GIHSN 8TH ANNUAL MEETING

19-20 October 2020

Foundation for
Influenza
Epidemiology

Sous l'égide de

Fondation
de
France

WELCOME TO THE GIHSN COMMUNITY!

Global Influenza
Hospital Surveillance
Network

ORGANISATION OF THE MEETING

❖ 19 OCTOBER 12:00–14:00 CET – PLENARY SESSION

- Update on the GIHSN and discussion of the Global Results for the 2019/2020 season.
- With an external speech from Dr Wenqing Zhang, WHO, on GISRS and the Covid impact

❖ 20 OCTOBER 9:00–12:00 & 14:00–17:00 CET – 2 REGION SPECIFIC SESSIONS

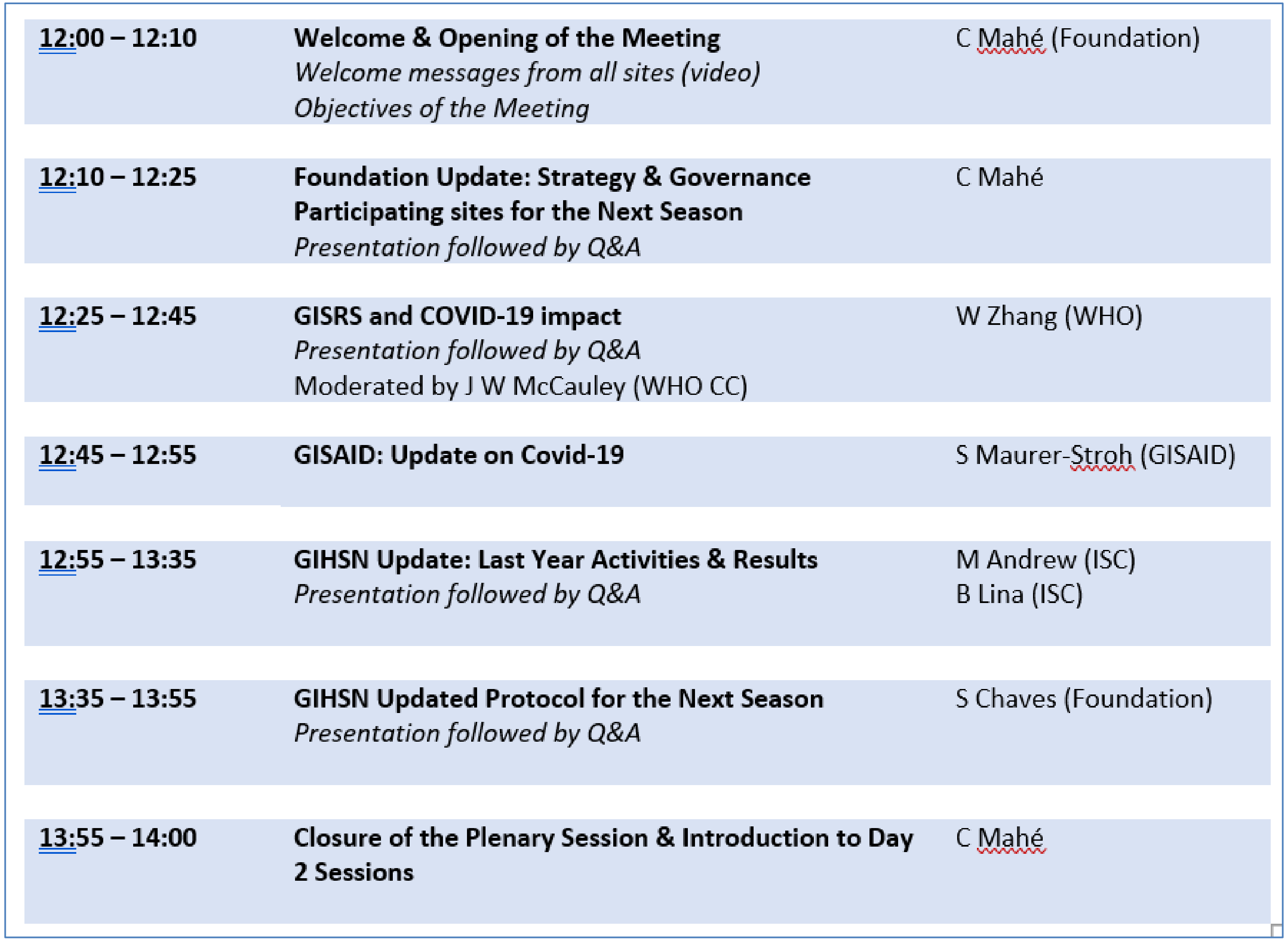
- Results by site
- Covid impact and implementation challenges for the coming season

WEBINAR RULES

- Except for the Speakers & Moderators, all attendees will be in "Listening only" mode.
- Your questions should be submitted using the Q&A button.
- Questions will be discussed after the presentations.
- Key questions not answered during the Q&A sessions will be answered in Day 2 sessions if relevant or via email after the webinar.

Thank you for your cooperation!

PLENARY SESSION 19 OCTOBER 12:00-14:00 CET AGENDA



12:00 – 12:10	**Welcome & Opening of the Meeting** *Welcome messages from all sites (video)* *Objectives of the Meeting*	C Mahé (Foundation)
12:10 – 12:25	**Foundation Update: Strategy & Governance** **Participating sites for the Next Season** *Presentation followed by Q&A*	C Mahé
12:25 – 12:45	**GISRS and COVID-19 impact** *Presentation followed by Q&A* Moderated by J W McCauley (WHO CC)	W Zhang (WHO)
12:45 – 12:55	**GISAID: Update on Covid-19**	S Maurer-Stroh (GISAID)
12:55 – 13:35	**GIHSN Update: Last Year Activities & Results** *Presentation followed by Q&A*	M Andrew (ISC) B Lina (ISC)
13:35 – 13:55	**GIHSN Updated Protocol for the Next Season** *Presentation followed by Q&A*	S Chaves (Foundation)
13:55 – 14:00	**Closure of the Plenary Session & Introduction to Day 2 Sessions**	C Mahé

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GIHSN 8TH ANNUAL MEETING, 19-20 OCTOBER 2020

FOUNDATION UPDATE: VISION & GOVERNANCE

Cédric MAHE, President, Foundation for Influenza Epidemiology

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France

BACKGROUND AND RATIONAL FOR THE FOUNDATION/GIHSN

- Effective influenza surveillance is essential for vaccine strain selection and pandemic preparedness
- WHO Global Influenza Surveillance and Response System (GISRS) relies on successful 70 years partnership with collaborating centers & NICs worldwide
- Nonetheless, additional components could strengthen GISRS:
  - Catalystic funding not to rely only on national funds (see COVID impact)
  - Additional focus on Severe Acute Respiratory Infection (essential part of WHO preferred product characteristics for flu vaccines in LMICs)
  - Linkage between virus genetic sequencing and clinical significance (better strain selection?)
  - Multiple respiratory pathogens detection (e.g. COVID, RSV) for economy of scale
  - Advanced analytics
- Private sector shares same goals regarding optimization of vaccine performance and the importance of awareness about severe respiratory outcomes → untapped potential for collaboration, synergistic funding
- **Toward a PPP funding mechanism for respiratory virus surveillance and control**

LATEST DEVELOPMENTS

- **Dialog with WHO GIP**
  - provision of data for the annual vaccine strain selection (NGS + clinical data)
  - Potential use the GIHSN to generate COVID-19 data: site feasibility conducted in April

- **Diversification of funding**: 2 new donors (Illumina and Seqirus) in addition of Sanofi Pasteur and IFPMA provide catalytic funding which complete national investments

- **Expansion of the sequencing activities:** strain sequencing platform, GISAID partnership

- **Discussion of a collaboration in respiratory virus surveillance and epidemiology with Institut Pasteur**

- **Potential link with Alliance for Influenza Pandemic Preparedness.** The Foundation is part of the Alliance and could be involved in the action plan (burden of disease awarness)

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GOVERNANCE

Cédric MAHE

Foundation for
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Epidemiology

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France

EXECUTIVE COMMITTEE MEMBERS

Executive Committee Members:

- Cédric Mahé, Sanofi Pasteur
- Erica Dueger, Sanofi Pasteur
- Mendel Haag, Seqirus
- Volker Liebenberg, Illumina
- Paula Barbosa, IFPMA
- Bruno Lina, Independent Scientific Committee
- John Paget, Independent Scientific Committee
- Melissa Andrew, Independent Scientific Committee

INDEPENDENT SCIENTIFIC COMMITTEE

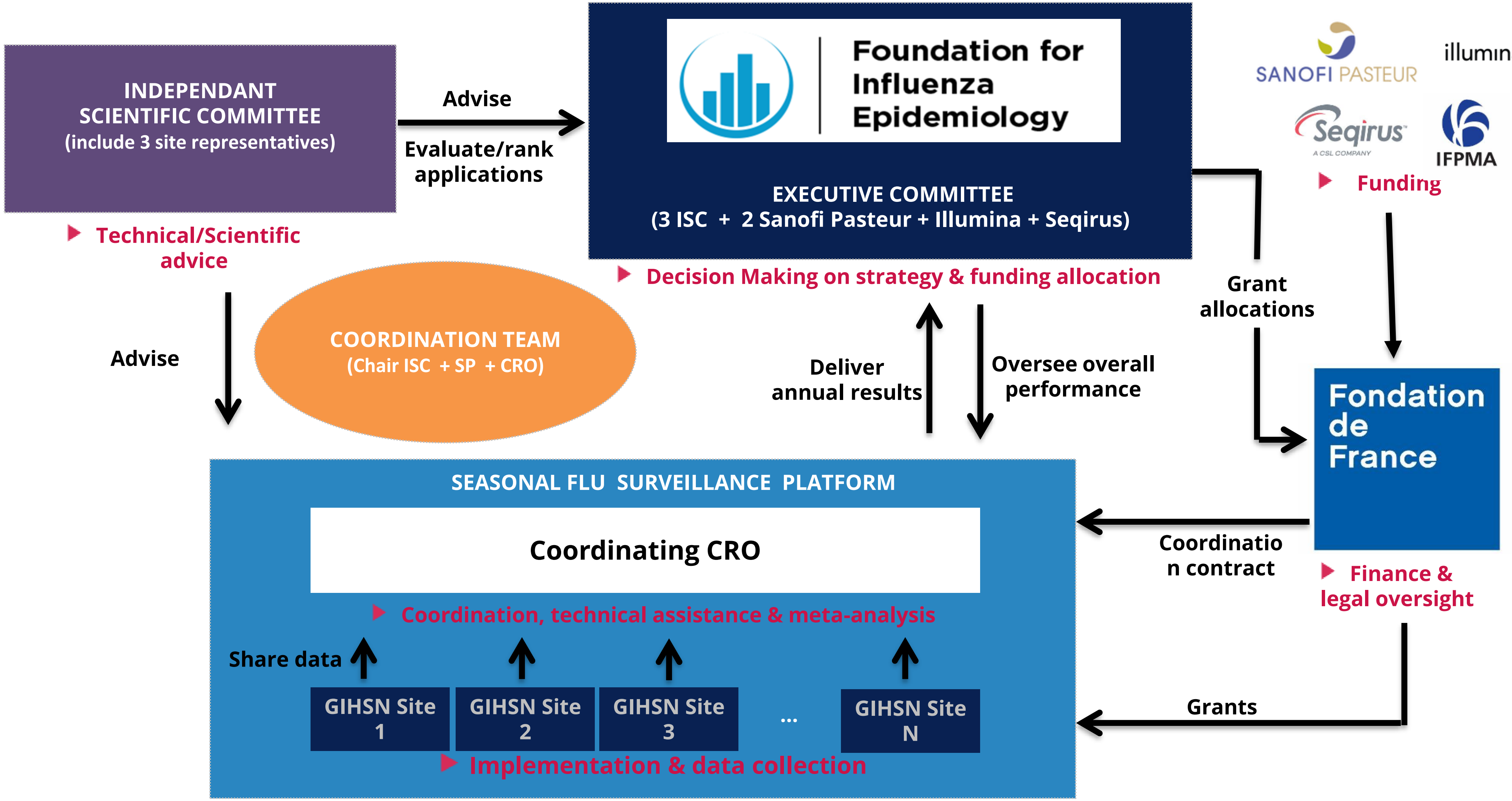
Mandate

- Review and advise on the scientific deliverables such as the protocol, analyses, interpretation of results, report(s), scientific communication and publications
- Advises on technical and scientific topics and provides specific recommendations
- Grading of the proposal to the tender
- 3 designated representatives at the Executive Committee

Composition

- The Committee is composed of 5 to 8 independent experts and 2-3 investigators from the GIHSN network
- Membership currently under renewal

FOUNDATION GOVERNANCE



INDEPENDANT SCIENTIFIC COMMITTEE
(include 3 site representatives)

▶ Technical/Scientific advice

Advise

Evaluate/rank applications

Foundation for Influenza Epidemiology

EXECUTIVE COMMITTEE
(3 ISC + 2 Sanofi Pasteur + Illumina + Seqirus)

▶ Decision Making on strategy & funding allocation

SANOFI PASTEUR
illumina
Seqirus
IFPMA

▶ Funding

Grant allocations

Fondation de France

▶ Finance & legal oversight

Advise

COORDINATION TEAM
(Chair ISC + SP + CRO)

Deliver annual results

Oversee overall performance

SEASONAL FLU SURVEILLANCE PLATFORM

Coordinating CRO

▶ Coordination, technical assistance & meta-analysis

Coordination contract

Share data

GIHSN Site 1

GIHSN Site 2

GIHSN Site 3

…

GIHSN Site N

▶ Implementation & data collection

Grants

SANOFI PASTEUR ROLE IN THE GOVERNANCE

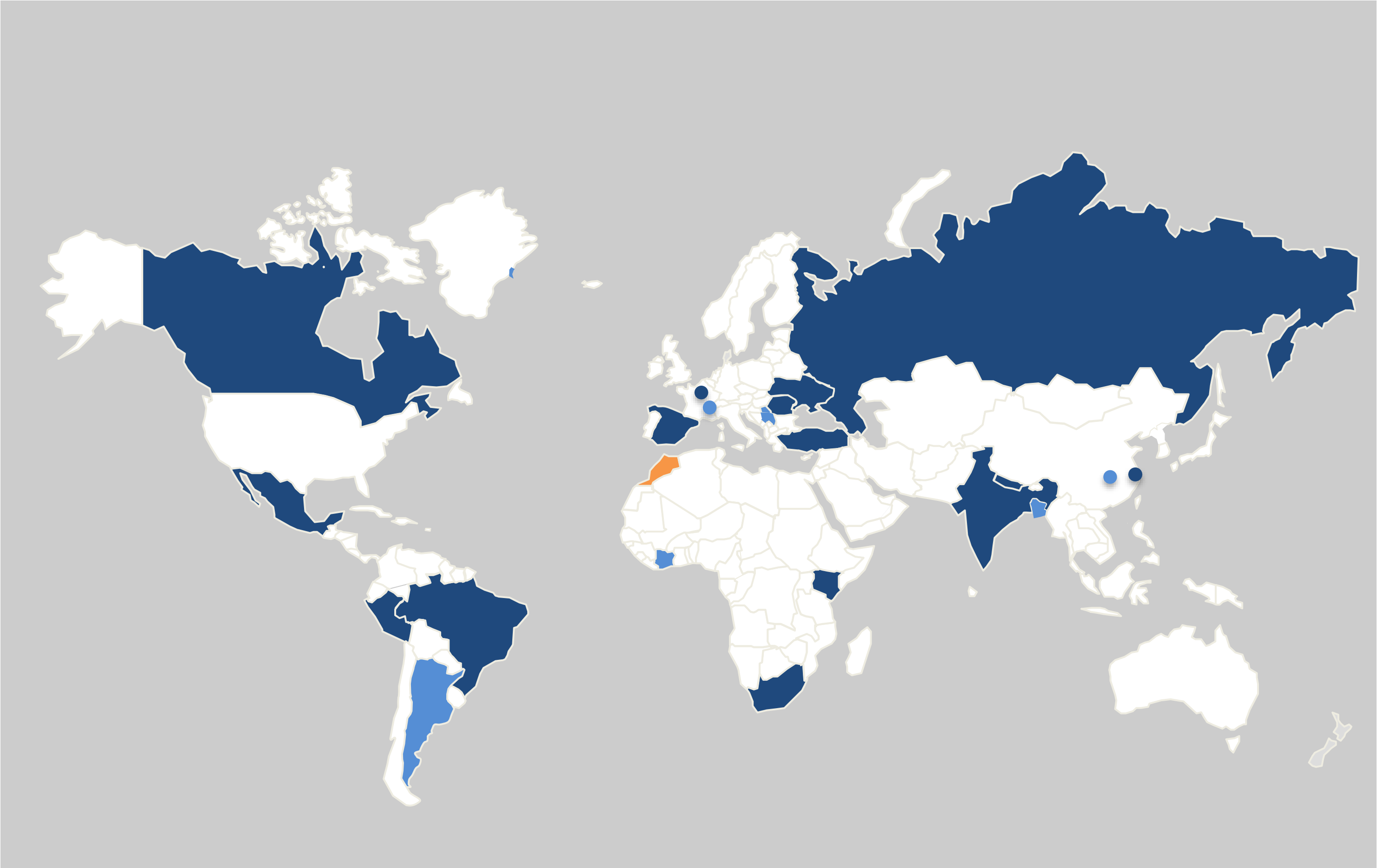
- **Contribution of FTEs from SP staff** (during this contribution, they do not represent SP interest)
    - Sandra Chaves (0,1 FTE - scientific)
    - Laurence Torcel-Pagnon (0,2 FTE- coordination)
    - Cédric Mahé (0,1 FTE - strategy & partnerships)
    - Myriam Beigeaud (0,1 FTE- admin)

SITES PARTICIPATING TO THE GIHSN IN THE 2019-2020 & 2020-2021 SEASON

North America
Canada
Mexico

South America
Brazil
Argentina
Peru

Eurasia
Romania
Serbia
France-Paris
France-Lyon
Ukraine
Spain
Russia (2)



🟦 2019-2020
■ 2019-2020 & 2020-2021
🟧 2020-2021

Africa
Ivory-Coast
South Africa
Kenya
Morocco

Middle East
Lebanon
Turkey

Asia/Pacific
China-Fudan
China-Wuhan
India
Nepal
Bangladesh

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GISRS AND COVID-19 IMPACT

Dr Wenqing ZHANG, Head of Global Influenza Program, WHO

Foundation for Influenza Epidemiology

Sous l'égide de

Fondation de France

GISRS and COVID-19 impact

Wenqing Zhang

GIHSN Global Annual Meeting 2020
19-20 October • Virtual meeting

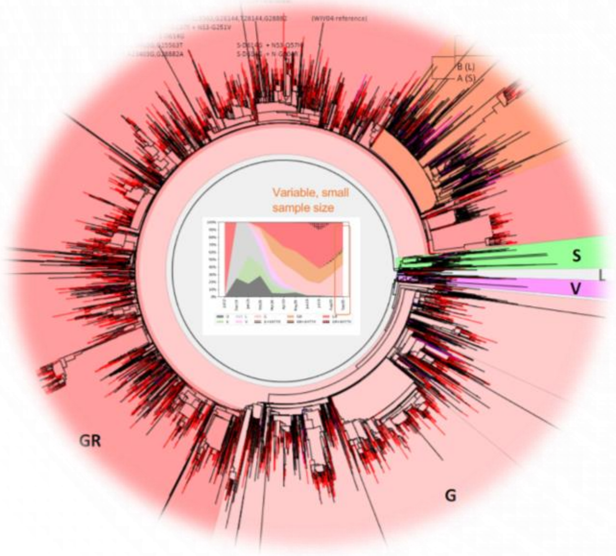
Response to COVID-19 pandemic:

GISRS in action since *day 1*

of the identification of SARS-CoV-2

TOP URGENT: GSD (Genetic sequence data) sharing

- GSD sharing – **critical for diagnostic** development, risk assessment ….
- **ABS** – Access and Benefit Sharing
- GISAID – the **GISRS mechanism** for influenza GSD sharing

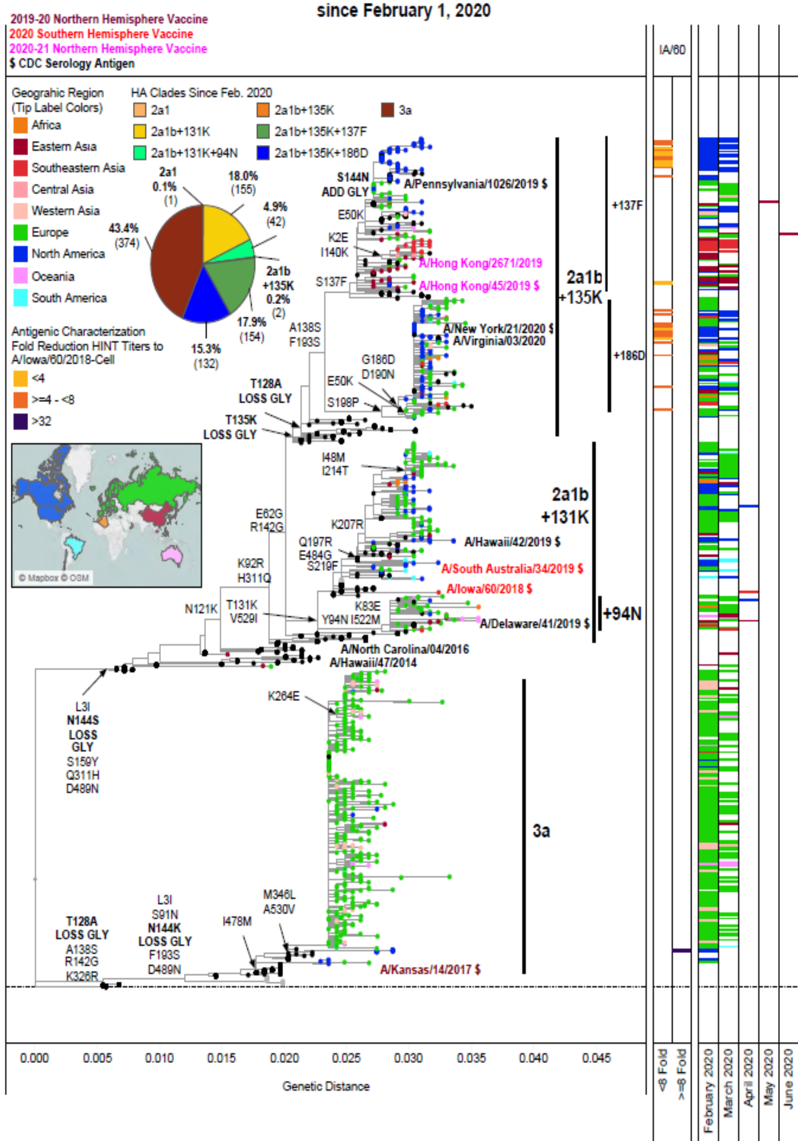


- 2020-01-10 1st GSD shared via GISAID (**< 48 hours**)

EpiFlu™ →→ EpiCoV™

- **~118K whole genomes** of SARS-CoV-2 as of 2 Oct 2020

Phylogenetic Analysis of A(H3N2) Hemagglutinin Genes Circulating Globally since February 1, 2020

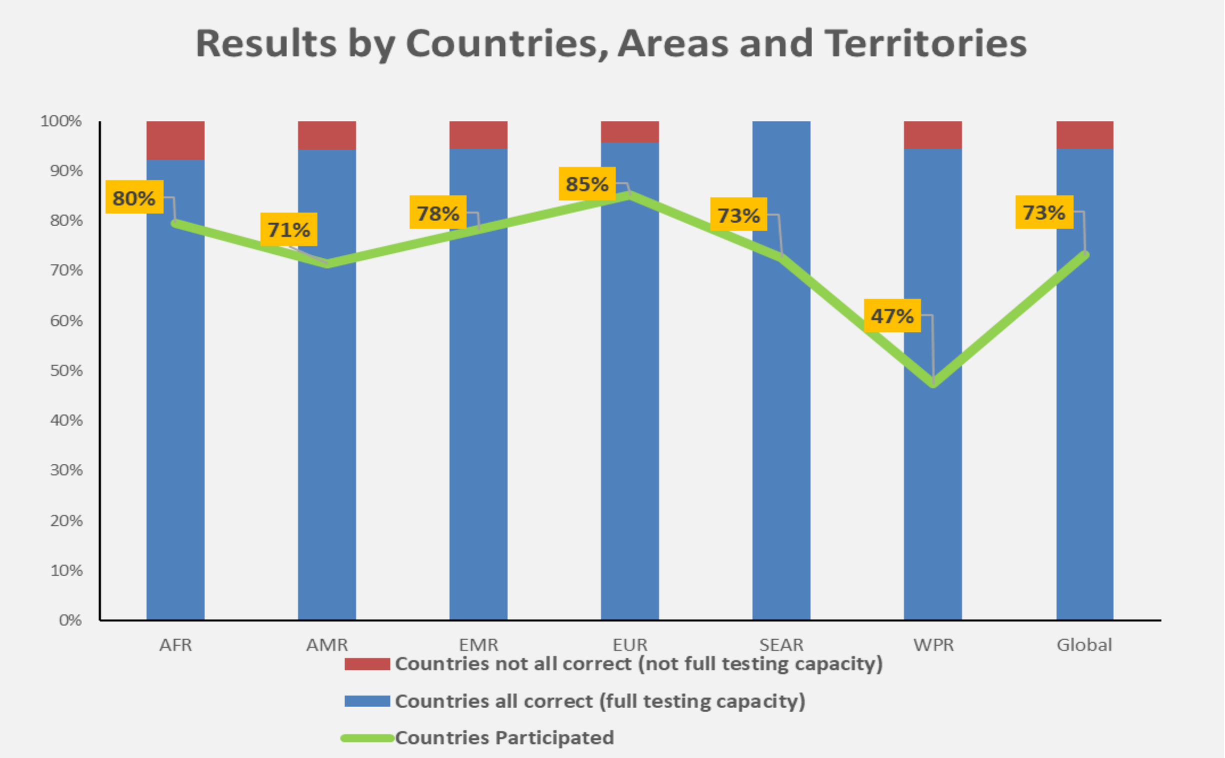


TOP URGENT: EQAP (external quality assessment program)

- Evaluate lab diagnostic quality of the novel virus SARS-CoV-2; understand the global capacity
- GISRS mechanism of annual EQAP for influenza since 2007
- Influenza EQAP → WHO COVID-19 EQAP
  - 8 Feb initiated discussion
  - Confirmed contract 15 March – 31 August
  - 16 April – 1st shipment going out

164 countries (233 labs) participated:

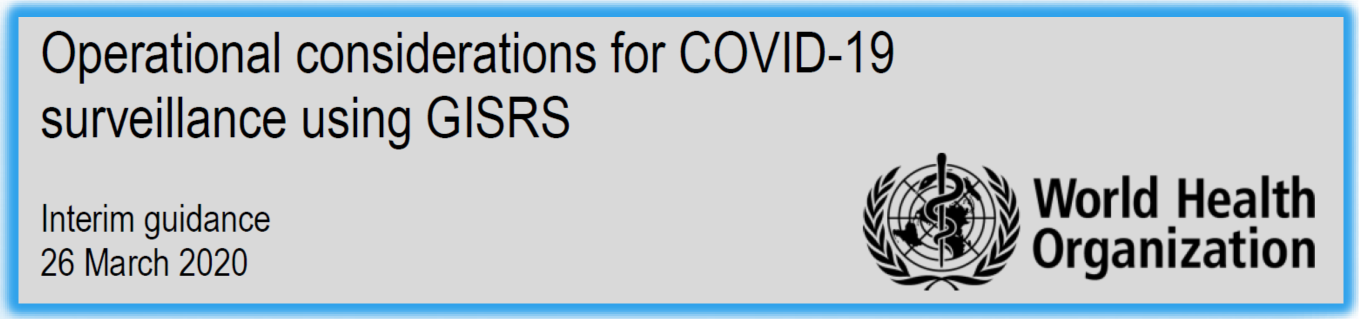
- **94%** participating labs all correct
- **95%** participating countries with all correctness full capacity in place
- **96%** of labs with 2019 influenza EQAP all correct record, all correct for COVID-19 virus



Capacity built through influenza readily → COVID-19 response

- **FluMart** → CoVMart: COVID data reporting
- GISRS influenza **shipping mechanism** → COVID-19 virus materials shipping
- Influenza pandemic **special study** protocols → COVID-19 serology and early investigation protocols
- ~90% national COVID-19 labs are **NICs** or labs associated with GISRS
- **GISRS mechanisms** e.g. TORs of H5RefLabs → COVID-19 Reference Labs

- **COVID-19 sentinel surveillance by GISRS**



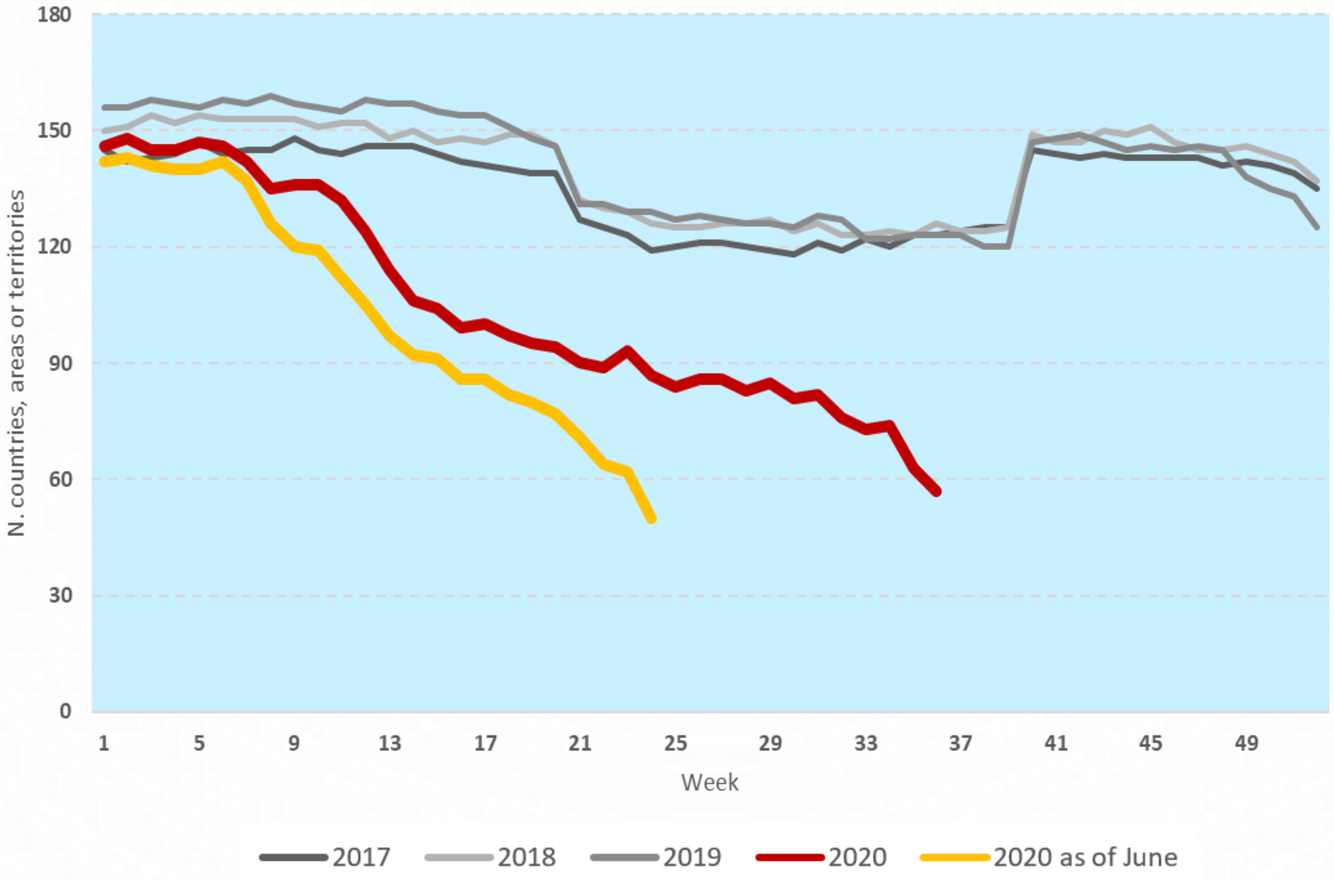
Operational considerations for COVID-19 surveillance using GISRS

Interim guidance
26 March 2020

World Health Organization

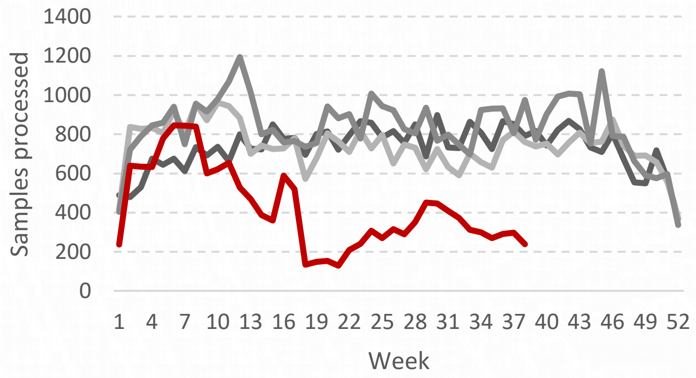
Impact on influenza surveillance and monitoring

Reporting to FluNet - global

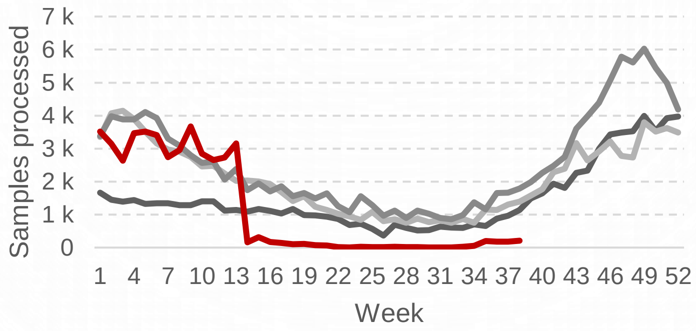


Specimens processed for influenza by WHO Region

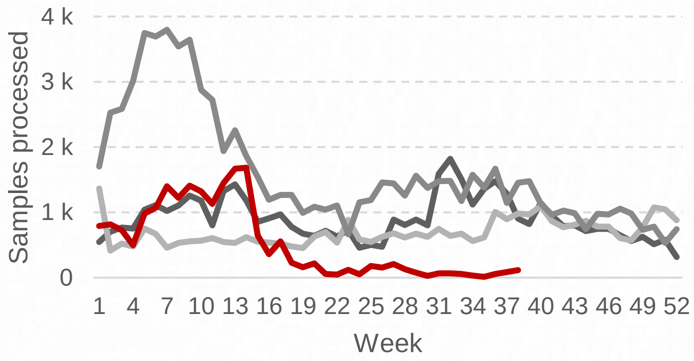
AFR



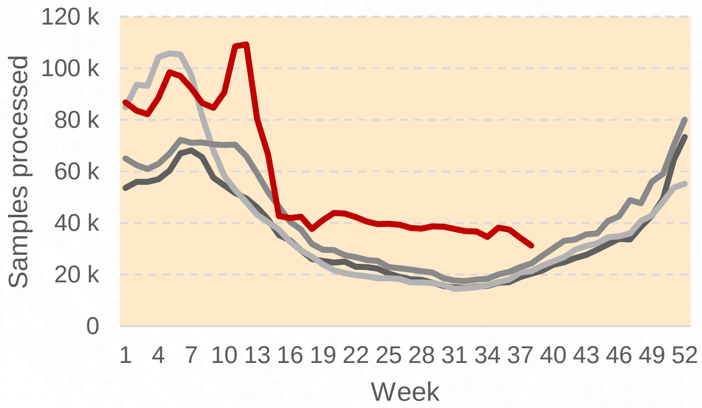
EMR



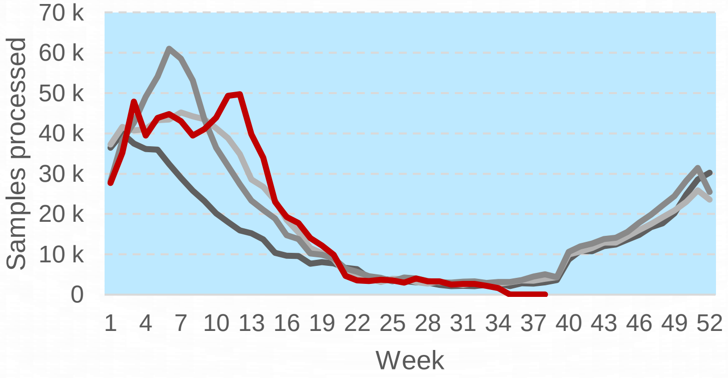
SEAR



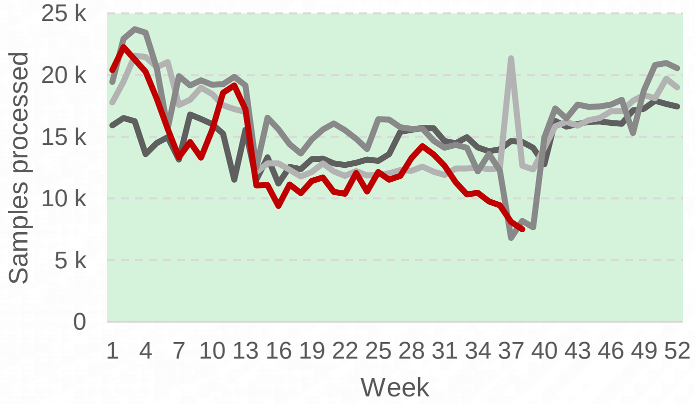
AMR



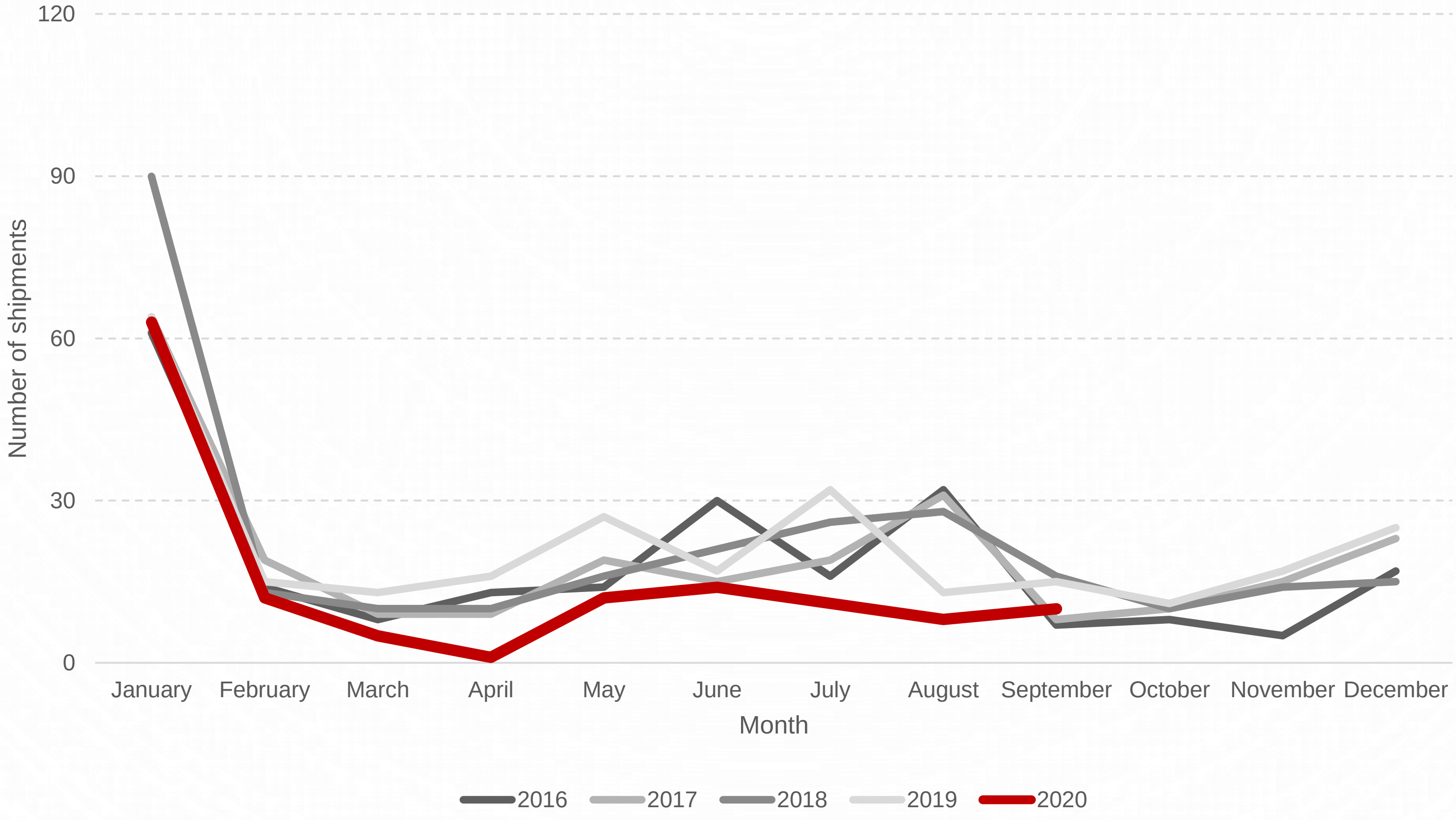
EUR



WPR

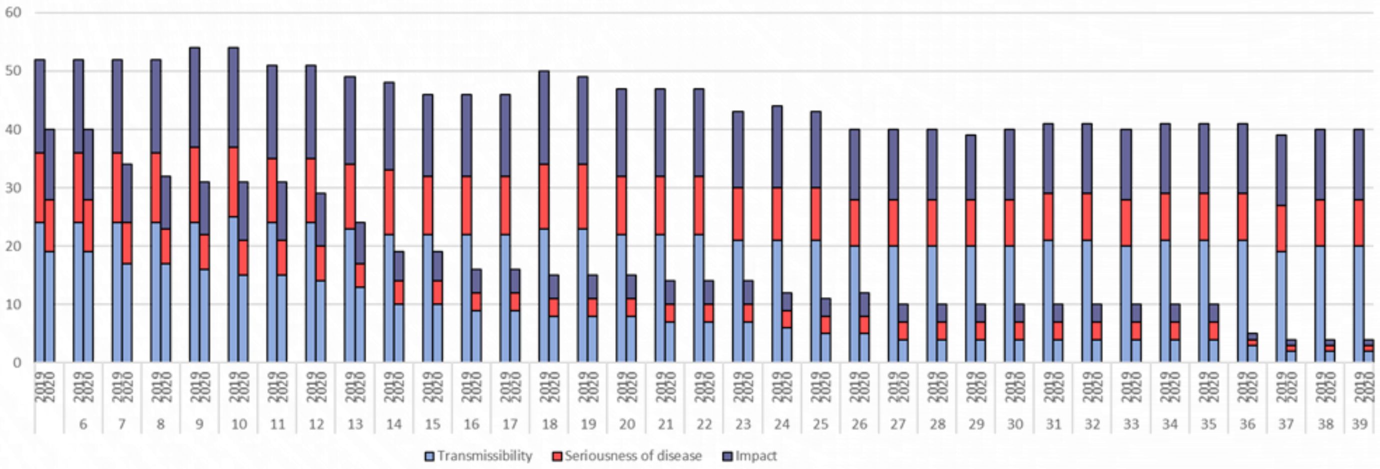


Shipments to WHO Collaborating Centres (via SFP)



Impact on influenza surveillance and monitoring

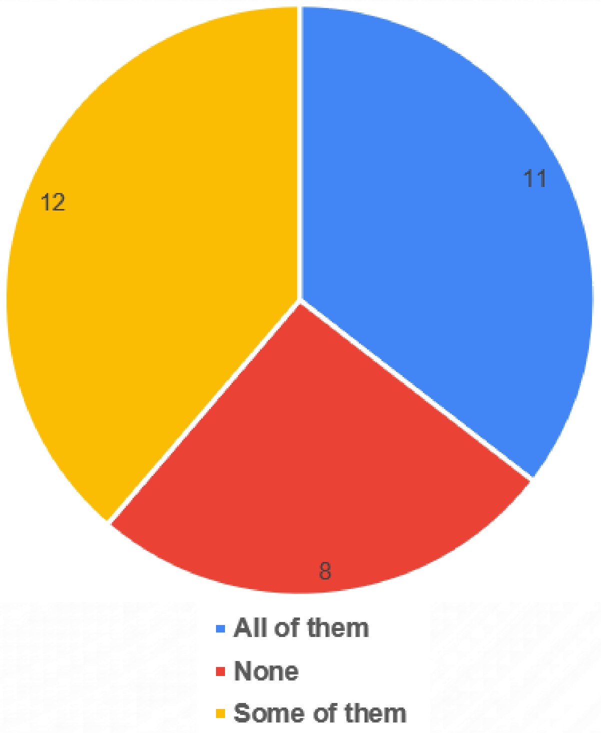
Reporting indicators of PISA



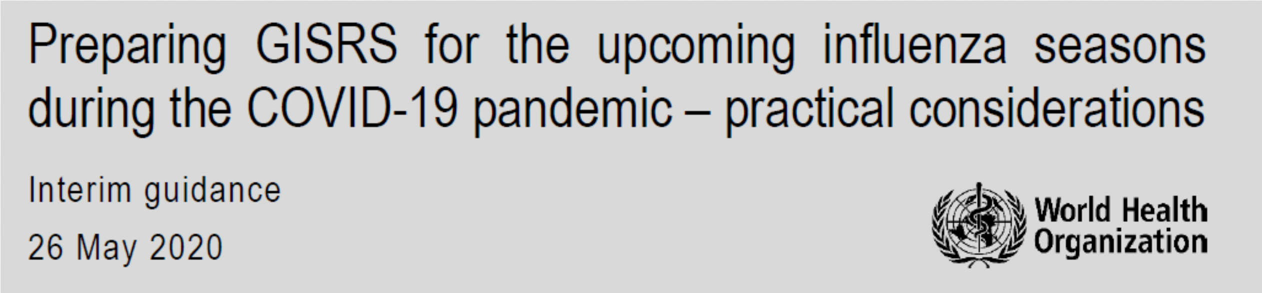
Total responses (n=31)

(from AFRO, AMRO, SEARO and WPRO)

Influenza sentinel hospitals (e.g. SARI surveillance) repurposed to COVID-19 designated hospitals?



WHO guidance - how to address the issue



Preparing GISRS for the upcoming influenza seasons during the COVID-19 pandemic – practical considerations

Interim guidance

26 May 2020

World Health Organization

Influenza

Preparing GISRS for the upcoming influenza seasons

In the context of the COVID-19 pandemic, GISRS, regional influenza networks, and national influenza surveillance systems should prepare for the co-circulation of influenza and SARS-CoV-2 viruses in the upcoming and subsequent influenza seasons and for the possible emergence of influenza viruses of pandemic potential. This document summarizes operational considerations to continue monitor the persistent influenza threat and maintain influenza surveillance while responding to the current COVID-19 pandemic.

Read the document

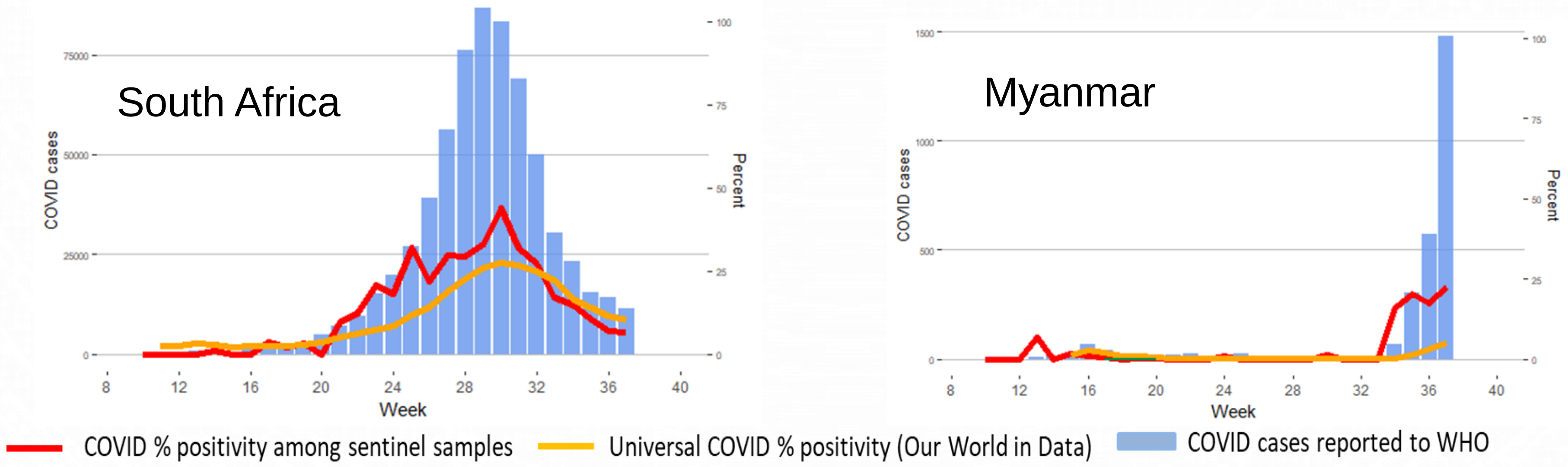
Before attempting influenza virus isolation in cells or eggs in BSL-2 settings, ensure the specimens **tested negative** for COVID-19

- **For the *persistent* influenza threat:** continuous surveillance, monitoring, and timely assessment of associated risks of seasonal, zoonotic, and pandemic influenza as specified in the WHO Terms of Reference of GISRS.
- **For the *current* COVID-19 response:** continued leverage of GISRS and associated surveillance systems for COVID-19 sentinel surveillance.

https://www.who.int/influenza/gisrs_laboratory/upcoming_flu_season/en/

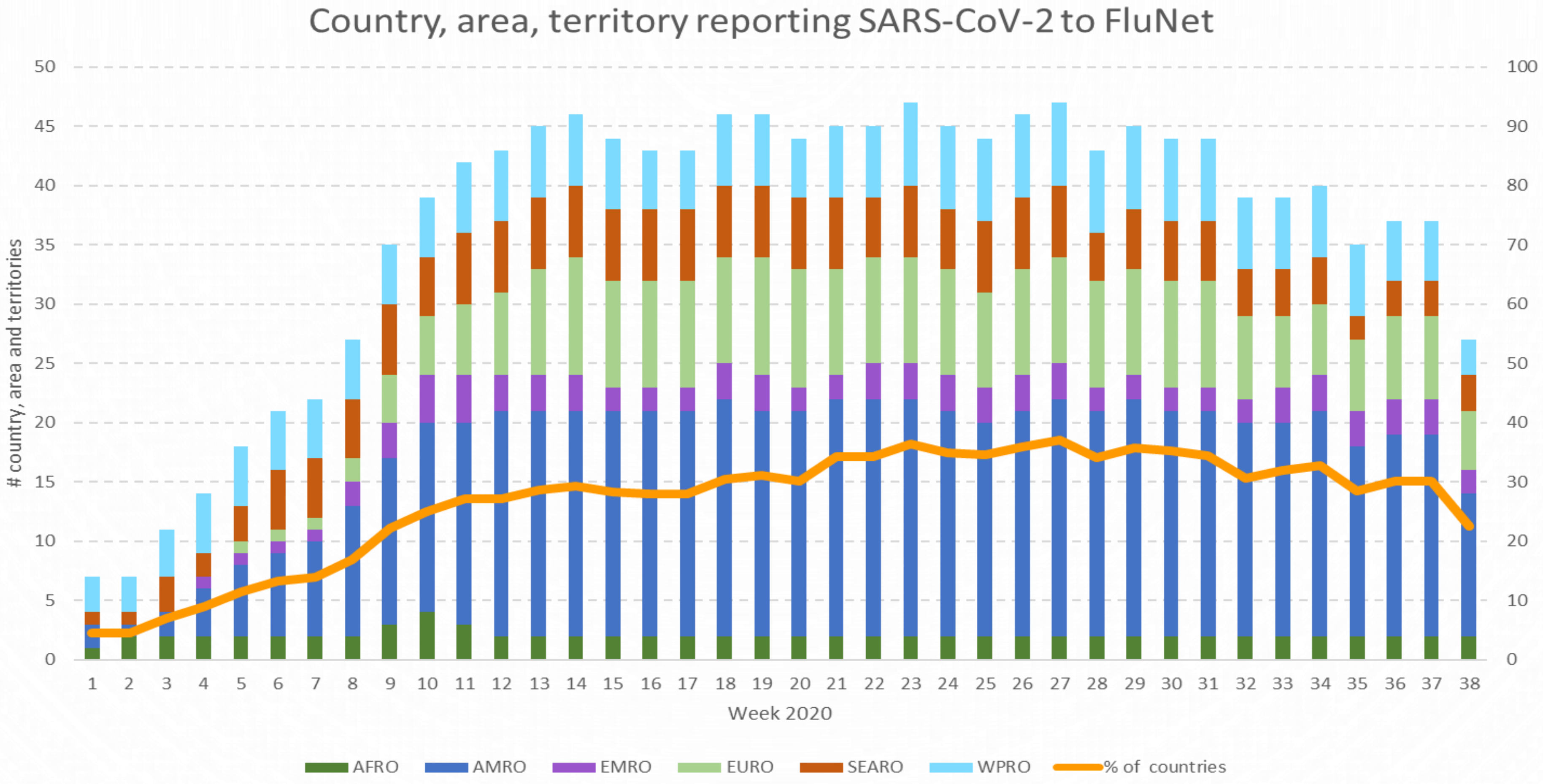
Optimize the use of GISRS influenza systems

- Enhance **vigilance** for the threat of influenza
- Surveillance for **co-circulation** of influenza and COVID-19
  - Utilize existing influenza sentinel surveillance systems – sustainable, practical
  - Atypical seasonality 2020 – strategies for *inter-seasonal* periods



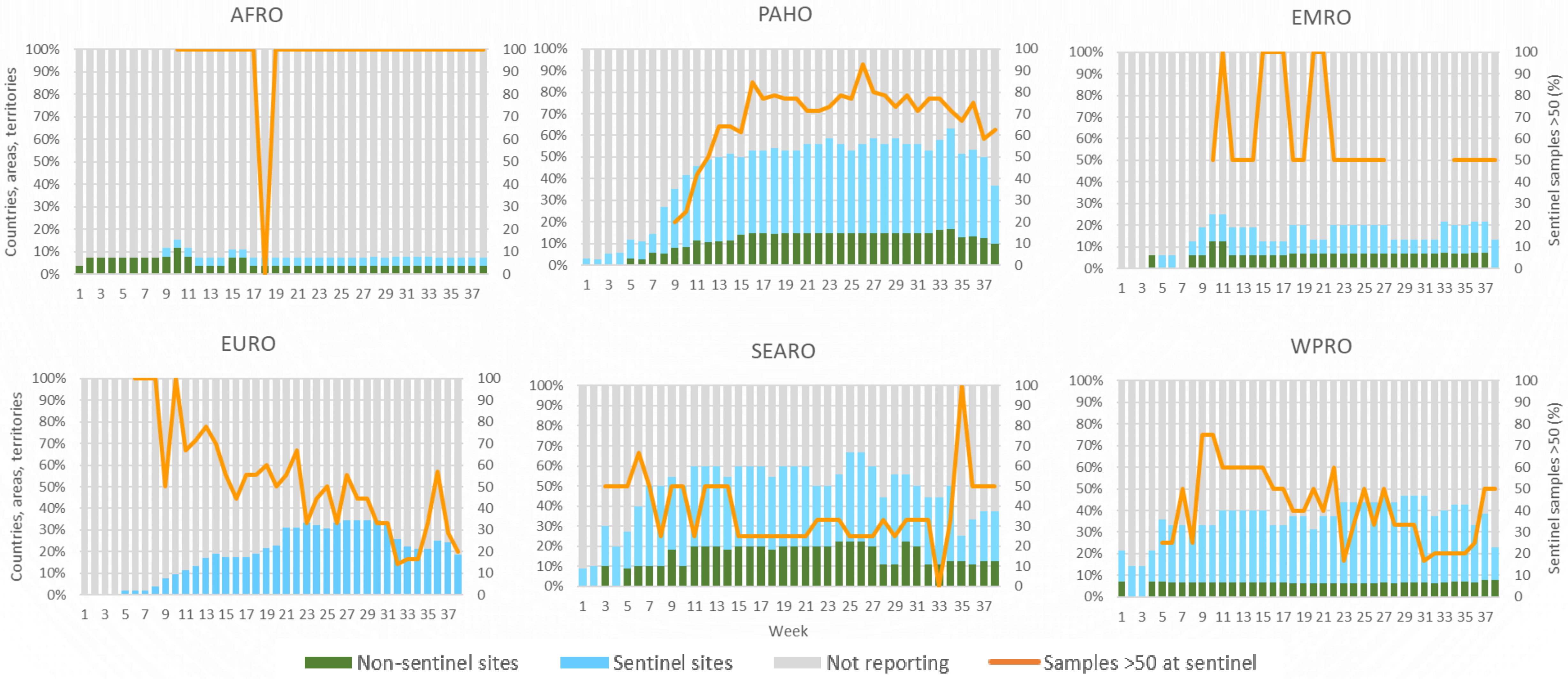
46 - 210	**Sentinel samples tested per week**	**4 - 730**
161 - 324,226	**Universal testing per week**	**441 - 20,755**

COVID-19 sentinel surveillance



Between week 26-39: 17 ~ 33 countries reported timely

COVID-19 sentinel surveillance by WHO Region



WHO e-Consultation 6-8 October

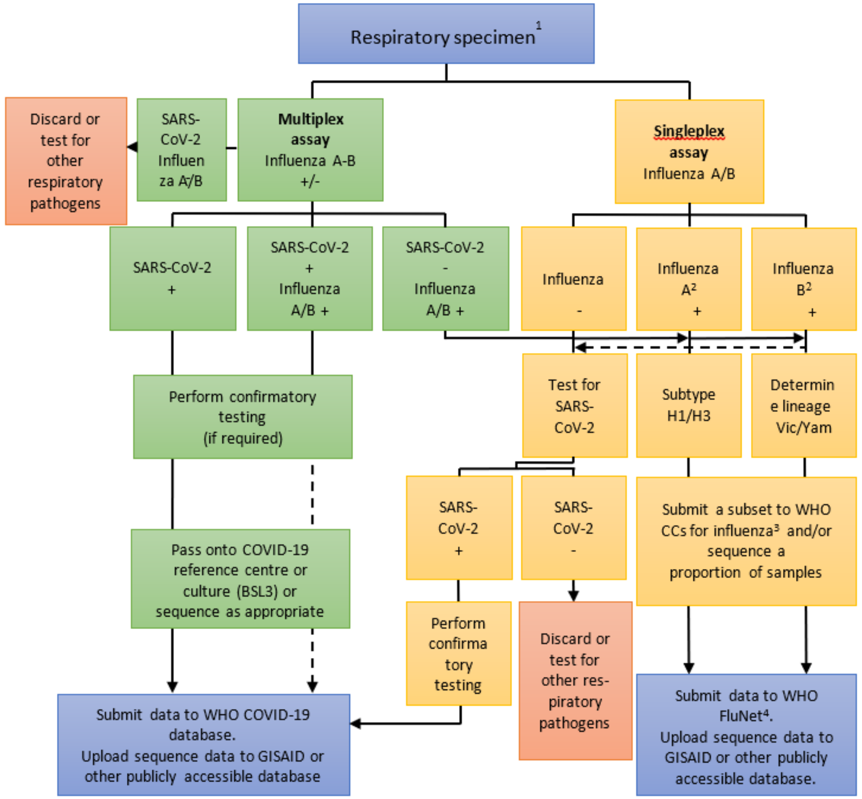
- main outcomes and observations

- Reassured **common ground** of a global system → GISRS and associated surveillance systems → influenza and COVID-19
- **Consensus** on essential components of the global systems for influenza and COVID-19 sentinel surveillance e.g. case definition, testing algorithms:
  - Primary roles and responsibility: influenza surveillance and monitoring
  - Whenever possible, add SARS-COVID-2 in sentinel surveillance
  - Clearer vision on how to function GISRS systems in the upcoming next 6-12 months
  - Real experience from Southern Hemisphere 2020 valuable
- Challenges real; **importance** and **benefits** of GISRS for both influenza and COVID-19 **not** fully understood by decision-making levels in many countries
- Importance of reporting to FluNet and FluID (for both influenza and COVID-19 surveillance data) **not** fully understood by some countries
- High expectation for **Multiplex** influenza+SARS-CoV-2 –*vs* – limited supply
  - CDC supply limited; commercial kits with constraints

What GIHSN can support

- Sustain sentinel surveillance
  - Secure 150 (minimum 50) per week of **quality** SARI/ILI/ARI specimens
- Test for influenza and SARS-COVID-2
  - When resource allows, test for both
- Report the aggregated results through same influenza reporting channel, same timing
  - Additional data fields already built into FluNet/FluID, including potential co-infections
- Vigilant of influenza threat
  - Continue GISRS function on influenza, especially now!

GISRS algorithm 1: when testing influenza influenza viruses as a first preference



Respiratory specimen[1]

Multiplex assay Influenza A-B +/-

SARS-CoV-2 Influenza A/B

Discard or test for other respiratory pathogens

SARS-CoV-2 +

SARS-CoV-2 + Influenza A/B +

SARS-CoV-2 - Influenza A/B +

Perform confirmatory testing (if required)

Pass onto COVID-19 reference centre or culture (BSL3) or sequence as appropriate

Submit data to WHO COVID-19 database. Upload sequence data to GISAID or other publicly accessible database

Singleplex assay Influenza A/B

Influenza -

Influenza A[2] +

Influenza B[2] +

Test for SARS-CoV-2

Subtype H1/H3

Determine lineage Vic/Yam

SARS-CoV-2 +

SARS-CoV-2 -

Perform confirmatory testing

Discard or test for other respiratory pathogens

Submit a subset to WHO CCs for influenza[3] and/or sequence a proportion of samples

Submit data to WHO FluNet[4]. Upload sequence data to GISAID or other publicly accessible database.

Acknowledgement

- **WHO GISRS** (Global Influenza Surveillance and Response System)
- GISRS associated **national/sub-national surveillance systems**
- **Countries** hosting GISRS institutions

- **WHO Global Influenza Programme**

Thank You

World Health
Organization

Global Influenza
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GISAID: UPDATE ON COVID-19

Sebastian MAURER-STROH, GISAID

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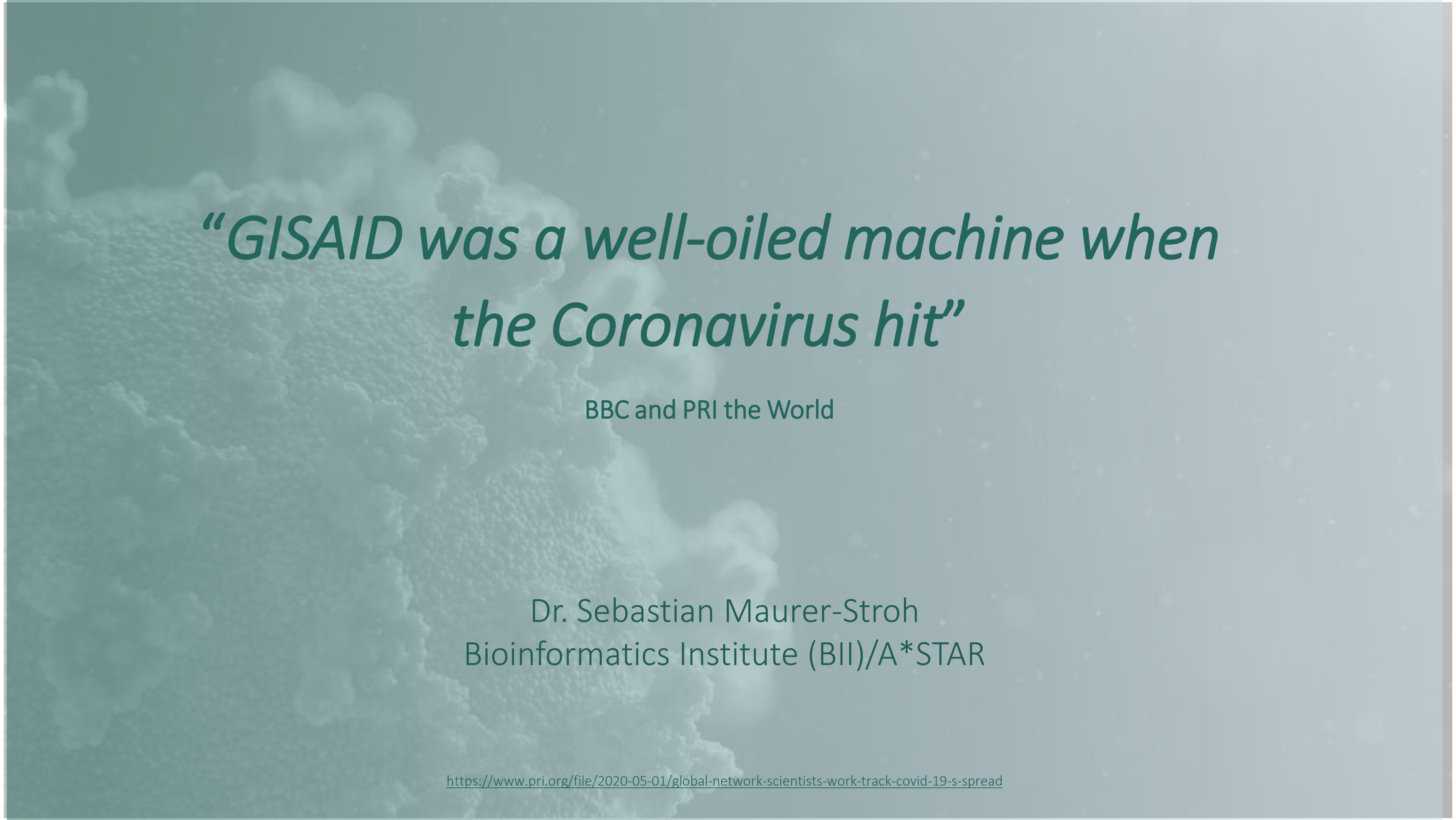


“GISAID was a well-oiled machine when the Coronavirus hit”

BBC and PRI the World

Dr. Sebastian Maurer-Stroh
Bioinformatics Institute (BII)/A*STAR

https://www.pri.org/file/2020-05-01/global-network-scientists-work-track-covid-19-s-spread

Near Real-Time Data Sharing begins 2009

Sharing the first and all subsequent genomes of the pandemic H1N1 influenza virus via GISAID (2009)

Rebecca Garten et al, U.S. CDC

Near Real-Time Data Sharing continues, e.g. 2013

Sharing the first and all subsequent genomes of the novel,
highly pathogenic H7N9 avian influenza virus via GISAID

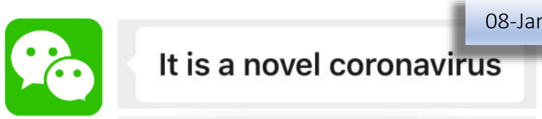
Tian Bai et al, China CDC

GISAID was ready for Disease X ==> newly emerging coronavirus

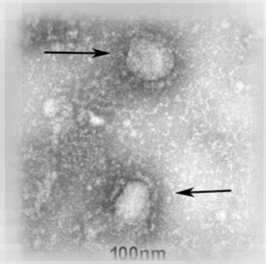

31-Dec-2019

XINHUANET

Viral pneumonia cases reported in central China


08-Jan-2020

It is a novel coronavirus




14-Jan-2020

World Health Organization (WHO)
@WHO

Replying to @WHO @WHOWPRO and @DrTedros

Whole genome sequences for the novel #coronavirus (2019-nCoV) from the Chinese 🇨🇳 authorities were shared with WHO and have also been submitted by Chinese authorities to the GISAID platform so that they can be accessed by public health authorities, laboratories and researchers.

World Health Organization Western Pacific and Tedros Adhanom Ghebreyesus

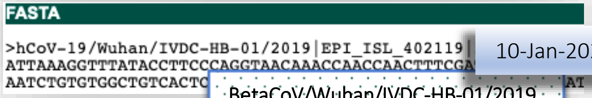
2020-01-08

Complete genomes sequenced

Less than 48 hours

2020-01-10

Shared with the world via GISAID


FASTA

```
>hCoV-19/Wuhan/IVDC-HB-01/2019|EPI_ISL_402119|
ATTAAAGGTTTATACCTTCCCAGGTAACAAACCAACCAACTTTCGA
AATCTGTGTGGCTGTCACTC
```

10-Jan-2020

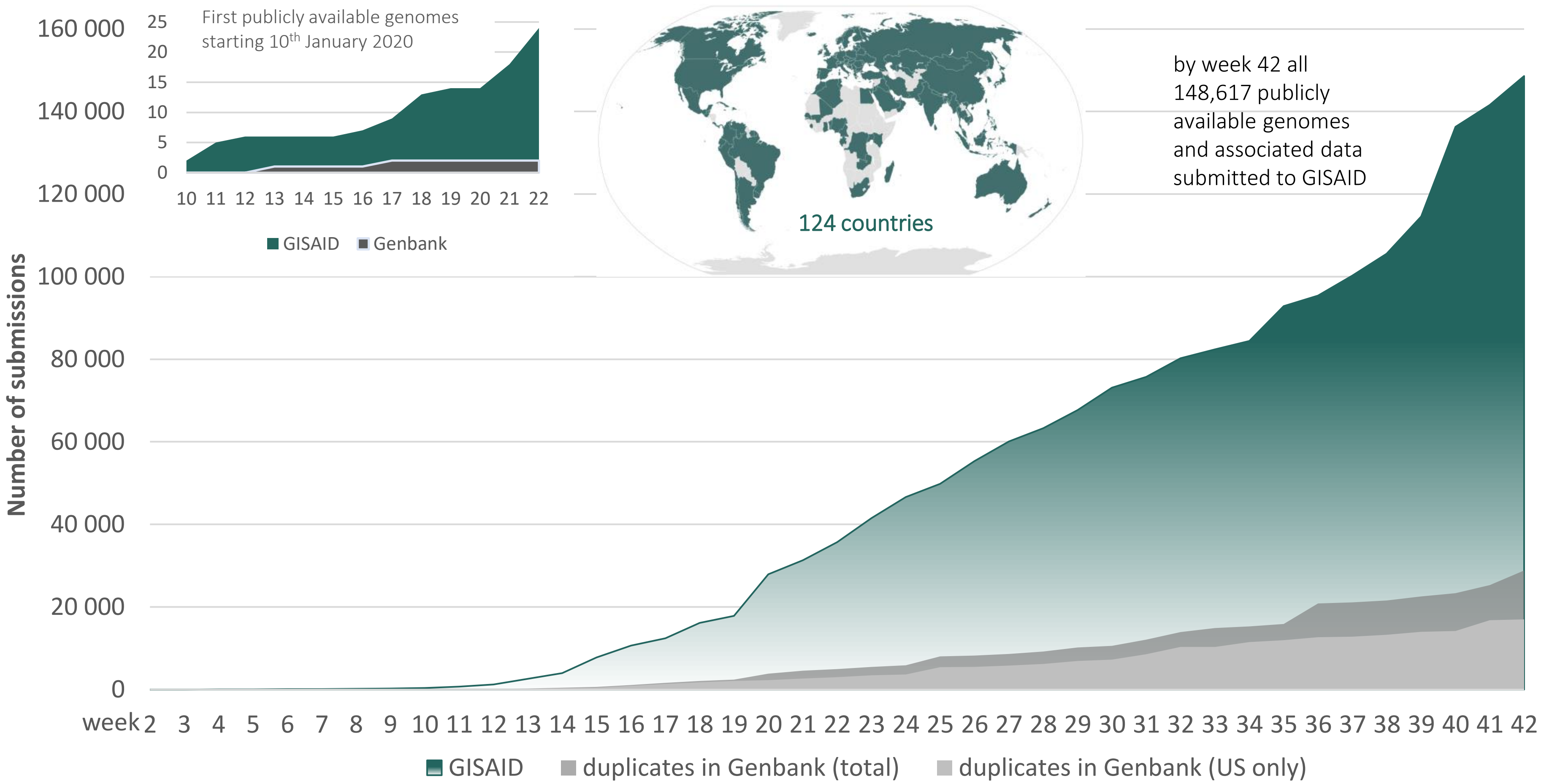
BetaCoV/Wuhan/IVDC-HB-01/2019
EPI_ISL_402119 via GISAID EpiCoV™

GISAID Data instantly yields Results for Targeted Response

1. Development of first diagnostics kits and refinement through ongoing surveillance for mutations
2. Identification of potential drug and vaccine targets on hCoV-19 through repurposing
3. Genomic epidemiology of hCoV-19, allows analysis of the exportation and importation events of viruses between countries, contact-tracing in countries, or identification of transmission chains
4. Evidence that the virus has not drifted to significant strain difference, with in particular the cell receptor binding pocket being followed closely
5. Identification of animal precursors of hCoV-19 (in bats and pangolins)

Real-time data sharing is not achieved by governmental Regulations

… it is incentivized by the confidence in transparent sharing mechanisms

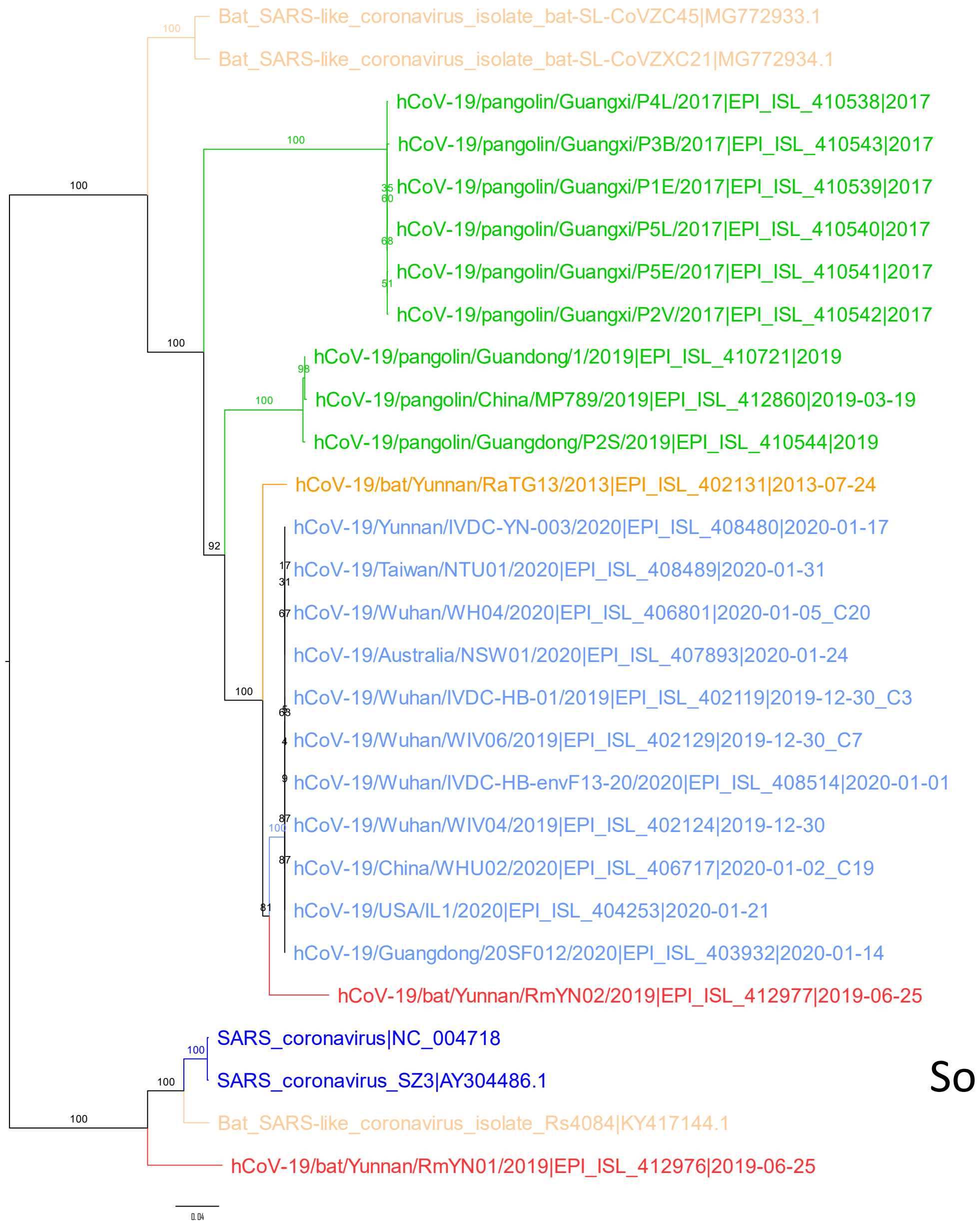


First publicly available genomes starting 10th January 2020

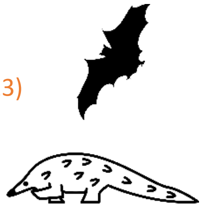
124 countries

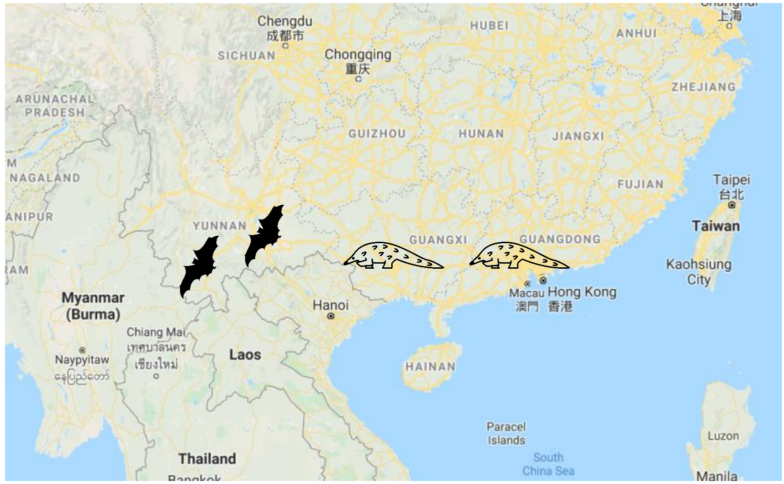
by week 42 all 148,617 publicly available genomes and associated data submitted to GISAID

Where did it come from?



Light Orange … previous bat CoVs
Orange … previous closest bat precursor (Yunnan 2013)
Red … new bat CoVs (Yunnan 2019)
Light blue … hCoV-19 2019-2020
Green … pangolin CoV (Southern China 2019)
Blue … SARS CoV





Southern China 2019: precursors in 2 species

by BII/GIS, A*STAR Singapore

Early outbreak genomes showed very low diversity, only a handful of mutations over 30,000 bases

	2019-12-24 Wuhan/IPBCAMS-WH-01	2019-12-30 Wuhan/HBCDC-HB-01	2019-12-30 Wuhan/IPBCAMS-WH-02	2019-12-30 Wuhan/IPBCAMS-WH-03	2019-12-30 Wuhan/IPBCAMS-WH-04	2019-12-30 Wuhan/IVDC-HB-01	2019-12-30 Wuhan/IVDC-HB-05	2019-12-30 Wuhan/WIV02	2019-12-30 Wuhan/WIV04	2019-12-30 Wuhan/WIV05	2019-12-30 Wuhan/WIV06	2019-12-30 Wuhan/WIV07	2020-01-01 Wuhan/IVDC-HB-04	**2020-01-08 Nonthaburi/61**	**2020-01-13 Nonthaburi/74**	2020-01-14 Guangdong/20SF012	2020-01-15 Guangdong/20SF013	2020-01-15 Guangdong/20SF014	2020-01-15 Guangdong/20SF025	2020-01-16 Zhejiang/WZ-01	2020-01-17 Guangdong/20SF028	2020-01-17 Zhejiang/WZ-02	2020-01-18 Guangdong/20SF040
2019-12-24 Wuhan/IPBCAMS-WH-01																							
2019-12-30 Wuhan/HBCDC-HB-01	4																						
2019-12-30 Wuhan/IPBCAMS-WH-02	9	7																					
2019-12-30 Wuhan/IPBCAMS-WH-03	4	2	7																				
2019-12-30 Wuhan/IPBCAMS-WH-04	3	1	6	1																			
2019-12-30 Wuhan/IVDC-HB-01	3	1	6	1	0																		
2019-12-30 Wuhan/IVDC-HB-05	5	3	8	3	2	2																	
2019-12-30 Wuhan/WIV02	5	3	8	3	2	2	4																
2019-12-30 Wuhan/WIV04	3	1	6	1	0	0	2	2															
2019-12-30 Wuhan/WIV05	5	3	8	3	2	2	4	4	2														
2019-12-30 Wuhan/WIV06	3	1	6	1	0	0	2	2	0	2													
2019-12-30 Wuhan/WIV07	5	3	8	3	2	2	4	4	2	4	2												
2020-01-01 Wuhan/IVDC-HB-04	6	4	9	4	3	3	5	5	3	5	3	5											
2020-01-08 Nonthaburi/61	3	1	6	1	0	0	2	2	0	2	0	2	3										
2020-01-13 Nonthaburi/74	3	1	6	1	0	0	2	2	0	2	0	2	3	0									
2020-01-14 Guangdong/20SF012	6	4	9	4	3	3	5	5	3	5	3	5	6	3	3								
2020-01-15 Guangdong/20SF013	6	4	9	4	3	3	5	5	3	5	3	5	6	3	3	0							
2020-01-15 Guangdong/20SF014	4	2	7	2	1	1	3	3	1	3	1	3	4	1	1	4	4						
2020-01-15 Guangdong/20SF025	6	4	9	4	3	3	5	5	3	5	3	5	6	3	3	0	0	4					
2020-01-16 Zhejiang/WZ-01	5	3	8	3	2	2	4	3	2	4	2	4	5	2	2	5	5	3	5				
2020-01-17 Guangdong/20SF028	4	2	7	2	1	1	3	3	1	3	1	3	4	1	1	4	4	2	4	3			
2020-01-17 Zhejiang/WZ-02	3	1	6	1	0	0	2	2	0	2	0	2	3	0	0	3	3	1	3	2	1		
2020-01-18 Guangdong/20SF040	4	2	7	2	1	1	3	3	1	3	1	3	4	1	1	4	4	2	4	3	0	1	

Thailand: First full genomes outside of China were still identical to the Wuhan consensus

World Health Organization (WHO) @WHO · Aug 19

Dr. Pilailuk Okada & her team 👩‍🔬👨‍🔬👩‍🔬 of microbiologists at the Thai National Influenza Centre worked around the clock and confirmed the first case of COVID-19 in Thailand - the first to be confirmed outside of China.

More #RealLifeHeroes stories 👉bit.ly/31lzl0X

Nucleotide (base) differences among early outbreak strains

Pilailuk Okada *et al.*
Euro Surveill. 2020 Feb 27; 25(8): 2000097.

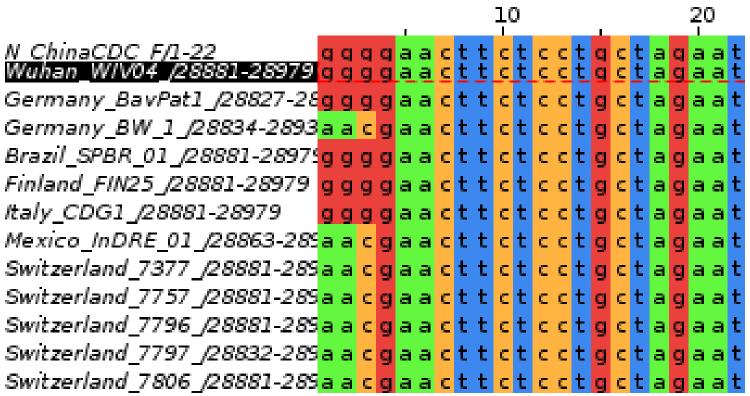
by BII, A*STAR Singapore

How can you detect it?

PCR-based (RNA amplification)

For active viral infection
Highly specific

Quick to develop
Lab-based

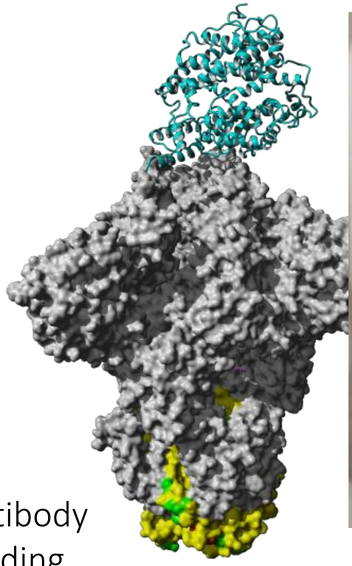


```
                                        10        20
N_ChinaCDC_F/1-22           ggggaacttctcctgctagaat
Wuhan_WIV04_/28881-28979    ggggaacttctcctgctagaat
Germany_BavPat1_/28827-28   ggggaacttctcctgctagaat
Germany_BW_1_/28834-2893    aacgaacttctcctgctagaat
Brazil_SPBR_01_/28881-2897  ggggaacttctcctgctagaat
Finland_FIN25_/28881-28979  ggggaacttctcctgctagaat
Italy_CDG1_/28881-28979     ggggaacttctcctgctagaat
Mexico_InDRE_01_/28863-28   aacgaacttctcctgctagaat
Switzerland_7377_/28881-28  aacgaacttctcctgctagaat
Switzerland_7757_/28881-28  aacgaacttctcctgctagaat
Switzerland_7796_/28881-28  aacgaacttctcctgctagaat
Switzerland_7797_/28832-28  aacgaacttctcctgctagaat
Switzerland_7806_/28881-28  aacgaacttctcctgctagaat
```

Serology-based (Antibody binding)

1. For later stage of infection
2. After infection (immune memory)

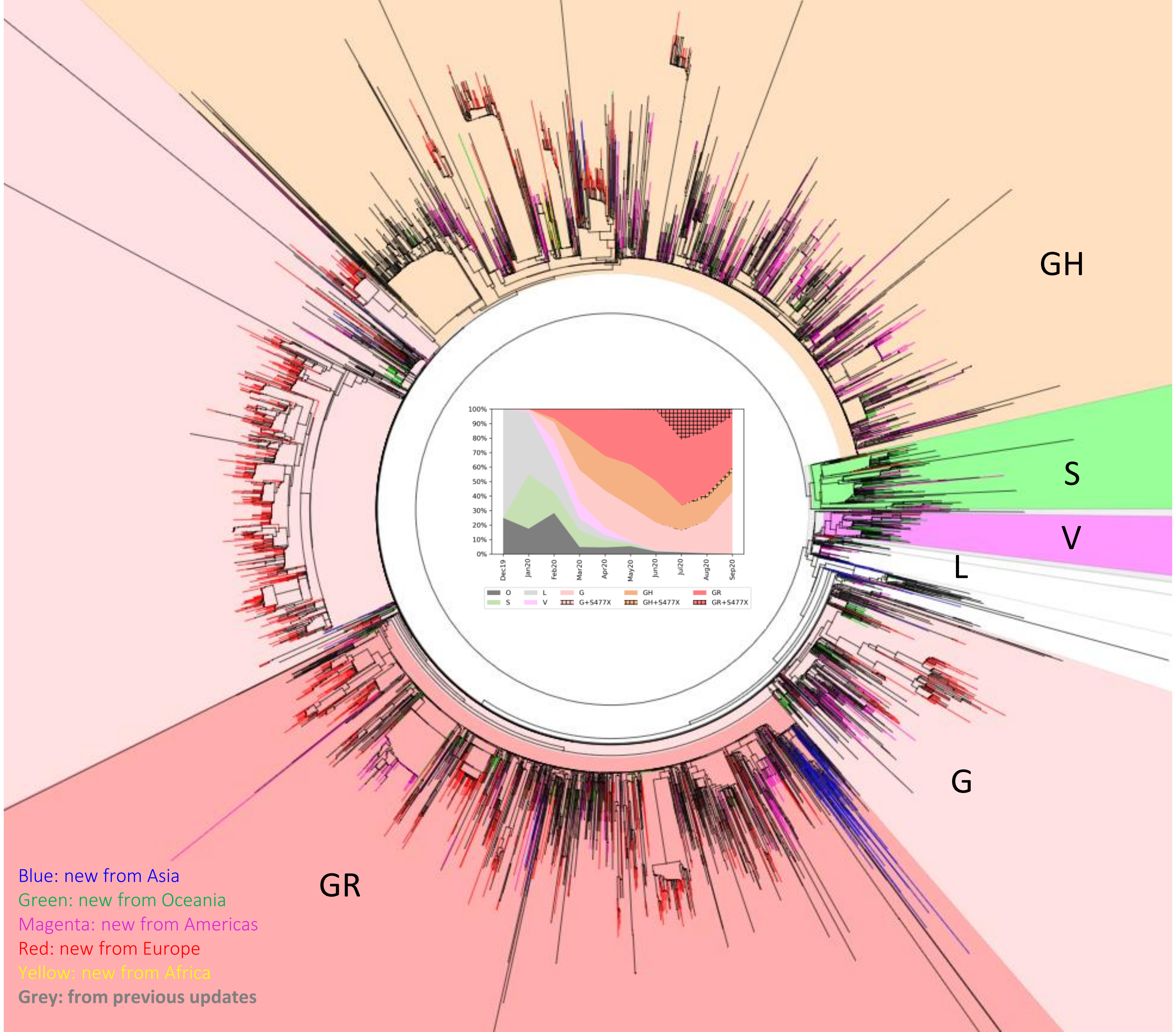
Slow to develop
Can become point-of-care



Antibody binding region (epitope)

by BII/GIS, A*STAR Singapore

Mutations leading to split into genetic groups (clades)



Blue: new from Asia
Green: new from Oceania
Magenta: new from Americas
Red: new from Europe
Yellow: new from Africa
Grey: from previous updates

Full genome tree derived from all outbreak sequences 2020-10-16

Notable changes:

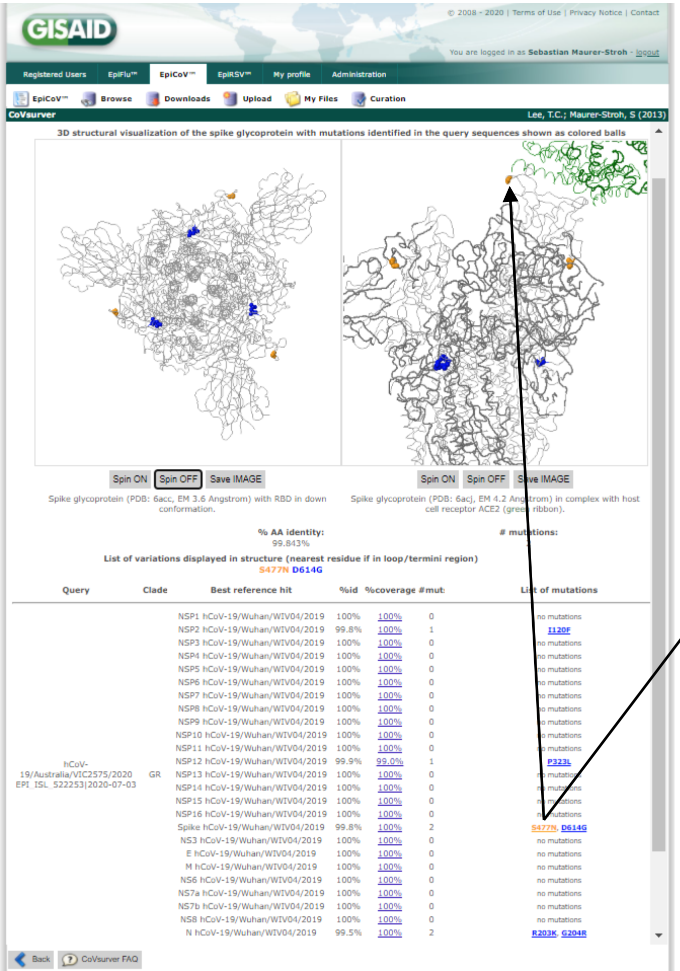
135707 full genomes (+3834) (excluding low coverage, out of 145201 entries)

Updated clades:
S clade 6358 (+70)
L clade 4181 (+53)
V clade 5251 (+48)
G clade [#S477X] 30972 [92] (+1329 [+0])
GR clade [#S477X] 53178 [7351] (+1151 [+5])
GH clade [#S477X] 31930 [618] (+1151 [+52])
Other clades 3837 (+32)

We gratefully acknowledge the Authors from Originating and Submitting laboratories of sequence data on which the analysis is based.

by BII/GIS, A*STAR Singapore

CoVsurver tool to analyse mutations – example spike S477N



CoVsurver Lee, T.C.; Maurer-Stroh, S (2013)

3D structural visualization of the spike glycoprotein with mutations identified in the query sequences shown as colored balls

Spike glycoprotein (PDB: 6acc, EM 3.6 Angstrom) with RBD in down conformation.

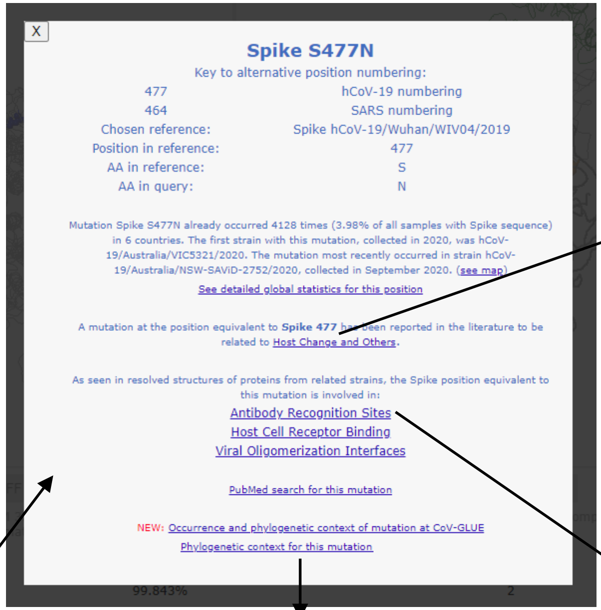
Spike glycoprotein (PDB: 6acj, EM 4.2 Angstrom) in complex with host cell receptor ACE2 (green ribbon).

% AA identity: 99.843%

 # mutations:

List of variations displayed in structure (nearest residue if in loop/termini region)
S477N D614G

Query	Clade	Best reference hit	%id	%coverage	#mut	List of mutations
hCoV-19/Australia/VIC2575/2020 EPI_ISL_522253|2020-07-03	GR	NSP1 hCoV-19/Wuhan/WIV04/2019	100%	100%	0	no mutations
		NSP2 hCoV-19/Wuhan/WIV04/2019	99.8%	100%	1	I120F
		NSP3 hCoV-19/Wuhan/WIV04/2019	100%	100%	0	no mutations
		NSP4 hCoV-19/Wuhan/WIV04/2019	100%	100%	0	no mutations
		NSP5 hCoV-19/Wuhan/WIV04/2019	100%	100%	0	no mutations
		NSP6 hCoV-19/Wuhan/WIV04/2019	100%	100%	0	no mutations
		NSP7 hCoV-19/Wuhan/WIV04/2019	100%	100%	0	no mutations
		NSP8 hCoV-19/Wuhan/WIV04/2019	100%	100%	0	no mutations
		NSP9 hCoV-19/Wuhan/WIV04/2019	100%	100%	0	no mutations
		NSP10 hCoV-19/Wuhan/WIV04/2019	100%	100%	0	no mutations
		NSP11 hCoV-19/Wuhan/WIV04/2019	100%	100%	0	no mutations
		NSP12 hCoV-19/Wuhan/WIV04/2019	99.9%	99.0%	1	P323L
		NSP13 hCoV-19/Wuhan/WIV04/2019	100%	100%	0	no mutations
		NSP14 hCoV-19/Wuhan/WIV04/2019	100%	100%	0	no mutations
		NSP15 hCoV-19/Wuhan/WIV04/2019	100%	100%	0	no mutations
		NSP16 hCoV-19/Wuhan/WIV04/2019	100%	100%	0	no mutations
		Spike hCoV-19/Wuhan/WIV04/2019	99.8%	100%	2	S477N, D614G
		NS3 hCoV-19/Wuhan/WIV04/2019	100%	100%	0	no mutations
		E hCoV-19/Wuhan/WIV04/2019	100%	100%	0	no mutations
		M hCoV-19/Wuhan/WIV04/2019	100%	100%	0	no mutations
		NS6 hCoV-19/Wuhan/WIV04/2019	100%	100%	0	no mutations
		NS7a hCoV-19/Wuhan/WIV04/2019	100%	100%	0	no mutations
		NS7b hCoV-19/Wuhan/WIV04/2019	100%	100%	0	no mutations
		NS8 hCoV-19/Wuhan/WIV04/2019	100%	100%	0	no mutations
		N hCoV-19/Wuhan/WIV04/2019	99.5%	100%	2	R203K, G204R



Spike S477N

Key to alternative position numbering:

477	hCoV-19 numbering
464	SARS numbering
Chosen reference:	Spike hCoV-19/Wuhan/WIV04/2019
Position in reference:	477
AA in reference:	S
AA in query:	N

Mutation Spike S477N already occurred 4128 times (3.98% of all samples with Spike sequence) in 6 countries. The first strain with this mutation, collected in 2020, was hCoV-19/Australia/VIC5321/2020. The mutation most recently occurred in strain hCoV-19/Australia/NSW-SAViD-2752/2020, collected in September 2020. (see map)

See detailed global statistics for this position

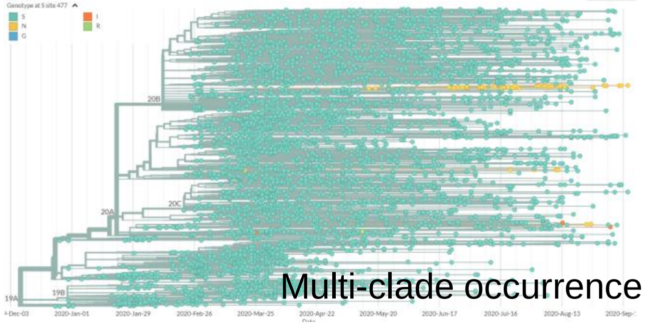
A mutation at the position equivalent to **Spike 477** has been reported in the literature to be related to Host Change and Others.

As seen in resolved structures of proteins from related strains, the Spike position equivalent to this mutation is involved in:

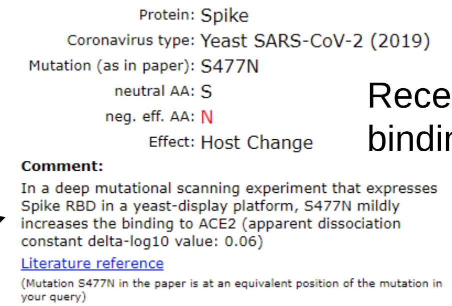
Antibody Recognition Sites
Host Cell Receptor Binding
Viral Oligomerization Interfaces

PubMed search for this mutation

NEW: Occurrence and phylogenetic context of mutation at CoV-GLUE
Phylogenetic context for this mutation



Multi-clade occurrence



Protein: Spike
Coronavirus type: Yeast SARS-CoV-2 (2019)
Mutation (as in paper): S477N
neutral AA: S
neg. eff. AA: N
Effect: Host Change

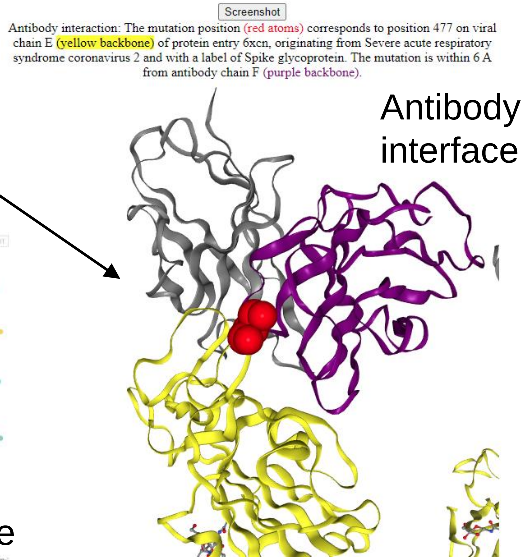
Comment:

In a deep mutational scanning experiment that expresses Spike RBD in a yeast-display platform, S477N mildly increases the binding to ACE2 (apparent dissociation constant delta-log10 value: 0.06)

Literature reference

(Mutation S477N in the paper is at an equivalent position of the mutation in your query)

Receptor binding



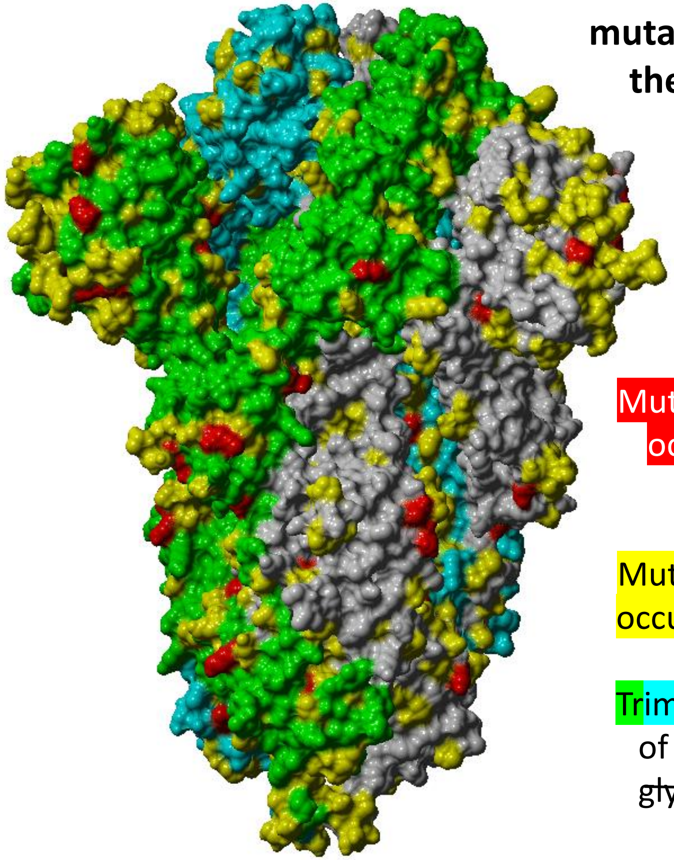
Antibody interaction: The mutation position (red atoms) corresponds to position 477 on viral chain E (yellow backbone) of protein entry 6xcn, originating from Severe acute respiratory syndrome coronavirus 2 and with a label of Spike glycoprotein. The mutation is within 6 A from antibody chain F (purple backbone).

Antibody interface

by BII/GIS, A*STAR Singapore

How can you treat it?

Vaccines, mAbs



Common spike mutations within the outbreak – Sep 2020

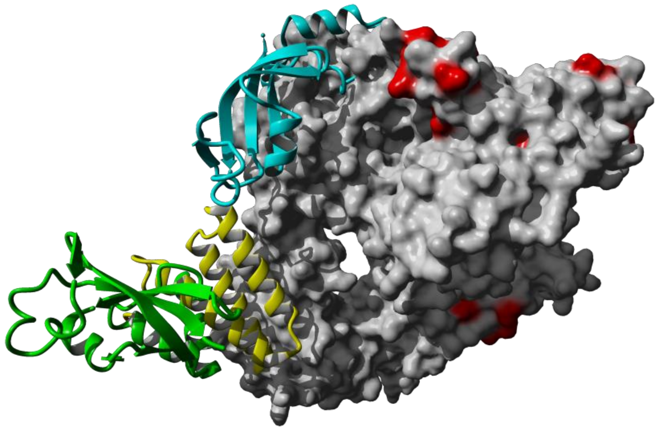
Mutations with occurrence >100

Mutations with occurrence >10

Trimer complex of viral spike glycoprotein

Surface antigen mutations appear random and not driven by antigenic selection (sites on top) so far

Small molecule drugs



Polymerase hCoV-19 vs SARS

nsp12 (gray=identical, red=mutated) complex with nsp7 (yellow) and nsp8 (cyan, green)

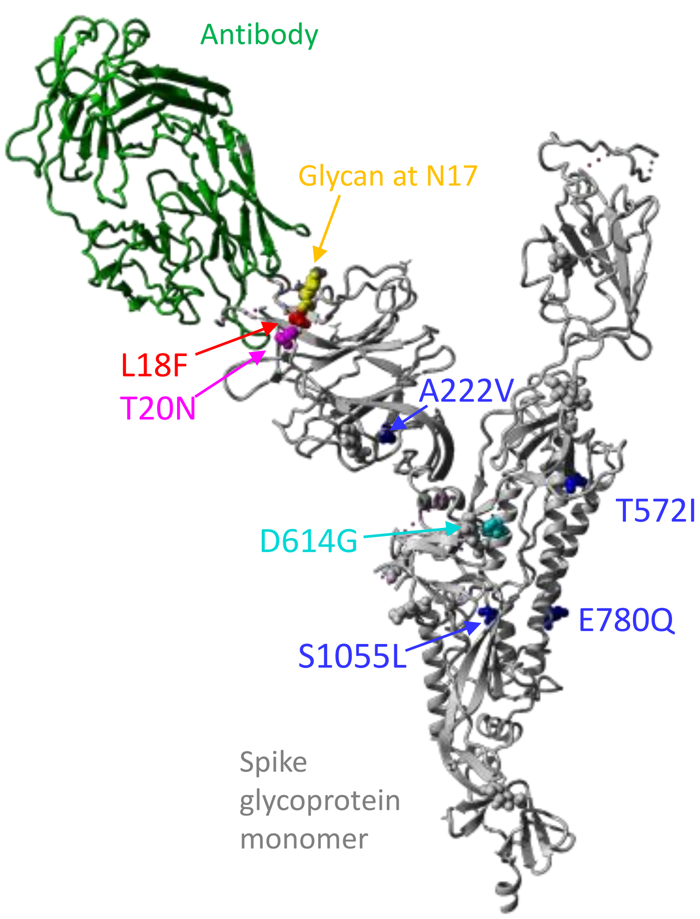
Inhibitors developed against the SARS-CoV polymerase have good potential to bind similarly to hCoV-19 -> **Drug repurposing**

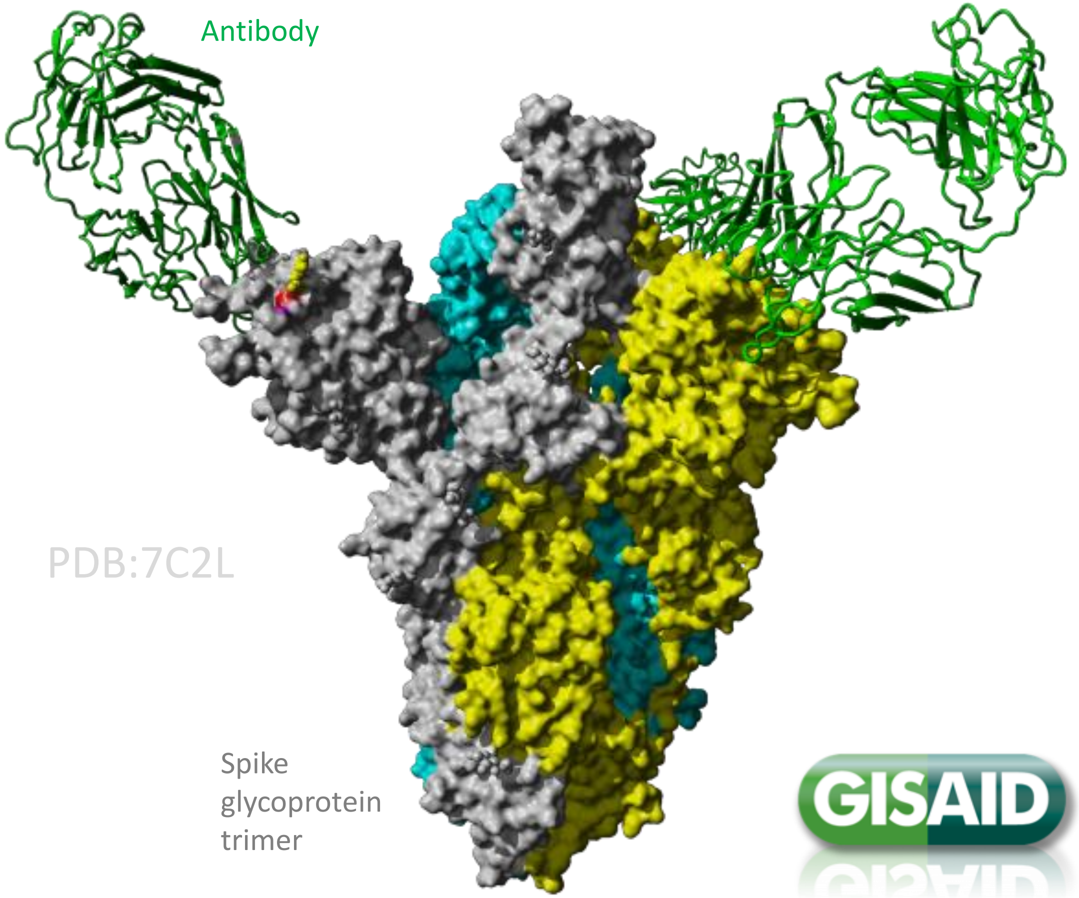
Remdesivir

by BII/GIS, A*STAR Singapore

How can you treat it?

4 reinfection cases spike glycoprotein comparison





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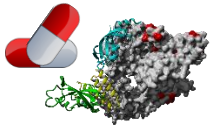
2 of 4 reinfection cases have mutations possibly interfering with the structural conformation of glycosylation sites in a region that is also broadly recognized by antibodies which would provide a hypothetical mechanism for immune escape potentially contributing to permitting second infection. However, this doesn't apply to all cases and many other factors could play a role too. Importantly, these mutations are rare and occur sporadically without causing large clusters so far.

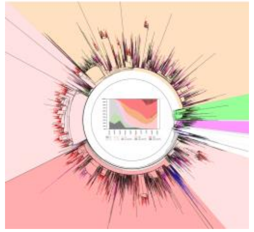
Summary – GISAID contributes to…

1. Development of first diagnostics kits and refinement through ongoing surveillance for mutations

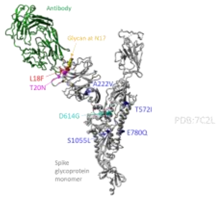
2. Identification of potential drug and vaccine targets on hCoV-19 through repurposing



3. Genomic epidemiology of hCoV-19, allows analysis of the exportation and importation events of viruses between countries, contact-tracing in countries, or identification of transmission chains



4. Evidence that the virus has not drifted to significant strain difference, with in particular the cell receptor binding pocket being followed closely



5. Identification of animal precursors of hCoV-19 (in bats and pangolins)

by BII/GIS, A*STAR Singapore

We gratefully acknowledge the Authors from Originating and Submitting laboratories of sequence and meta data.

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Hospital Surveillance
Network

www.gihsn.org

GIHSN 8TH ANNUAL MEETING, 19-20 OCTOBER 2020

GIHSN GLOBAL RESULTS FOR THE 2019/2020 SEASON

Dr Melissa K ANDREW, Independent Scientific Committee

Foundation for
Influenza
Epidemiology

Sous l'égide de
Fondation
de
France

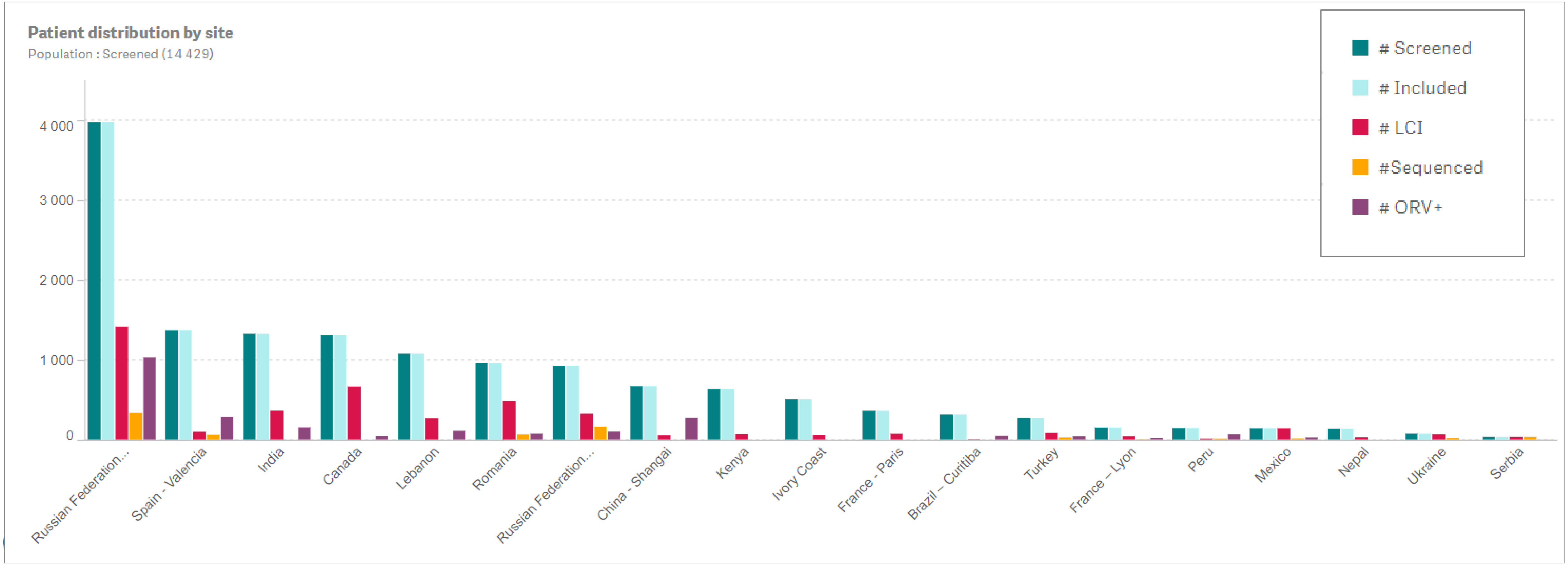
2019/2020: 20 SITES HAVE SHARED THEIR DATA ON THE GIHSN PLATFORM

#included = **14 429**

#LCI = **4 326**

#sequenced = **753**

#ORV+ = **2 298**



QUICK OVERVIEW OF THE DATA COLLECTION PROCESS (1/2)

All sites apply a standardized protocol

- Key focus : Link clinical and virologic data (including whole genome sequence) from hospitalized patients with acute respiratory infections, with emphasis on lab-confirmed influenza cases

Trained study staff on site collect relevant information

- 2 questionnaires (<5 years old / 5 years old and more)

All patients meeting the inclusion criteria and providing consent will be swabbed. Samples are sent to reference laboratory for RT-PCR or tested on site.

WGS must be generated for a minimum of 50-100 flu positive specimens.

- If the site has no WGS capacity, specimens can be sent to the National Influenza Center in Lyon, France, under Terms of Reference for sharing materials

QUICK OVERVIEW OF THE DATA COLLECTION PROCESS (2/2)

Results of WGS are shared on the GISAID platform with a “GIHSN” tag.

Epi data are collected for positive samples that have been sequenced and, if possible, for all positive cases and negative cases (for sequenced specimens, the questionnaires include a GISAID number to allow linkage between WGS results and clinical information).

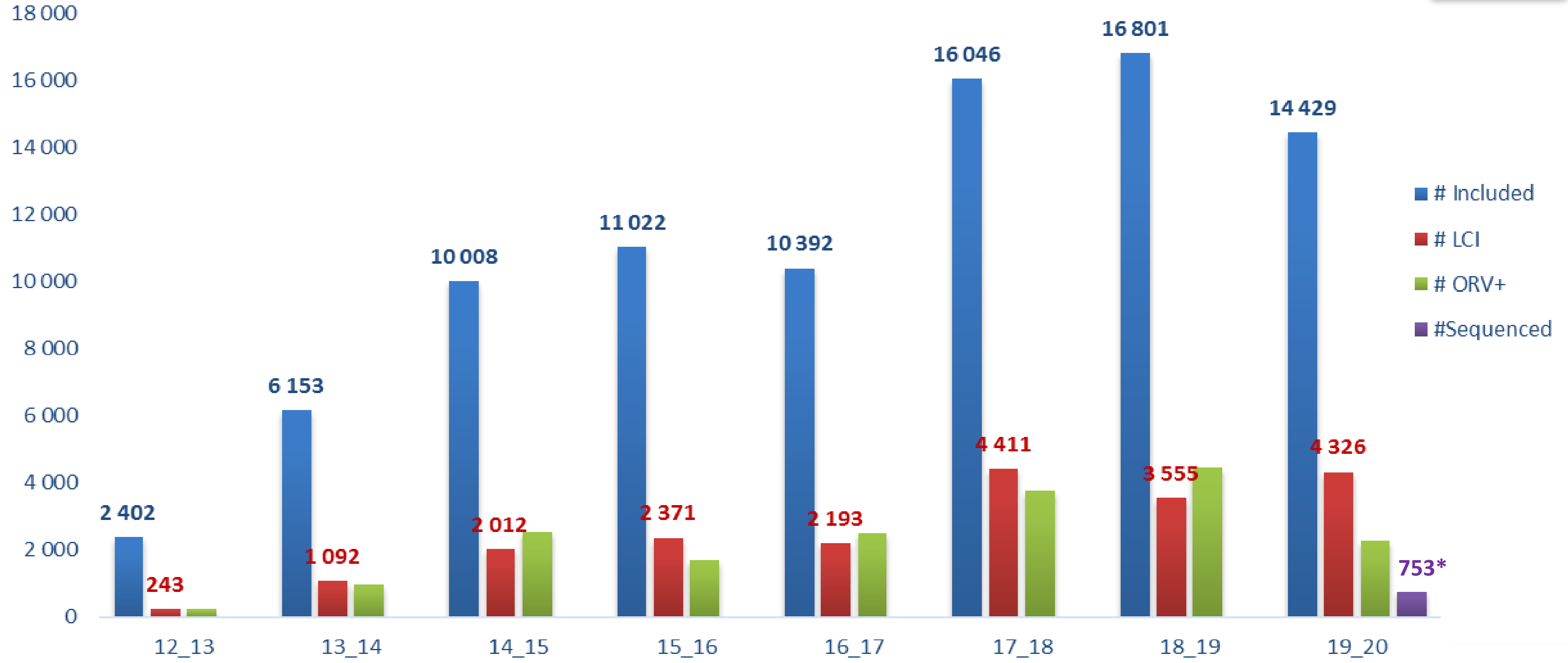
Questionnaires are uploaded on the GIHSN Data platform using a e-CRF or excel files.

Descriptive analysis and outcomes

(Data as of 9/10)

GLOBAL PATIENT INCLUSION
– NEARLY 90 000 PATIENTS OVER 8 YEARS

N= 87 253



# SITES	4	5	6	8	12	18	18	19

*sequenced samples shared with GISAID

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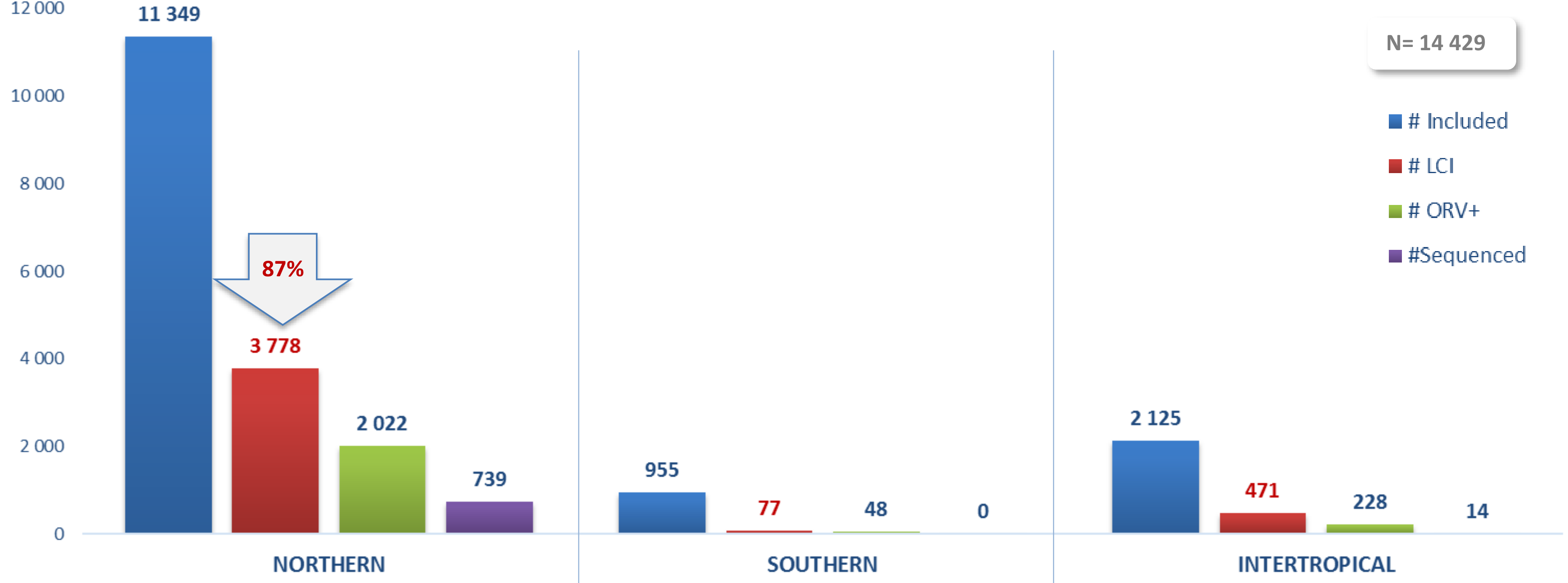
6th Global Annual Meeting

CONTRIBUTION BY HEMISPHERE
SEASON 2019-2020



13 SITES :
CANADA
CHINA
FRANCE – LYON & PARIS
LEBANON
MEXICO
ROMANIA
RUSSIA – MOSCOW & ST PETERSBURG
SERBIA
SPAIN
TURKEY
UKRAINE

3 SITES :
BRAZIL
KENYA
SOUTH AFRICA
(ANALYSIS PENDING)

4 SITES :
INDIA
IVORY COAST
NEPAL
PERU

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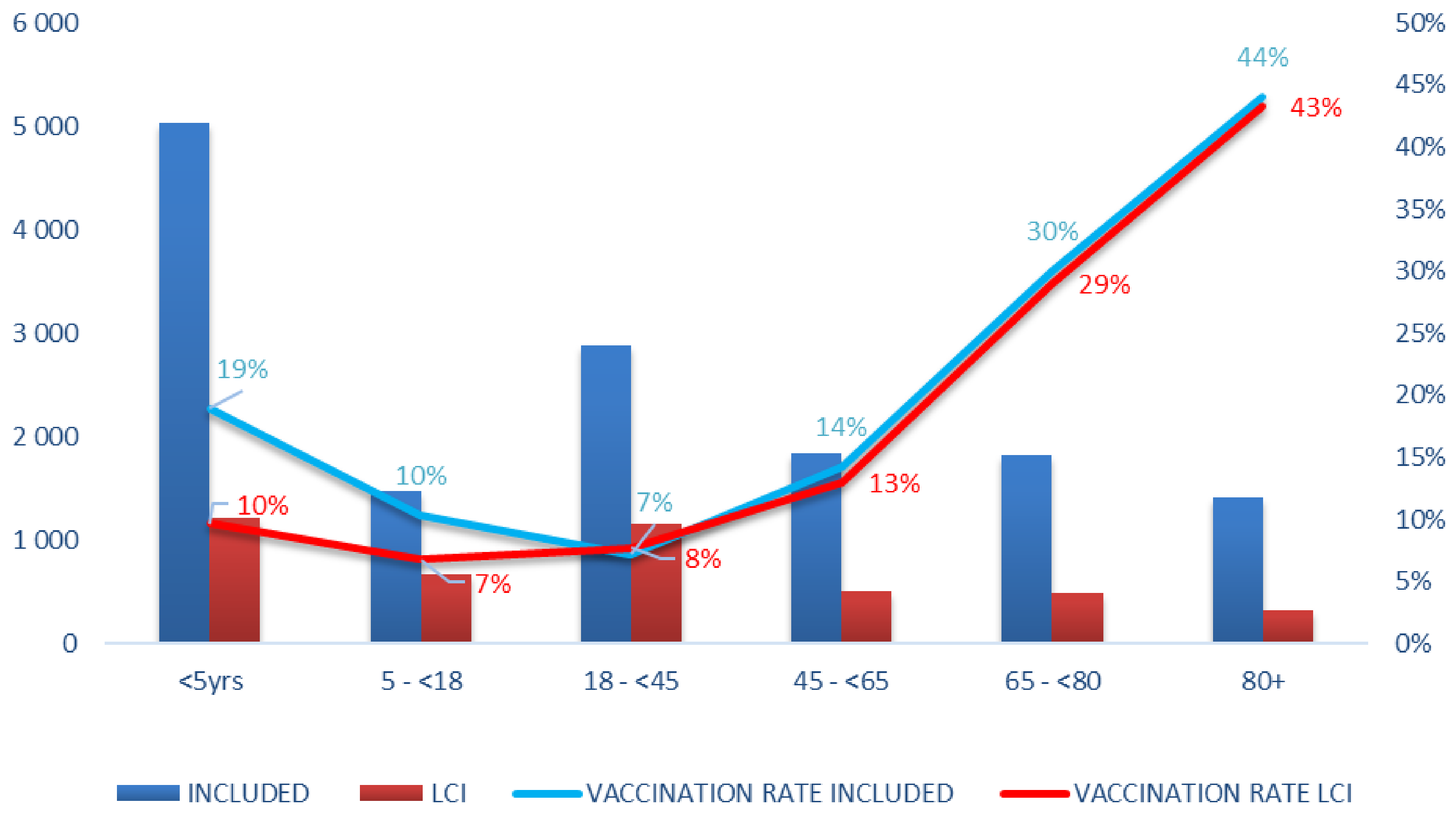
2019-2020 GLOBAL
AGE DISTRIBUTION & VACCINATION RATE

N= 14 429



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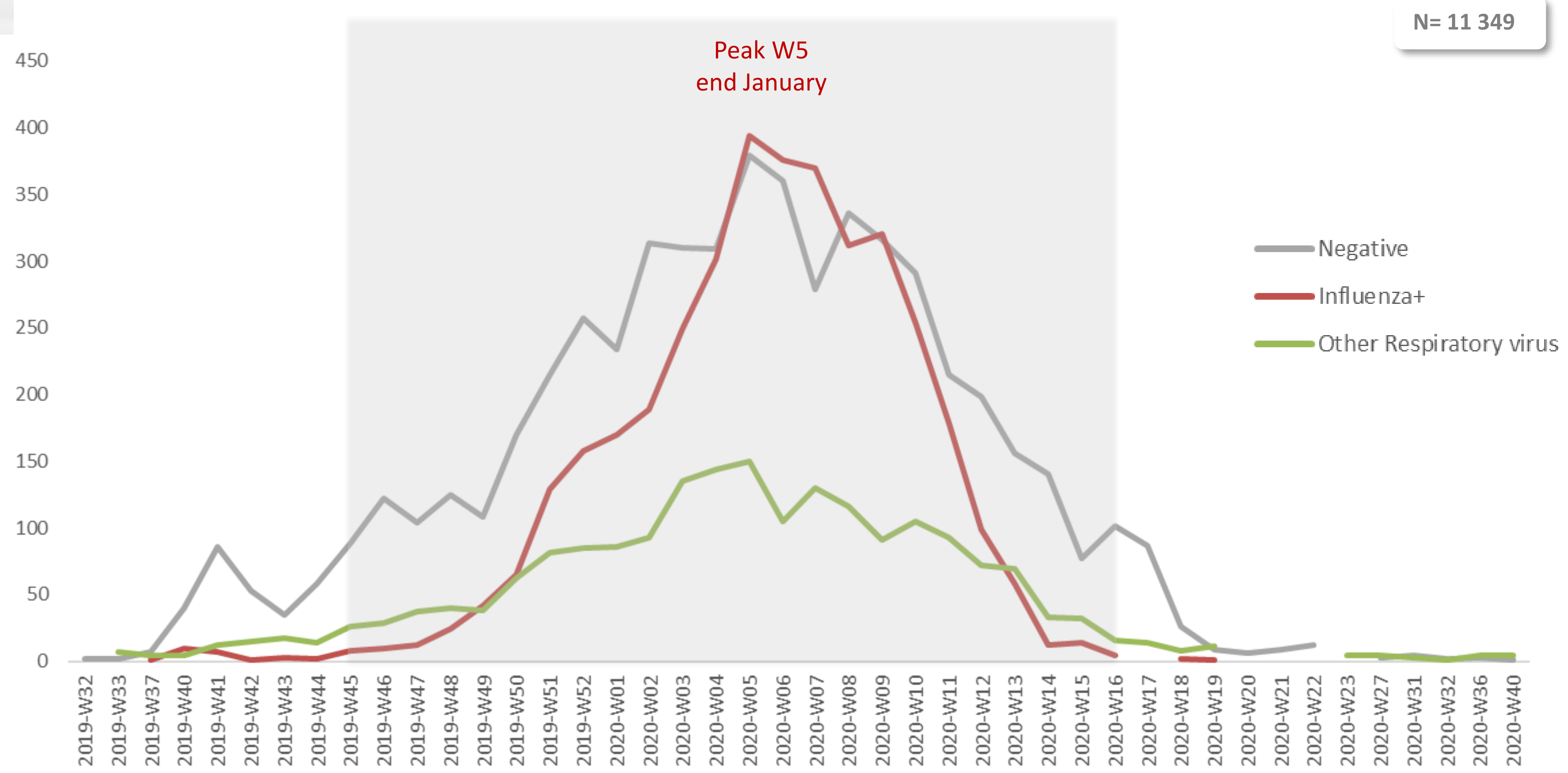
2019-2020 EVOLUTION OF INFLUENZA CASES NORTHERN HEMISPHERE

N= 11 349



Flu season : W45 early November 2019 – W16 early April 2020

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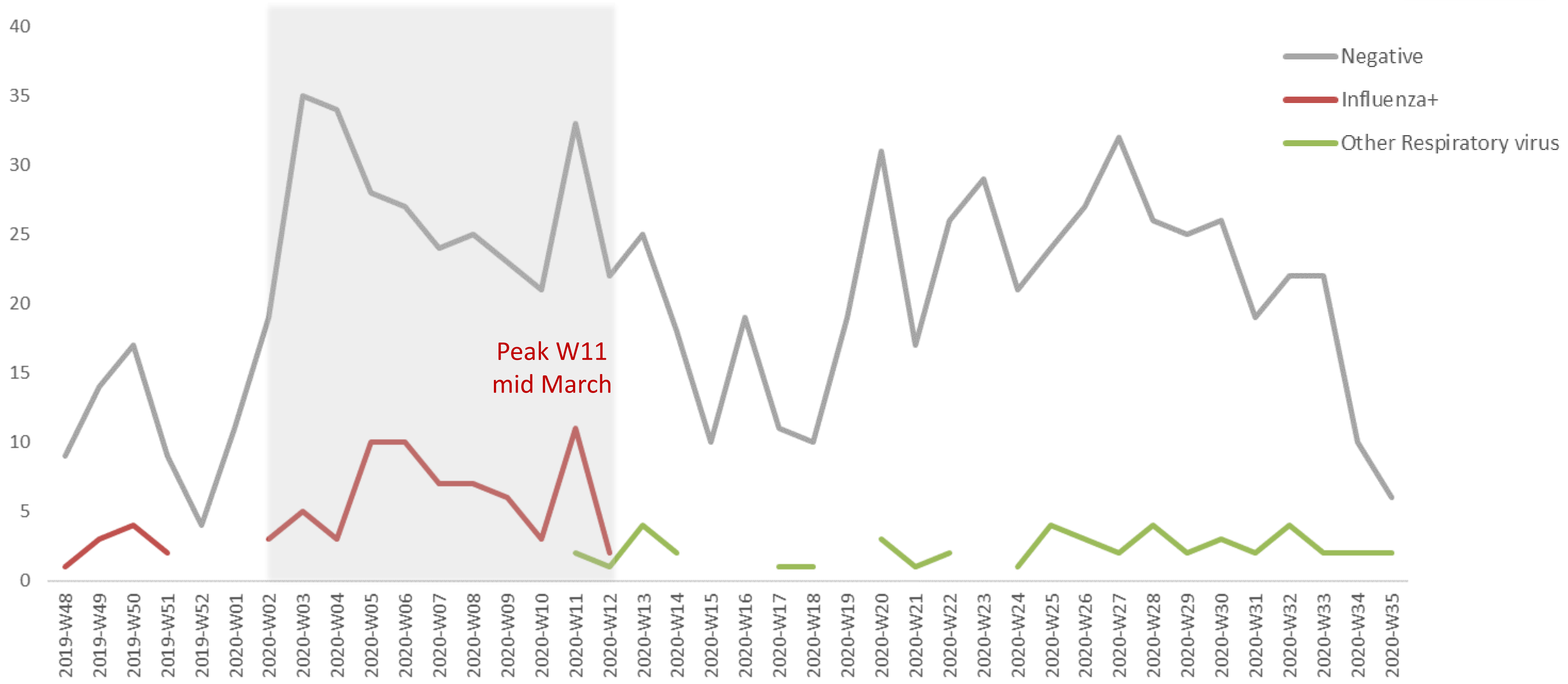
2019-2020 EVOLUTION OF INFLUENZA CASES SOUTHERN HEMISPHERE

N= 955



« Season » : W2 mid January – W12 mid March

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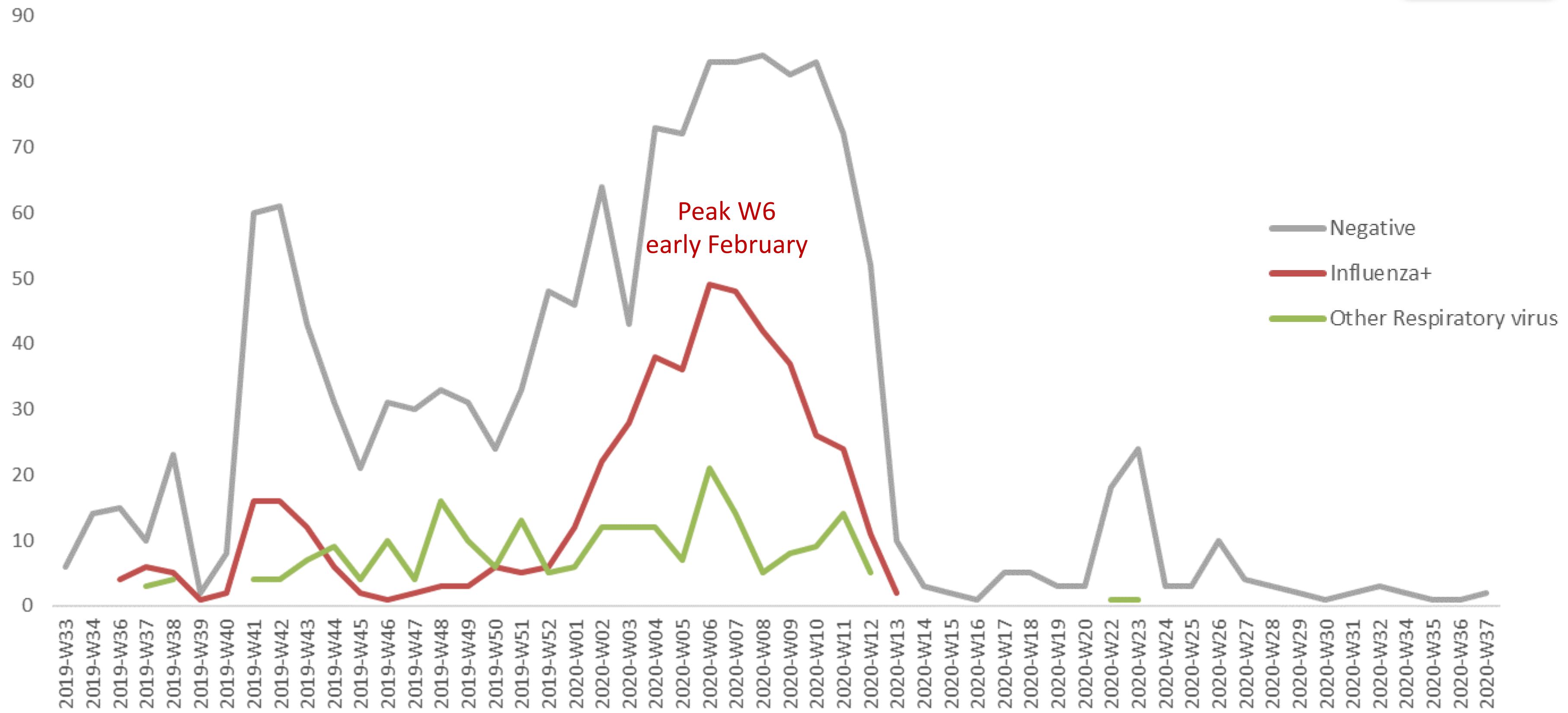
2019-2020 EVOLUTION OF INFLUENZA CASES INTERTROPICAL HEMISPHERE

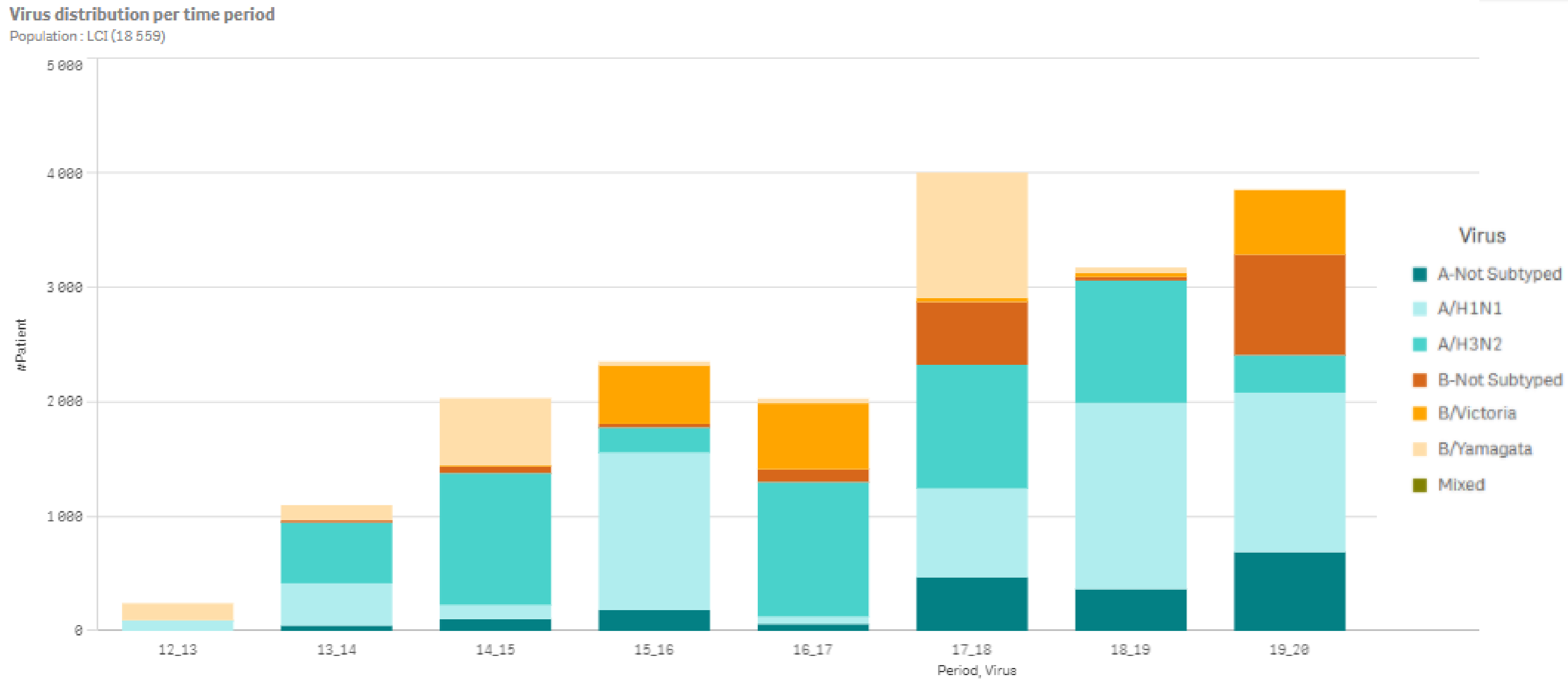
N= 2 125



Year-round surveillance

INFLUENZA VIRUS STRAIN EVOLUTION OVER MULTIPLE SEASONS: NORTHERN HEMISPHERE

N=18 559



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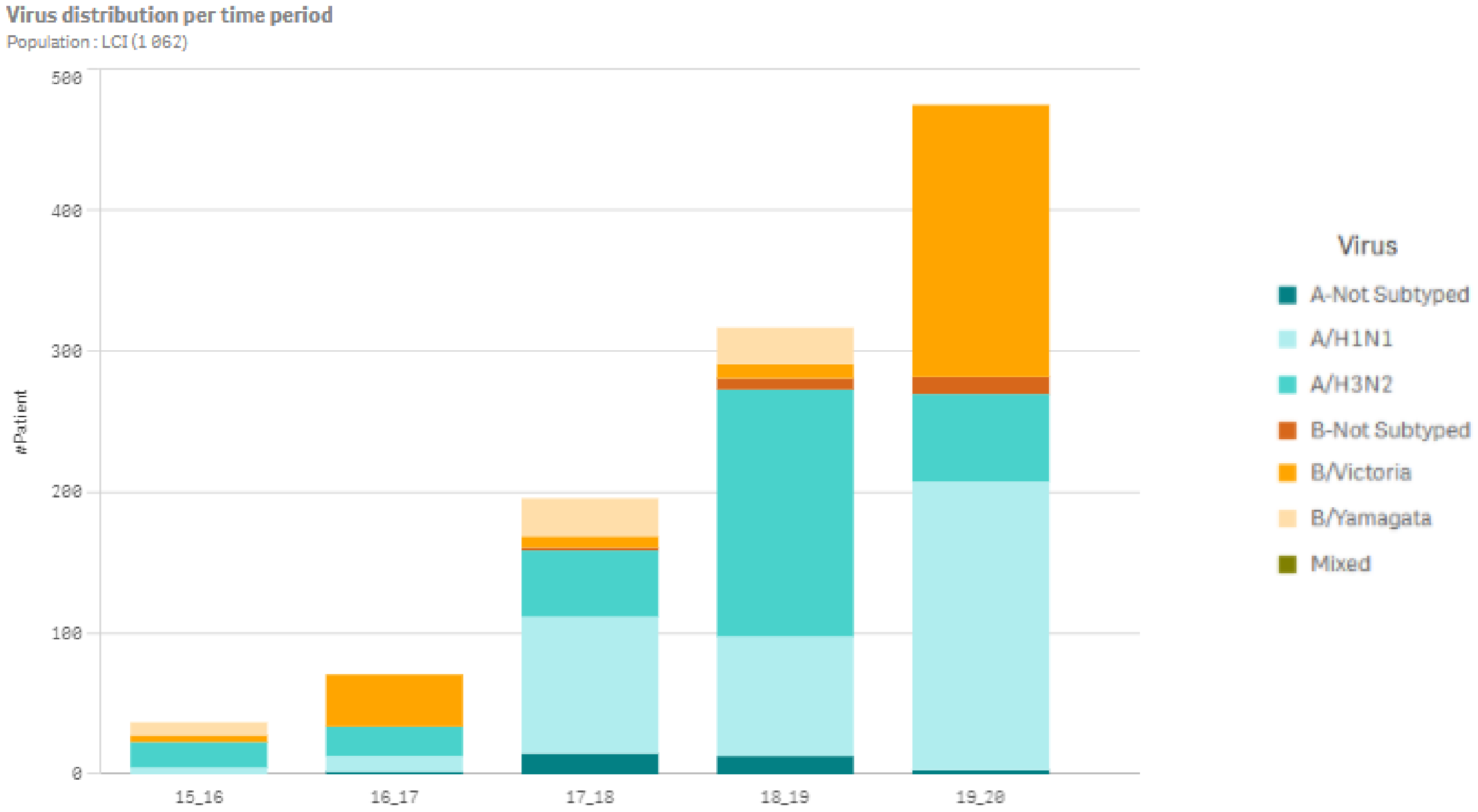
INFLUENZA VIRUS STRAIN EVOLUTION: INTERTROPICAL REGIONS

N=1 062



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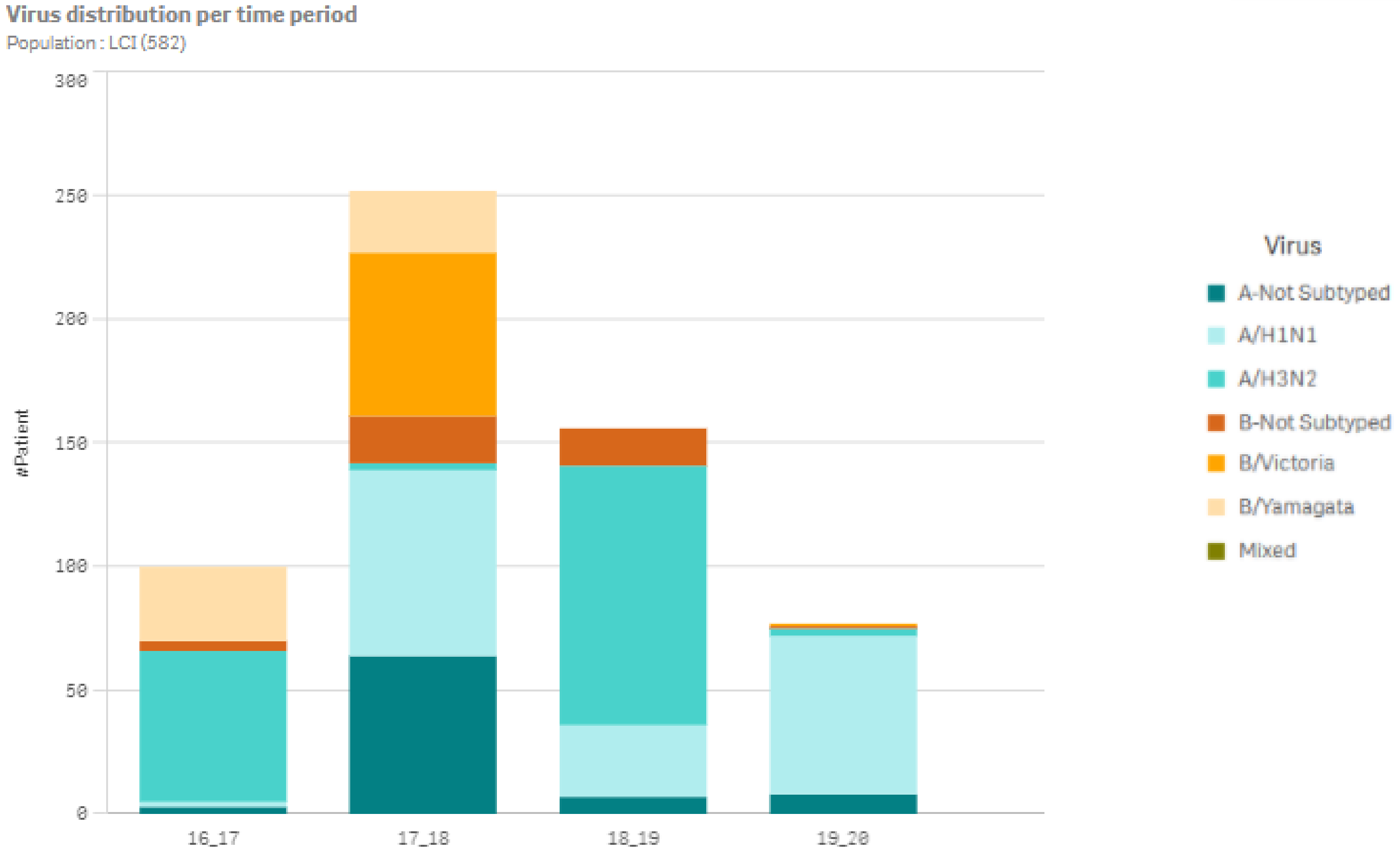
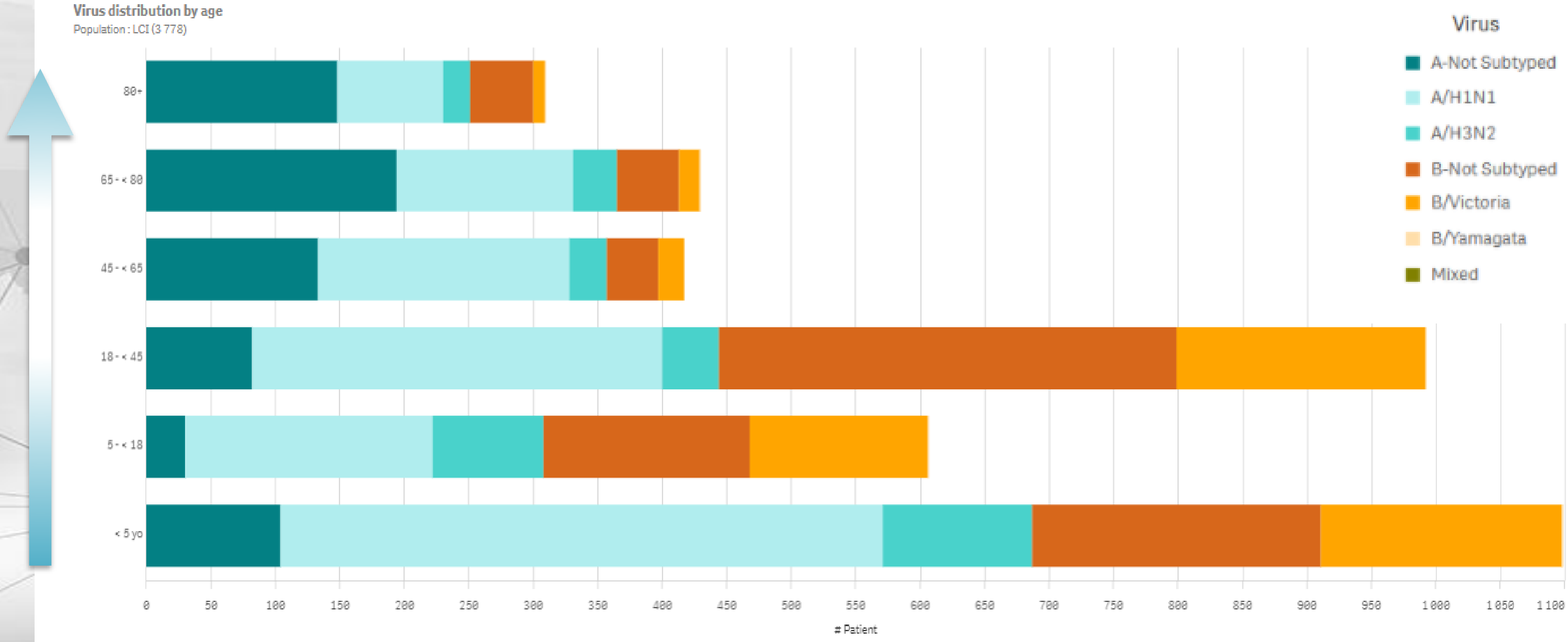
INFLUENZA VIRUS STRAIN EVOLUTION: SOUTHERN HEMISPHERE

N=582



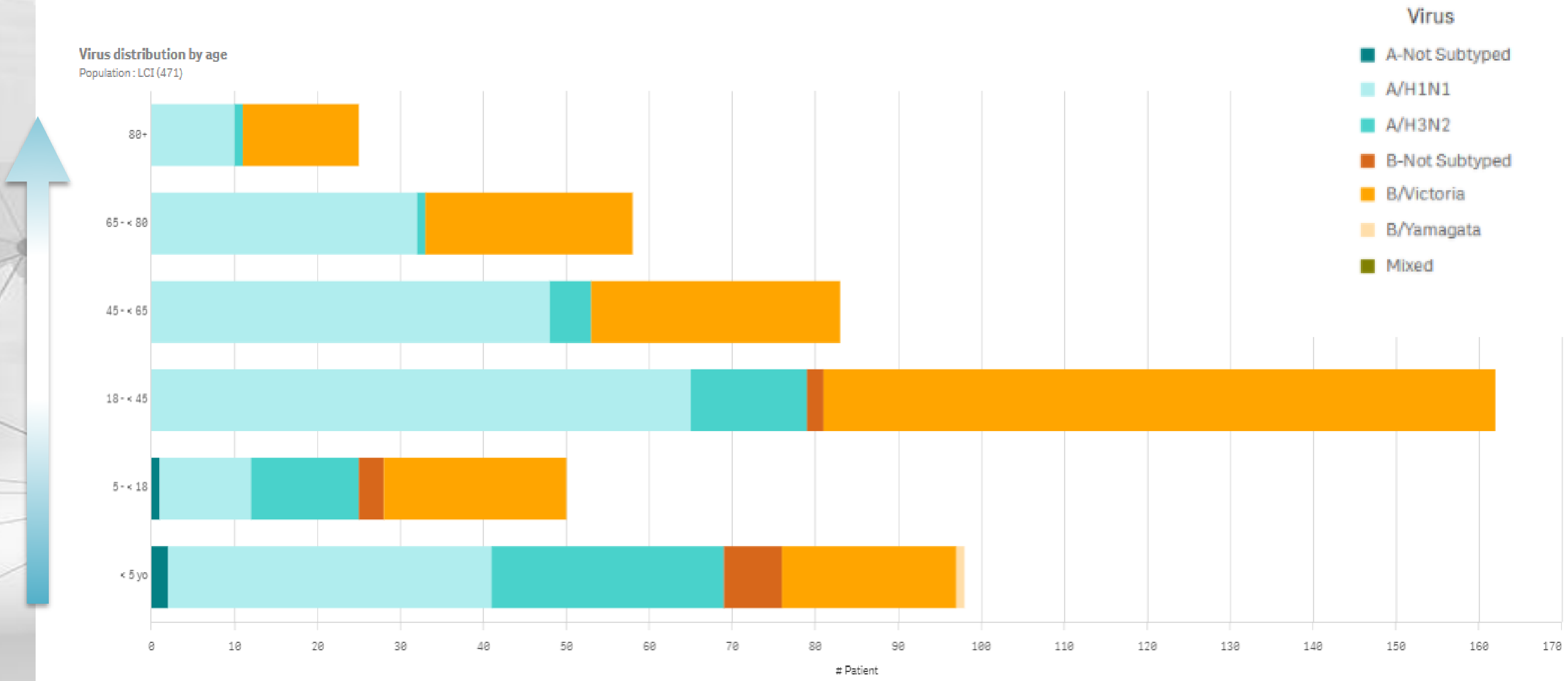
2019-2020 INFLUENZA VIRUS STRAIN DISTRIBUTION PER AGE GROUP - NORTHERN HEMISPHERE

N=3 778



2019-2020 INFLUENZA VIRUS STRAIN DISTRIBUTION PER AGE GROUP - INTERTROPICAL HEMISPHERE

N=471



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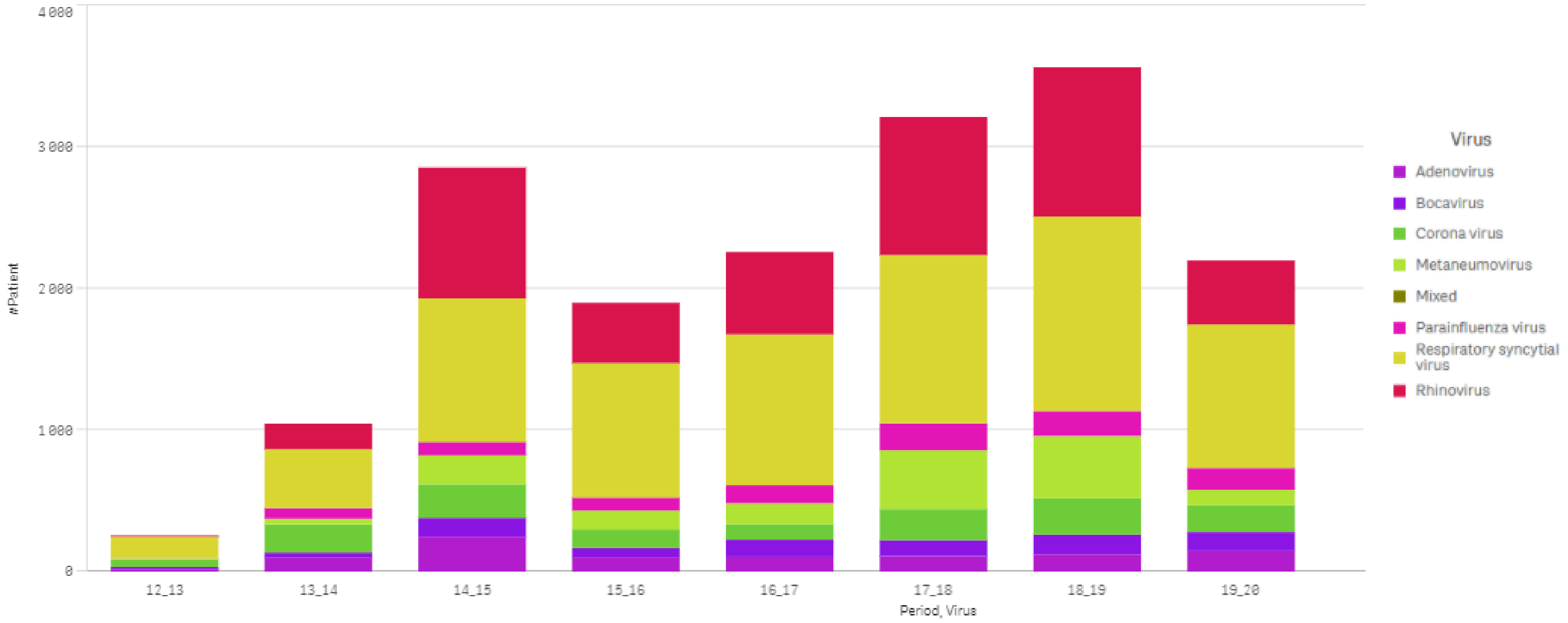
6th Global Annual Meeting

OTHER RESPIRATORY VIRUS STRAINS EVOLUTION OVER MULTIPLE SEASONS: NORTHERN HEMISPHERE

N=15 734

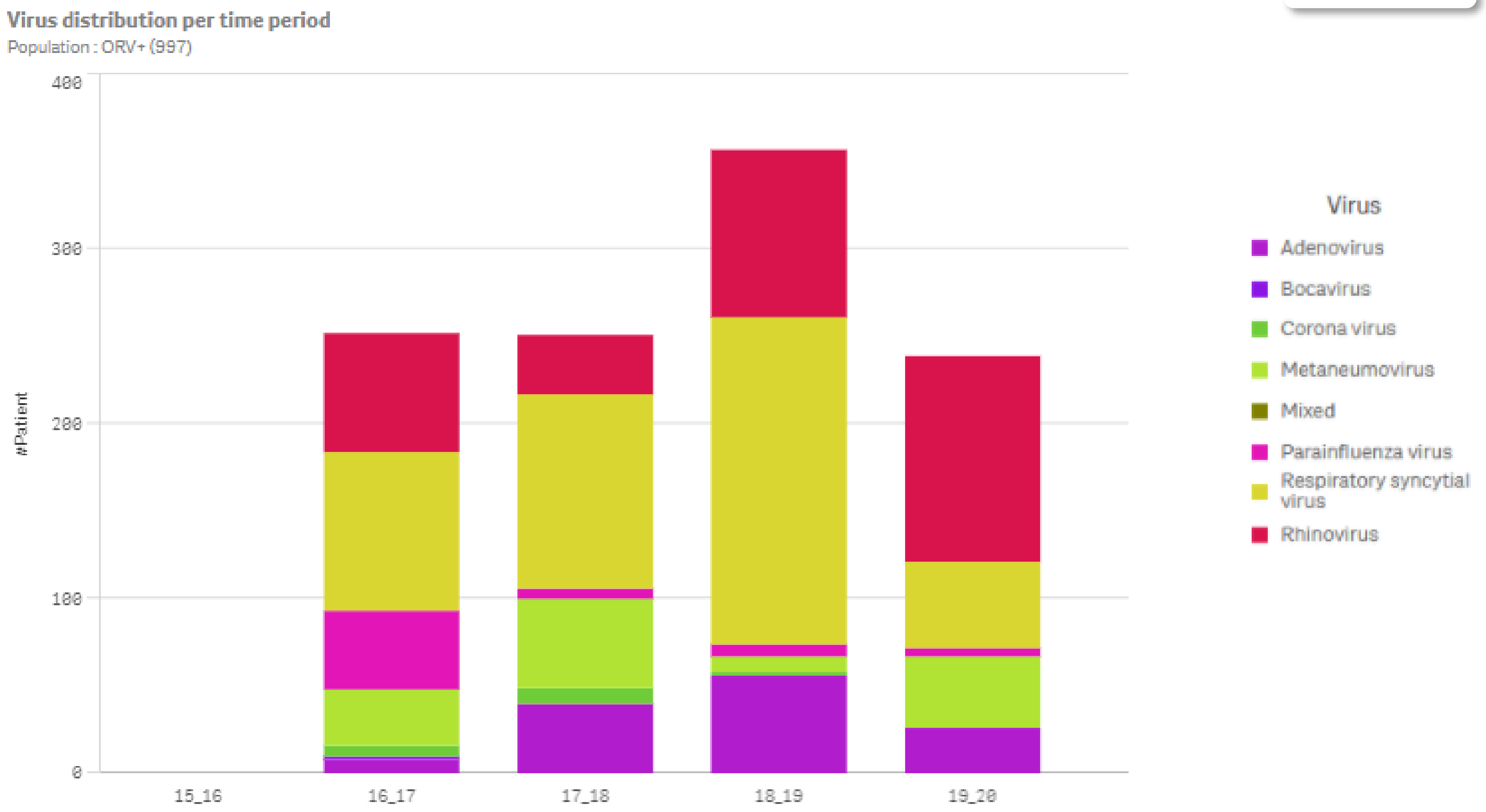
Virus distribution per time period

Population : ORV+ (15 734)



OTHER RESPIRATORY VIRUS STRAIN EVOLUTION: INTERTROPICAL REGIONS

N=997



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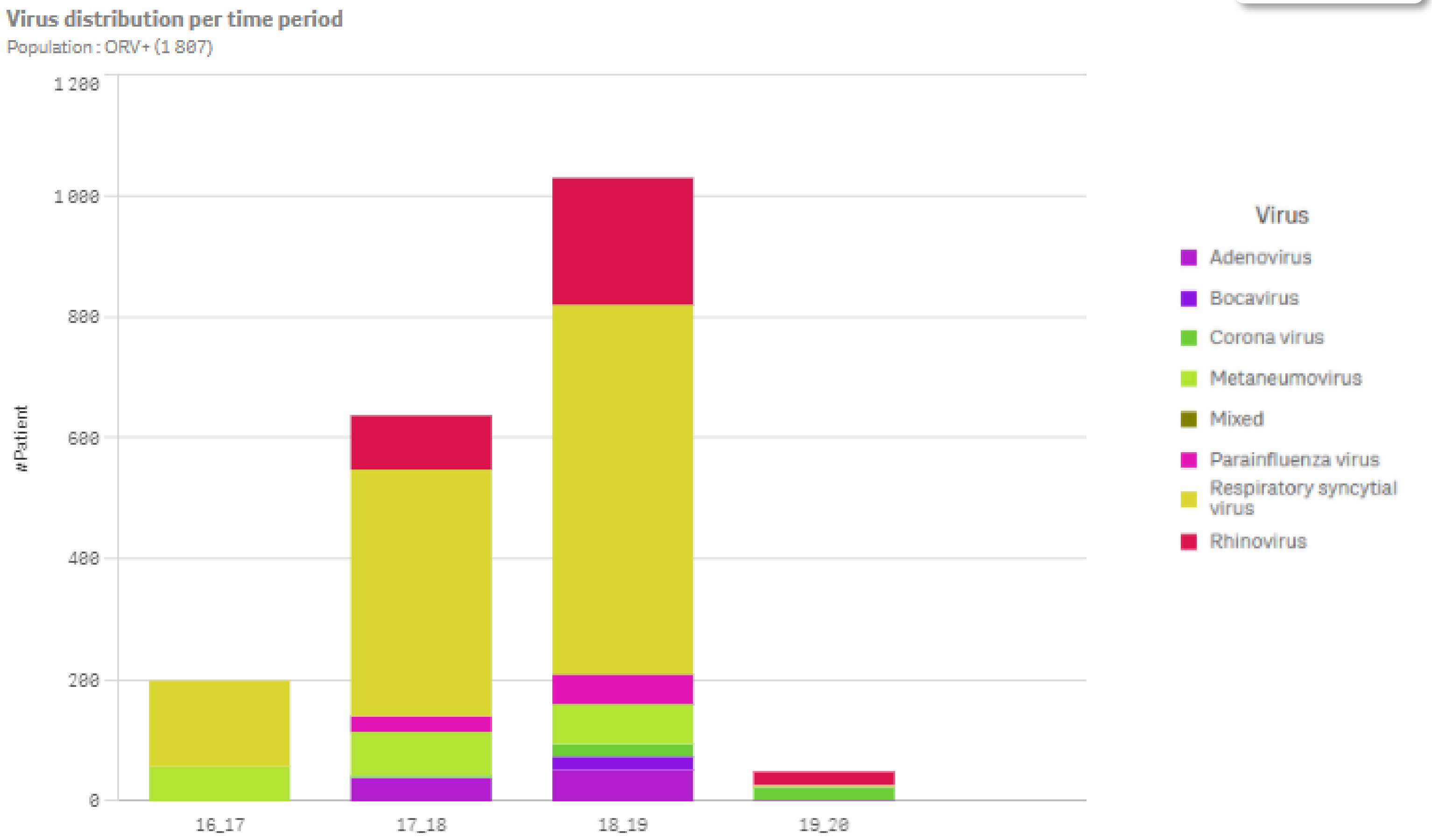
OTHER RESPIRATORY VIRUS STRAINS EVOLUTION: SOUTHERN HEMISPHERE

N=1 807



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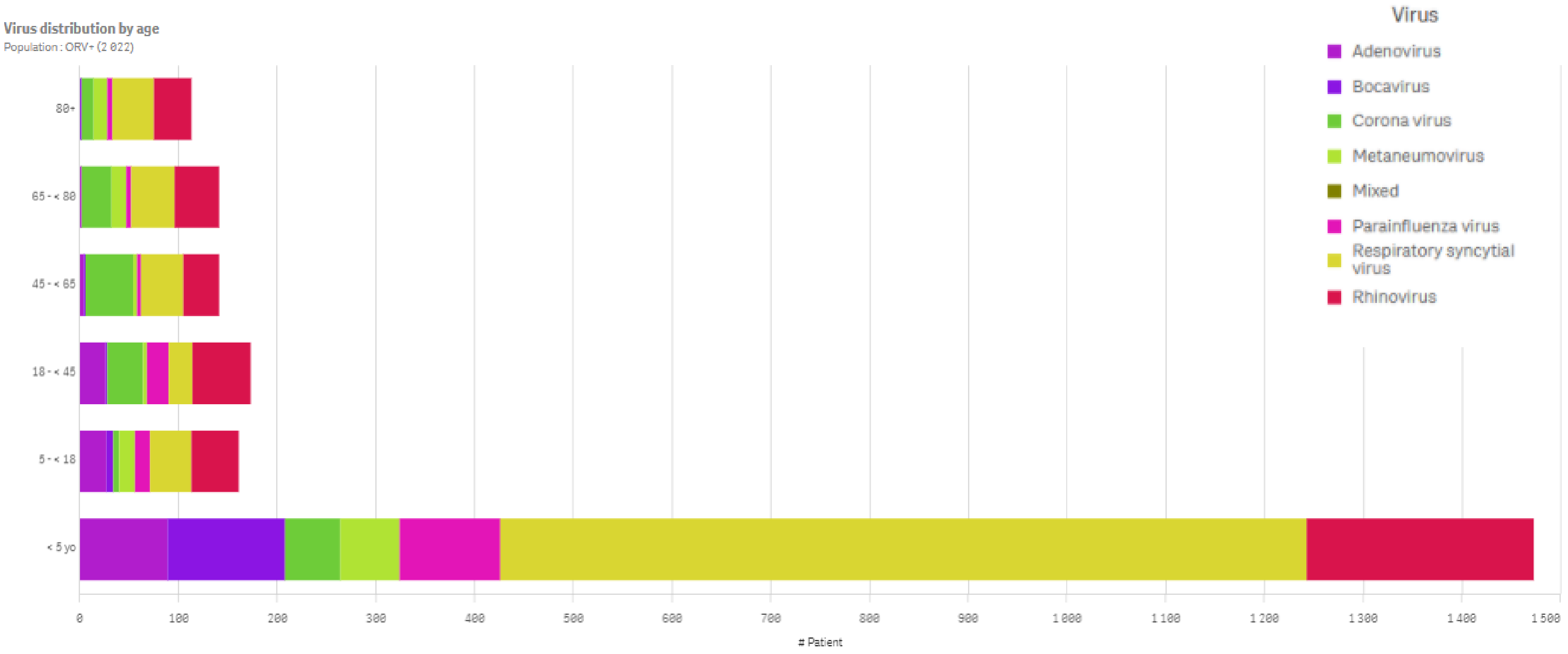
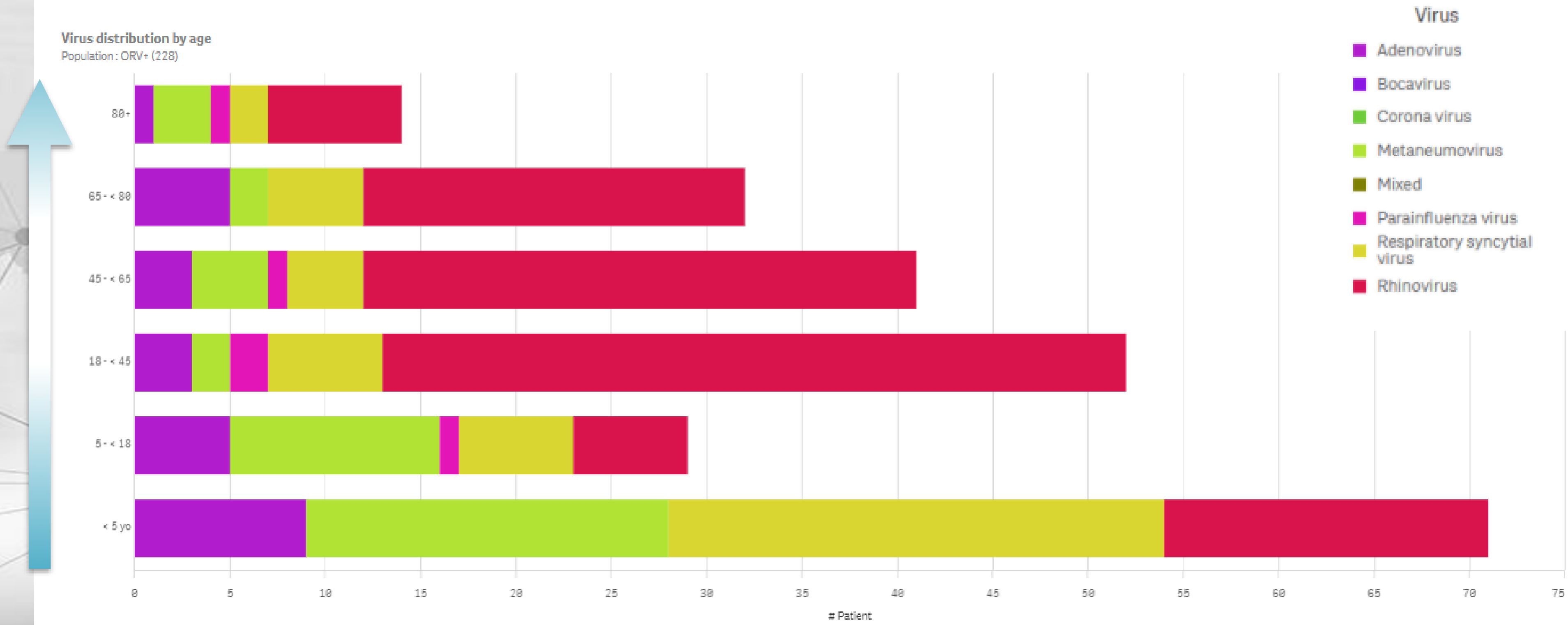
2019-2020 OTHER VIRUS STRAIN DISTRIBUTION PER AGE GROUP - NORTHERN HEMISPHERE

N=2 022



2019-2020 OTHER VIRUS STRAIN DISTRIBUTION PER AGE GROUP - INTERTROPICAL REGIONS

N=228



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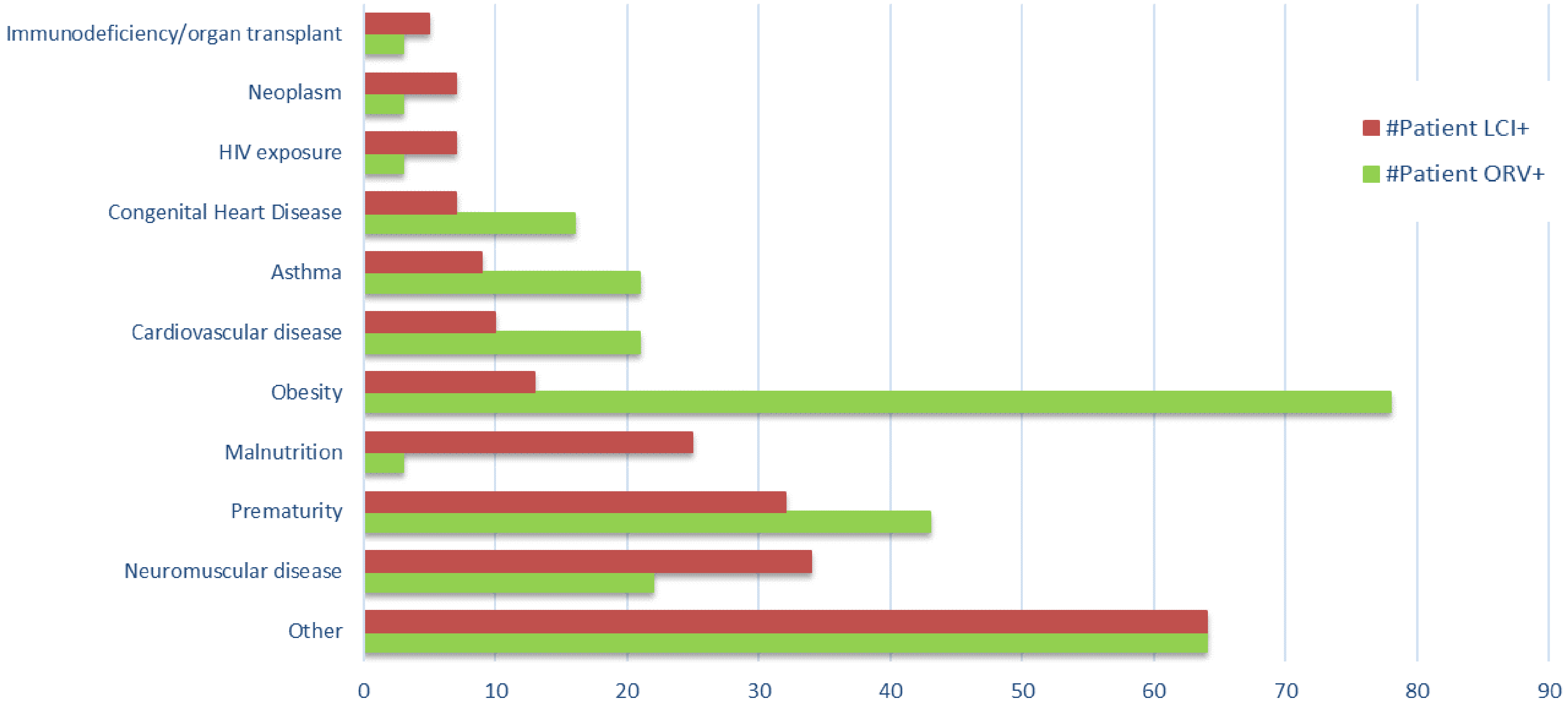
CHRONIC CONDITIONS LCI+ VS ORV+ PATIENTS <5

N= 2 629



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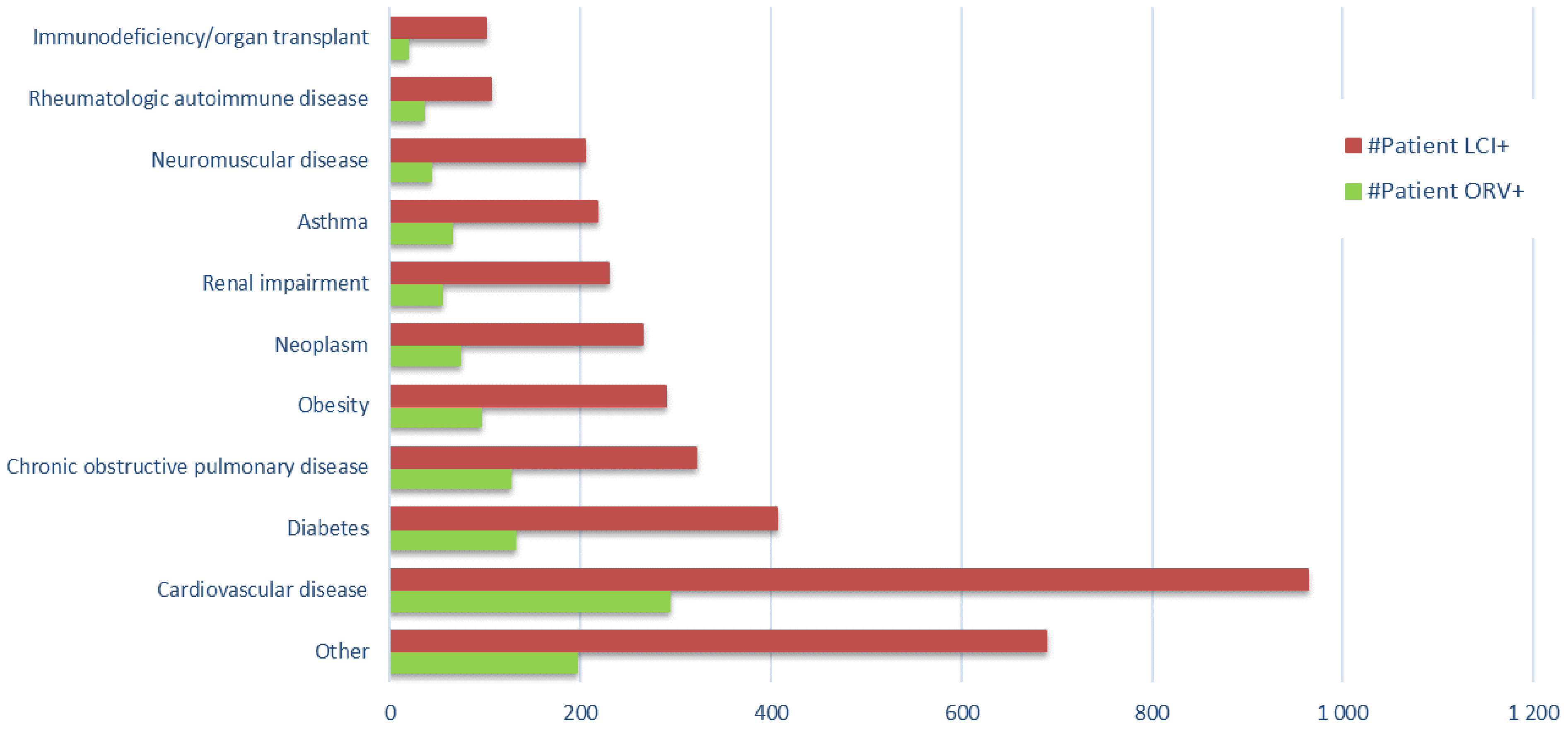
CHRONIC CONDITIONS LCI+ VS ORV+ PATIENTS >=5

N=3 995



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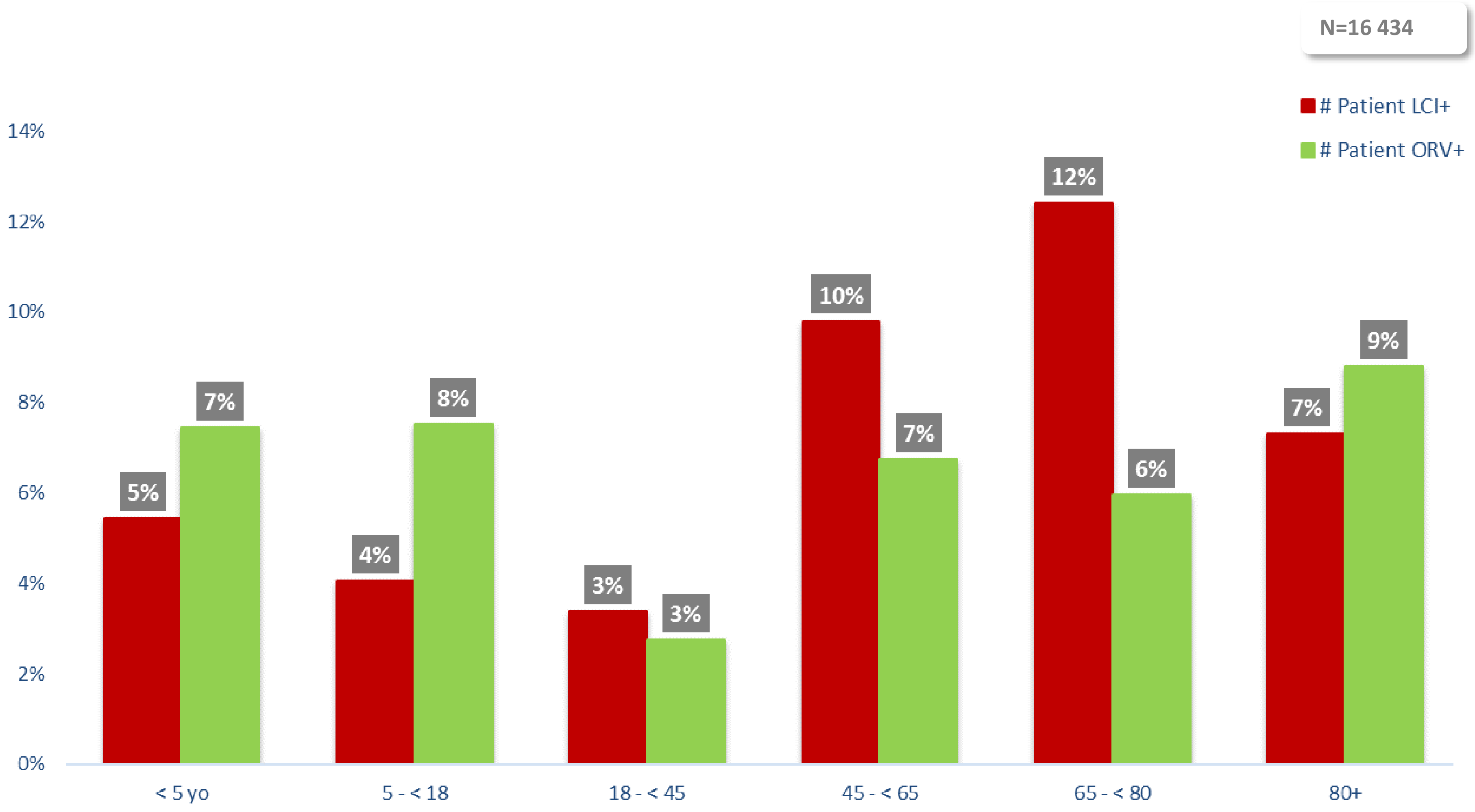
ICU ADMISSION PER AGE GROUP

LCI+ VS ORV+



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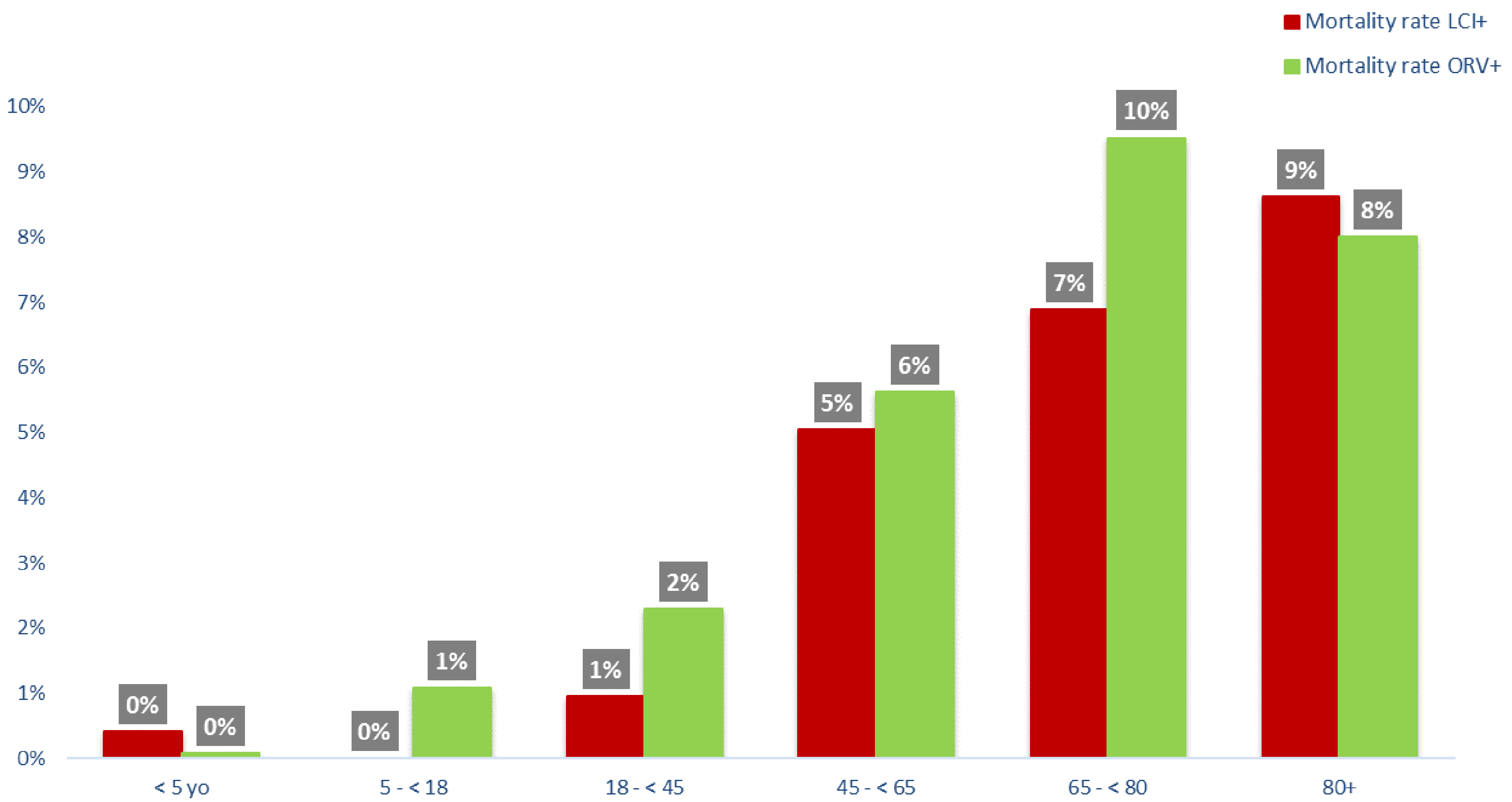
MORTALITY PER AGE GROUP

LCI+ VS ORV+

N=16 434



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STRAIN SEQUENCING 2019/2020

Bruno LINA, University of Lyon, GIHSN Independent Scientific Committee

Foundation for
Influenza
Epidemiology

Sous l'égide de

Fondation
de
France

TECHNICAL ISSUES

Shipment:

- Transport by World Courrier (organized Open Health)
- Predefined dates were not applicable
- Additional extra sequences not always used

Material:

- Extracted RNA (volume 60µL per specimen, ct<30 and below)

Documentation:

- Excel table called « GISAID epiflu uploader » with completed mandatory fields

GIHSN STRAIN SEQUENCING PERSPECTIVES FOR 2019-2020

SITES USING VIRPATH LAB FOR SEQUENCING

- ☐ India (100) 3 shipments: week 4 of nov, week 1 of jan, mar
- ☐ Nepal (65) 3 shipments: week 4 of nov, week 1 of jan, mar
- ☐ Kenya (100) 3 shipments week 1 of dec, jan, mar
- ☐ France – Lyon (50) (real-time)
- ☐ France – Paris* (100) 3 shipments week 1 of dec, jan, mar
- ☐ Russia – Moscow (60) 3 shipments week 2 of dec, jan, mar
- ☐ Serbia (100) 3 shipments week 2 of dec, jan, mar
- ☐ Ukraine (60) 3 shipments week 2 of dec, jan, mar

- ☐ Peru (50 HN-HS) 3 shipments week 1 of jan, jul, sept
- ☐ Bangladesh (100 HN-HS) 3 shipments week 2 of jan, jul, sept

- ☐ Argentina (75 HS) 3 shipments week 2 of may, jul, sept

TOTAL / 860 incl 250HS

GIHSN STRAIN SEQUENCING REALITY FOR 2019-2020

SITES USING VIRPATH LAB FOR SEQUENCING

- ☐ India (111) 3 shipments: week 4 of Jan, week 2 of Feb
- ☐ **Nepal (0) 0 shipment**
- ☐ Kenya (63) 2 shipments week 2 Feb, week 2 Sept
- ☐ France – Lyon (42) (almost real-time)
- ☐ France - Paris (33) 1 shipments week 2 Sept
- ☐ **Russia – Moscow (0) 0 shipment**
- ☐ Serbia (50) 2 shipments week 2 Jan, week 1 Mar
- ☐ Ukraine (61) 3 shipments week 2 Jan, week 1 mar, week 4 Jun
- ☐ Lebanon (87) week 2 Jul
- ☐ Peru (14) 1 shipments week 1 sept
- ☐ **Bangladesh (0) 0 shipments**
- ☐ Ivory Coast (pending)
- ☐ **Argentina (0) 0 shipments**

TOTAL / 461 plus 215 off-site

GIHSN SHIPMENT PERSPECTIVES FOR 2019-2020

Prepared 2019-2020 calendar for shipments/data sharing

2019

2020

Shipments on Tuesdays

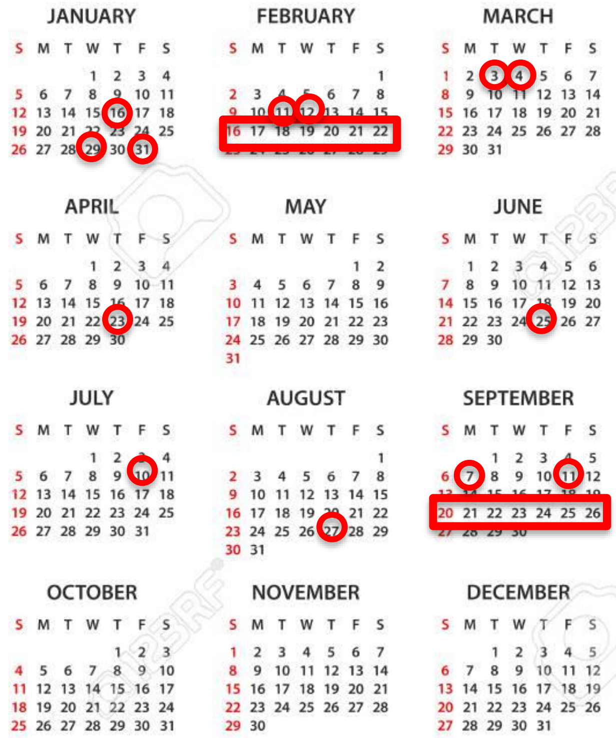
GIHSN SHIPMENT REALITY FOR 2019-2020

Prepared 2019-2020 calendar for shipments/data sharing

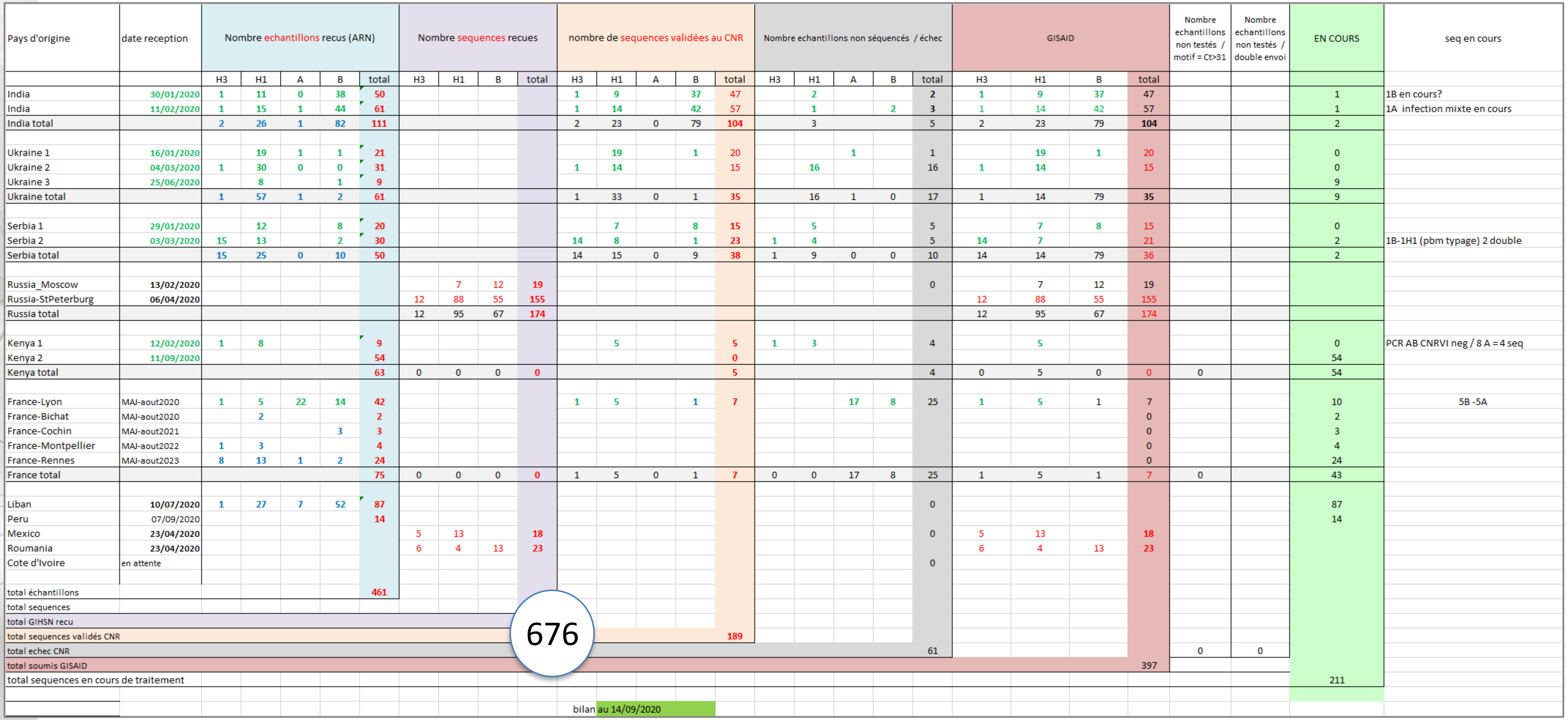
2019

2020

Shipments on Tuesdays



SUMMARY OF GIHSN SEQUENCE ANALYSIS



Pays d'origine	date reception	Nombre echantillons recus (ARN)					Nombre sequences recues				nombre de sequences validées au CNR					Nombre echantillons non séquencés / échec					GISAID				Nombre echantillons non testés / motif = Ct>31	Nombre echantillons non testés / double envoi	EN COURS	seq en cours
		H3	H1	A	B	total	H3	H1	B	total	H3	H1	A	B	total	H3	H1	A	B	total	H3	H1	B	total				
India	30/01/2020	1	11	0	38	50					1	9		37	47		2			2	1	9	37	47			1	1B en cours?
India	11/02/2020	1	15	1	44	61					1	14		42	57		1		2	3	1	14	42	57			1	1A infection mixte en cours
India total		2	26	1	82	111					2	23	0	79	104		3			5	2	23	79	104			2	
Ukraine 1	16/01/2020		19	1	1	21						19		1	20			1		1		19	1	20			0	
Ukraine 2	04/03/2020	1	30	0	0	31					1	14			15		16			16	1	14		15			0	
Ukraine 3	25/06/2020		8		1	9																					9	
Ukraine total		1	57	1	2	61					1	33	0	1	35		16	1	0	17	1	14	79	35			9	
Serbia 1	29/01/2020		12		8	20						7		8	15		5			5		7	8	15			0	
Serbia 2	03/03/2020	15	13		2	30					14	8		1	23	1	4			5	14	7		21			2	1B-1H1 (pbm typage) 2 double
Serbia total		15	25	0	10	50					14	15	0	9	38	1	9	0	0	10	14	14	79	36			2	
Russia_Moscow	13/02/2020							7	12	19										0		7	12	19				
Russia-StPeterburg	06/04/2020						12	88	55	155											12	88	55	155				
Russia total							12	95	67	174											12	95	67	174				
Kenya 1	12/02/2020	1	8			9						5			5	1	3			4		5					0	PCR AB CNRVI neg / 8 A = 4 seq
Kenya 2	11/09/2020					54									0												54	
Kenya total						63	0	0	0	0					5					4	0	5	0	0	0		54	
France-Lyon	MAJ-aout2020	1	5	22	14	42					1	5		1	7			17	8	25	1	5	1	7			10	5B -5A
France-Bichat	MAJ-aout2020		2			2																		0			2	
France-Cochin	MAJ-aout2021				3	3																		0			3	
France-Montpellier	MAJ-aout2022	1	3			4																		0			4	
France-Rennes	MAJ-aout2023	8	13	1	2	24																		0			24	
France total						75	0	0	0	0	1	5	0	1	7	0	0	17	8	25	1	5	1	7	0		43	
Liban	10/07/2020	1	27	7	52	87														0							87	
Peru	07/09/2020					14																					14	
Mexico	23/04/2020						5	13		18										0	5	13		18				
Roumania	23/04/2020						6	4	13	23											6	4	13	23				
Cote d'Ivoire	en attente																			0								
total échantillons						461																						
total sequences																												
total GIHSN recu																												
total sequences validés CNR															189													
total echec CNR																				61					0	0		
total soumis GISAID																								397				
total sequences en cours de traitement																											211	
											bilan	au 14/09/2020																

676

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19/10/2020

STRAIN SEQUENCING: DATA AVAILABLE

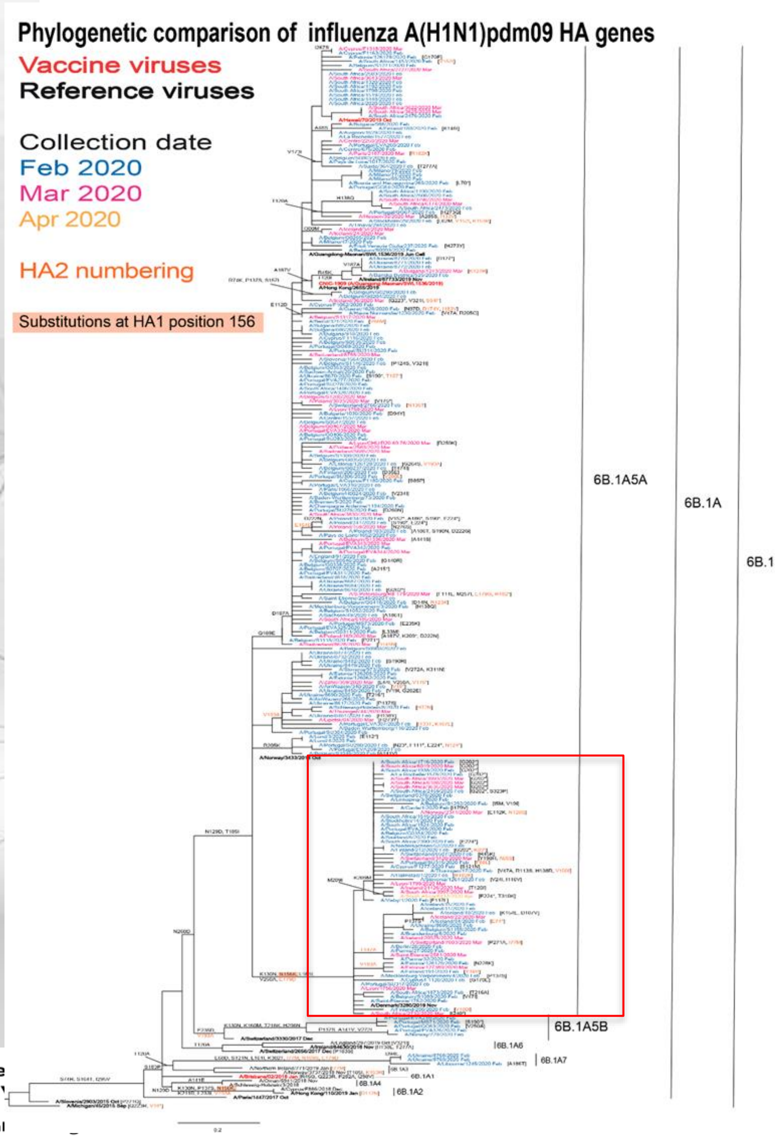
Majority of A(H1N1)pdm09, a minority of A(H3N2) viruses.

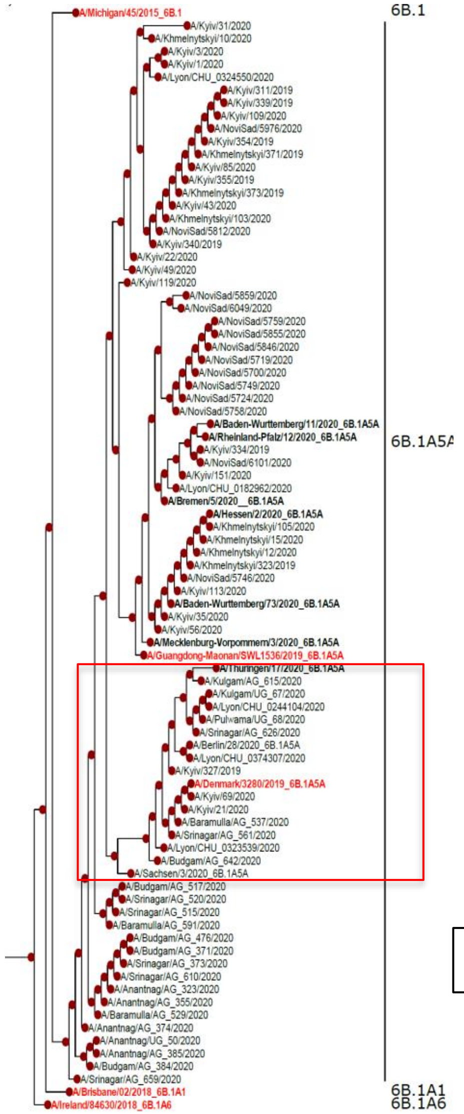
B Victoria strains majority of the detected B viruses, no B Yamagata detected in the network.

Phylogenetic analysis not completed :

- sequences from off-sites not all receved
- sequencing of the last strains still pending (late arrivals)

PRELIMINARY COMPARISON GISRS – GIHSN : H1N1PDM09





K130N, N156K, L161I, V250A in HA1

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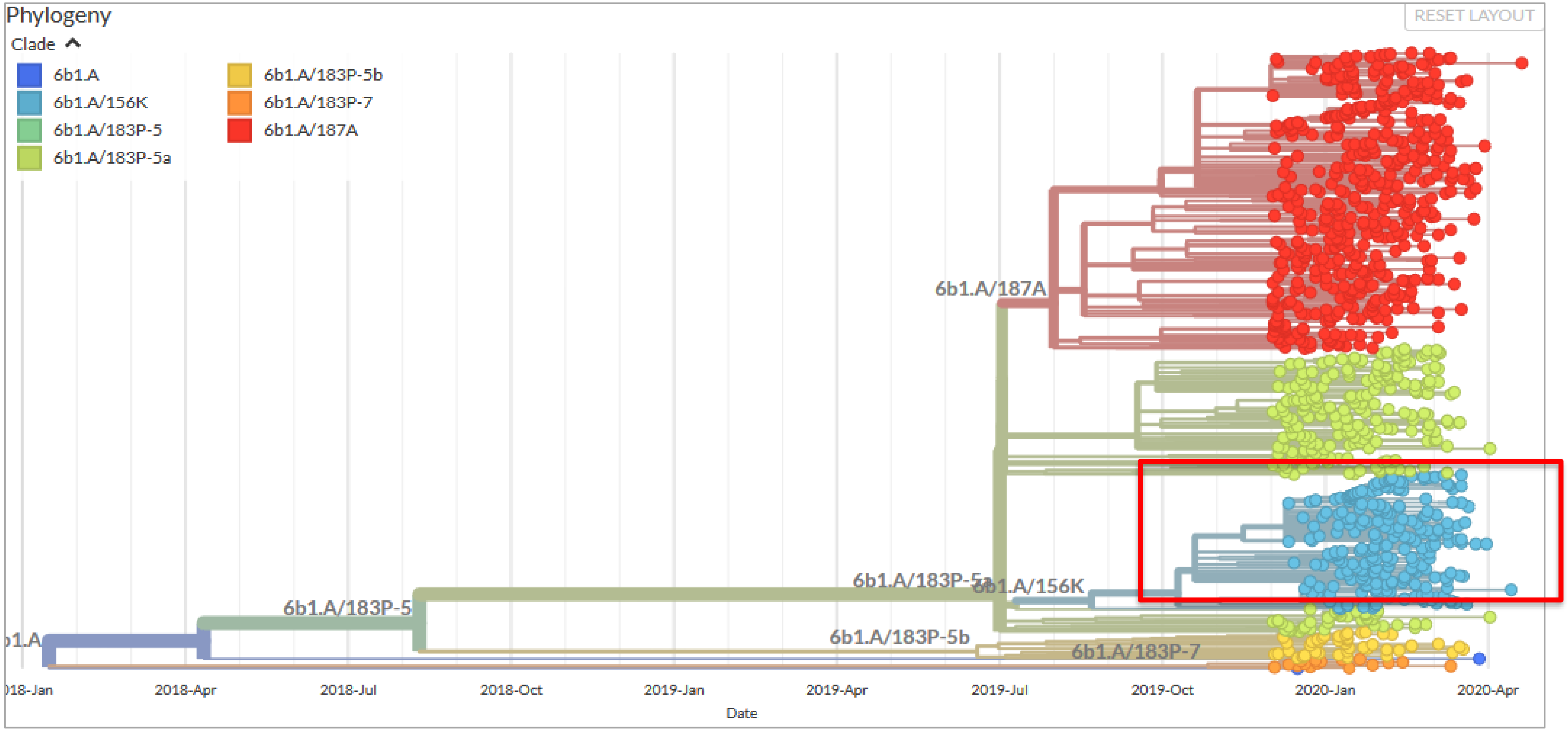
PHYLOGENY OF RECENT H1N1PDM09 (INCL 6B1.A/156K)



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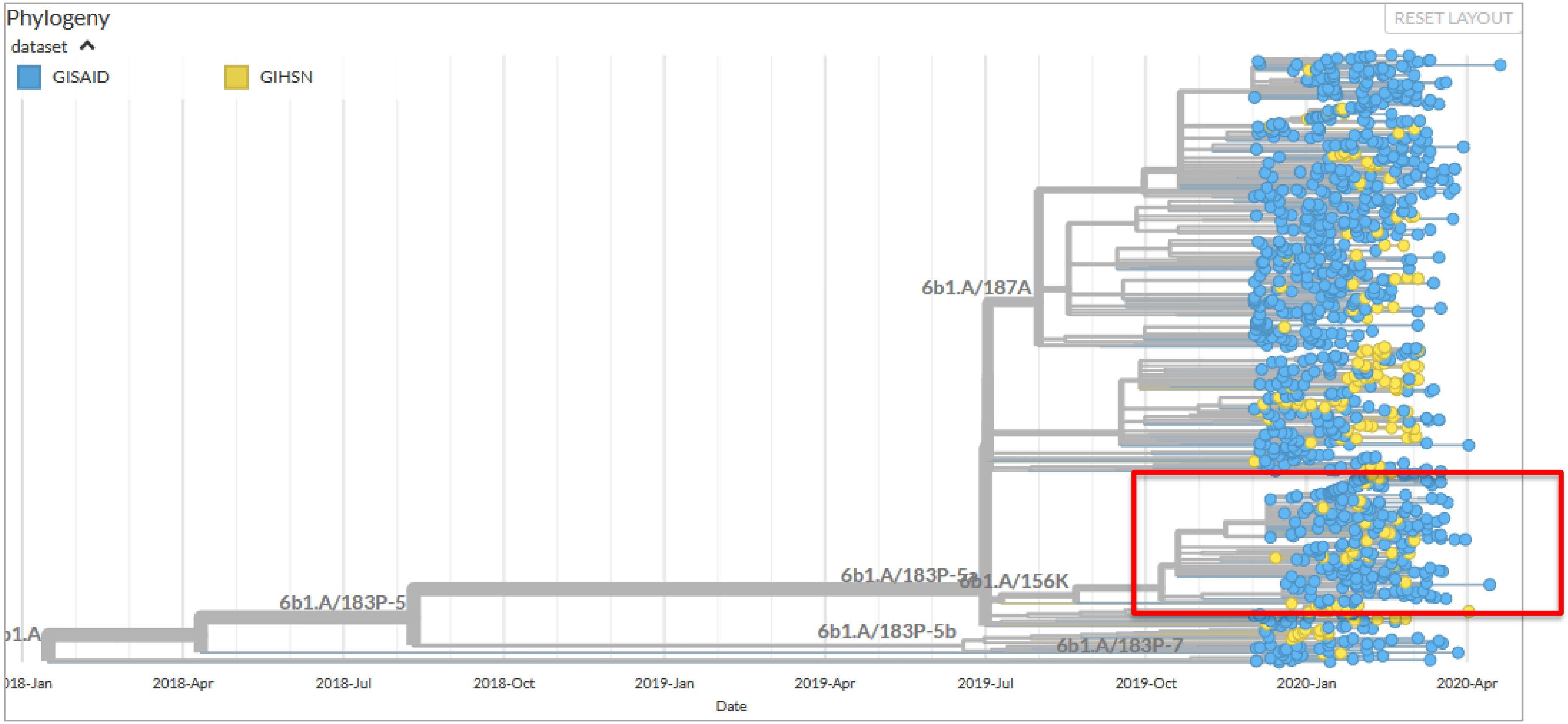
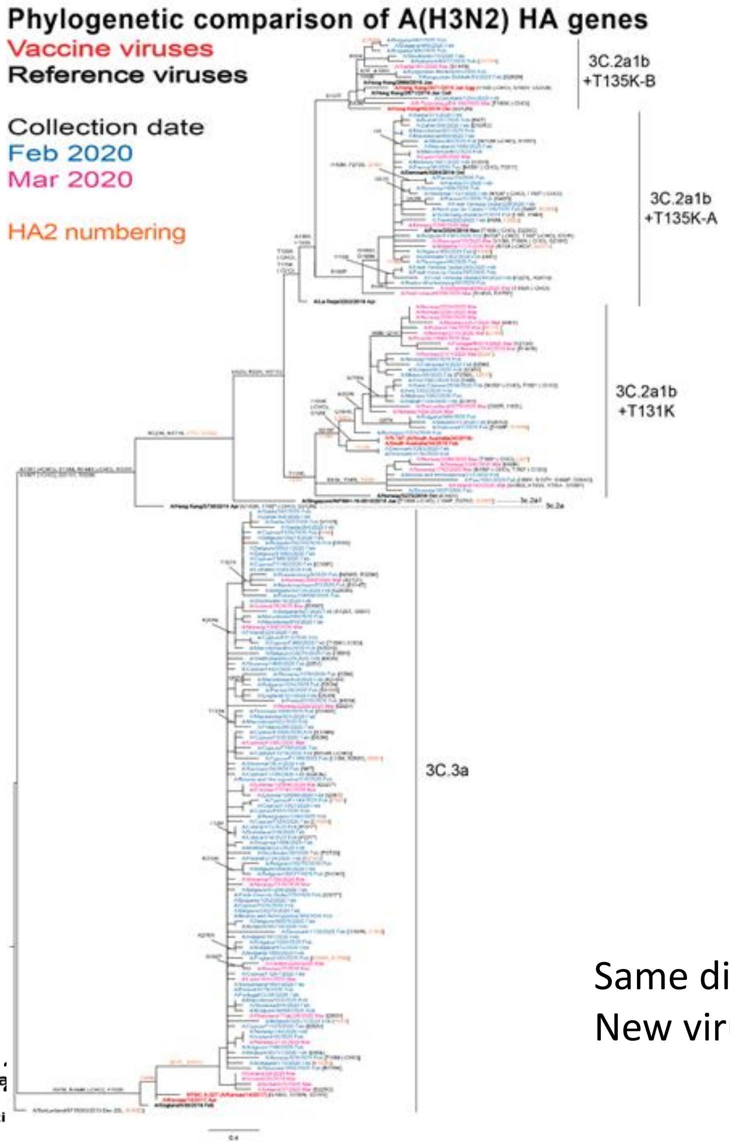
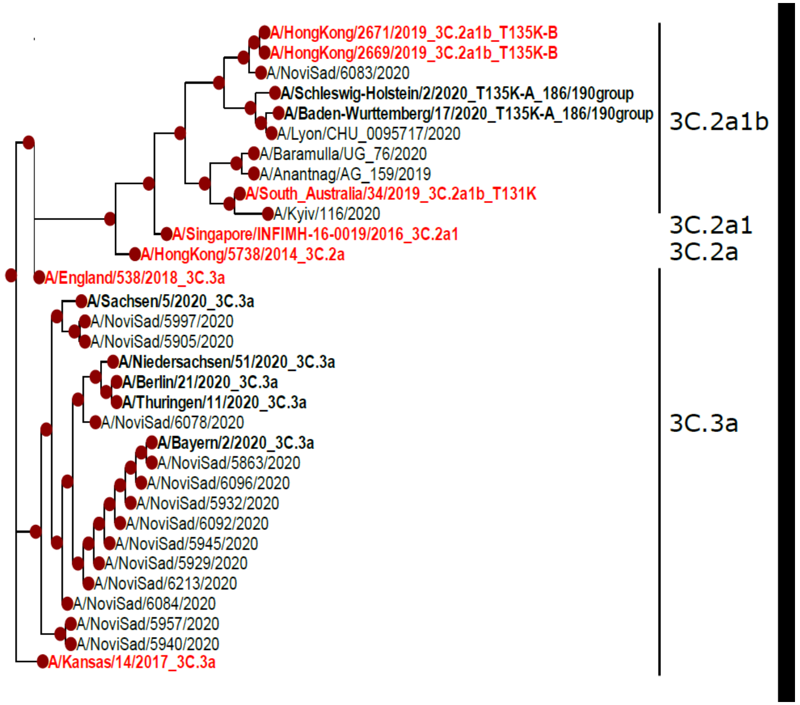
PHYLOGENY OF RECENT GIHSN H1N1PDM09 (INCL 6B1.A/156K)



19/10/2020

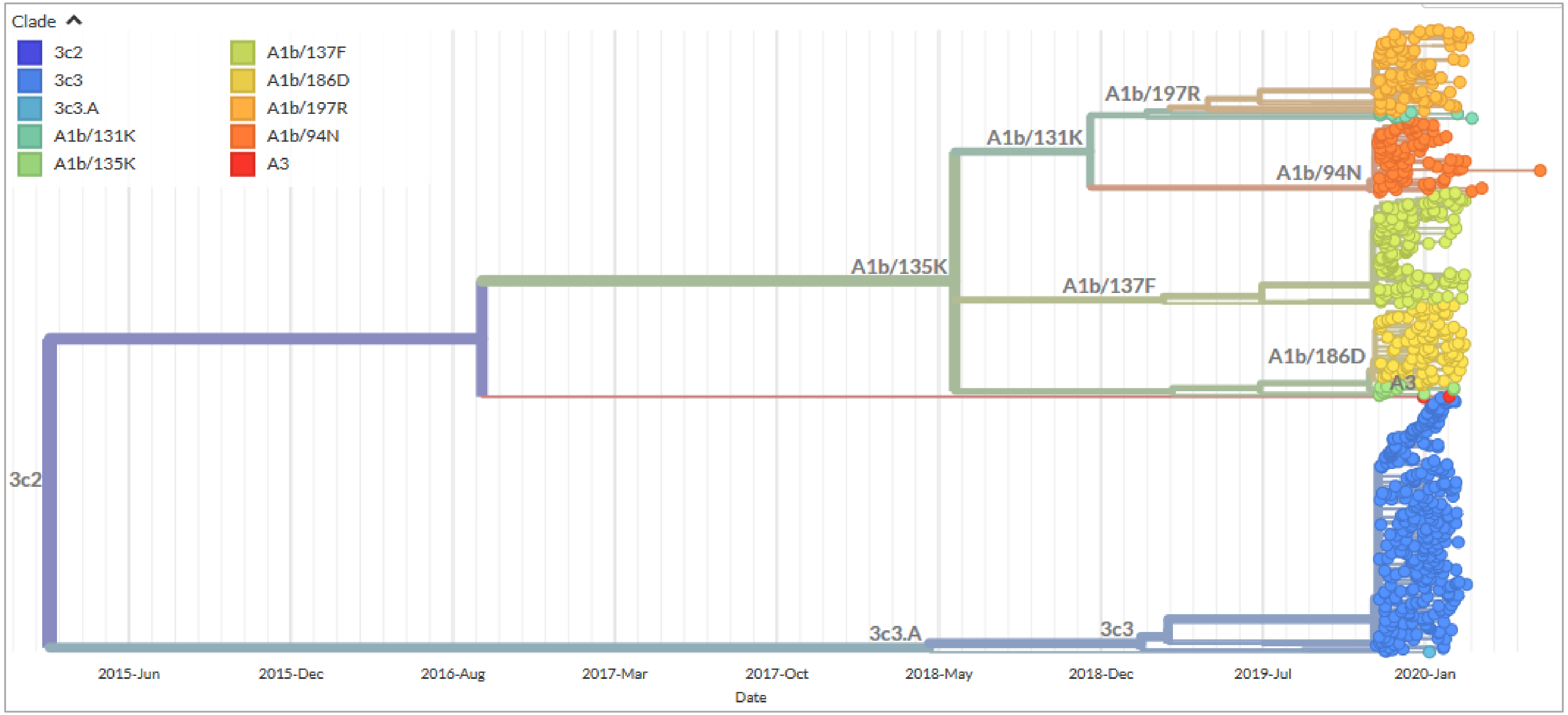
PRELIMINARY COMPARISON GISRS – GIHSN : H3N2





Same diversity (T135K-A and T135K-B), but limited number of viruses.
New viruses to be sequenced

PHYLOGENY OF RECENT H3N2 (3C.2A1B SUBCLADES)



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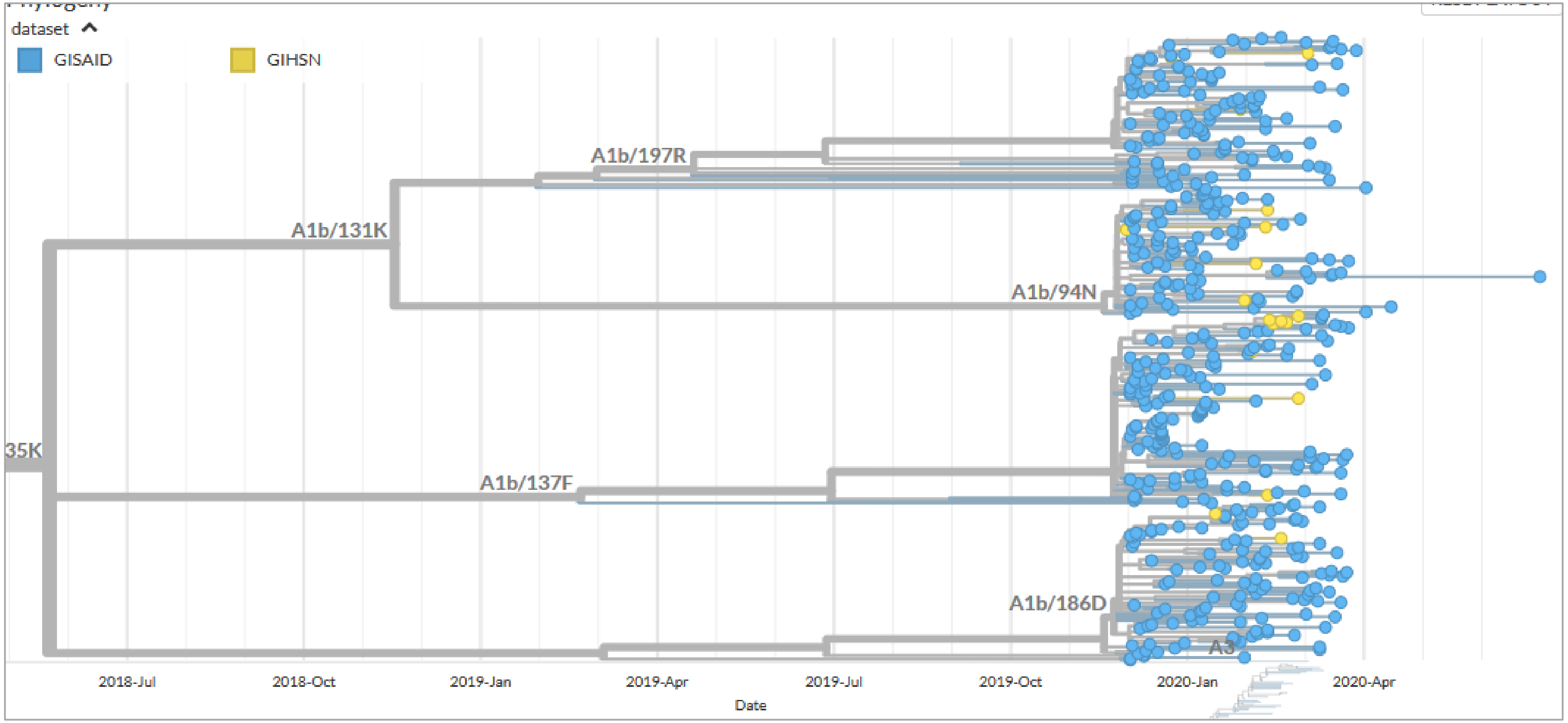
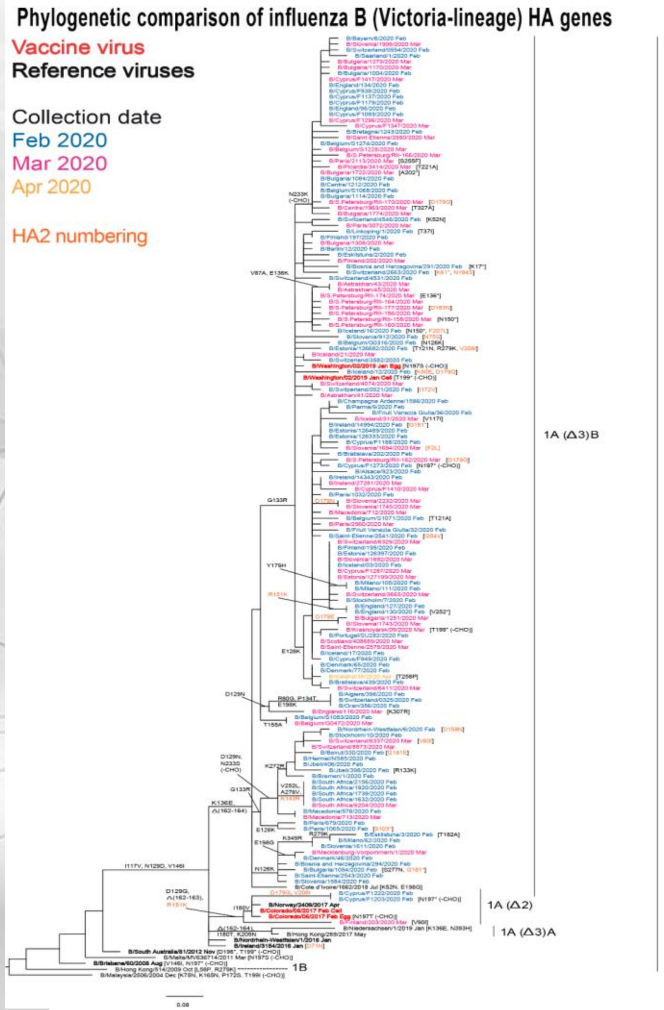
PHYLOGENY OF RECENT GIHSN H3N2 (3C.2A1B SUBCLADES)

Clade 3c.2A1b



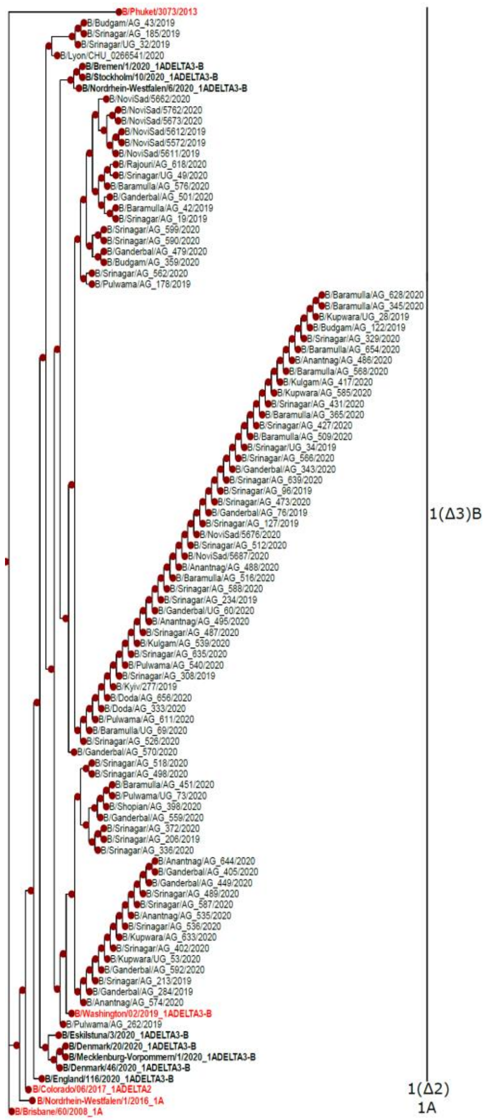
PRELIMINARY COMPARISON GISRS – GIHSN : B VICTORIA



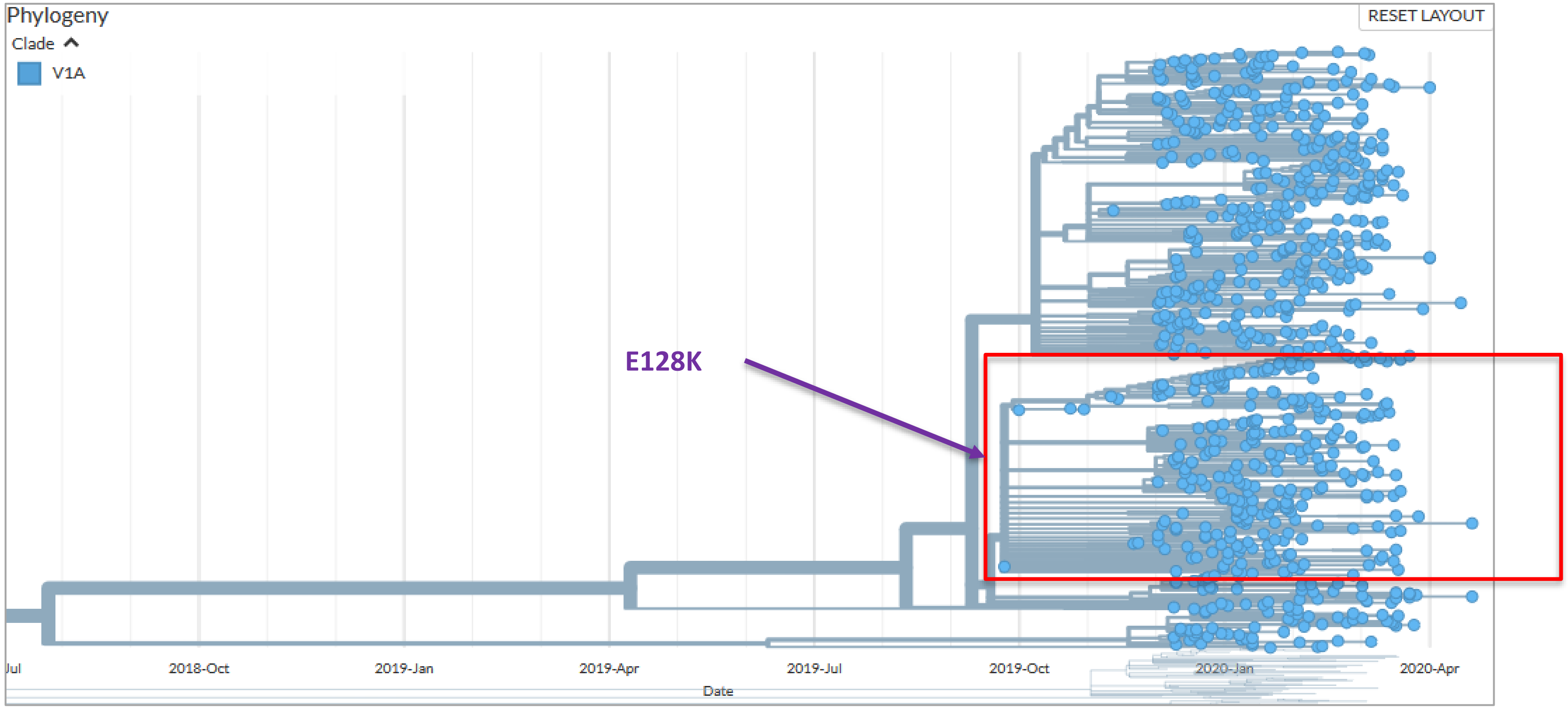
Δ162-164, K136E, G133R

B/Washington/02/2019

E128K → ?

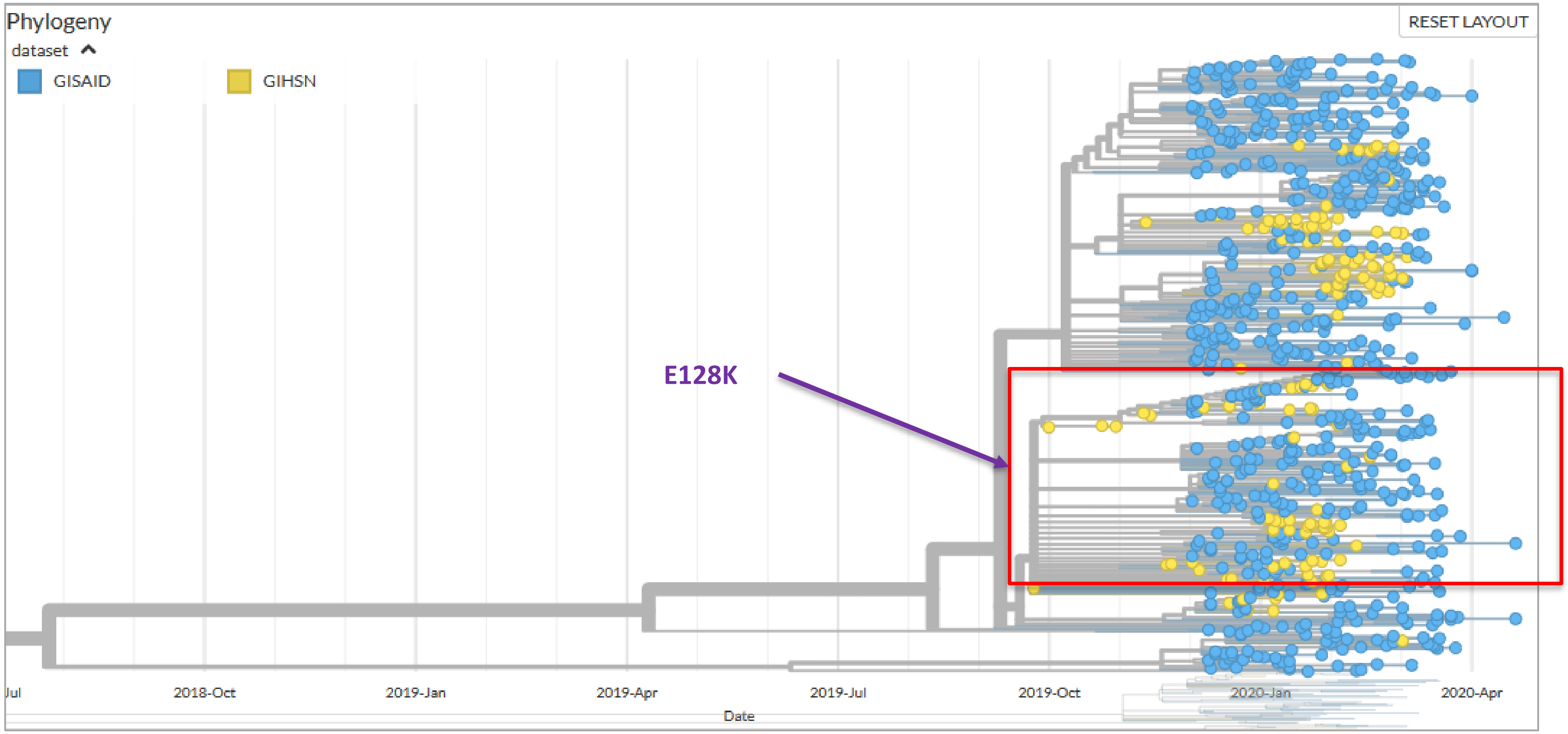


PHYLOGENY OF RECENT B VICTORIA (Δ162-164 1A SUBCLADE)



E128K

PHYLOGENY OF RECENT GIHSN B VICTORIA (Δ162-164 1A SUBCLADE)



E128K

SUMMARY

- More input from the sites than last year
- Some very participative labs
- Completion of the data not finished yet
- Overall 500 sequences generated from the Lyon lab

- Very large representation of the A(H1N1)pdm09 and B Victoria from hospital cases
- Sharing of sequence data and GISAID upload satisfactory
- Good feedback from sites

- Improvement in TaT for sequence production and sharing
- Improvement in shipment of material

EVOLUTION OF THE ENVIRONMENT

Acquisition of a Mosquito platform

- Reduction of cost per sequence
- Better preparation for the sequencing (automation)

Illumina nextseq on site (confirmed)

- Improved TaT
- dedicated staff

Hiring of a Bio-Ingeneer (Hadrien REGUES) and a PhD student (Gregory QUEROMES)

- Provide analytical and comparison tools
- involved in the wet and dry lab
- Development of a website for better interaction with the sites

ACKNOWLEDGEMENTS

Staff from Lyon NIC

Gwendoline Burfin
Hadrien Regue
Solene Brun
Marine Jourdain

Maude Bouscambert
Laurence Josset
Martine Valette

Surveillance GISRS Data

John McCauley
GISRS network

System for Data collection

GISAID

Source of Data

GIHSN sites

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GIHSN SURVEILLANCE PROTOCOL 2020/21

Sandra CHAVES, MD, MSc, Executive Officer Foundation for Influenza Epidemiology

Foundation for
Influenza
Epidemiology

Sous l'égide de

Fondation
de
France

OBJECTIVES

- Expand international laboratory and surveillance capacity and data sharing
- Support the biannual WHO vaccine strain selection process
- Link clinical and virologic (including whole genome sequence) data from hospitalized patients with acute respiratory infections
- Describe the distribution of the different influenza strains (A/H1N1, A/H3N2, B/Yamagata, B/Victoria) among these severe cases over a wide range of geographic areas

ELIGIBILITY CRITERIA

- Patients with an acute process
- Patients whose indication for admission was any of a predefined set of conditions, described as possibly associated with a recent influenza infection (list provide to sites)
- Study nurse or attending clinician will identify eligible cases in the hospital admission log, chart review or available records
- All eligible patients hospitalized in the previous 72 hours with hospital stay of at least 1 night would be screened

INCLUSION CRITERIA

- Patients ≥5 years will be included in the study if they are hospitalized within <u>7 days</u> of community onset influenza like-illness, defined as

Modified ECDC definition of influenza like-illness (ILI)
<u>Combination of</u>:
At least <u>one</u> of the following four systemic symptoms (ICD-9-CM code): Fever o feverishness (780.6), headache (784.0), myalgia, (729.1) or malaise (780.79);
AND
At least <u>one</u> of the following four respiratory symptoms (ICD-9-CM code): Cough (786.2), sore throat (787.2), shortness of breath (786.05), or nasal congestion (478.19)

- Patients <5 years will be included if admission associated with any of the conditions listed as part of eligibility criteria – if onset within 7 days from admission

SAMPLE COLLECTION

Each patient meeting the inclusion criteria and providing consent would have the following specimens collected:

- A nasopharyngeal (NP) or nasal swab combined with an oropharyngeal (OP) swab in a viral transport media (VTM)

Samples are sent to reference laboratory for RT-PCR or tested on site

Note: There may be some variation on specimen collected by site that need to be captured

Nasal and throat swabs combined are well accepted and the yield is like NP/OP combined

WGS must be generated for **a minimum of 50-100 flu positive specimens**

➢ If the site has no WGS capacity, specimens can be sent to the National Influenza Center in Lyon, France, under Terms of Reference for sharing materials

SAMPLE MANAGEMENT AND LABORATORY PROCEDURES

- Samples kept at –20ºC until sent to reference laboratory. Multiplex real-time RT-PCR
- Influenza A/B viruses (influenza A subtyped and influenza B lineage identified)

New

- **Testing for SARS-CoV-2 simultaneously (?)**
- Other respiratory pathogens *(* human coronavirus, metapneumovirus, bocavirus, respiratory syncytial viruses, adenovirus, parainfluenza viruses, rhinovirus) optional
  - ✓ Analysis for respiratory viruses other than influenza can be carried out after the study ends (if samples are stored appropriately)

New

- Storage (-20C or -70C) of all <u>influenza positive and negative study samples</u> for a minimum of <u>one year</u>
- All influenza positive (and SARS-CoV-2 positive, if performed) samples plus a subset of 30% of negative samples should be stored for <u>an additional 3 years</u>
  - ✓ This will assure sample availability for additional retrospective investigations (e.g. SARS-CoV-2, testing of lab diagnostic tools or investigation of emerging new pathogens)

GENOME SEQUENCING

- Whole genome sequencing (WGS) must be generated for a **minimum of 50-100 influenza positive specimens**
- Samples for WGS will be selected using specific criteria to be agreed upon by the GIHSN Independent Scientific Committee (ISC) prior to the start of the 2020/21 influenza season
- If the site has no WGS capacity, specimens can be sent to the National Influenza Center in Lyon, France, under Terms of Reference for sharing materials in GISRS
  - ✓ Shipments are organized by OpenHealth

Hemisphere	***Early season***	***ICU/deaths and vaccine failures***	***Samples per month***
Northern	*all samples until 15 January*	*All*	*10-30 (during season)*
Southern	*all samples until 15 July*	*All*	*10-30 (during season)*
Intertropical	*NA*	*All*	*5-15 (all year)*

EPI AND CLINICAL DATA COLLECTION

- Trained study staff collect relevant information by a combination of face-to-face interview with patient or caretaker and attending physicians, and by reviewing clinical records (to capture clinical outcome data)
- Influenza vaccination status is self-reported (patient or caretaker/ representative)
    - If patient had received the influenza vaccine for the current season, date of vaccination is captured
    - Whenever possible vaccination information will be validated by existing registries, vaccination cards or through contacting the place where the vaccine was administered

QUESTIONNAIRES – WHAT IS NEW??

- Two questionnaires still available (children <5 years vs. those ≥5 years)
- Capture information on testing for specific pathogens (including SARS-COV-2)
- **In the ≥5 years questionnaire**
  - ✓ Added few extra variables to assess clinical presentation (nausea and vomiting, diarrhea, new loss or taste or smell, chest pain)
  - ✓ Clarify severity questions to be captured at admission and frailty score to be done in all patients 50 years and older
- **In the <5 years questionnaire**
  - ✓ Added signs and symptoms for acute episode (not collected before), accommodating also those associated with COVID-19

QUESTIONS?


WE'RE MEETING TO TALK ABOUT COL-
WHAT'S "COL"?
IT LOOKS LIKE HIS SCREEN FROZE.
SHOULD WE WAIT?
YEAH, LET'S WAIT.
I WAS ON MUTE ...I AGREE.
HI, SORRY I'M LATE. WHAT DID I MISS?
-LABORATION.
TOM FISH BURNE
© marketoonist.com

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CLOSURE & INTRODUCTION TO DAY 2

Cédric MAHE, Foundation for Influenza Epidemiology

Foundation for
Influenza
Epidemiology

Sous l'égide de
Fondation
de
France

20 OCTOBER: 2 REGION SPECIFIC SESSIONS - DISCUSS SITE RESULTS & IMPLEMENTATION CHALLENGES

9:00–12:00 CET

SITES SESSION 1

CHINA - FUDAN
CHINA - WUHAN
INDIA
BANGLADESH
NEPAL
LEBANON
TURKEY
RUSSIA - ST PETERSBURG
RUSSIA – MOSCOW
UKRAINE
SERBIA
ROMANIA

14:00–17:00 CET

SITES SESSION 2

CANADA
MEXICO
BRAZIL
ARGENTINA
PERU
SOUTH AFRICA
KENYA
IVORY COAST
SPAIN
FRANCE - PARIS
FRANCE - LYON

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THANK YOU!

Global Influenza Hospital Surveillance Network