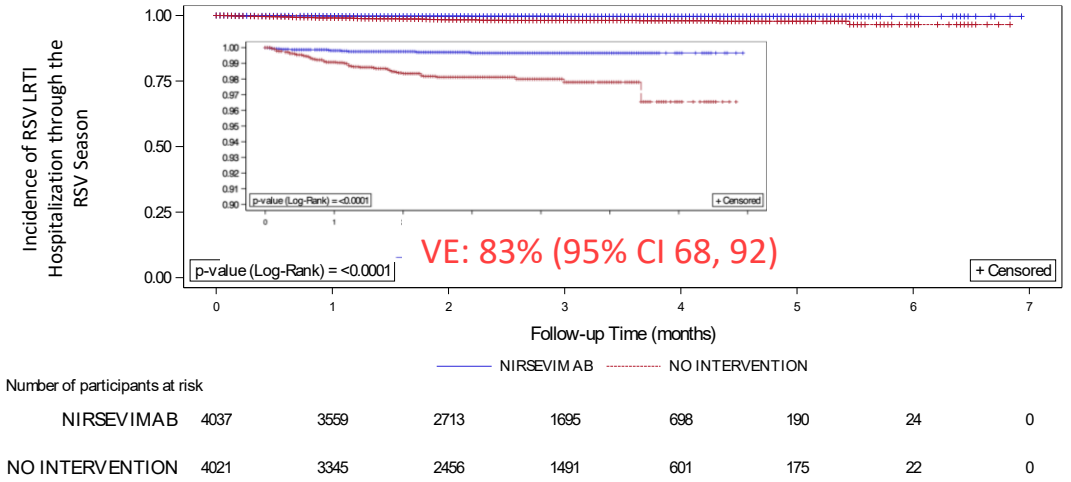
Classical Trial Design



Hammitt LL, et al. Nirsevimab for Prevention of RSV in Healthy Late-Preterm and Term Infants. New England Journal of Medicine. 2022;386(9).

Open-Label Phase 3b

data collected in a real-world setting during the 2022-2023 RSV season



Drysdale S, et al. Efficacy of nirsevimab against RSV lower respiratory tract infection hospitalization in infants: preliminary data from the HARMONIE phase 3b trial. Presented at 41st Annual Meeting of the European Society for Paediatric Infectious Diseases in Lisbon, 2023.

RSV: human respiratory syncytial virus
VE: vaccine efficacy/effectiveness

IV. Post-Graduate Training

	Title	
WP 1	Burden of respiratory viruses	1 Phd + 1 post doc + 3 MSc
WP 2	Evolution of respiratory viruses	1 Phd + 1 post doc + 1 MSc
WP 3	Vaccine performance	1 Phd + 1 MSc

Thank you