



GLOBAL INFLUENZA HOSPITAL SURVEILLANCE NETWORK (GIHSN)

Standard Operating Procedures (SOP) for fieldwork and data collecting activities

Version 6.0

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Updated version by OpenHealth Company based on the recommendations of the Independent Scientific Committee of the GIHSN

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History of modifications

All modifications from previous version will not be listed here.

This version 6 includes major changes in both questionnaires:

- Inclusion criteria for patients 5 years of age or more modified to: *“all eligible patients hospitalized in the previous **72** hours and who have stayed in the hospital for at least 1 night, who are able to communicate (alt. through a proxy), who have given consent to participate in the study **and** who are experiencing symptoms in the last 7 days prior to admission”*. Nasal congestion was added in the ILI respiratory symptoms.
- Inclusion criteria for patients less than 5 years of age modified to: *“all eligible patients hospitalized in the previous **72** hours and who have stayed in the hospital for at least 1 night, who are able to communicate (alt. through parent or tutor), who have given consent to participate in the study **and** who are experiencing symptoms of the actual acute episode in the last 7 days prior to admission.”*
- A few chronic diseases were added on both questionnaires
- Questions were added on the use of antibiotics and vaccination in the previous season.
- Several questions on severity were added for both patient groups and a frailty score for patients 5 years of age and more
- And importantly, to meet the study objectives, a chapter on Data Linking was added to be able to link sequencing data submitted on the **GISAID EpiFlu™ database** platform with the clinical data submitted on the GIHSN platform (via the on-line questionnaires).
- All data sharing will be done on-line through the on-line questionnaires on the GIHSN platform.



The GIHSN

The Global Influenza Hospital Surveillance Network (GIHSN) is a platform able to generate strong epidemiological and medical evidence on **influenza severity** and to support vaccine strain selection through **timely sharing of clinical and laboratory data**. The GIHSN is a network of not-for profit institutions coordinating local hospitals in several countries following the same core protocol.

The GIHSN is a unique hospital active surveillance network using a standard protocol complementary to WHO GISRS, offering:

- The largest yearly case series of patients hospitalized with influenza worldwide from all age groups for both NH and SH allowing to better understand flu severity and related risk factors;
- A strong opportunity to inform WHO vaccine strains selection by linking clinical data with viral genome sequencing information;
- An alert system in case of pandemic/strain mutation, contributing to improve countries response and international collaboration.

GIHSN SOP's aims

This SOP is a tool to support the homogeneity and the consistency of fieldwork procedures for all sites included in the GIHSN study.

Our goal is that the studies in each site are performed in a uniform standardized manner.

- Notation: Text in 'red' refers to the questionnaire questions; the questionnaires are attached as Annex 3 and 4.

General Information

An active surveillance system will be established at each study site for the screening of patients (prospective ascertainment of all consecutive admissions that qualify them for eligibility as they enter the hospital with an acute condition possibly related with a recent influenza virus infection).

The screening of patients will take place during the influenza season. The criteria to define the influenza season should be decided before hand in each site's local protocol.

Study questionnaires will be filled in with the information obtained from admission enrolment lists and hospital registries and, after informed consent,



through face to face interviews with the patients, through the review of clinical records and through consultations with the patients' physicians and nurses.

Data Collection

Data is collected via the **on-line GIHSN study Core Questionnaires** on the GIHSN web-based platform which can be accessed by all GIHSN members through the GIHSN website (www.gihsn.org). IDs and password are personal and communicated by OpenHealth Coordination Team. Further explanation on how to access the platform in Annex 6.

Minimum dataset collected is based on the aforementioned GIHSN study Core Questionnaires (*Annex 3 and Annex 4*). Each site/country can decide to collect additional data for own local study purposes.

Site communication

A telephone kick-off meeting will be performed between the Site and the OpenHealth coordination team, together with follow-up calls during the season to assure a complete understanding of methods and procedures.

The Coordination Team members will assist the sites continuously, by telephone and/or by e-mail.

The questionnaire in detail

Please note that all questions should be answered. Sites will have the opportunity for non-mandatory questions to use a "do not know"- choice if the information is not available.

Questionnaires can be filled in and **saved** progressively and **submitted** only once all questions have been properly answered. Once they have been submitted, questionnaires cannot be modified any longer.

Please note that concerning questionnaires with pending sequencing data, the questionnaires need to be **saved** as and when clinical data are been collected but **submitted** only once the sequencing data has been shared on the GISAID database and a GISAID Accession Number has been obtained and entered as a last step into the questionnaire.



Eligibility

The patient is considered eligible if:

1. Admitted through emergency doors or study participating wards for an acute condition.
2. Admitted in the previous 72 hours and has stayed in hospital for at least 1 night (therefore a patient admitted before midnight of the previous day).
3. Admitted due to any acute condition possibly associated with an influenza infection (*admission diagnosis listed in Annex1*).
4. He/she is experiencing symptoms in the last 7 days prior to admission

The first 3 points should be confirmed by looking at admission logs or clinical records. If the patient does not comply with these eligibility criteria, then there is no need to open a questionnaire for the patient. Please continue screening for other eligible patients.

If the patient complies with the above eligibility criteria and **'complies with any acute clinical conditions listed in Annex 1 at admission'**, then please open a questionnaire, and tick 'Yes' to signify that the patient complies with any of the admission diagnosis listed.

Please make sure that the main **'Admission diagnosis code'** is recorded according to the International Classification of Diseases code (ICD).

Please specify which version of ICD code is used, either **'ICD-9 code or ICD-10 code'**, by ticking the box that is found next to either possibility.

The **'Date of Admission'** is the date at which the patient arrives to the hospital.

Identification of Patient

If the patient is eligible, then a patient study identification number should be assigned and all the following data regarding the patient's general information should be filled in:

The **'Hospital ID'** corresponds to, if the study site has more than 1 hospital included in the study, the code number that has been given to the individual hospital. For example, if one of the study sites was Sydney, and there were 6 hospitals from Sydney participating in the study, then I may code the hospitals: Hospital # 1, Hospital # 2, Hospital # 3, Hospital # 4, Hospital # 5 and Hospital # 6. The hospital ID's should be communicated to the Coordination Office in the beginning of the study. Needs to be a numeric value.



The '**Patient study identification number**' corresponds to a unique identification number for each unique **admission episode**. Each patient should have a different identification number. It can be composed of numbers/letters/symbols but should be unique for each patient and each episode. Please note that a patient could be included more than once if he/she gets admitted after the current episode and complies with all criteria for eligibility and inclusion.

The GIHSN study should comply with all applicable laws, government standards, regulations, licenses, and guidelines, including, without limitation the Good Epidemiological Practices (GEP), all applicable laws and regulations concerning the protection of personal information and/or conferring privacy rights on any individual and each study site needs to guarantee personal data protection (confidentiality) by using anonymous Study Site databases in data sharing processes.

Therefore, please never send patient's name and/or personal health care identification number to the Coordination Office.

For the '**Sex**' of the patient, please identify either female or male by ticking the corresponding box.

The '**Age**' is expressed in years for patients 5 years and more, and in months for patients less than 5 years old (59 months or less). Please make sure that the age is correctly filled in, in order to avoid miscalculations of age.

Communication & Consent

After gathering general data about the patient, you will now need to interview the patient (/proxy/parents/tutors).

Please precise if it is '**Possible to communicate with the patient**', with the patient himself/herself or through a proxy/parent/tutor, by ticking 'Yes' or 'No'.

If you are not able to communicate please tick in 'No' in the questionnaire. This could be due to language barriers, to the patient having already been discharged, having no proxy present, or the patient having neuronal damage, or to any other circumstance.

If you were unable to communicate with the patient, please consider this questionnaire **closed**.

If you are able to communicate please tick in 'Yes' in the questionnaire and go on to see if the patient gives consent to participate in the study.



Informed consent is required for all patients before going any further with the questionnaire. You will need to specify if the **'patient, or a proxy, gives consent to participate in the study.'**

In case the patient has not reached legal age or is impaired, the parents, tutors or relatives should sign the Informed Consent (***please, follow local legislations***).

Aspects that should be stressed about the study processes in order to receive informed consent:

- Inform about objectives and procedures of the study
- Inform that participation is voluntary and that the patient can refuse to participate and withdraw her/his consent at any point in time
- Inform that some health and social questions will be asked, and samples will be taken in order to identify the viruses present in their specimen
- All information compiled for the study is confidential
- The study has been reviewed and approved by the Ethical Committee
- The patient is free to ask any questions about the study

There should be two Informed Consents forms per patient. After signing, one copy will be kept by the patient and the other copy by the study team.

If the patient does not give consent, please tick 'No' and close the questionnaire. If the patient gives consent, please make sure that you tick 'Yes' and before going further in the questionnaire please check that all previous information in the questionnaire is filled in and completed.

Informed consent withdrawal

Patients can withdraw Informed Consent whenever they feel like it and can ask for their data not to be used for the study analysis.

All information about withdrawals should be documented. If the patient withdraws consent, then the **'informed consent'** question should be changed to a 'No' to signify that the patient did not give consent to participate in the study.

Patients will be excluded due to lack of consent.

Influenza like-illness (ILI)

For patients 5 years or older

Patients 5 years or older will need to comply with the **'ILI case definition'** (ECDC), shown in the box below, relating to the **'patient's symptoms in the last 7 days prior to admission'**.

Please tick the boxes to indicate the symptoms that the patient has or does not have.

If the patient **'Complies with the GIHSN case definition'**, the ILI case definition plus the 7-days criteria, please tick 'Yes' and continue the questionnaire. If the patient



does not comply with the ILI case definition, please tick 'No' and close the questionnaire.

European Centre for Diseases Control (ECDC) definition of influenza like-illness (ILI):

- A Combination of:

At least one of the following four **ILI systemic symptoms**:

- Fever or feverishness
- Headache
- Myalgia
- Malaise

At least one of the following three **ILI respiratory symptoms**:

- Cough
- Sore throat
- Shortness of breath

Including also:

- Nasal congestion

The patient/parent/tutor/proxy needs to refer to seven days or less BETWEEN onset of symptoms AND the date of hospital admission

For patients less than 5 years old

Ask the parent/tutor if the symptoms of 'admission diagnosis' the patient has been diagnosed with have '**begun in the last 7 days prior to admission**'. According to the answer, the patient will be considered eligible or not.

For all patients

After having gathered ALL the information mentioned until this point, if the **patient does NOT fulfil** the GIHSN case definition of ILI case definition plus 7 days criteria (for 5 years or more) or an admission diagnosis occurring in the last 7 days prior to admission (patients less than 5 years old), please thank the patient for having spent the time with you to answer the previous questions and **close** the questionnaire.

After having gathered ALL the information listed above, if the **patient DOES fulfil** the GIHSN case definition of ILI case definition plus 7 days criteria (for 5 years or more) or an admission diagnosis occurring in the last 7 days prior to admission (patients less than 5 years old), then you can consider this patient as **included population** into the study (see Flow Diagram in Annex 2).



These **included patients** will be swabbed and all further questions in the questionnaire will need to be completed.

Swabbing

GIHSN protocol requires two samples per patient; the two swabs will be introduced in one unique tube of viral transport medium that will be sent to the laboratory.

For those < 14 years old,

1. A nasopharyngeal swab
2. A nasal swab

For those 14 years old or more

1. A nasopharyngeal swab
2. A pharyngeal swab

Please note that each site elaborates its own protocol and can decide to make minor changes in swabbing.

The '**Date of swabbing**' will be recorded for each patient. **Please make sure that this date is at a later date than the date of admission.**

Procedure Collection:

1. Put on a surgical mask, eye protection and gloves.
2. Explain the procedure to the subject and parent or legal guardian.
3. Get the sampling material ready: swab applicator and one universal viral transport medium (UTM) tube (Copan).
3. Have patient blow nose to remove excess nasal secretions.
4. Remove cap from the transport media tube (Previous to use we recommend keeping UTM tubes stored at 2-8°C).
5. Remove flocked swab (see picture 1, Copan, Italy) from bundle. Use only synthetic fiber swabs with plastic shafts. Do not use calcium alginate swabs or swabs with wooden shafts, as they may contain substances that inactivate some viruses and inhibit PCR testing.

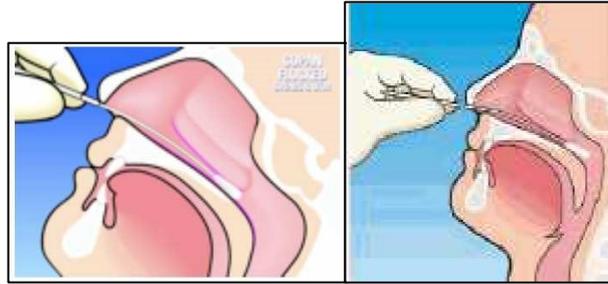


Picture 1

Nasopharyngeal Swab (NP)

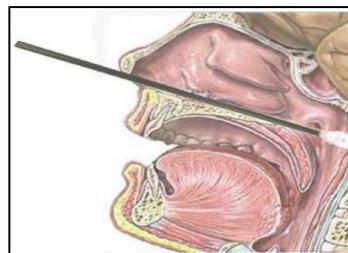
1. Insert dry swab through one nostril straight back (not upwards), along the floor of the nasal passage until reaching the posterior wall of the nasopharynx (see Picture 2).





Picture 2

The distance from the nose to the ear gives an estimate of the distance the swab should be inserted (see picture 3).



Picture 3

Link to video showing this procedure: Sample Collection: Nasopharyngeal Swab Procedure – COPAN <https://vimeo.com/40590348>

Tip: The patient may gag or show other signs of discomfort. It may help to instruct patients to sit with head against a wall/chair back to reduce the tendency of pulling away during this procedure.

Note: Do not force swab. If resistance is encountered during swab insertion, remove it and attempt insertion in the opposite nostril.

2. Rotate swab gently for 5-10 seconds, and then remove (see Figure 4).



Figure 4

3. The tip of the swab is placed immediately into a collection sterile tubes containing 2–3 ml transport medium (rotate swab gently for 5-10 seconds) and the applicator stick is broken off (see Figure 5).



Figure 5

4. Label the transport system tube appropriately with the patient study identification number and date of collection.

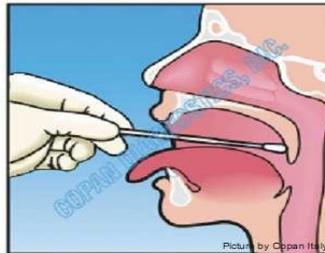
Nasal swabs (N)

1. Tipped swab is inserted into the nostril for a few seconds before being slowly withdrawn using a rotating motion.
2. The tip of the swab is placed immediately into a collection sterile tubes containing 2–3 ml transport medium (rotate swab gently for 5–10 seconds) and the applicator stick is broken off (see Figure 5).
3. Label the transport system tube appropriately with the patient study identification number and date of collection.

Link to video showing this procedure: Sample Collection: Nasal Swab Procedure – COPAN <https://vimeo.com/40590286>

Pharyngeal swabs (P)

1. Insert dry swab through one the posterior pharynx are swabbed vigorously, avoiding tongue and tonsillar areas (see picture 6).



Picture 6

2. The tip of the swab is placed immediately into a collection sterile tubes containing 2–3 ml transport medium (rotate swab gently for 5–10 seconds) and the applicator stick is broken off.



3. Label the transport system tube appropriately with the patient study identification number and date of collection.

Link to video showing this procedure: Sample Collection: Combination Nasal/Throat Swab Procedure – COPAN <https://vimeo.com/40589687>

Additional useful and detailed information can be found at WHO Manual for the laboratory diagnosis and virological surveillance of influenza.

Storage, packing, shipping, and transporting specimens

Refrigerate specimen at 2-8°C up to 72 hours; if exceeding 72 hours, freeze at between -20°C to -50°C and ship on dry ice. Specimens for virus isolation should be placed at 4 °C immediately after collection and promptly transported to the laboratory. In order to prevent loss of infectivity, repeated freezing and thawing must be avoided.

All specimens must be pre-packed to prevent breakage and spillage. Send specimens with cold packs or other refrigerant blocks that are self-contained, not actual wet ice. This prevents leaking and the appearance of a spill. When large numbers of specimens are being shipped, they should be organized in a sequential manner in boxes.

In summary

Additional useful and detailed information can be found at the current WHO guidance on the transporting of infectious substances (WHO:

Guidance on regulations for the Transport of Infectious Substances 2015-2016; available at:

http://www.who.int/ihr/publications/who_hse_ihr_2015.2/en/).

Transport the swab: NP, P or N specimens combined, placing swabs in the same vial.

A combined (meaning that two swabs will be taken separately) nasopharyngeal and a pharyngeal or nasopharyngeal and a nasal swab (depending on age), is to be obtained from each included patient, using preferentially Flocked Swabs (for instance, Copan, Italy) shown in picture 1. The reference provided is convenient as one size and type can be used for all age groups minimizing logistics conundrums. The two swabs (combined; two swabs one tube) will be introduced into one unique vial with 3 mL UTM, for instance, Copan, and kept at least at -20 °C and preferably -50°C if stored at the hospital until shipped to the reference laboratory. Daily, freezer temperature should be recorded twice, and the records kept in the study file.

Sample vials should be all labelled and correctly identified.

Sample shipments to reference laboratory records should be kept at site (with date of shipment and identified samples).



Once in the laboratory the samples will be kept around -70° C. Then, a multiplex real time PCR will be performed to all samples to detect the presence of influenza virus A (H1N1 / H3N2) and B (Yamagata / Victoria)

Testing for other respiratory viruses is optional and it will be each sites'/countries' decision to perform these tests or not.

A laboratory protocol for sample management and PCR methods should be available at each site if requested and a copy sent to the GIHSN Coordination Office at the beginning of the season.

Laboratory results

Please indicate first if the **'Patient has a positive flu result?'** by ticking 'yes' or 'no', or 'inadequate sample' if this was the case.

In the questionnaire, whenever the result is positive for any virus please tick the box next to the virus. If there is a mixed infection of two or more viruses, please indicate which viruses. Otherwise, for the viruses not tested by protocol in the lab (for instance the site does not perform RT-PCR for other respiratory viruses and restricts the study to influenza) then no mark is to be included in the questionnaire for these viruses.

Please indicate also **'if a co-infection has been detected'** by ticking 'yes' or 'no', or 'inadequate sample' if this would be the case.

If the sample is negative, the subsequent questions in the questionnaire are not mandatory. If the sample is positive however, the questionnaire has to be fulfilled.

Sequencing

Besides quantifying the distribution of the different influenza strains, the objective of the Network is to share clinical information linked with genetic sequencing of influenza strains to support the biannual vaccine strain selection process of the WHO's formal recommendation for the composition of human influenza vaccines. Each site is therefore asked to sequence a selection of flu positive samples.

Sequencing scheme for all patients, per hemisphere:



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

If no capacities to generate genetic sequence data (GSD) are available onsite, the site may ship its specimens to the GIHSN sequencing platform in Lyon. Refer to separate documents describing this process.

Patient characteristics

Height

For patients less than 5 years old only, please enter the patient's 'Height' in cm.

Weight

For patients less than 5 years old only, please enter the patient's 'Weight' in Kg.

Pregnancy status

Only for patients 5 years and more, record the 'Pregnancy status' by ticking 'yes', 'no', or 'none-applicable' for male patients.

If pregnant, please record the number of 'Pregnancy weeks', for instance, week 8 will be '8'.

Chronic conditions

Indicate whether the patient has any 'Chronic conditions' at the time of admission by ticking either 'Yes' or 'No'. If yes, tick the box(es) of the corresponding chronic disease(s). At least one box has to be ticked.

The questions will be answered using information from medical records or questioning the patient. In the case that the patient tells us that a chronic condition exists, but this is not recorded in the clinical records, then please record the information provided by the patient. If no information on the existence of



underlying conditions or previous prescriptions is obtained from the above-mentioned sources the answer will be 'No' to all questions.

Use of antivirals & antibiotics

Indicate if the patient has received a '**Prescription of an antiviral for the current episode**'. If yes, indicate also, if known, the starting date of the treatment.

Answer 'Yes' only in case neuraminidase inhibitors (see list below) have been taken by the patient for the current illness episode, such as:

- Oseltamivir
- Zanamivir
- Peramivir
- Favipiravir

Indicate also if the patient has received a '**Prescription of an antibiotics preceding admission**' and the treatment starting date.

Frailty rate

Only for the patient group 5 years and older, relying on the frailty scale in annex 5, please record the '**baseline frailty score of the patient, prior to onset of the current illness**' indicating the fitting category between 1-9.

This is an optional question. If you did not ask the question, please tick 'did not ask'.

Vaccination status

Information regarding vaccination status is to be obtained from the face-to-face interview with patient and/or from patient records or registries if available.

The patient will be asked if he/she was '**Vaccinated against influenza for the current season**'. Please tick 'Yes', 'No' or 'Do not know', according to the patient's answer.

Patients less than 5 years are also to be asked if '**2 doses of vaccine have been administered**'.

The patient will then be asked to recall if he/she was '**Vaccinated more than 14 days before onset of the ILI symptoms**'. Please tick either a 'Yes', a 'No', or a 'Do not know' according to the patient's answer.



The patient will also be asked if he/she was '**Vaccinated in the preceding season**'. The possible answers are 'Yes', 'No' or 'Do not know'. Please tick either a 'Yes', a 'No', or a 'Do not know' for all patients accordingly to patients' answers. If the patient says he has not been vaccinated or does not remember being vaccinated but in the records there is evidence that the patient was vaccinated, the patient will be considered '**vaccinated**' and recorded as such.

Severity

Hospital records will be used to record the severity status of the patient at admission.

6 questions are to be looked up in the hospital records for all patients in order to evaluate the severity of the patient, ticking the corresponding answer 'Yes', 'No', or 'Do not know', or the requested value:

- '**Confusion/lethargy at admission**',
- '**Blood pressure (systolic/diastolic)**' expressed in mmHg
- '**Respiratory rate at admission**' expressed in breaths per minute for patients 5 years, and older and for patients less than 5 years '**Oxygen saturation value on ambient air at admission**' expressed in %,
- '**Supplemental oxygen without mechanical ventilation**',
- '**Vasopressor support**' and
- '**Mechanical ventilation**'.

For patients 5 years and older it is also asked if they are experiencing '**Apnea**'.

Outcome

Hospital records will be used to record the outcome of the patient.

Hospital records will be looked at to see if the patient was '**Admitted to the Intensive care Unit (ICU)**' or not. Please tick either a 'Yes' or a 'No', for all patients. Use the hospital records to see whether the patient died during the admission or not. Please tick either a 'Yes' or a 'No', for all patients to signify '**Death while hospitalized**'.

Use the records to inform about the '**Discharge/death date**' respecting the date format YYYY-MM-DD, and also if the patient was discharged to another hospital



by ticking 'Yes', 'No', or 'Do not know' according to the available information. Please control that the date is superior to admission date.

The '**Main diagnosis at discharge/death**' will be recorded for all patients by entering the ICD code for:

- 1) '**Main discharge/death diagnosis**';
- 2) '**Secondary 1 diagnose**' and
- 3) '**Secondary 2 diagnose**'

Please specify also which ICD code is used, either '**ICD-9 code or ICD-10 code**', by ticking the box that is found next to either possibility.

For patient group 5 years and older and additional question could be asked (optional question) concerning the '**Frailty score of the patient at discharge**' by entering a score from 1 to 9.

Data Linking

Two last questions are to be filled in to allow for the linking of clinical and virologic data:

A first question to confirm whether the sample was '**Submitted to GISAID EpiFlu™ database**', by ticking the appropriate box; 'Yes', 'No', or 'No, failed sequencing'.

If you answered 'yes' to the previous question, you are also asked to enter the '**GISAID Accession Number (EPI_ISL)**'

After filling in all the questions of the questionnaire, please do not forget to press 'SUBMIT'.



Annex 1: Admission diagnosis

For Patients 5 years of age or older	ICD 9 Codes	ICD 10 Codes
Acute upper or lower respiratory disease	382.9; 460-466	J00-J06, J20-J22, H66.90
Acute myocardial infarction or acute coronary syndrome	410-411 and 413-414	I20-I25.9
Acute asthma or exacerbation	493.92	J45.901
Acute Heart failure	428-429.0	I50-I50.9; I51.4
Pneumonia and influenza	480-488	J09-J18
Bronchitis and exacerbations of Chronic Pulmonary Obstructive disease	490, 491.21 and 491.22,	J40; J44.0; J44.1
Acute respiratory failure	518.82	J96
Myalgia	729.1	M79.1
Acute metabolic failure (diabetic coma, renal dysfunction, acid-base disturbances, alterations to the water balance)	250.1- 250.3; 584-586; 276-277	E11.9, E10.9, E11.65, E10.65, E10.11, E11.01, E10.641, E11.641, E10.69, E11.00, E10.10, E11.69, N17.0, N17.1, N17.2, N17.8, N17.9, N18.1, N18.2, N18.3, N18.4, N18.5, N18.6M N18.9, N19, E87.0, E87.1, E87.2, E87.3, E87.4, E87.5, E87.6, E87.70, E87.71, E87.79, E86.0, E86.1
Altered consciousness, convulsions, febrile convulsions, syncope and collapse	780.01-780.02; 780.09; 780.2; 780.31-780.32	R40.20, R40.4, R40.0, R40.1, R55, R56.00, R56.01
Dyspnea/respiratory abnormality	786.0	R06.0, R06-R06.9
Respiratory abnormality	786.00	R06.9
Shortness of breath	786.05	R06.02

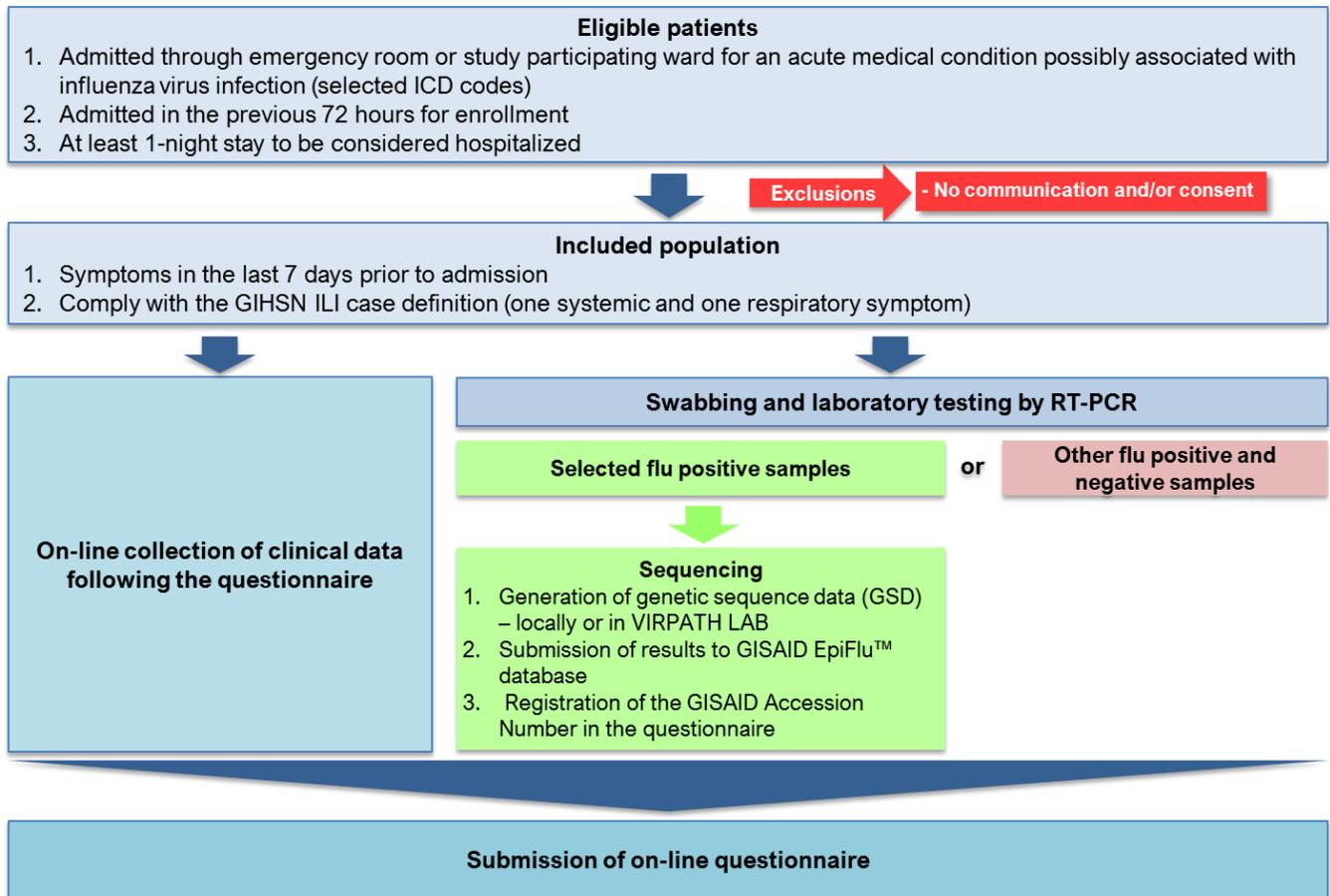


Respiratory abnormality, not otherwise specified	786.09	R06.3, R06.00, R06.09, R06.83
Respiratory symptoms/chest symptoms	786.9	R06.89
Fever or fever unknown origin or non-specified	780.6-780.60	R50, R50.9
Cough	786.2	R05
Sepsis, Systemic inflammatory response syndrome	995.90-995.94	R65.10, R65.11, R65.20, A41.9

For Patients less than 5 years of age	ICD 9 Codes	ICD 10 Codes
Acute upper or lower respiratory disease	382.9; 460 to 466	J00-J06, J20-J22
Dyspnea, breathing anomaly, shortness of breath, tachypnea (polypnea)	786.0; 786.00; 786.05-786.07; 786.09; 786.9	R06.0, R06, R06.9, R06.3, R06.00, R06.09, R06.83, R06.02, R06.82, R06.2, R06.89
Acute asthma or exacerbation	493.92	J45.901
Pneumonia and influenza	480 to 488	J09-J18
Acute respiratory failure	518.82	J96
Acute heart failure	428-429.0	I50-I50.9; I51.4
Myalgia	729.1	M79.1
Altered consciousness, convulsions, febrile convulsions	780.01-780.02; 780.09; 780.31-780.32	R40.20, R40.4, R40.0, R40.1, R56.00, R56.01
Fever or fever unknown origin or non-specified	780.6-780.60	R50, R50.9
Cough	786.2	R05
Gastrointestinal manifestations	009.0; 009.3	A09.0; A09.9
Sepsis, Systemic inflammatory response syndrome, not otherwise specified	995.90-995.94	R65.10, R65.11, R65.20, A41.9
Nausea and vomiting	078.82; 787.0; 787.01-787.03	R11; R11.0; R11.10 - R11.12; R11.2



Annex 2: Flow diagram





- ✓ Headache Yes No
- ✓ Myalgia Yes No

b) ILI respiratory symptoms

- ✓ Cough Yes No
- ✓ Sore throat Yes No
- ✓ Shortness of breath Yes No
- ✓ Nasal congestion Yes No

8) Does the patient comply with the GIHSN ILI case definition* and the 7 days criteria? Yes No

**GIHSN ILI case definition: at least one of the symptoms listed in question 7a AND one of the symptoms listed in question 7b.*

If the answers to questions 1 and 8 are Yes and the conditions for inclusion described at the top of the page are fulfilled, please proceed with swabbing and laboratory testing by RT-PCR followed by sequencing of selected positive specimens and continue filling in the questionnaire. If no capacities to generate genetic sequence data (GSD) are available onsite, the site may ship its specimens to the GIHSN sequencing platform in Lyon.

If No, to these two questions, then please consider this questionnaire closed.

Sequencing scheme for all samples (patients of all ages):

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



Swabbing

9) **Date of swabbing** (yyyy-mm-dd)

|_|_|_|_|_| - |_|_| -
|_|_|

Do not
know

Laboratory Results

10) **a. Does the patient have a positive flu result?**

Yes

No

Inadequate
sample

b. If yes, tick the boxes corresponding to the positive virus(es)

- H1N1pdm09
- H3N2
- B/Yamagata
- B/Victoria
- Influenza A no lineage
- Influenza B no lineage

11) **a. Did you test for other respiratory viruses (optional)?**

Inadequate
sample

b. If yes, tick the boxes corresponding to the positive virus(es)

- Corona virus
- Metaneumovirus
- Respiratory syncytial virus
- Adenovirus
- Bocavirus
- Parainfluenza virus
- Rhinovirus

Yes

No

12) **Have you detected a co-infection?**

Inadequate
sample

Yes

No

If the answer to question 10a is Yes, please continue filling in the questionnaire.

If no to this question, the completion of the questionnaire is requested but not mandatory.

Submission of samples to GISAID EpiFlu™ database via the GISAID platform:

GIHSN Standard Operating Field Procedures

V.6.0 December 2019

24/36





All sequenced samples are to be submitted on the platform on a continued basis
(http://gisaid.org/EPI_ISL/123456)

Clinical outcomes

Patient characteristics

13) a. Pregnancy status

Yes

No

Non-applicable

b. If yes, pregnancy weeks:

 weeks

Do not know

14) a. Does the patient have any chronic conditions?

Yes

No

Not asked

b. If yes, indicate which ones

- Cardiovascular disease
- Chronic obstructive pulmonary disease
- Asthma
- Diabetes
- Immunodeficiency (**except HIV**) / Organ transplant
- Renal impairment
- Rheumatologic disease / Autoimmune disease
- Neurological or neuromuscular disease
- Cirrhosis / Liver disease
- Neoplasm (active)
- Obesity
- Active tuberculosis
- HIV infection
- Leukemia
- Hemoglobinopathies
- Other

15) a. Prescription of antiviral for the current episode

Yes

No

b. Starting Date (yyyy-mm-dd)





- 16) a. Prescription of antibiotics preceding this admission? Yes No Do not know
- b. Starting Date (yyyy-mm-dd) |_|_|_|_| - |_|_| - |_|_|

- 17) What is the baseline frailty score of the patient, prior to onset of the current illness? (category 1-9) (see annex 2 for definition of the scale) Category |_|_| Did not ask

Vaccination Status

- 18) Vaccination status:
- a. Influenza vaccination for the current season Yes No Do not know
- b. Vaccinated more than 14 days before onset of the ILI symptoms Yes No Do not know
- c. Influenza vaccination in the preceding season? Yes No Do not know

Severity

- 19) Confusion at admission Yes No Do not know
- 20) Blood pressure (systolic/diastolic) |_|_|_|_| / |_|_|_|_| mmHg Do not know
- 21) Respiratory rate at admission (breaths per minute) |_|_| bpm Do not know
- 22) Supplemental oxygen without mechanical ventilation Yes No Do not know
- 23) Vasopressor support Yes No Do not know
- 24) Mechanical ventilation Yes No Do not know
- 25) Apnea Yes No Do not know

Outcome

- 26) ICU admission Yes No Do not know



- 27) Death while hospitalized Yes No Do not know
- 28) Discharge/death date (yyyy-mm-dd)
- 29) Discharge to another hospital Yes No Do not know
- 30) a. Main diagnose at discharge/death (letter/code.subcode)
 b. Secondary 1 diagnose at discharge/death (letter/code.subcode)
 c. Secondary 2 diagnose at discharge/death (letter/code.subcode)
 d. ICD used ICD-9 ICD-10
- 31) What is the frailty score of the patient at discharge? (category 1-9) Did not ask
See annex 2 for definition of the scale

Data Linking

- 32) GISAID EpiFlu™ database sharing:
- a. Did you submit the sample to GISAID EpiFlu™ database? Yes No No, failed sequencing
- b. If yes, please enter the GISAID Accession Number (EPI_ISL)
The GISAID Accession Number needs to be completed for the data linkage (clinical/sequencing).

End of the questionnaire. Please send the questionnaire to PI for recording.



Annex 4: Core Questionnaire, Patients Less Than 5 Years Old

Core questionnaire: Patients less than 5 years of age
Version 7.4 November 2019

QUESTIONNAIRE TO BE FINALIZED FOR ALL PATIENTS TESTED FLU POSITIVE and if possible, also for negatives

for all eligible patients hospitalized in the previous **72** hours and who have stayed in the hospital for at least 1 night, who are able to communicate (alt. through parent or tutor), who have given consent to participate in the study **and** who are experiencing symptoms of the actual acute episode in the last 7 days prior to admission

Screening

- 33) Does the patient comply with any of the admission diagnosis listed in **Annex 1?** Yes No
- c. Admission diagnosis (letter/code.subcode) |_|_|_|_|. |_|_|_|_|
- d. ICD used ICD-9 ICD-10
- 34) Date of admission (yyyy-mm-dd) |_|_|_|_| - |_|_| - |_|_|
- 35) What is the hospital ID? |_|_|_|_|_|_|_|_|
- 36) Patient study identification number |_|_|_|_|_|_|_|_|_|_|_|_|_|_|
- 37) Sex Female Male
- 38) Age (in months) |_|_|_|_|
if the patient < 1 month, use the value 0
e.g. 4 years old = 48 months

If the answers to questions 1 and the conditions for inclusion described at the top of the page are fulfilled, please proceed with swabbing and laboratory testing by RT-PCR followed by sequencing of selected positive specimens and continue filling in the questionnaire.
If no capacities to generate genetic sequence data (GSD) are available onsite, the site may ship its specimens to the GIHSN sequencing platform in Lyon.



If No to question 1, then please consider this questionnaire closed.

Sequencing scheme for all samples (patients of all ages):

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

Swabbing

39) Date of swabbing (yyyy-mm-dd)

- -

Do not know

Laboratory Results

40) a. Does the patient have a positive flu result?

Yes

No

Inadequate sample

c. If yes, tick the boxes corresponding to the positive virus(es)

- H1N1pdm09
- H3N2
- B/Yamagata
- B/Victoria
- Influenza A no lineage
- Influenza B no lineage

41) a. Did you test for other respiratory viruses (optional)?

Yes

No

Inadequate sample

b. If yes, tick the boxes corresponding to the positive virus(es)

- Corona virus



- Metaneumovirus
- Respiratory syncytial virus
- Adenovirus
- Bocavirus
- Parainfluenza virus
- Rhinovirus

42) Have you detected a co-infection?

Yes

No

Inadequate sample

*If the answer to question 8a is Yes, please continue filling in the questionnaire.
If no to this question, the completion of the questionnaire is not mandatory.*

*Submission of samples to GISAID EpiFlu™ database via the GISAID platform:
All sequenced samples are to be submitted on the platform on a continued basis
(http://gisaid.org/EPI_ISL/123456)*

Clinical outcomes

Patient characteristics

43) Height (Round up to the nearest integer)

|_|_|_| cm

Do not know

44) Weight (Round up to the nearest integer)

|_|_|_| kg

Do not know

45) a. Does the patient have any chronic conditions?

Yes

No

Not asked

b. If yes, indicate which ones

- Cardiovascular disease
- Chronic obstructive pulmonary disease
- Asthma
- Diabetes
- Immunodeficiency (genetic, acquired or induced)
- Renal impairment
- Rheumatologic disease / Autoimmune disease
- Neurological or neuromuscular disease





- Cirrhosis / Liver disease
- Neoplasm (active)
- Obesity
- Malnutrition
- Active tuberculosis
- HIV exposure
- Prematurity
- Down Syndrome or any other developmental

handicap

- Congenital Heart Disease
- Other

46) a. Prescription of antiviral for the current episode Yes No

b. Starting Date (yyyy-mm-dd) |_|_|_|_| - |_|_| - |_|_|

47) a. Prescription of antibiotics preceding admission? Yes No Do not know

b. Starting Date (yyyy-mm-dd) |_|_|_|_| - |_|_| - |_|_|

Vaccination Status

48) Vaccination status:

a. Influenza vaccination for the current season Yes No Do not know

b. If yes, were 2 doses of vaccine given to the patient? Yes No Do not know

c. Vaccinated more than 14 days before onset of the ILI symptoms Yes No Do not know

d. Influenza vaccination in the preceding season? Yes No Do not know

Severity

49) Confusion/lethargy at admission Yes No Do not know

50) Blood pressure (systolic/diastolic) |_|_|_| / |_|_|_| mmHg Do not know

51) Oxygen saturation value on ambient air (%) at admission |_|_|_| % Do not know

52) Supplemental oxygen without mechanical ventilation Yes No Do not know



Annex 5: Frailty Scale

The frailty scale according to the categories defined below. If a subject is in between levels use best judgement.

Category 1: Very Fit. People who are robust, active, energetic and motivated. The people commonly exercise regularly. They are among the fittest for their age.

Category 2: Well. People who have no active disease symptoms but are less fit than category 1. Often, they exercise or are very active occasionally, e.g. seasonally

Category 3: Managing Well. People whose medical problems are well controlled but are not regularly active beyond routine walking.

Category 4: Vulnerable. While not dependent on others for daily help, often symptoms limit activities. A common complaint is being “slowed up”, and/or being tired during the day.

Category 5: Mildly Frail. These people often have more evident slowing, and need help in high order IADLs (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.

Category 6: Moderately Frail. People need help with all outside activities and with keeping house. Inside, they often have problems with stairs and need help with bathing and might need minimal assistance (cuing, standby) with dressing.

Category 7: Severely Frail. Completely dependent for personal care, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months)

Category 8: Very Severely Frail. Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.

Category 9: Terminally Ill. Approaching the end of life. This category applies to people with a life expectancy <6 months, who are not otherwise evidently frail.



Annex 6: On-line tool

Here below is described how to access the on-line questionnaires via the GIHSN homepage.

How to log in:

GIHSN HOMEPAGE

foundationforinfluenza@ghsn.org

Global Influenza Hospital Surveillance Network

HOME ABOUT US THE NETWORK RESULTS BY SEASON PUBLICATIONS JOIN THE GHSN

CALL FOR PROPOSAL 2019-2020 INFLUENZA SEASON

May 27th, 2019

Launch of a Call for proposal 2019-2020 Influenza Season. Linking clinical to virological and genetic data in existing influenza surveillance networks.

[Read the call and apply](#)

FLU

GIHSN - Login

User Name
Password
 Remember me

[Log In](#)

[Forgot my password](#)

Open Health

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Choose the on-line data collection tool (The Data Analysis tool allows you to visualize the data):



LANDING PAGE



Global Influenza
Hospital Surveillance
Network

MORIZET Maria
OpenHealth Company
Warning ! Your password will
expire in 21 days.



Copyright GIHSN 2018 4 3

A pop-up question allows you to choose the questionnaire (5 years and older or Less than 5 years):

DATA COLLECTION TOOL



Global Influenza
Hospital Surveillance
Network

TEST - VANNES #1



How old is the patient?

52
Registered Core
Questionnaire



52
Validated Core
Questionnaire

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[Back to Top](#)

Questions are then to be filled in accordingly. There are several options on the bottom of the page after each chapter; 1) save the questionnaire, being able go back and complete with additional information if necessary, 2) cancel the questionnaire, 3) print





the questionnaire or 4) submit the questionnaire once all the questions have been finalized (after that no possibility to edit/modify):

The screenshot displays the 'DATA COLLECTION TOOL' interface. At the top, there is a blue header with the text 'DATA COLLECTION TOOL'. Below this, the 'Global Influenza Hospital Surveillance Network' logo and name are visible on the left, and 'TEST - VANNES #1' with a power icon is on the right. A navigation bar contains tabs for 'Screening', 'Swabbing', 'Clinical outcomes', and 'GISAID Number'. The 'Screening' tab is active, and the section title 'Screening' is centered. The form contains eight questions:

- 1) Does the patient comply with any of the admission diagnosis listed [here](#)? Yes No
- 2) Date of admission: [calendar icon]
- 3) What is the hospital ID?:
- 4) Patient study identification number:
- 5) Sex: Female Male
- 6) Age (Years):
- 7) Is it possible to communicate with the patient or a proxy? Yes No
- 8) Does the patient give consent to participate in the study? Yes No

At the bottom, there is a navigation bar with buttons for 'Previous', 'Save', 'Cancel', 'Print', 'Submit', and 'Next'. A small '5' is visible in the bottom right corner of the interface.