

# GIHSN 7TH ANNUAL MEETING, PARIS, OCTOBER 13-15TH 2019 WELCOME & INTRODUCTION

#### Cédric Mahé, Catherine Commaille-Chapus



Foundation for Influenza Epidemiology



# **WELCOME & INTRODUCTION OF PARTICIPANTS**

- 55 participants, 25 countries
- A growing network:
  - 18 sites, 60 hospitals this season
  - 21 sites, 90 hospitals for the upcoming season
- An operational platform for data generation, capacity building and data sharing/valuation:
  - More than 3,500 documented cases of hospitalizations from influenza per season
  - Already up to 7 seasons of data generated including NH and SH data (>74,000 patients records available)
- Stronger scientific oversight



# **OBJECTIVES OF THE MEETING**

- Review the individual and global results of the 2018-2019 season
- Exchange around the new GIHSN protocol and the evolution of the Network
- Present the new sites for the 2019-2020 season
- Discuss the strain sequencing process in order to optimize the GIHSN contribution to the WHO Strain Selection meetings
- Discuss how to value and communicate the generated data



# **AGENDA: MONDAY 14TH OCTOBER**

8:30 - 8:45	Welcome & Introduction to the meeting	C Mahé (FIE) C Commaille (OpenHealth)
8:45 - 10:30	Site results 1 (Poster Session with question-and- answer session) Sites 1 - 10 Moderated by: Elena Burtseva, member of ISC	Site Investigators
10:30 - 11:00	Coffee break	
11:00 - 12:30	Site results 2 (Poster Session with question-and- answer session) Sites 11 - 19 Moderated by: Marta Nunes, member of ISC	Site Investigators
12:30 - 14:00	Buffet Lunch	
14:00 - 14:40	GIHSN Results Season 2018-2019 (presentation followed by discussions)	Dr M Andrew (ISC)
14:40 - 16:00	Round Table Discussion – Strain Selection Process: Current & Future Challenges	Dr W Zhang (WHO) Dr P Bogner (GISAID) Pr J McCauley (WHO CC)
	Moderated by: Cedric Mahé (FIE)	Pr B Lina (Lyon University)
	- //	
16:00 - 16:30	Coffee break	
16:30 - 17:00	Contribution of the GIHSN to the Strain Selection Meeting – Feedback on the 2018-2019 Season & Prospects for the Next Season	Pr B Lina (Lyon University)
17:00 - 17:45	GIHSN Implementation for the Next Season -Evolution of the Governance of the Foundation -New Design of the GIHSN Implementation -Participating sites for the 2019-2020 Season	C Mahé (FIE)
17.45 - 18:00	Discussion & closure of Day 1	



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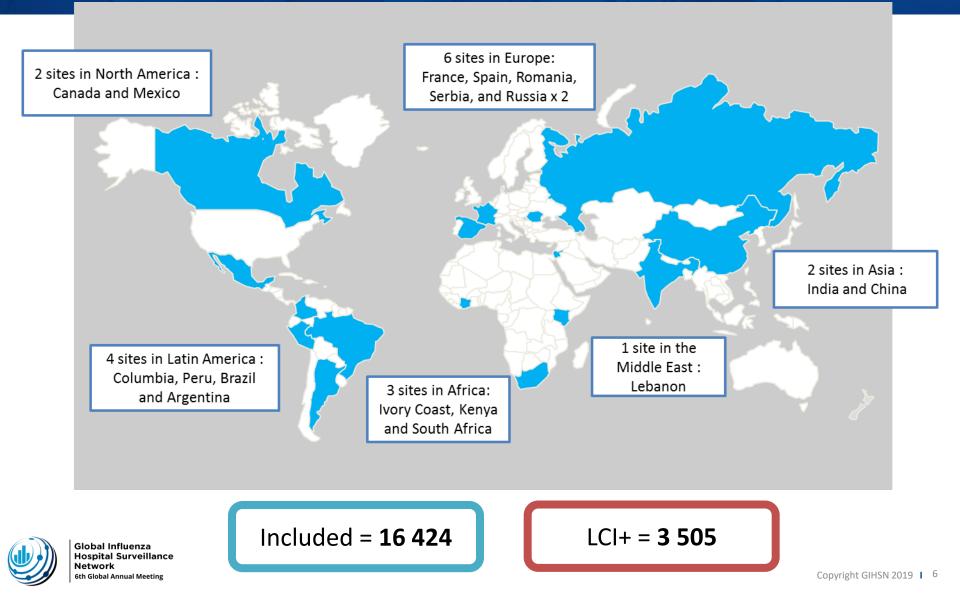
Network

# **AGENDA: TUESDAY 15TH OCT**

8:30 - 8:45	First day wrap-up & objectives of Day 2	C Commaille (OpenHealth)
		AU 11
8:45 – 10:15	Workshop Session 1: New Protocol Implementation -Implementation of the new questionnaire -Data Entry -Need for support	All sites
	Moderated by: Sandra Chaves (FIE)	
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10:15 - 10:45	Coffee break	
10:45 - 12:00	Workshop Session 2: Strain Sequencing Process -Timing of sequencing -Strain selection - Strain logistics between sites & Lyon Moderated by: Bruno Lina (ISC)	All sites
12:00 - 12:45	Dissemination & Publications (Globally and Locally) - Update on current manuscript development - Posters presented at Options X - Publication plan & International conferences 2019- 2020 - Manuscript writing process 2018-2019 season & rules of authorship	Pr B Lina (ISC)
12:45 - 13:00	Closing	C Mahé (FIE)
13:00 - 14:00	Buffet lunch	



# SEASON 2018-2019: 18 SITES, 60 HOSPITALS





# GIHSN 7TH ANNUAL MEETING, PARIS, OCTOBER 13-15TH 2019 POSTER SESSIONS: SITES RESULTS

#### All Site Investigators



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# **POSTER SESSION 1**

#### Moderator : Dr. Elena Burtseva (Scientific Committee)

Sites : South America – Africa - Asia Argentina Peru Brazil Columbia China - Shanghai India **Ivory Coast** South Africa Kenya Tunisia 35 min poster round

60 min short presentation by each site investigator & questions and answers



# **POSTER SESSION 2**

#### Moderator : Dr. Marta Nunes (Scientific Committee)

# Sites : North America - Middle East - Europe Mexico Canada Lebanon France - Lyon Romania Russia - Moscow Russia - St Petersburg Serbia Spain

35 min poster round 55 min short presentation by each site investigator & questions and answers





# GIHSN 7TH ANNUAL MEETING, PARIS, OCTOBER 13-15TH 2019 GIHSN RESULTS SEASON 2018-2019

#### Dr Melissa K. Andrew (Scientific Committee)



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# Study objectives and protocol - Modifications for 2018-2019 season



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# **GIHSN STUDY OBJECTIVES**

#### **Primary objectives**

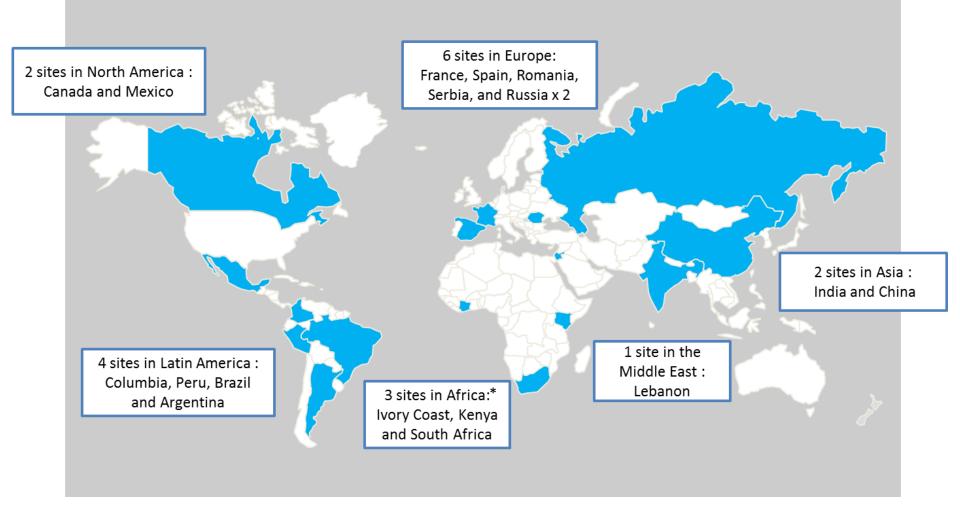
- 1. To evaluate the burden of severe influenza disease, defined as hospitalization related to community acquired influenza or complications following an influenza infection
- 2. To quantify the distribution of the different influenza strains (A/H1N1, A/H3N2, B/Yamagata, B/Victoria) among these severe cases

#### Secondary objectives

- 1. Notice: the GIHSN goals are related to influenza epidemiology [Optional: If testing for other respiratory viruses is performed] To estimate the relative incidence of influenza compared to other respiratory viruses
- 2. [Optional: If vaccine coverage is sufficient for some age group] To measure the effectiveness of influenza seasonal vaccines to prevent these hospitalizations using a case control design



# GIHSN DATA BASE 2018 – 2019 : 19 SITES ARE SHARING THEIR DATA





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\*The Tunisian site which was not a part of the Network this year has also shared data

# **UPDATED PROTOCOL**

Changes were implemented for the season 2018-2019 in order to simplify the protocol :

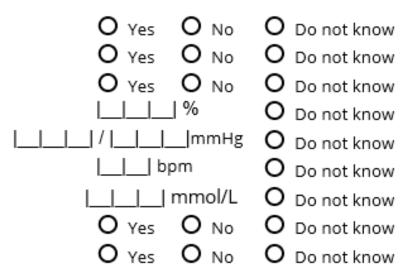
- A few historical exclusion criteria were removed such as :
  - Resident
  - Hospitalization in the last 30 days
  - Patient living in an institution
- ✓ Variables that were not relevant for analysis were removed and the section « laboratory results » was also simplified
- ✓ Adding the answer « Do not know » for many questions in order to allow for more data collection
- ✓ « Education levels » were replaced by « occupation »
- ✓ Adding of a Severity section allowing for analysis on severity



# **NEW SEVERITY SECTION**

#### Severity

- 26) Hypoxia at admission
- 27) Confusion at admission
- 28) Lethargy at admission
- 29) Oxygen saturation value on ambient air (%)
- 30) Blood pressure (systolic/diastolic)
- 31) Respiratory rate at admission (breaths per minute)
- 32) Blood Urea Nitrogen (mmol/L units)
- 33) Supplemental oxygen without mechanical ventilation
- 34) Vasopressor support

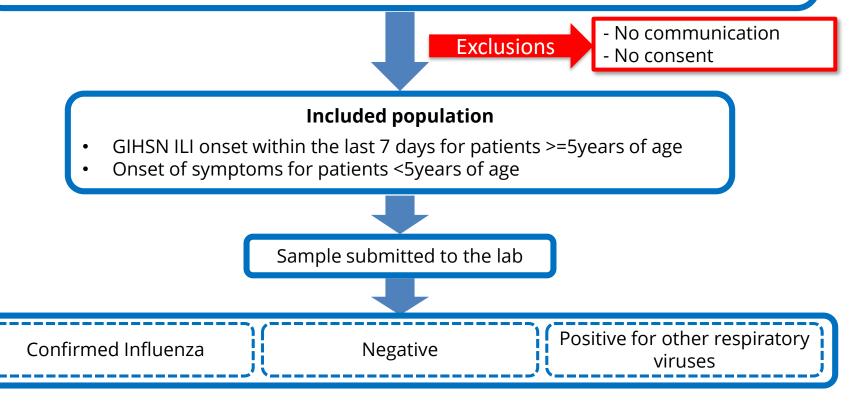




# **PROTOCOL 2018-2019**

#### **Eligible patients**

- Admitted through emergency doors or study participating wards for an acute condition.
- Admitted in the previous 48 hours and having stayed in hospital for at least 1 night.
- Main complaint for admission possibly related to influenza infection.





# **CURRENT ELIGIBILITY CRITERIA**

#### **Eligibility criteria**

Enrolment is based on:

- 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\*
- In this case, [a study nurse, doctor...] will identify by hospital admission registries, chart review or available records, all eligible patients hospitalized in the previous 48 hours and has stayed in hospital for at least 1 night (therefore a patient admitted before midnight of the previous day).

\*Admission diagnoses possibly associated with an influenza infection. International Classification of Diseases Code version 9 and 10. Codes are listed in the protocol and in annex of the questionnaire



# **CURRENT INCLUSION CRITERIA**

#### **Inclusion criteria**

Patients **<u>5 years old and older</u>** will be included in the study if they refer to a <u>seven</u> <u>days or less</u> antecedent of a community onset influenza like-illness (see definition in table 2).

Table 2. Modified European Centre for Diseases Control definition of influenzalike-illness (ILI)

#### **Combination of:**

at least one 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); at least one of the following three respiratory symptoms (ICD-9-CM code): b) Cough (786.2), sore throat (787.2) or shortness of breath (786.05).

Patients <u>less than 5 years</u> will be included if indications for admission, occurred within seven days or less between the beginning of symptoms and admission to hospital.



# **PROTOCOL SWABBING PROCEDURES**

#### Swabbing procedures :

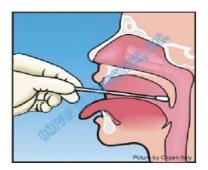
A nasopharyngeal swab for all patients and a pharyngeal swab for adults (14 years of age or older) and a nasal sample for children (less than 14 years old) will be obtained from each patient in case they comply with inclusion criteria and give consent.

#### Nasopharyngeal swab





#### Pharyngeal swab





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# Data Analysis – Descriptive analysis and outcomes

(Data as of 25/9)



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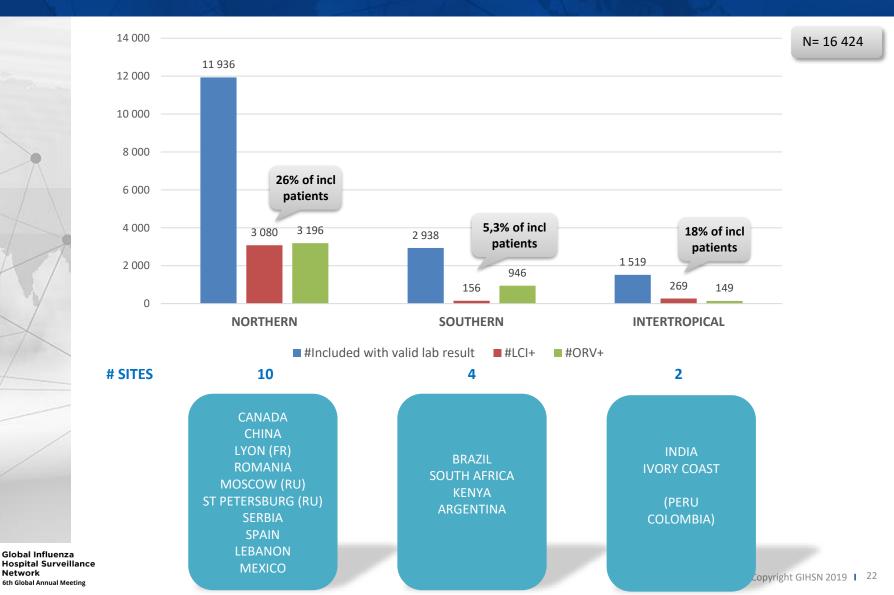
# **GLOBAL PATIENT INCLUSION** EVOLUTION OVER 7 YEARS



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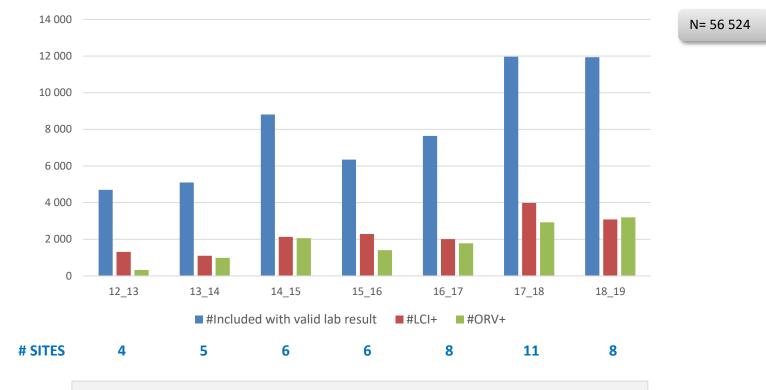
\*data from Colombia and Peru are not included Copyright GIHSN 2019 | 21

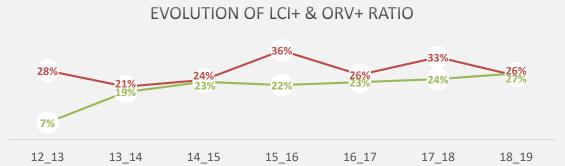
# **CONTRIBUTION PER ZONE 2018-2019**



Network

# NORTHERN HEMISPHERE – 16 SITES SINCE 2013



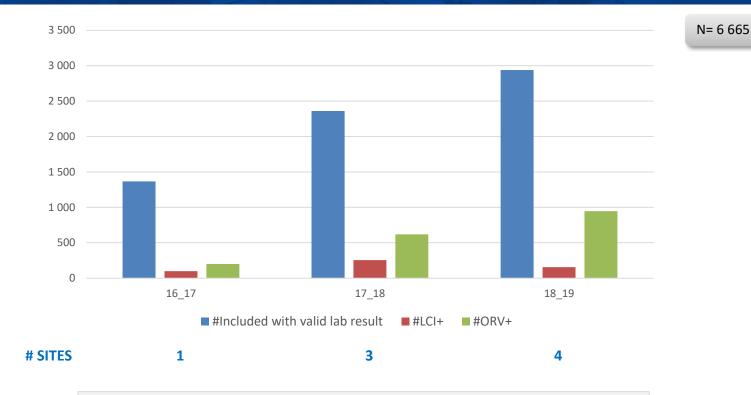


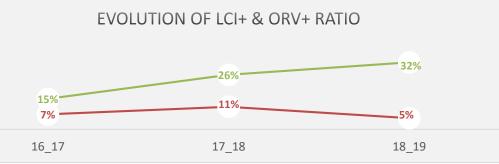


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# **SOUTHERN HEMISPHERE – 5 SITES SINCE** 2013

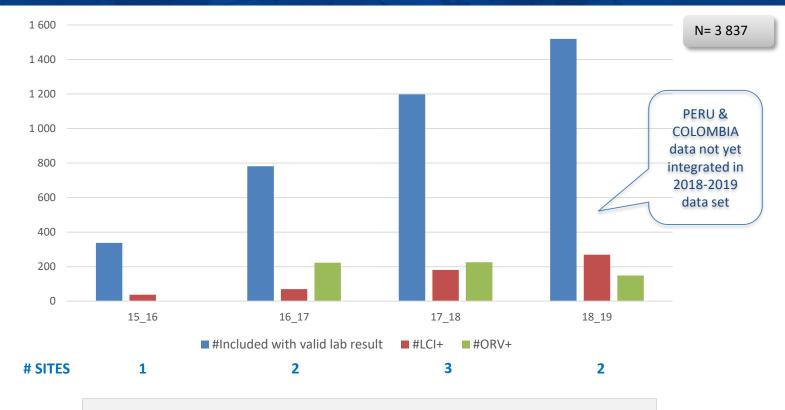






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# **INTERTROPICAL HEMISPHERE – 4 SITES SINCE** 2013







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#### GLOBAL AGE & GENDER DISTRIBUTION PATIENTS INCLUDED (W/ VALID RESULTS) 2018-2019



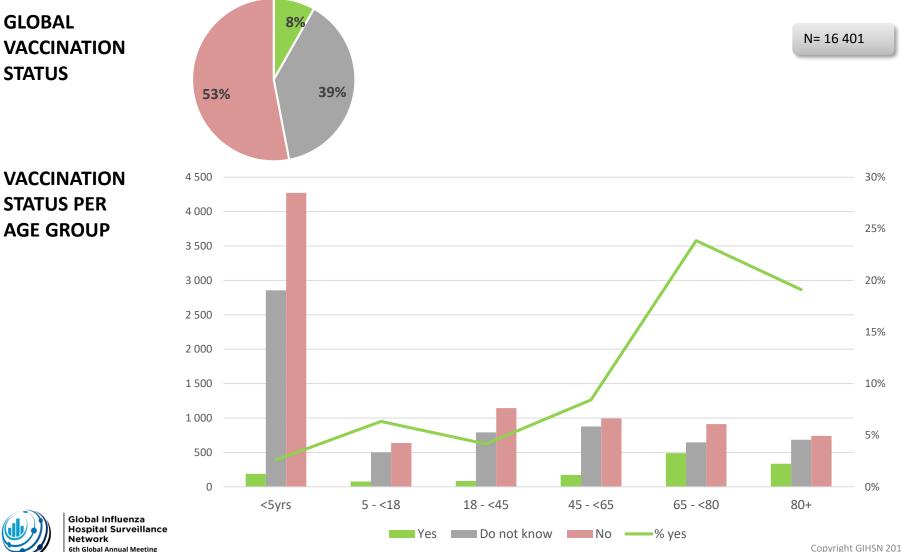
# VACCINATION RATE EVOLUTION VACCINATION RATE VS INCLUDED PATIENTS



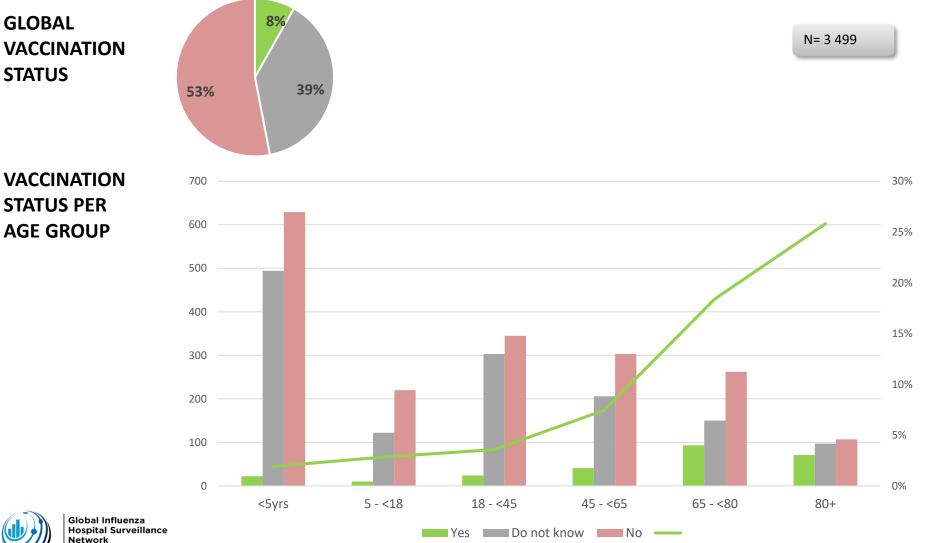


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#### **VACCINATION STATUS BY AGE GROUP INCLUDED PATIENTS 2018-2019**



#### VACCINATION STATUS BY AGE GROUP LCI+ PATIENTS 2018-2019



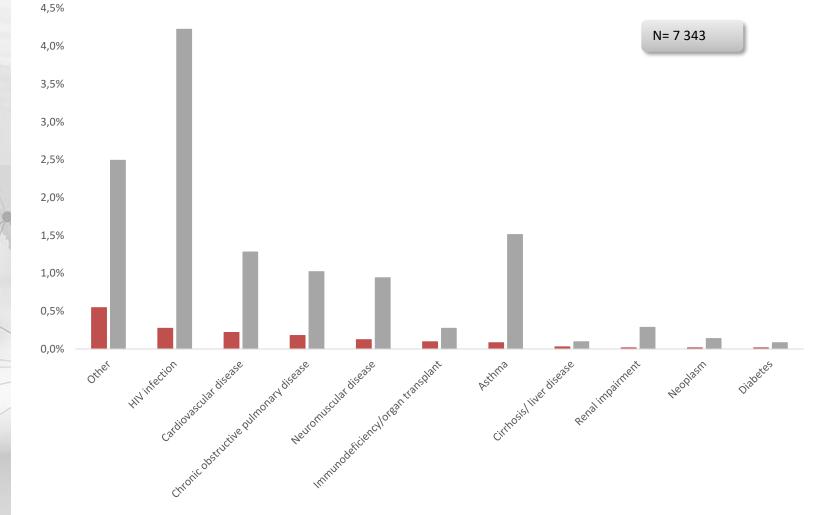
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#### INFLUENZA POSITIVES PER AGE GROUP LCI+ 2018-2019



#### INFLUENZA STATUS PER CHRONIC CONDITION PATIENTS <5

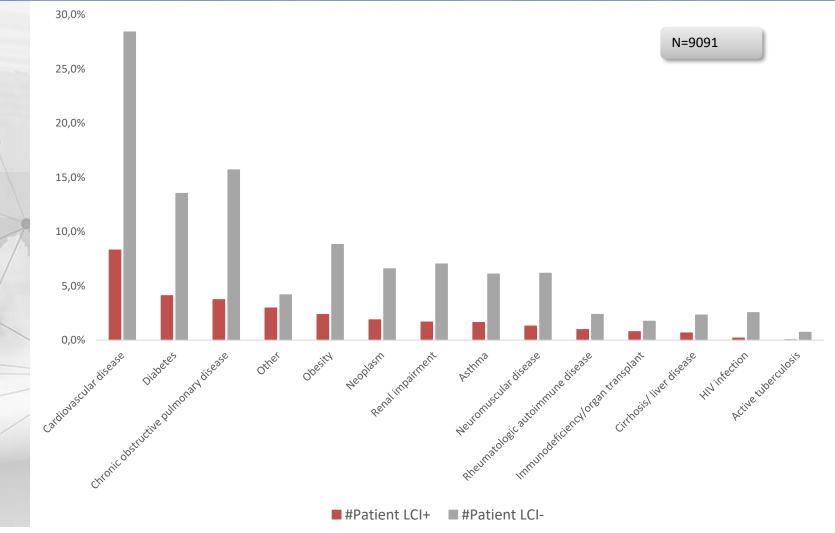


#Patient LCI+ #Patient LCI-



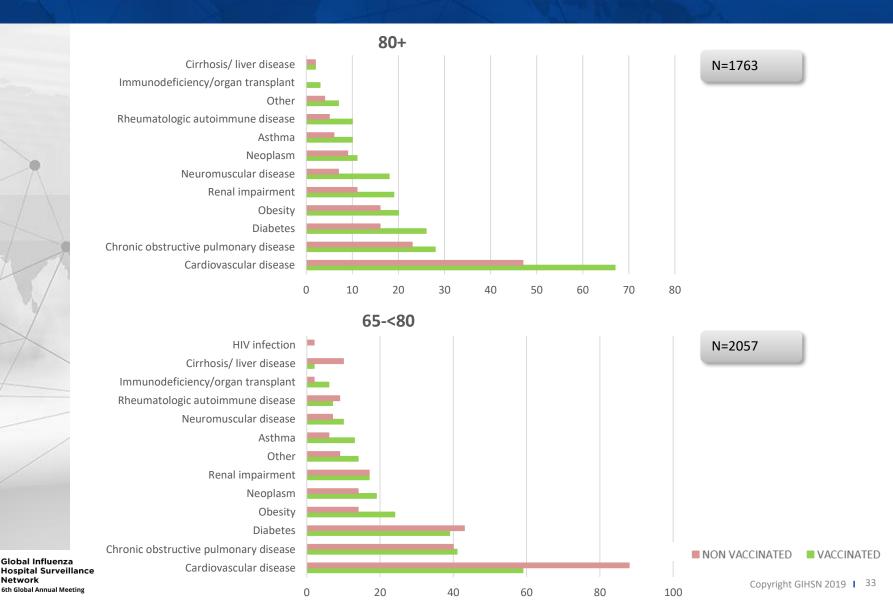
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#### INFLUENZA STATUS PER CHRONIC CONDITION PATIENTS >=5

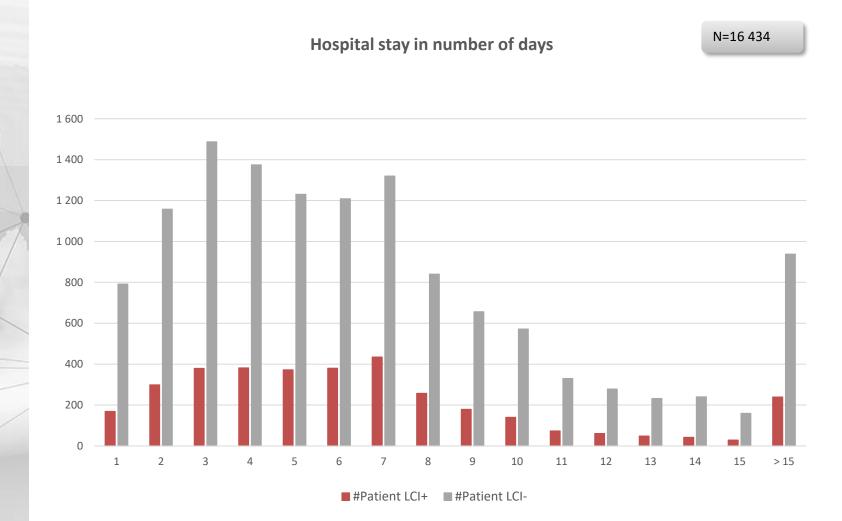




#### CHRONIC CONDITIONS IN OLDER AGE GROUPS LCI+ VACCINATED VS NON VACCINATED



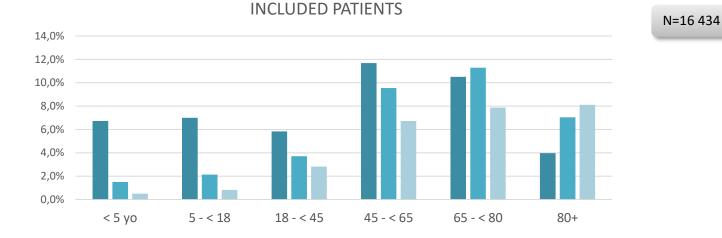
# LENGTH OF HOSPITAL STAY LCI+ VS LCI-





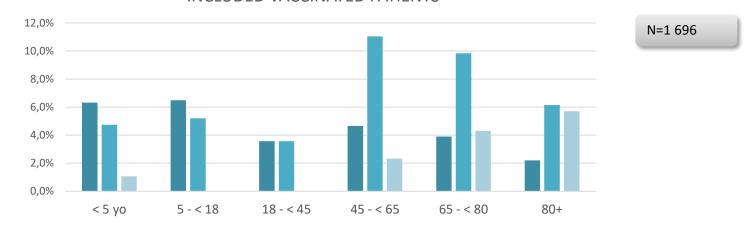
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# **OUTCOME SEVERITY BY AGE GROUP**



#### INCLUDED VACCINATED PATIENTS

■ %ICU admission ■ %Ventilation



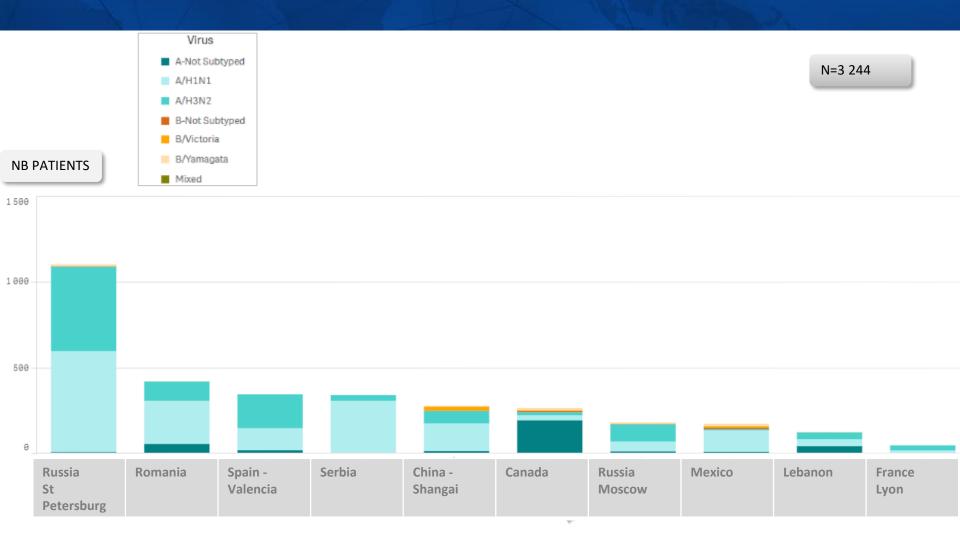
%Death



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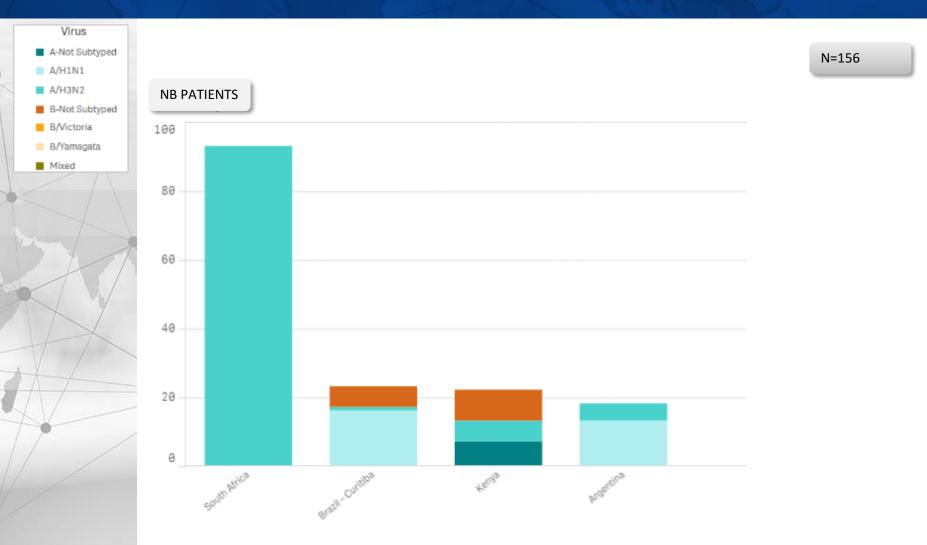
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# **VIRUS DISTRIBUTION NORTHERN HEMISPHERE**





## **VIRUS DISTRIBUTION SOUTHERN HEMISPHERE**





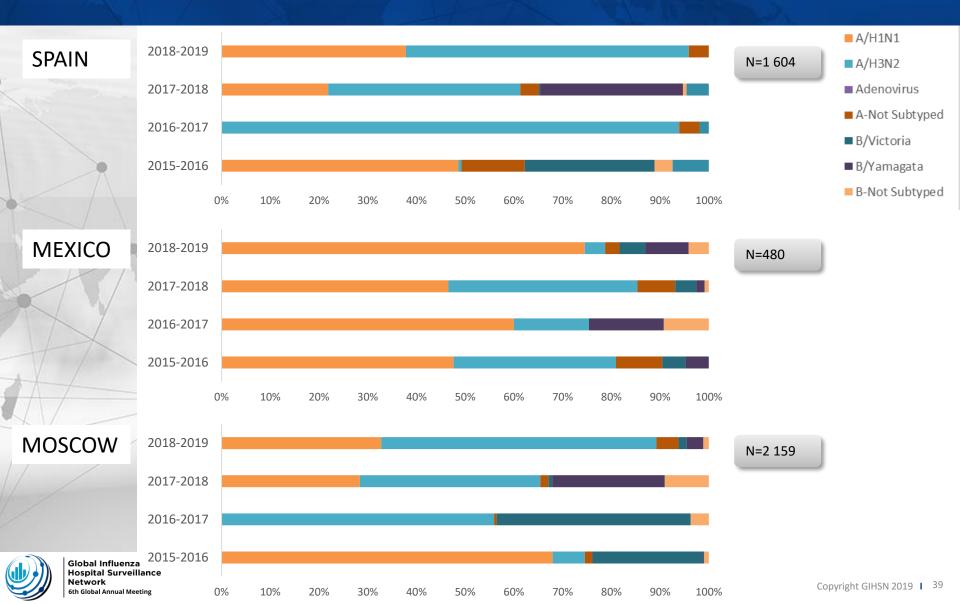
## VIRUS DISTRIBUTION INTERTROPICAL HEMISPHERE



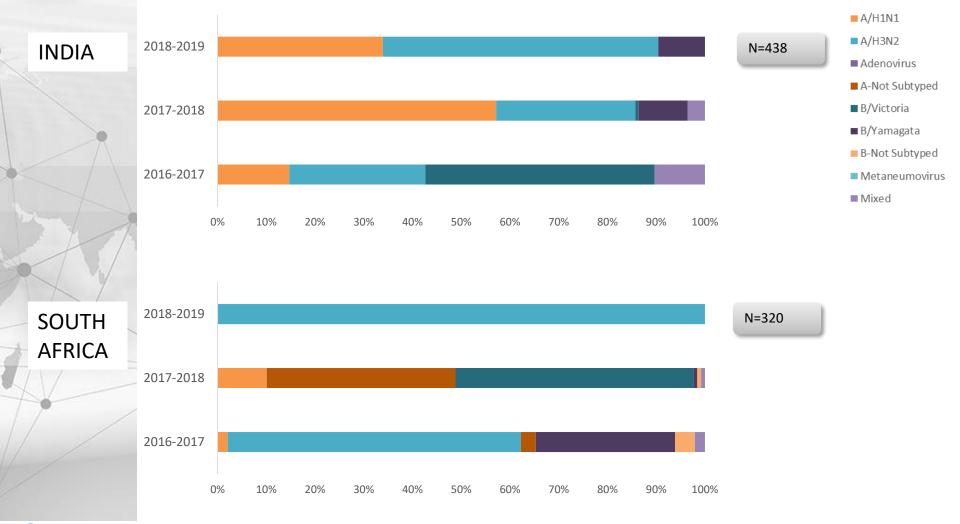


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#### VIRUS DISTRIBUTION OVER 4 SEASONS SITES IN NORTHERN HEMISPHERE



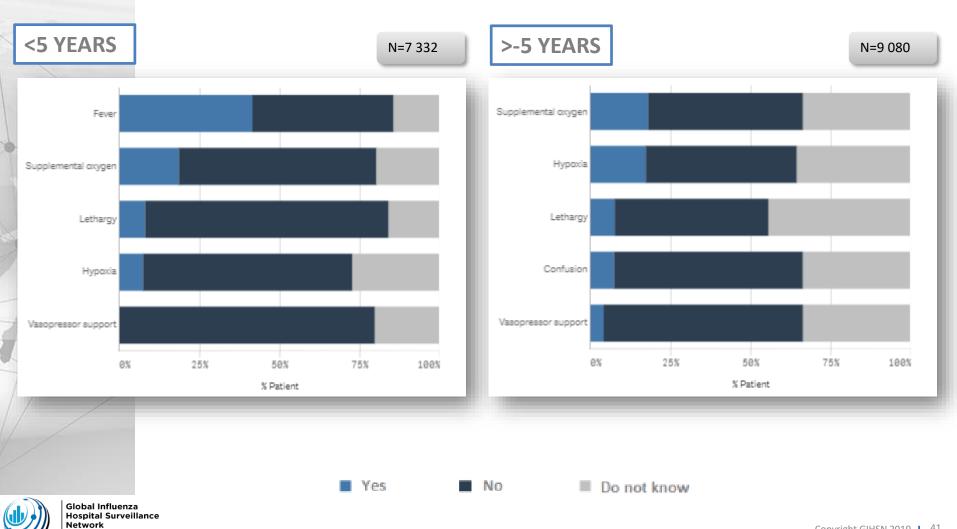
## VIRUS DISTRIBUTION OVER 3 SEASONS SITES IN SOUTHERN & INTERTROPICAL HEMISPHERES





#### **SEVERITY INDICATORS INCLUDED PATIENTS**

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## SEVERITY INDICATORS **PATIENTS <5 YEARS**



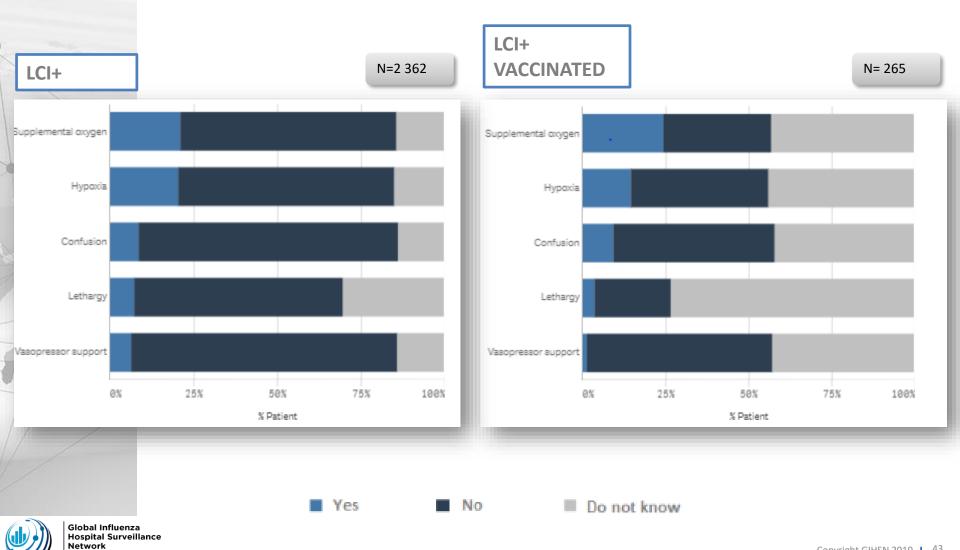
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#### **SEVERITY INDICATORS PATIENTS >-5 YEARS**

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#### **SEVERITY INDICATORS OLDER PATIENTS 65+**

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## GIHSN 7TH ANNUAL MEETING, PARIS, OCTOBER 13-15TH 2019 STRAIN SELECTION PROCESS: CURRENT & FUTURE CHALLENGES



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## **STRAIN SELECTION PROCESS: CURRENT & FUTURE CHALLENGES**

# **ROUND TABLE:**

- Dr. Wenqing ZHANG (WHO)
- Dr. Peter BOGNER (GISAID)
- Pr. John McCAULEY (WHO CC)
- Pr. Bruno LINA (Lyon University)
- Moderated by: Cédric MAHE (FIE)





#### CONTRIBUTION OF THE GIHSN TO THE STRAIN SELECTION MEETING – FEEDBACK ON THE 2018-2019 SEASON & PROSPECTS FOR NEXT SEASON

Pr. Bruno LINA

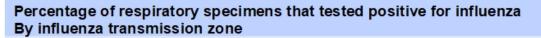


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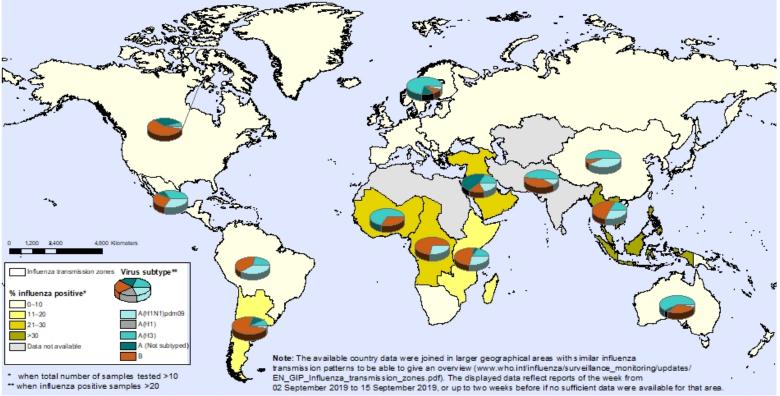


#### Influenza surveillance: diversity





Status as of 27 September 2019

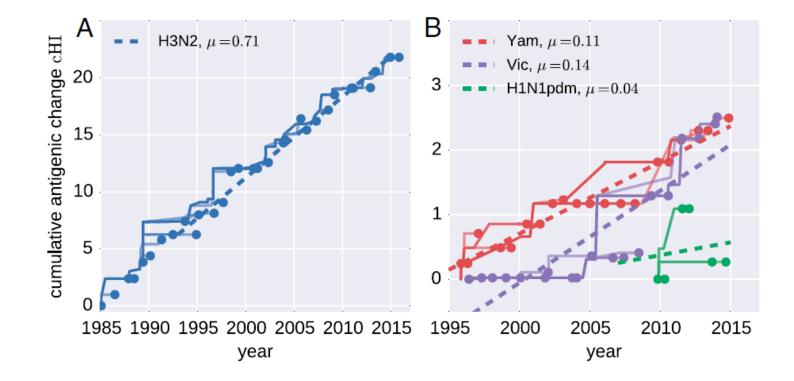


The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, tentory, oity or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: Global Influenza Surveillance and Response System (GISRS), FluNet (www.who.int/flunet)



# The evolutive trend of the Influenza viruses is type/sub-type/lineage dependant





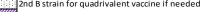
Global Influenza Hospital Surveillance Network 6th Global Annual Meeting Neher RA et al, PNAS 2016

#### As a consequence:

# Annual changes in the influenza vaccine composition

#### NH vaccine composition

	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	201
A(H3N2)																						
A/Sydney/5/97																						
A/Moscow/10/99																						
A/Fujian/411/2002																						
A/California/7/2004																						
A/Wisconsin/67/2005																						
A/Brisbane/10/2007																						
A/Perth/16/2009																						
A/Victoria/361/2011																						
A/Texas/50/2012																						
A/Switzerland/9715293/2013																						
A/Hong Kong/4801/2014																						
A/Singapore/INFIMH-16-0019/2016																						
A/Switzerland/8060/2017																						
A/Kansas/14/2017																						
A(H1N1)																						
A/Beijing/262/95																						
A/New Caledonia/20/99																						
A/Solomon Islands/3/2006																						
A/Brisbane/59/2007																						
A/California/7/2009																						
A/Michigan/45/2015																						
A/Brisbane/02/2018																						
В																						
B/Beijing/184/93 (Yam)																						
B/Sichuan/379/99 (Yam)																						
B/Hong Kong/330/2001 (Vic)																						
B/Shanghai/361/2002 (Yam)																						
B/Malaysia/2506/2004 (Vic)																						
B/Florida/4/2006 (Yam)																						
B/Brisbane/60/2008 (Vic)																						
B/Wisconsin/1/2010 (Yam)																						
B/Massachusetts/2/2012 (Yam)																						
B/Phuket/3073/2013 (Yam)																						
B/Colorado/06/2017 (Vic Δ-2)	İ				Ì		İ	ľ					1									



2nd B strain for quadrivalent vaccine OMS recommendation

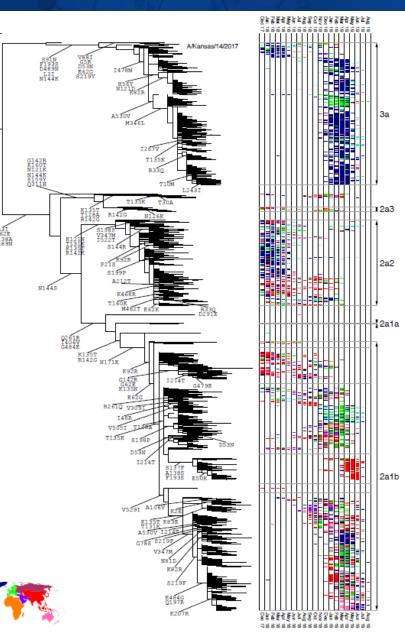


# H3N2 current evolution: multiple clades and sub-clades

H3

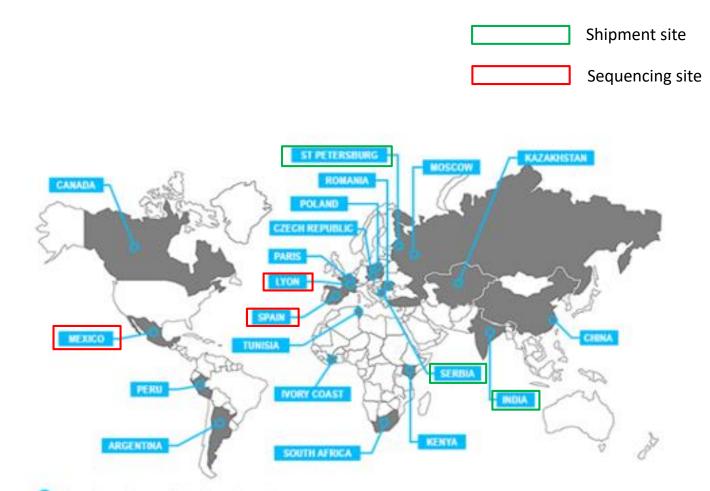
N1458 8157L





Global Influenza Hospital Surveillance Network 6th Global Annual Meeting Project:

Use GIHSN to provide WGS real-time data to analyse strain variation and evolution. 2018-19 phase 1 feasability study





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## Results for the 2018-2019 feasability study

#### Summary :

- 1 6 sites provided data
- 2 Overall, approx 200 whole genome sequences have been obtained
- 3 Shipments have been difficult to organize
- 4 Difficulty to provide real-time data by the GIHSN sequencing lab
  - For the sequence fasta files
  - For the GISAID upload
  - For the feedback to the originating labs

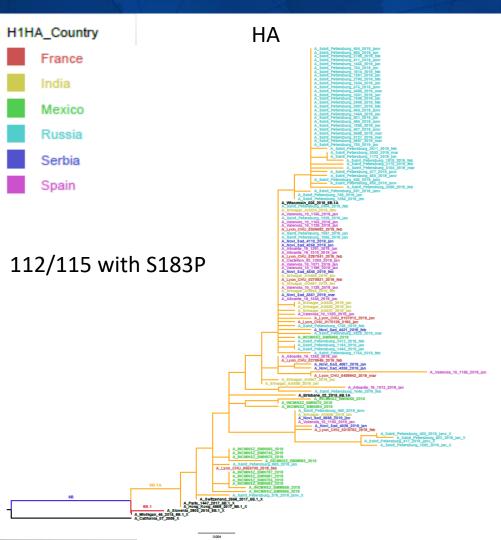


## Results for the 2018-2019 feasability study

Country	date	٢	Nb specimei			Nb sequ	ences		NI	b validated	sequences	5	Nb non tested specimens Ct>31	Nb non tested specimens / double shipment	Ongoing	seq failure	
		H3	H1	В	total	H3	H1	В	total	H3	H1	В	total				
Russia_jan	28/01/2019	8	15	0	23	0	0	0	0	8	15	0	23	0		0	0
Russia_apr	25/04/2019	39	56	0	95	0	0	0	0	30	43	0	73	8	4	1	9
Russia tot	1	47	71	0	118	0	0	0	0	38	58	0	96	8	4	1	9
France	03/2019	31	13	0		0	0	0	0	26	9	0	35	6		0	3
India	18/02/2019	15	10	5	30	0	0	0	0	15	10	4	29			0	1
Spain	02/2019	0	0	0	0	5	15	0	20	5	15	0	20			0	0
Serbie	09/04/2019	10	10		20	0	0	0	0	10	9	0	19			0	1
Mexico (pas de NA)	02/2019	0	0	0	0	0	14	0	14	0	14	0	14			0	0
N N /					0				0				0			0	0
					0				0				0			0	0
1-1-1-					0				0				0			0	0
					0				0				0			0	0
					0				0				0			0	0
					0				0				0			0	0
total specimens					212												
total sequences									34								
									246								
total sequences													213				
														14	4		
total seq failure																	14



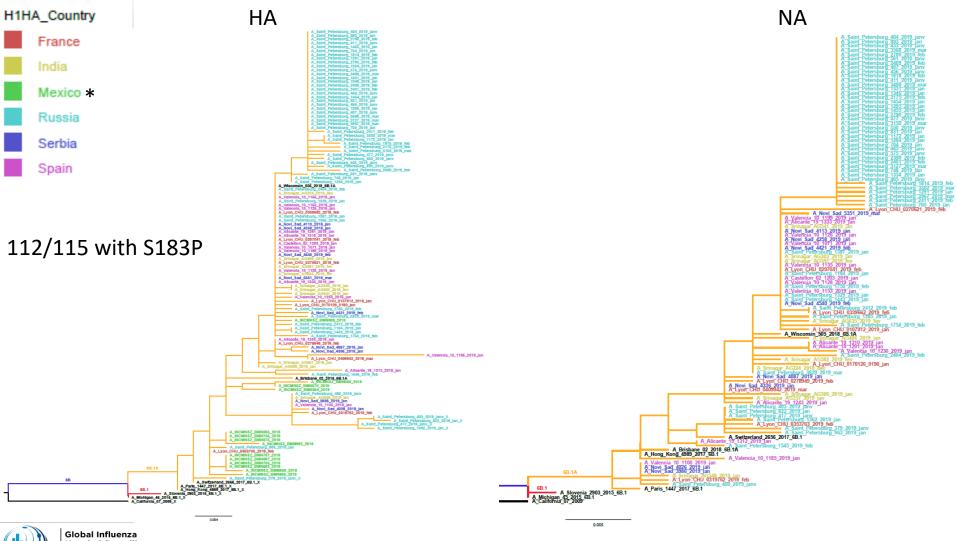
# H1N1pdm09





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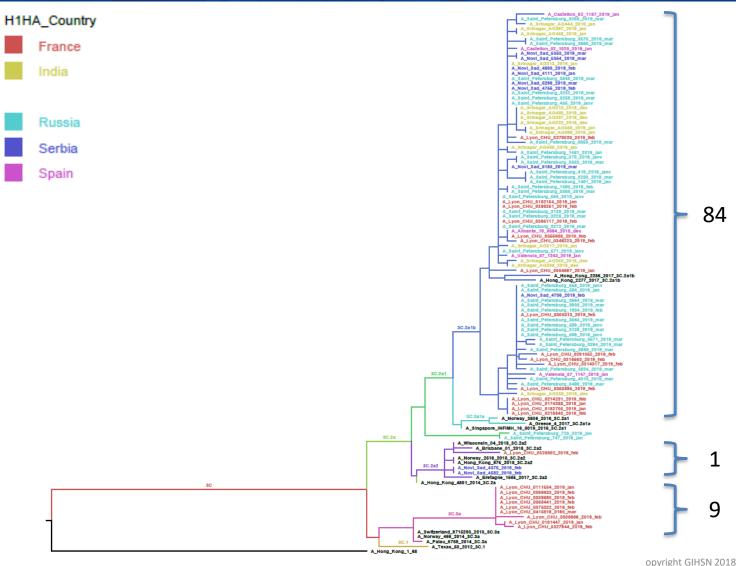
# H1N1pdm09



# H3N2 HA

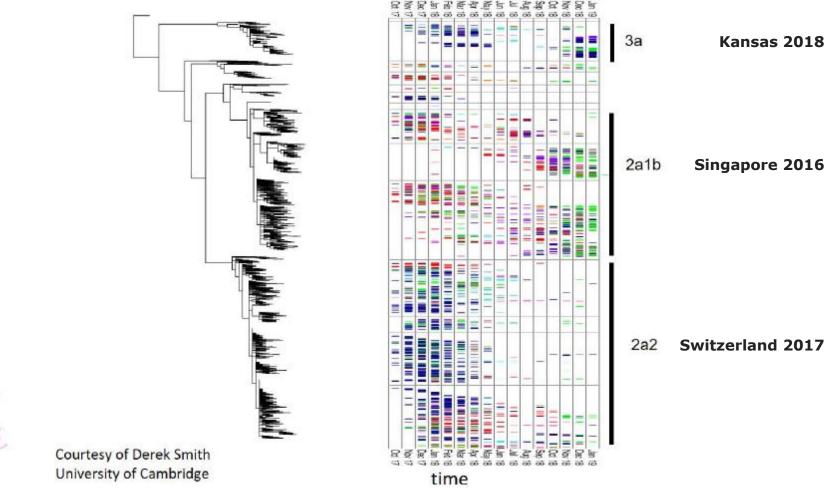


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0.02

#### H3N2 clade evolution 2017-2019



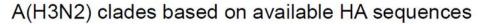
North America South America Europe Africa Middle East Russia E SE Asia Oceania

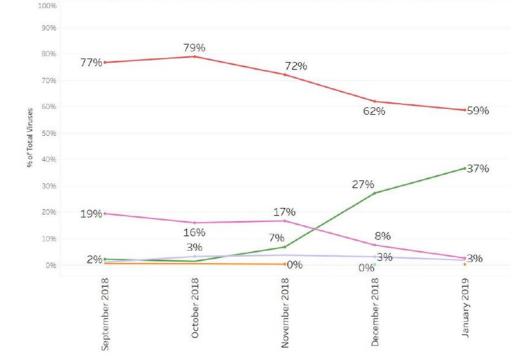




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# Discrepancies between GIHSN and WHO A(H3N2) clade evolution 2017-2019 (as of feb 2019)





But, the extent of the GIHSN data is limited...



Global Influenza Hospital Surveillance Network 6th Global Annual Meeting 3C Clades

2a1

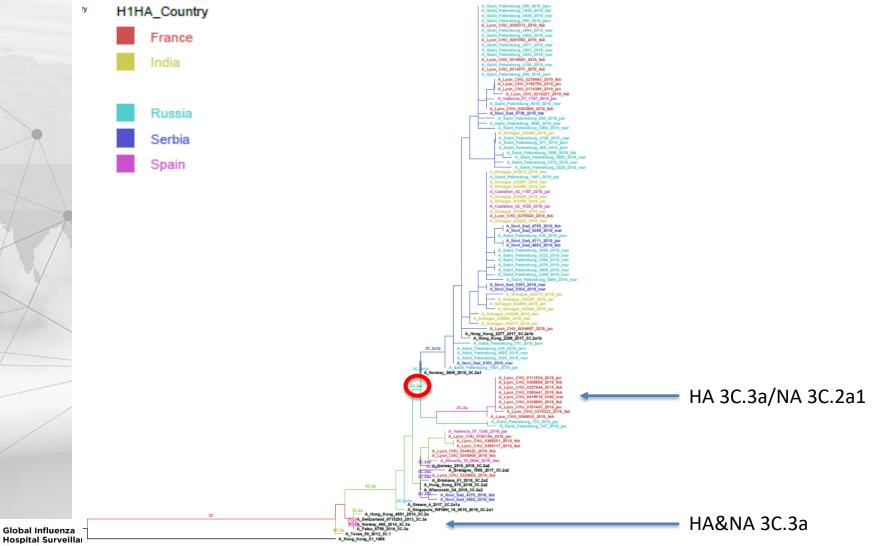
2a2

2a3

2a4

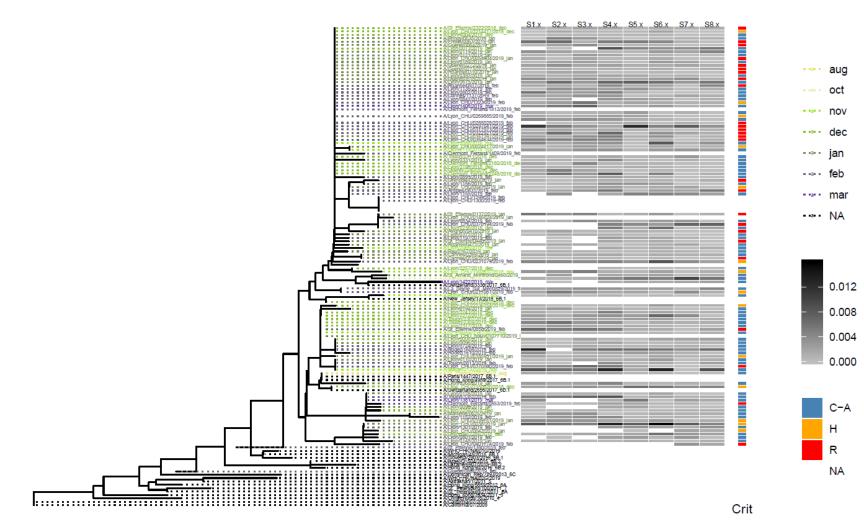
2a1b

# H3N2 NA



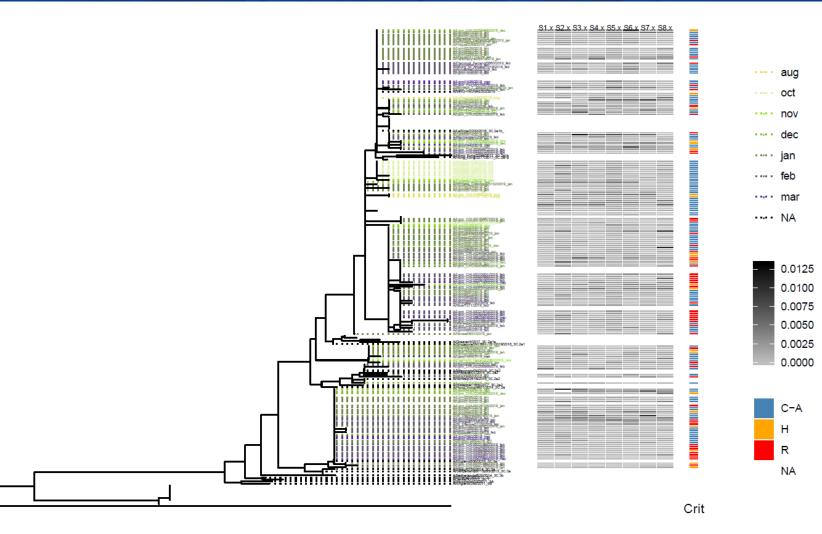
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## Sequence variability and severity: H1N1pdm09





## Sequence variability and severity: H3N2





## Conclusions

This first year confirmed the potential of GIHSN to provide a complementary set of data for WHO and other stakeholders

consensus sequence minority variants

Need for better organisation (see project)

better integration into GISRS define the reporting procedure (who does what)



#### Acknowledgements



#### NIC & Hospital Lyon:

- Bruno Simon
- Marine Jourdain
- Gwendolyne Burfin
- Estelle Gallice
- Rolf Kramer
- Alexandre Gaymard
- Gregory Destras
- Laurence Josset
- Florence Morfin
- Martine Valette

#### GIHSN sites and ISC:

- John Paget
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- Daria Danilenko
- Xavier Lopez-Labrador
- Robert Steiner
- Marta Numes
- Christine Commaille-Chapus
- Clothilde El Guerche-Seblain



#### WHOcc Crick Institute :

- John McCauley
- Rod Daniels



WHO cc in Cambridge (Institute of Zoology)

- Derek Smith
- Sarah James





## GIHSN 7TH ANNUAL MEETING, PARIS, OCTOBER 13-15TH 2019 GIHSN IMPLEMENTATION FOR THE NEXT SEASON

#### Cédric Mahé



Foundation for Influenza Epidemiology



# FOUNDATION FOR INFLUENZA EPIDEMIOLOGY: GOVERNANCE PRINCIPLES

**Dedicated fund** created in 2015 under the *Fondation de France* aegis: **Fondation for Influenza Epidemiology** 

**Mandate:** Support the epidemiological and virological research on influenza

#### Governance

- > Funding to the GIHSN is allocated through a yearly call for tender
- Selection is made by an Executive Committee

#### **Key principles**

- > Applicants must be non-for-profit institutions
- Data generated through the projects is owned by sites but contributes to Foundation related projects (yearly pooled analysis)
- Coordination and technical support is provided Open Health Company



# THE INDEPENDENT SCIENTIFIC COMMITTEE

#### 9 experts with an increased decision-making ability since last season

- 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 NEW
- > 3 designated representatives at the Executive Committee NEW

#### Independent experts

- Jill Ferdinand (CDC, USA)
- Feng Luzhao (CDC, China)
- Bobby Reiner (IHME, USA)
- Bruno Lina (Univ of Lyon, France)
- Justin Ortiz (Univ of Maryland, USA)
- John Paget (NIVEL, Nederland)

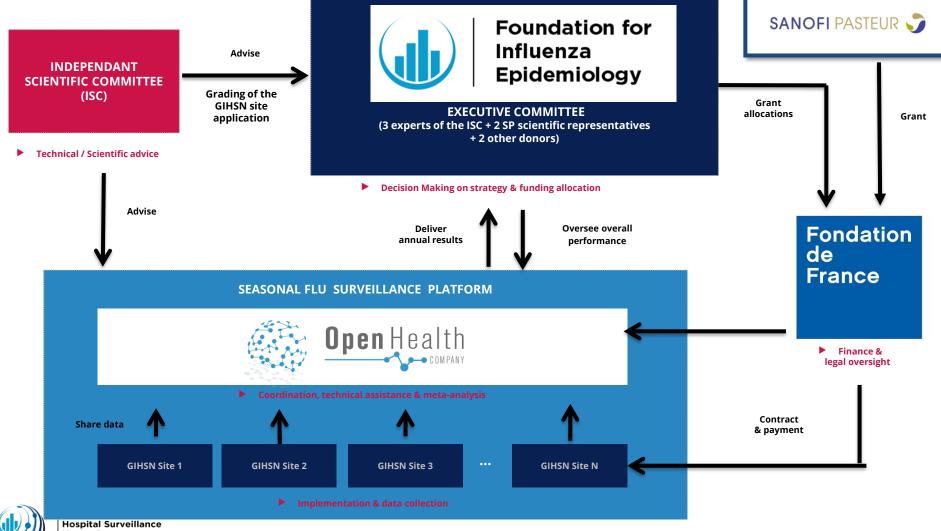
#### Investigators

- Elena Burtseva (Moscow)
- Marta Nunes (South Africa)
- Melissa Andrew (Canada)

Secretariat is managed by OpenHealth Company



## **FOUNDATION GOVERNANCE**



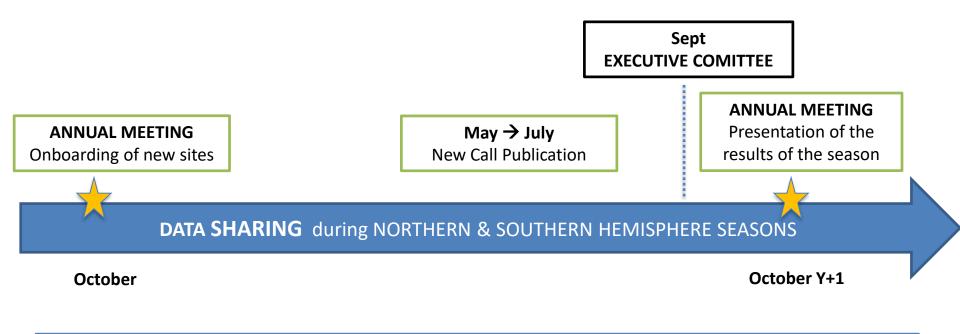
Network 6th Global Annual Meeting

## FOUNDATION FOR INFLUENZA EPIDEMIOLOGY UPDATE

- GIHSN network: 60 hospitals in 18 countries in 2018-2019
  - More than 3,500 documented cases of hospitalizations from influenza per season
  - Already up to 7 seasons of data generated including NH and SH data (>74,000 patients records available)
- **Diversification of funding**: small funding from IFPMA/IVS. Discussion ongoing with Seqirus
- **Expansion of the sequencing activities:** strain sequencing platform, GISAID partnership
- Formal dialog with WHO GIP and provision of data for the annual vaccine strain selection (NGS + clinical data)



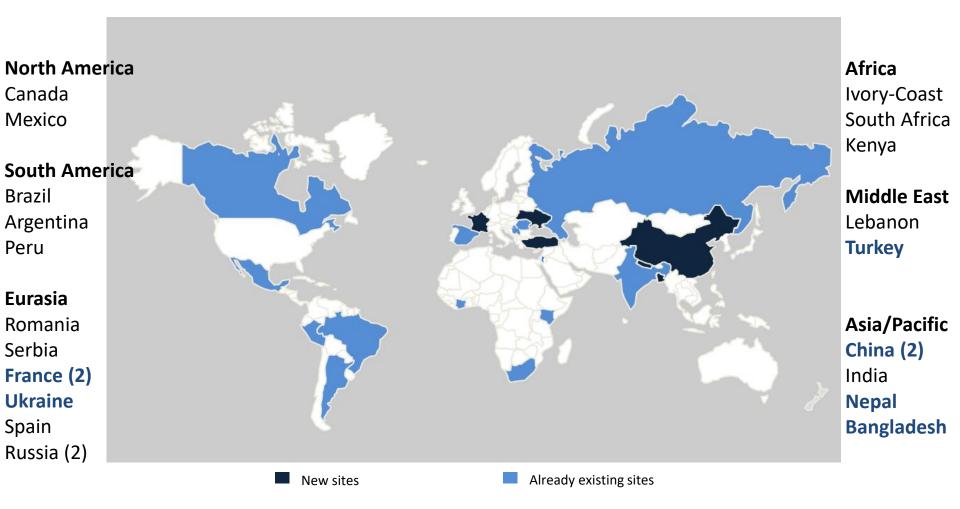
## **GIHSN TIMELINES**



ISC meeting (2 per year) : Protocol review, Publication plan validation, ...



## MAP OF GIHSN SITES FOR THE SEASON 2019-2020 (21 SITES - 6 NEW)





## **NEXT STEPS**

#### Administrative aspects & funding allocations

**Contacts**: Foundation for Influenza Epidemiology (Sandra Chaves)

Fondation de France (Charlotte Von Thienen Bardinet)

- After acceptation of the grant, a letter of engagement including a description of milestones and payment terms is prepared for the site.
- When needed, a contract can be prepared by the institution to be signed by the Foundation

#### Study implementation & Kick-off TC

**Contacts:** Open Health Company (Catherine Commaille-Chapus, Maria Morizet)

- Sites are invited to start the seasonal <u>active</u> surveillance in accordance with national surveillance
- Open Health is planning to set individual Kick-off TC to review the study implementation, data collection
- Sites are encouraged to share data on the data web tool, once a week.



# EVOLUTION OF THE STRATEGY AND RELATED DATA COLLECTION

- Stronger focus on strain circulation and their clinical significance (disease severity, vaccine failure) – burden and vaccine effectiveness not always feasible in most countries
- Stronger focus on timeliness, geographical representativeness
- Need to reduce cost per sites (for sustainability)
- Engagement of NICs and WHO CCs

#### **Operational considerations**

- Data collection for LCI only (with a lower number of variables)
- Linkage between clinical data and virus sequencing
- Timely availability of data (e-crf + GISAID)
- Offer of support for sequencing





# GIHSN 7TH ANNUAL MEETING, PARIS, OCTOBER 13-15TH 2019 DISCUSSION & CLOSING DAY 1



Foundation for Influenza Epidemiology



# **DISCUSSION & CLOSING OF DAY 1**

- Feedback from sites on the discussed results
- "First reactions" on the new protocol
- Important points to take "home"





# GIHSN 7TH ANNUAL MEETING, PARIS, OCTOBER 13-15TH 2019 OPENING DAY 2

#### Catherine Commaille-Chapus



Foundation for Influenza Epidemiology



# **OBJECTIVES DAY 2**

- Discussion on the implementation of the new protocole – exchange on the site organization and individual challenges
- Practical discussion on the strain sequencing process : sites doing their own sequencing vs sites needing to coordinate with Lyon for sequencing
- Present local and global publications and start discussing the publication plan relating to the 2019-2020 season data





# **AGENDA: TUESDAY 15TH OCT**

8:30 - 8:45	First day wrap-up & objectives of Day 2	C Commaille (OpenHealth)					
8:45 - 10:15	Workshop Session 1: New Protocol Implementation -Implementation of the new questionnaire -Data Entry -Need for support	All sites					
	Moderated by: Sandra Chaves (FIE)						
10:15 - 10:45	Coffee break						
10:45 - 12:00	Workshop Session 2: Strain Sequencing Process	All sites					
10:45 - 12:00	Workshop Session 2: Strain Sequencing Process -Timing of sequencing -Strain selection - Strain logistics between sites & Lyon Moderated by: Bruno Lina (ISC)	All sites					
12:00 - 12:45	Dissemination & Publications (Globally and Locally) - Update on current manuscript development - Posters presented at Options X - Publication plan & International conferences 2019- 2020 - Manuscript writing process 2018-2019 season & rules of authorship	Pr B Lina (ISC)					
12:45 - 13:00	Closing	C Mahé (FIE)					
13:00 - 14:00	Buffet lunch						





# WORKSHOP SESSION 1: NEW PROTOCOL IMPLEMENTATION

Dr. Sandra CHAVES



Foundation for Influenza Epidemiology



## **RESEARCH OBJECTIVE 2019-2020**

- I. Support international capacities developed through the Global Influenza Surveillance and Response System (GISRS) of laboratories to increase the availability of <u>clinical information linked with genetic sequencing</u> of influenza virus strains
- II. <u>Support</u> the biannual <u>vaccine strain selection process</u> of the WHO's formal recommendation for the composition of human influenza vaccines



### SIMPLIFIED DATA COLLECTION

- ✓ Data collection for laboratory-confirmed influenza (LCI) cases only
  - ✓ 50 to 100 cases/site
- ✓ **Timely upload of data** (e-crf + GISAID)
  - ✓ Weekly uploads of clinical and lab data
  - ✓ Linkage between clinical data and virus sequencing
- ✓ Support for sequencing capacities GIHSN center in Lyon, coordination by Open Health company (OHC)



#### **CLINICAL DATA**

#### EPI and CLINICAL VARIABLES TO BE COLLECTED

#### **Smoking habits**

**Pregnancy status** 

**Chronic medical conditions** 

Prescriptions of antiviral for the current episode

Influenza vaccination for the current and previous season (self-reported y/n)

Supplemental oxygen without mechanical ventilation

**Vasopressor support** 

**ICU** admission

**Mechanical ventilation** 

Death while hospitalized

Discharge/death date (yyyy-mm-dd)

**GISAID Accession Number (EPI\_ISL)** 



### Workshop :

- Group discussion (6 groups) ~20 min followed by presentations: Only « key » challenges and opportunities
- Plenary discussion on identified key issues ~30 min
- Live demo of on-line questionnaire ~5 min





# **ISSUES TO DISCUSS**

- 1. How these changes would affect your site (pros and cons)?
  - Reduce workload? No change in case finding strategy? Easy to manage?
  - Can leverage on other sites in the country?
- 2. TIMELY is key!
  - How feasible is to commit to weekly reporting?
- 3. Capacity for FGS
  - Available in site? Interested in sequencing inhouse? Batches \_ weekly ?
- 4. Questionnaire any thoughts?



Global Influenza Hospital Surveillance Network 6th Global Annual Meeting



# WORKSHOP SESSION 2: STRAIN SEQUENCING PROCESS

Pr. Bruno LINA



Foundation for Influenza Epidemiology



# STRAIN SEQUENCING CRITERIA – FOR DISCUSSION

Sample target : 50 – 100 per site

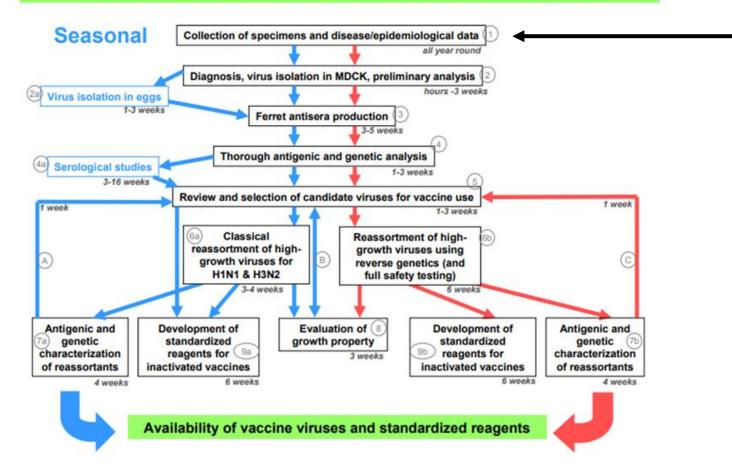
Sample selection criteria for sequencing :

- 1. All early season samples (before Jan 15), vaccine failure or severe case (ICU admission/ventilation/death)
- A subset of the other samples collected across the season : 15-25 per months depending on the total number expected (50-100)





#### Process of influenza vaccine virus selection and development





## **GIHSN** strain sequencing perspectives for 2019-2020

# SITES WITH ONSITE SEQUENCING

- □ Mexico\*
- Brazil
- **Canada**
- □ Spain\*
- **Lebanon**
- Ivory Coast
- **Gouth Africa**
- **U** Turkey
- □ Argentina
- China X 2
- Russia-St Petersburg\*
- Romania

#### SITES USING VIRPATH LAB FOR SEQUENCING

- India
- Bangladesh
- □ Nepal
- □ France Lyon
- **Given Service Paris**
- Russia Moscow
- **Gamma** Serbia
- **Ukraine**
- □ Argentina
- D Peru
- □ Kenya



Global Influenza Hospital Surveillance Network 6th Global Annual Meeting

### **GIHSN strain sequening perspectives for 2019-2020**

Better link between the sites and the sequencing platform

Clarification on the circulation of the Data and the specimens from the sites (WHO/GISRS requirements)

Predefine for each site the dates of shipment of material to the GIHSN platform

Use a standardised data set for the shipment





# GISAID batch upload facility

#### GISAID epiflu Uploader: the communication tool

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## **GIHSN** strain sequencing perspectives for 2019-2020

Better link between the sites and the sequencing platform

Clarification on the circulation of the Data and the specimens from the sites (WHO/GISRS requirements)

Predefine for each site the dates of shipment of material to the GIHSN platform

Use a standardised data set for the shipment

Predefine who is responsible for the upload of sequences (fasta files) in the GISAID database



#### Prepare 2019-2020 calendar for shipments/data sharing

# 2019

# 2020

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The GIHSN sequencing plaform will provide sequence data for 11 sites

This needs to be organized

number of specimens per site date of shipments reporting procedure sharing with members (GIHSN/NIC /WHO)

Integration of the data obtained from the other sequencing sites

Work with different stakeholders to address unmet needs



#### Acknowledgements



#### NIC & Hospital Lyon:

- Bruno Simon
- Marine Jourdain
- Gwendolyne Burfin
- Estelle Gallice
- Rolf Kramer
- Alexandre Gaymard
- Gregory Destras
- Laurence Josset
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- Clothilde El Guerche-Seblain



#### WHOcc Crick Institute :

- John McCauley
- Rod Daniels



WHO cc in Cambridge (Institute of Zoology)

- Derek Smith
- Sarah James





# GIHSN 7TH ANNUAL MEETING, PARIS, OCTOBER 13-15TH 2019 DISSEMINATION & PUBLICATIONS

Pr. Bruno LINA



Foundation for Influenza Epidemiology



# DATA OWNERSHIP & ACCESS TO THE DATA

- Data collected at site level remains the proprietary of the site.
- Each contributing site has full access to the data through a secured platform managed by Open Health Company.
- Open Health Company has access to the raw data for epidemiological research fulfilling the following conditions:
  - Analyses are performed for research purposes in line with the mandate of the Foundation (i.e. surveillance and monitoring of influenza and other respiratory viruses)
  - Analyses are exclusively performed with strictly anonymous and aggregated data
  - Any analyses plan need to be approved beforehand by the Independent Scientific Committee (ISC) of the Foundation



# **GIHSN PUBLICATION RULES**

- All analyzed results need to be submitted to ISC before publication.
- Scientific publications and conference communications mention GIHSN contributing sites with main investigators names in the authorship in line with the ICJME rules.
- Sites will be informed upfront for any additional planned data analysis beyond the annual pooled analysis.
- Sites have the possibility to opt-out.



### **ORGANIZATION OF WORK PROPOSALS**

#### Seasonal pooled analysis

- 1 manuscript in peer reviewed journal, and conferences, research question to be proposed/defined by the ISC
- Authors: ISC & GIHSN group of authors (volunteering GIHSN principal site investigators can be included in the list of authors provided they commit to the ICJME rules and the manuscript development timeframe)

#### **Specific topics publications**

- 1 manuscript per year
- Topics proposed by GIHSN members and validated by the ISC
- i.e severity analyses, Burden of disease in specific populations
- Authors: Group of authors including volunteers GIHSN investigators and led by one member of the ISC
- Analyses : OpenHealth

Analyses : OpenHealth



#### Medical Writing supported by the Foundation

#### SPECIFIC TOPICS ANALYSES RESEARCH PROPOSALS AND ABBREVIATED REPORTS



Global Influenza Hospital Surveillance Network

#### **Research Project Proposal**

This research proposal should include a detailed description of a proposed study designed to investigate a given problem. It must answer the questions: What you plan to accomplish, why do you want to do it and how are you going to do it?

This proposal will be presented to the Scientific Committee for approval and must be led by a member of this Committee.

The proposal should provide details for the following sections:

- 1. Project Title
- 2. Investigator(s)
- 3. Introduction
  - a. Background
  - b. Statement of the research problem
  - c. Rationale of the proposed study

#### 4. Objectives

This section should contain a general objective of the research and specific objectives presented as primary and secondary objectives.

#### 5. Data variables

Identify the key variables (Independent variables, dependent variables, cofounding variables and background variables).



- a detailed description of a proposed study designed to investigate a specific question
- Should explain: rationale to develop the analyses, research questions, identification of variables, data period extraction
- Organisation of work: who will be part of the authors group, roles and responsibilities

The proposal is presented to the ISC for approval and must be led by a member of this Committee.



### MANUSCRIPT SEASON 2017-2018 : COMPLICATED HOSPITALIZATION DUE TO INFLUENZA FOR PUBLICATION IN BMC PUBLIC HEALTH

#### Complicated hospitalization due to influenza: Results from the Global Hospital

#### Influenza Network for the 2017-2018 season

Bruno Lina<sup>1-3,\*</sup>, Alexandre Georges<sup>4</sup>, Elena Burtseva<sup>5</sup>, Marta C. Nunes<sup>6,7</sup>, Melissa K. Andrew<sup>8</sup>, Guillermo M. Ruiz-Palacios<sup>9</sup>, Luzhao Feng<sup>10</sup>, Jan Kyncl<sup>11</sup>, Philippe Vanhems<sup>12-14</sup>, Justin R. Ortiz<sup>15</sup>, John Paget<sup>16</sup>, and Robert C. Reiner<sup>17</sup> on behalf of the GIHSN 2017–2018 study group<sup>†</sup>

- ✓ 1st outline June 14th
- ✓ Draft 1 July 16th
- ✓ Draft 2 September 13thFinal version expected forend of November

#### Authorship :

- The main manuscript is developed by the Scientific Committee with Chairman Bruno Lina and sites who have volunteered to write (Czech Republic, Lyon and Mexico)
- In the group authorship are mentioned : main investigators of all sites
- Other investigators or research staff can be mentioned in the acknowledgements



# **INTERNATIONAL CONFERENCES IN 2020**

- IDWeek, 02-06 Oct 20 (abstract deadline 01 May 20; LB abstract deadline 08-Aug-20)
- ECCMID Paris, France 18-21 Apr 20 (abstract deadline 27 Nov 19; LB abstract deadline 20 Feb 20)
- ESPID 06-11 May 20 (abstract deadline 15 Jan 20) ۲
- ISPOR, Orlando, FL, USA 16-20 May 20 •
- American Diabetes Association 12-16 Jun 20 (abstract deadline 12 Jan 20; LB abstract deadline 16 Mar 20)
- 7<sup>th</sup> ESWI Valencia, Spain 13-16 September 2020 (abstract deadline 15-May-2020; LB • abstract deadline 15-Aug-20)
- International Society for Pharmacoepidemiology (36 ICPE) Berlin, Germany 26-30 • Aug 20 (abstract deadline 13 Feb 20)
- AAFP Family Medicine Experience (FMX 2020) Chicago, IL, USA 13-17 Oct 20 (abstract deadline 03 Apr 20)
- ISPOR-AP, Seoul, S. Korea 12-15 Nov 20 (abstract deadline 18 Mar 20) ٠
  - ISPOR-EU, Milan, IT 14-18 Nov 20 (abstract deadline 24 Jun 20)



Global Influenza

Network

### **GIHSN POSTERS PRESENTED AT OPTIONS X**

During the **OPTIONS X** (Singapore, August 2019) a poster

(Scientific Committee represented by Pr Bruno Lina)

of the GIHSN network was presented

Local posters was also presented.





Global Influenza Hospital Surveillance Network 6th Global Annual Meeting

# Developments of the global influenza hospital surveillance network to support better monitoring of influenza virus genetic evolution: The GIHSN-SevVIR network

#### Bruno LINA<sup>1</sup>, John Pagel<sup>2</sup>, Melissa K Andrew<sup>3</sup>, Luzhao Feng<sup>4</sup>, Justin R Ortla<sup>6</sup>, Daria Danilenko<sup>4</sup>, Xavier Lopez-Labrador<sup>7</sup>, Robert C Reiner Jr<sup>4</sup>, Marta C Nunes<sup>9</sup>, Catherine Commaille-Chapus<sup>10</sup>, Clotilde El Guerche-Seblain<sup>11</sup>

rate Centre, HCL & CRI team Vipoth, Insem UTITI, CNIS 5308, INS, UCBL, Fonces, Topyl Spid Decase Control and Prevention, Branch of Seguritory Infectious Database Deviate of Infectious and National Infeature Centre, Branch Prevention, Topyland Public Head ccs: "Dept Spidemiology, NVEL Netherlands: "Dathcase University / Canadian Center or of Intections Disease. China: "University of Maryland / School of Medicine. United by Laboratory. Genomics and Health Asea. Spin: "University of Washington, Institute citz <sup>4</sup>Chinese Center for Di search institute of influence th Metrics Sciences, United States: "Medical i rs, South Africa, Department of Science and I

#### INTRODUCTION

 After seven seasons of active influenza surveillance, the Global Influenza Hospital. Surveiliance Network (CHSN) is leveraging capacities to link clinical and virological data.

The main objective is to analyze and monitor influenze viruses' characteristics from hospitalized cases, and to provide this information to WHO for vaccine strain composition

#### METHODS

Rgure 1. Map of GIHSN laboratory capacities

 During the 2018-2019 season, a coordinated approach was developed by the French National Reference Laboratory for respiratory viruses (ind Influenza) in Lyon.

 GHSN surveillance sites and associated laboratories were mapped for their sequencing capa chies.

Astandardized method was proposed using Whole Genome Sequencing and the sites were invited either to share information from sequenced strains or send material for sequencing in Lyon.

This sequencing data was linked to detailed epidemiological and clinical information on hospitalized patients collected by GHSN.

#### decisions. RESULTS

OBJECTIVE

#### Countries mapping

All eighteen countries participating in GHSN have laboratory capacity for Influenze typing and subtyping (Figure 1).

Sixteen laboratories participated in the sequencing data survey, eleven (including nine national reference laboratories) perform strain sequencing and share their sequence data with WHO's GISRS network via the GISAID platform.

Three laboratories (Melencia, St. Petersburg, Lyon) shared reports with the WHO ahead of the February Vaccine composition meeting.

Strain sequencing results

6 GIHSN sites provided viruses for sequencing.

#73 A(H3N2),105 A(H1N1)pdm09 and 4 B Yam were sequenced by these laboratoria s.

• 70 A(H3N2) belonged to clade 3C.2a1b while only 2 viruses were from clade. 3C.2a, and 1 from clade 3C.2a fa (Figure 2)

All 105 A(H1N1)pdm09 belonged to the 68.1A clade, and 100/105 had the S183P substitution as described in the A.Brisbane 2/2018 reference strain. (Figure 3)

 Only B Yamagata viruses have been sequenced by the GHSN lab, close to the B/Phuket/3073/2013 virus



samples of nce and strain set

#### FUNDING STATEMENT

The Sequencing study platform is supported by the Foundation of Influenza Epidemiology (RE), which is partly funded by Sanof Pasteur.

#### CONTACT AUTHOR

brung.line@univ-lyon1.fr





Global Influenza **Hospital Surveillance** Network **6th Global Annual Meeting** 





Figure 3. Phylogenetic tree of the GIHSN A (H1 N1)pdm09 strains detected during the 2018-2019 season. Strains with a X are \$183

# **REMINDER OF ICJME RULES**

"Recommendations intended to ensure that contributors who have made substantive intellectual contributions to a paper are given credit as authors, but also that contributors credited as authors understand their role in taking responsibility and being accountable for what is published "

# The ICMJE recommends that authorship be based on the following 4 criteria:

- Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
- Drafting the work or revising it critically for important intellectual content; AND
- Final approval of the version to be published; AND
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.





# GIHSN 7TH ANNUAL MEETING, PARIS, OCTOBER 13-15TH 2019 CLOSING OF THE MEETING

#### Thank You All !



Foundation for Influenza Epidemiology

