The University Of Sheffield.

PRIEST

The PRIEST study: Pandemic Respiratory Infection Emergency System Triage

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The PRIEST study: Pandemic Respiratory Infection Emergency System Triage
Planned investigation:

Research objectives

We aim to optimise the triage of people using the emergency care system (111 and 999 calls, ambulance conveyance, or hospital emergency department) with suspected respiratory infections during the COVID-19 pandemic and identify the most accurate triage method for predicting severe illness among patients using the urgent and emergency care system for suspected respiratory infection.

Our specific objectives during the pandemic are:

1. To report any important emerging findings regarding the performance of the emergency care triage method (or methods) used for suspected respiratory infections during a pandemic
2. To identify clinical characteristics and routine tests associated with under-triage (false negative assessment) or over-triage (false positive assessment) during a pandemic
3. To determine the discriminant value of alternative triage methods for predicting severe illness in patients presenting with suspected respiratory infection during a pandemic
4. To inform policy makers and practitioners during a pandemic of the study's emerging findings.

Our specific objectives after the first wave and, potentially for subsequent waves, of the pandemic are, for the hospital (emergency department):

1. To determine the discriminant value of emergency department triage methods for predicting severe illness in patients presenting with suspected pandemic respiratory infection
2. To determine the accuracy of presenting clinical characteristics and routine tests for predicting severe illness
3. To determine the independent predictive value of presenting clinical characteristics and routine tests for severe illness
4. To develop new triage methods based upon presenting clinical characteristics alone or presenting clinical characteristics, electrocardiogram (ECG), chest X-ray and routine blood test results, depending upon the data available and the predictive value of variables evaluated in objective 3

Our specific objectives after the first wave and, potentially for subsequent waves, of the pandemic are, for prehospital services (NHS 111 and emergency ambulance services):

1. To link NHS 111 calls, identified as potentially relating to COVID19, to participating hospital and NHS Digital data, to determine whether patients calling NHS 111 were appropriately advised or provided with an ambulance response, in terms of whether they were admitted to hospital or suffered an adverse outcome.
2. To link ambulance ePR data to hospital and NHS Digital data, to determine whether patients attended by ambulance were appropriately advised to self-care at home or

transported to hospital, in terms of whether they were admitted to hospital or suffered an adverse outcome.

3. To use ambulance ePR data recording patient characteristics to determine which patient characteristics, when recorded prehospital, are useful in predicting adverse outcome and determine the discriminant value of early warning scores, such as NEWS2, for predicting adverse outcome.
4. To explore the potential for data mining to provide new insights into the prediction of adverse outcome among patients contacting NHS 111 or ambulance services with suspected COVID-19.

Existing research

Prior to the 2009 H1N1 pandemic, the United Kingdom (UK) influenza pandemic contingency plan predicted around 750,000 excess emergency department attendances and 82,500 excess hospitalisations during a pandemic [1]. A 2011 consultation document suggested that a pandemic could result in 50% of population having some symptoms, of whom 30% would seek primary care and 1-4% would need hospital admission [2]. The Pandemic Influenza Advisory Committee Subgroup on Modelling have estimated a likely clinical attack rate of 3-35% (worst case scenario 50%), with 10-25% of these to have complications and a peak demand in the worst case scenario of 13% of the population being ill [3].

Pandemic planning needs to encompass a wide range of potential scenarios, but even projections at the less severe end of the spectrum could cause substantial problems of overcrowding at emergency departments that are already often working close to capacity. Methods of triage for patients presenting to the emergency department with suspected pandemic influenza and other respiratory infections are therefore required and need to be fair, robust and reproducible [4].

The term triage is often used to describe a brief initial assessment in the emergency department to determine patient order of priority in the queue to be seen. In this proposal we use the term triage more broadly to include the full process of emergency department assessment, potentially including investigations such as blood tests and X-rays, and apply it to decision-making regarding whether the patient should be admitted and whether they should be referred for high dependency or intensive care. We also include prehospital triage processes involving the NHS111 and ambulance services.

Emergency department triage methods need to accurately predict the individual patient's risk of death or severe illness. The predicted risk can then guide decision-making. Patients with a low risk may be discharged home, those with a high risk admitted to hospital, and those with a very high risk referred for high dependency or intensive care. Risk predictors need to recognise that thresholds for decision making may differ as a pandemic progresses and resource availability differs.

Health Protection Agency (HPA) guidance prior to the 2009 pandemic, supported by the British Thoracic Society and British Infection Society, recommended the use of the CURB-65 pneumonia score [5] for patients with suspected influenza-related pneumonia. This score uses five variables (confusion, urea level, respiratory rate, blood pressure and age) to generate a score between zero and five. Subsequent Department of Health guidelines on

surge capacity in a pandemic also considered use of a physiological-social score (Pandemic Modified Early Warning Score (PMEWS)) [6]. This score uses physiological variables, age, social factors, chronic disease and performance status to generate a score between zero and seven. National guidance specific to the 2009 H1N1 pandemic included a swine flu hospital pathway for emergency department management with seven criteria, any one of which predicts increased risk and the need for hospital assessment [7].

We used the autumn/winter phase of the 2009 H1N1 pandemic in Sheffield and Manchester to evaluate the discriminant value of three potential systems for triage of pandemic respiratory infection patients in the emergency department: CURB-65, PMEWS and the swine flu hospital pathway [8,9]. However, the pandemic in these areas was less severe than predicted and only five patients of the cohort of 481 met our predefined criteria for critical illness. Within this cohort the discriminant value (c-statistic) of the three systems for predicting critical illness was moderate (CURB-65 0.78 (95% confidence interval (CI) 0.58 to 0.99), PMEWS 0.77 (0.55 to 0.99) and the swine flu hospital pathway 0.70 (0.45 to 0.96)). Their performance in predicting hospital admission was worse: CURB-65 0.65 (95% CI, 0.54 to 0.76), PMEWS 0.76 (0.66 to 0.86) and the swine flu hospital pathway 0.62 (0.51 to 0.72). These findings suggested that clinicians were not using the recommended triage methods when deciding whether to admit or discharge patients, and raised concerns about the accuracy of these methods for predicting adverse outcome.

Other research during the pandemic cast doubt on the utility of existing triage systems. The SwiFT study of patients admitted to critical care with H1N1 found 68% scored 0 or 1 using CURB-65 (i.e. recommended for hospital discharge)[10]. This is supported in evidence from a Canadian seasonal flu cohort, where no triage system performed well in predicting intensive care admission (c-statistics PMEWS 0.63 (0.57-0.69), CURB-65 0.58 (0.52-0.64)[11]. The best discriminator in this cohort was SMART-COP, a system specifically developed to predict intensive care admission in community-acquired pneumonia [12] which achieved a c-statistic of 0.73 (0.67-0.79) but has not to our knowledge been examined in a pandemic cohort. The SwiFT study [10] also developed a new score based on systolic blood pressure, temperature, heart rate, respiratory rate, neurological status and inspired oxygen concentration to predict adverse outcome. The SMART-COP and SwiFT scores therefore offer alternative triage methods that require validation in a pandemic. We are not aware of any other new scores to emerge since the 2009 pandemic.

In addition to our study and SwiFT, a number of cohort studies were undertaken during the 2009 H1N1 pandemic to identify risk factors for poor outcome in various groups (see appendix). The predominant predictors of adverse outcome were chronic co-morbidities and obesity [13-18] with conflicting evidence regarding the risk of pregnancy [10,15]. Acute physiological disturbances, particularly hypoxia, were also found to have prognostic value [10,14, 19-25]. Further studies [26-61] have confirmed these findings and identified a number of other predictors of adverse outcome, but no well validated and widely accepted prediction rules have been developed.

The existing research therefore suggests that, although there are a number of patient characteristics and clinical measures that can predict adverse outcome, the available data do

not support the use of any specific triage methods in suspected pandemic respiratory infection.

We developed the PAINTED study (PAndemic INfluenza Triage in the Emergency Department) to evaluate emergency department triage methods during a pandemic, based on pre-pandemic pilot work and a protocol that would be placed in "hibernation" until a pandemic occurred. Pilot work showed that a standardised data collection form that doubled as a clinical record was acceptable to clinicians and could be used to collect research data in an influenza pandemic, but analysis may be limited by missing data [62].

There have been a number of developments since the PAINTED protocol was written that have created a need to update the protocol:

1. Emergence of COVID-19 has resulted in a need for the study to be applicable to other respiratory infections, specifically COVID-19.
2. Ambulance services are increasingly training and supporting paramedics to manage patients without transport to hospital and NHS 111 has pathways that advise alternatives to emergency ambulance dispatch. This has created a need for triage methods to be applicable to prehospital use.
3. Electronic patient report forms, triage records and hospital records are increasingly used as alternatives to paper records.

The development of electronic records means that the original intention of the pandemic portfolio studies, to produce findings that would influence practice during the pandemic, is now more achievable. However, a detailed analysis using a locked data set to compare alternative triage methods and develop new methods would not be completed until it was too late to influence practice during a pandemic. Furthermore, although there are limited data to support current triage methods, emergency departments and ambulance services need to use a triage method to manage demand as soon as a pandemic develops. The objectives and analysis of the study therefore need to focus on using descriptive interim analysis to improve the triage method in use.

Research methods

We plan to undertake an observational cohort study using routine electronic data capture from people using the emergency care system (via 111 and 999 calls, ambulance conveyance, or hospital emergency department) with suspected respiratory infections during a pandemic.

Planned inclusion/exclusion criteria

We will include all adults and children with suspected respiratory infection during the pandemic who present at the emergency department of a participating hospital, call 111 or emergency ambulance services or are attended by an ambulance from a participating ambulance trust. The inclusion criteria for each group are detailed below.

Emergency department

Patients will be eligible for inclusion if they meet the current clinical diagnostic criteria [63] of fever (≥37.8°C) and at least one of the following respiratory symptoms, which must be of acute onset: persistent cough (with or without sputum), hoarseness, nasal discharge or

congestion, shortness of breath, sore throat, wheezing, sneezing; or if they meet any future clinical diagnostic criteria recommended by the Department of Health and Social Care.

Inclusion will be determined on the basis of the assessing clinician recording on the patient record that the patient has suspected pandemic infection, which will result in standardised data being collected.

NHS 111 telephone service

We will include any patient who contacted the NHS 111 telephone service operated by Yorkshire Ambulance Service NHS Trust (YAS) who, in the last triage of a call, had a COVID-19 related final disposition recorded. COVID-19 related dispositions were implemented within the NHS 111 triage system from 18th March 2020; we may seek to identify records belonging to potential COVID-19 patients who contacted the NHS 111 telephone service before this time by examining other likely final symptom groups (e.g. "breathing problems, breathlessness or wheeze", "cough", or "fever").We will exclude those with a missing NHS number (estimated to be 2% of NHS 111 breathing pathway calls).

Emergency ambulance service

We will include any patient who was a subject of a Yorkshire Ambulance Service NHS Trust (YAS):

1. Emergency Operations Centre call in which there was no ambulance response but the call was managed according to the Advanced Priority Medical Despatch triage card 36 (a pandemic triage process for patients with suspected COVID); or,
2. ambulance response and the attending ambulance staff recorded a clinical impression of suspected or confirmed COVID on the patient's clinical record.

Predictor variable data collection

Participating emergency departments will be provided with paper forms that can be integrated into the patient record and used to collect standardised triage assessment data. The form can be used at triage or at full patient assessment, and will form part of the clinical record. It can also be used by the emergency department to guide triage assessment. For example, the data recorded can be used to recommend diversion away from the hospital if criteria are not met or admission to hospital if criteria are met. The form will include key variables used in recommended triage methods, such as PMEWS and the swine flu hospital pathway, and other variables considered to be potentially useful predictors of adverse outcome. We will allow participating sites to adapt the form to their local circumstances, for example omitting variables that are already routinely collected.

We will retrospectively extract routinely collected data from participating ambulance service data systems as specified in Table 1 below. The data will be shared with the University of Sheffield project team as detailed in the "Data linkage" section below.

Table 1: Data items to be collected from ambulance service data systems

NHS111	**Ambulance – Computerised Dispatch System**	**Ambulance – Electronic Patient Record**
Identifiable data Date of Birth* Postcode of residence* NHS Number*	**Identifiable data** Name (Surname & Forename)* Date of Birth* Postcode of residence* NHS Number*	**Identifiable data** Name (Surname & Forename)* Date of Birth* Postcode of residence* NHS Number*
Call details Date & time Patient age Type Patient gender Passed to clinician Call back made Time of clinician assessment	**Call details** Incident number Incident Date Incident Time(s) Patient age Patient gender Chief complaint (reason for call) Priority category Dispatch code/disposition Destination hospital and department or ward Stop code	**Call details** Incident number Incident Date Incident Time Patient age Patient gender Destination hospital (transported patients) Reason for non-transport Referral to other service - type Pre-alert to hospital
Patient assessment Initial assessment pathway (call reason) Call handler identified symptom group Call handler identified symptom discriminator Call handler disposition Clinician identified symptom group Clinician identified symptom discriminator Clinician disposition Final symptom group Final symptom discriminator Final Disposition		**Patient assessment & management** Physiological observations (e.g. pulse, BP, Respiratory rate, oxygen saturation, level of consciousness, NEWS) Airway intervention – type Cardiac or respiratory arrest present Cardiac or respiratory arrest outcome (died or ROSC) Advice provided (non-transported patients) Supplementary oxygen provided Drugs administered (name, dosage, route) Main clinical (working) impression [diagnosis]
		Free text fields** Presenting complaint & history Previous medical history/comorbidities Examination findings Care plan decision

* Data item required for the purposes of linkage with NHS Digital outcome data; DOB will also be used to derive age at activity; postcode will be used to derive deprivation score, care home resident status, rural/urban status, and output area (social-demographic) classification.
** We seek approval for participating ambulance services to provide the whole clinical free text field contained in the ePR to the University of Sheffield study team to allow the predictive value of this information to be explored through data mining. It is acknowledge that data captured in free-text may, inadvertently, contain information relating to individuals other than the patient. This data item will be considered fully identifiable in all our processing and analyses.

Planned Interventions
The study will be observational and will not change patient care, other than introducing standardised data recording in emergency departments. Participating hospitals and ambulance trusts will use whatever triage method is determined to be most appropriate on the basis of national and local guidance. Decisions to transport the patient to hospital or admit the patient to hospital will be made on the basis of clinician discretion, drawing upon whatever guidance and triage methods are in place. We anticipate that a clinical pathway similar to the swine flu clinical pathway or PMEWS is likely to be in operation and guiding triage decisions at most hospitals and ambulance services. The participating sites will be free to adapt the standardised form to local needs, so that it is used for routine clinical care.

We will evaluate triage methods used to determine whether a patient suspected to be infected with pandemic respiratory infection should be admitted to hospital or not, and whether they should be admitted to intensive or high dependency care. These may include the CURB-65 score, PMEWS, the swine flu hospital pathway, SMART-COP, the SwiFT score and any new methods developed before the next pandemic. We will also evaluate the actual triage decisions made by NHS111 (self-care, GP contact or ambulance response), ambulance service responders (transport to hospital or leave at home) and the emergency department (admit to hospital or discharge). Finally, we will develop two new emergency department triage methods based upon (a) presenting clinical characteristics alone and (b) presenting clinical characteristics, electrocardiogram (ECG), chest X-ray and routine blood test results.

The first score will only use variables available at initial patient assessment, i.e. history and examination, including simple technologies such as automated blood pressure measurement and pulse oximetry. This triage method can be used to assess patients for the need for hospital investigation and identify patients that can be discharged without further assessment. It could potentially be used, with appropriate validation, to assess patients in the community.

The second triage method will be based upon all available emergency department data, including routine blood tests, ECG and chest X-ray findings. This triage method can be used for two potential purposes: (1) Identification of patients with a low risk of adverse outcome who can be discharged home after emergency department assessment; and (2) Identification of high-risk patients who are likely to need high dependency or intensive care.

We will evaluate the ability of each method to predict whether patients die or require respiratory, cardiac or renal support. We will not evaluate the impact of triage methods upon patient care. Intervention in the study will therefore only consist of data collection and follow-up. Patient management will continue according to whatever Department of Health and Social Care guidance is in place at the time of the pandemic.

We will evaluate triage methods separately for adults and children. Adverse outcome from COVID-19 appears to be strongly related to older age and the existence of co-morbidities. Furthermore, physiological measures have different normal ranges in adults and children, and different associations with adverse outcome.

Proposed outcome measures

Patients who die or require respiratory, cardiovascular or renal support they will be defined as having an adverse outcome. If patients survive to 30 days without requiring respiratory, cardiovascular, or renal support they will be defined as having no adverse outcome. If a severe pandemic leads to hospital resources being overwhelmed we will categorise patients as having an adverse outcome if they were deemed to have needed respiratory, cardiovascular, or renal support but were denied this due to lack of resources.

Respiratory support is defined as any intervention to protect the patient's airway or assist their ventilation, including non-invasive ventilation or acute administration of continuous positive airway pressure. It does not include supplemental oxygen alone or nebulised bronchodilators. Cardiovascular support is defined as any intervention to maintain organ perfusion, such as inotropic drugs, or invasively monitor cardiovascular status, such as central venous pressure or pulmonary artery pressure monitoring, or arterial blood pressure monitoring. It does not include peripheral intravenous cannulation and/or fluid administration. Renal support is defined as any intervention to assist renal function, such as haemoperfusion, haemodialysis or peritoneal dialysis. It does not include intravenous fluid administration.

We have selected an outcome measure that has a relatively clear definition and unequivocally indicates a case in which hospital admission and high dependency care would be desirable. The disadvantage of this definition is that it excludes patients who might benefit from other aspects of hospitalisation, such as nursing care, oxygen supplementation or intravenous fluids. However, oxygen and intravenous fluids are often administered to patients with little clinical need for these treatments, administration is often poorly recorded and administration may be based on the clinical variables being tested in this project rather than objective clinical need. Including these treatments in our definitions of respiratory or cardiovascular support would thus carry a substantial risk of over-estimating the prevalence of serious outcome and of over-estimating the association between predictor variables and outcome.

We will also not attempt to determine whether deaths were likely to be amenable to treatment and will thus not explore the issue of whether treatment would be futile. It is possible that a severe pandemic could result in a need to identify cases where treatment would be futile, but this is beyond the scope, and possibly incompatible with the aims, of this proposal.

Hospital follow up and data management
Follow up data can be captured by local research staff conducting a search of local patient records and inputting patient outcomes onto the study database.

At participating hospitals, research nurses employed by each hospital (and funded by the Clinical Research Network) will identify patients with suspected respiratory infection for whom standardised data were collected. The research nurse will check the hospital computer system for deaths or hospital admissions. If death or hospital admission has occurred the research nurse will retrieve hospital notes to record details of any adverse events. Once complete the research nurse will enter data into a secure online database provided by the Sheffield Clinical Trials Research Unit (CTRU).

Research nurses will review the hospital records of all admitted patients who has suspected pandemic respiratory infection (initial or subsequent attendance up to 30 days) to determine whether the criteria for adverse outcome are met. If the criteria are not met or if there is no record of hospital admission, then it will be assumed that there was no adverse outcome. The research nurse will also collect more detailed data from two specific patient groups:

1. The records of patients who were not admitted to hospital at initial attendance but had an adverse outcome (false negative triage decision) will be reviewed in detail to identify any potential predictors of adverse outcome that could have improved triage
2. The records of patients who were admitted to hospital at initial attendance but did not have an adverse outcome (false positive triage decision) will be reviewed to determine the reason for admission, and specifically which positive triage criteria could have prompted admission.

For patients with an adverse outcome (admitted on initial attendance, or false negatives), at 30 day follow-up site research staff at hospitals may be asked to retrospectively collect any missing data from the standardised baseline assessment, as required for the study. Additional non identifiable patient data may also be collected from patients with adverse outcomes that could have helped to predict adverse outcome, e.g. long-term conditions, ethnicity, lifestyle (smoking, alcohol, drug use), recent travel history, patient history, and medications. This additional information will allow for a greater understanding of which patients may require prioritisation during a pandemic. For false positives may also collect the reason for patient admission.

Once complete the research nurse will securely transfer data to the Sheffield Clinical Trials Research Unit (CTRU). Patient NHS number and date of birth are being collected and sent to the University of Sheffield for linkage purposes with outcome data and to allow additional data enquiries at sites.

In the case of Scottish sites involved in the study, their equivalent of the NHS number – the Community Health Index (CHI) number – will not be available to the research team. However, at the discretion of the sites involved, the local principal investigator may hold the link between the CHI and study number to enable such a cross-check.

Data linkage and management of linked datasets

Patients recruited through participating hospital emergency departments in England, and eligible patient contacts with NHS111 and the emergency ambulance service, will be linked to subsequent records of care provided at English hospitals and English death registration data to identify patient outcomes and adverse events in the 30 days after the initial contact. We will request relevant hospital care data and death registration data for the identified study population held by NHS Digital. We will use data from the Emergency Care Data Set (ECDS) for attendances at emergency departments, Admitted Patient Care (APC) data for general inpatient care; and, Adult Critical Care (ACC) data for information on intensive care during inpatient stays. These data provide information on clinical aspects of care, diagnoses, type and length of stay and discharge destination. We will also request demographic and ONS death registration data (held by NHS Digital) to identify patients' ethnicity and socioeconomic status and all deaths amongst the study population that occurred outside of hospital. We will use GPES Data for Pandemic Planning and Research (GDPPR) held by NHS Digital to obtain more complete information on the COVID19-relevant patient risk factors and comorbidities for our cohort. We will use data held by NHS England to describe the property classification for each patient's place of residence. Refer to Appendix II for a summary of all data sources.

We will use experience gained from two successful projects previously used in Sheffield to create linked prehospital and hospital datasets, the "Connected Health Cities: Data linkage of urgent care data" study [https://www.sheffield.ac.uk/scharr/sections/hsr/cure/projects/cured-rd/home] and a NIHR study that linked ambulance data with hospital and mortality data (10). In brief, we will use the following stepwise strategy for both NHS111 and 999 contacts:

1. Yorkshire Ambulance Service will identify and extract all records for the eligible study population* from all service contacts recorded in YAS's information systems within the specified time period. YAS will prepare datasets for each extract, contingent on YAS's information systems and the structure in which the data is stored and routinely extracted. At a minimum, separate datasets will be created for the NHS111 and ambulance ePR data. These datasets will include patient identifiable data (NHS111 datasets will contain: NHS number, date of birth, sex, postcode of residence, ambulance service datasets will contain: NHS number [not always populated], names (first and surname), date of birth, sex, postcode of residence/incident) to enable subsequent linkage with core-PRIEST data and data held by NHS Digital. These datasets will be encrypted by YAS before being uploaded to University of Sheffield IT infrastructure over a secure connection to a location accessible only to authorised members of the University of Sheffield project team and those YAS employees responsible for transferring the data extracts.
   (*YAS will honour NHS national patient 'opt-outs' identified amongst all records for which an NHS Number was captured. YAS will not supply records identified as belonging to patients who have 'opted-out'.)
2. Using the data provided by YAS and that from the core PRIEST cohort, the University of Sheffield (UoS) data management team will partition each dataset into two datasets: one containing only the patient identifiers (NHS number, sex, date of birth, postcode of residence) and the other containing data for analyses (with no direct

identifiers present). From the patient identifier datasets, a further dataset will be produced consisting of all distinct combinations of patient identifiable information (NHS number, names, sex, date of birth, postcode of residence) present across all datasets with a unique identifier for each record. This dataset will be uploaded to NHS Digital's secure severs via NHS Digital's Secure Electronic File Transfer (SEFT) service.

3. NHS Digital will identify individuals amongst the uploaded records and will create a further dataset that links the supplied unique identifier to an NHS Digital generated pseudo-identifier, to enable linkage to data held by NHS Digital. NHS Digital will then extract records for all* identified individuals within datasets they hold from which we seek data (ECDS, APC, ACC, and death registrations). Where a record is found the requested variables (refer to NHS Digital Data Fields (Appendix III) for details) will be extracted together with the pseudo-identifier. NHS digital will supply, via their SEFT service, the data extracted from their national dataset together with the dataset linking each UoS supplied unique identifier to an NHS Digital generated pseudo-identifier. (*NHS Digital will honour NHS national patient 'opt-outs' and will not supply information on these patients. These patients will be "lost to follow-up".)
4. The UoS data management team will use the NHS Digital provided pseudo-identifiers to identify individuals across all study datasets (core PRIEST, NHS111 and ambulance data, and NHS Digital data) and will produce de-identified extracts for analyses (i.e extracts will not contain direct identifiers such as: patient names, NHS Number, date of birth/death, postcode).

We will share NHS Numbers (only) of patients in the Pre-hospital PRIEST cohort (that is patients in the NHS 111 telephone or Emergency Ambulance data supplied by YAS and/or patients identified by English NHS hospital Trusts participating in the core-PRIEST study) with NHS England for the purpose of NHS England to supply back to the University of Sheffield NHS Number and associated property classification of each patient's place of residence (e.g. "Care / Nursing Home", "Prison", "House In Multiple Occupation", etc.) only. We will supply this data to NHS England under a Data Sharing Agreement that limits NHS England's processing, storage and retention of this data to fulfil the objective of supplying property classification to the University of Sheffield only. All data will be transferred using a secure (authenticated and encrypted) electronic communication method.

Data will be stored and processed on a secure virtual machine hosted on the University of Sheffield's IT infrastructure in compliance with Information Governance practices assured by conformance with the NHS DSPT. All data management, processing and storage will be in accordance with NHS HRA authorisations (including CAG recommendations) and data sharing agreements made with NHS Digital, Yorkshire Ambulance Service and hospital trusts participating in the PRIEST study.

The linked datasets will provide information on the large pre-hospital NHS111 and ambulance population who contact these services with potential COVID-19 disease or symptoms, including those who have no hospital ED attendance or admission. By also including and linking the PRIEST cohort we will obtain better follow-up data and identify whether or not these patients were 'pre-triaged' by the NHS111 or ambulance service before arriving at ED.

Proposed sample size

The sample size will ultimately depend upon the size and severity of the pandemic. Our pragmatic data collection methods will ensure that we maximise any opportunity to evaluate emergency department triage methods in a pandemic.

Our experience in the 2009 pandemic has shown us that pre-pandemic estimates of case hospitalisation and case fatality rates can be very misleading and that sample size estimates must take into account considerable uncertainty in these estimates. Nevertheless, we have also shown that informative findings can be generated even in a pandemic with a very low rate of adverse outcome.

Given that most cases of suspected pandemic respiratory infection (even in a severe pandemic) do not result in an adverse outcome, the key variable in determining study power is the number of cases with an adverse outcome. A single cohort including at least 150 cases with adverse outcome would allow us to estimate the c-statistic of a triage method, clinical variable or test with a standard error of 0.03 (assuming the true c-statistic was 0.8). The table below shows the standard error resulting from samples with smaller numbers of adverse outcomes.

N with adverse outcome	Standard error (assuming c-statistic was 0.8)
150	0.033
125	0.036
100	0.040
75	0.046
50	0.056

A sample with N=150 adverse outcome would estimate the sensitivity of a dichotomised rule, variable or test with a standard error as outlined in the table below, depending on the sensitivity at the threshold used. Estimates of specificity would obviously be very precise given the anticipated low prevalence of adverse outcome.

Sensitivity	Lower limit of 95% CI
1.00	0.98
0.95	0.90
0.90	0.84
0.85	0.78
0.80	0.73

The same cohort could be used to identify independent predictors of outcome and develop new triage methods (objectives 3 and 4). The number of variables that could be tested as independent predictors of outcome in a multivariable model and for inclusion in a triage method would depend upon the sample size. Based on the rule of thumb of needing at least 10 events for each independent regression variable in a logistic regression, a cohort with 150 cases with adverse outcome would allow us to test up to 15 parameters [26].

These estimates assume that each triage method and predictor variable will be used and tested on the whole cohort. However, we plan to explore whether different patients require

different triage methods, particularly whether a different triage method is required for children and adults. Data from the 2009 H1N1 pandemic suggest that around a quarter to a third of adverse outcomes may occur in children [14,33]. To increase the probability that we will have at least 50 cases with adverse outcome among children we will aim to recruit a total of 200 cases with adverse outcome rather than 150.

If we assume that the prevalence of adverse outcome is the same as our 2009 cohort (1%) then we would need to collect data from 20,000 cases to identify 200 with an adverse outcome. We have therefore used this estimate in planning, although it is likely to be a overestimate of the total numbers required given the mild nature of the 2009 pandemic. A more severe pandemic would allow more precise estimates to be made with no additional costs or would allow us to reduce the total number of cases required to identify 200 with an adverse outcome.

If we are able to develop a new triage method that appears to have superior discriminant value to existing methods then we would want to validate this method in a new cohort. A sample including 421 cases with adverse outcome would provide 80% power to compare an area under the ROC curve of 0.85 versus 0.90 at 5% significance, assuming a correlation of 0.6 between scores. We have not included validation of a new triage method in our objectives because this would require (a) successful development of a new method and (b) a much larger sample size, with associated costs and assumptions about pandemic severity. However, if the pandemic is severe (i.e. the prevalence of adverse outcome exceeds 3%, so the number with adverse outcome exceeds 450) we will split the cohort into two equal cohorts to allow testing of existing rules and derivation of new rules on one half and validation of new rules, with comparison to existing rules, on the other.

We plan to collect data across 40 hospitals and have based our sample size calculation on the assumption of receiving 500 completed forms, including an average of 5 adverse outcomes, per hospital over the course of the pandemic.

Sample size recalculation

We update our justification for developing a multivariable prediction model based on the recommended approach of Riley et al [65]. With 20,000 cases, 200 outcomes (an assumed Nagelkerke R-squared (R^2_N) of 15%, shrinkage of ≥0.9 and R^2_N change ≤5%) this will allow us to investigate more than 20 potential covariates without overly compromising the potential overfitting.

Recruiting past 20,000 cases, or observing a larger proportion of adverse outcomes, will increase the likelihood of having enough adverse outcome events to split the cohort and both develop and validate a new triage tool. A minimum of 100 events will ensure we are able to validate the new triage tools (Collins, 2015) [66] and give indication of its value, although more patients than this would be needed to formally compare its performance against the best existing triage tool.
The number of children with adverse outcomes is likely to be low in number, and we are unlikely to be able to build a formal prognostic model for children.

Prehospital sample size

The sample size for pre-hospital data will be determined by the pandemic and the available data. We estimate an average of 20 patients per hospital per day (100 patients per day from across YAS), which will provide a total of 9000 patients within 3 months. We will aim to collect sufficient data to identify 200 cases with an adverse outcome of around 40 per participating hospital (adverse outcome rate 2.2%), which current projections suggest hospitals will exceed. We have no information on the accuracy of existing triage tools but following the recommended approach of Riley et al [65] (including an assumed Nagelkerke R-squared (R^2_N) of 15%, shrinkage of >=0.9 and R^2_N change <=5%) this will allow us to investigate more than 20 potential covariates without overly compromising the potential overfitting.
9000 patients allows us to estimate the area under the ROC (AUROC) to within a standard error of approximately 0.02 providing the AUROC is at least 0.75 [67]. The accuracy of the sensitivity and positive predictive value (PPV) depends primarily on the prevalence of adverse outcomes and of positive prognoses respectively. For the former, the 200 expected cases will ensure a sensitivity of 0.8 will be estimated to a standard error of 0.028 and therefore with a 95% CI lower limit of 0.74).The estimated PPV will be estimated more accurately than the sensitivity since more than 200 will likely be classified as having suspected diagnosis: for indication, if 1000 patients are prioritised (i.e. a PPV cut-off of <=20%), the PPV of this rule has a standard error of 0.013.

Statistical analysis
Analysis will be undertaken in two ways:

1. Emerging data prospectively collected regarding triage of patients in the Emergency Department will be analysed weekly while data collection is ongoing
2. Full analysis at the end of the first wave of the pandemic (and after any subsequent wave, if appropriate), after data collection is complete or at another point as determined by the specific pandemic characteristics

Weekly analysis of the emerging data will involve descriptive presentation of:

1. The number and geographical distribution of new cases
2. The proportion with an adverse outcome and details of adverse outcomes
3. Potential predictor variables identified in patients who were not admitted at initial presentation but had an adverse outcome
4. Triage criteria identified in patients who were admitted to hospital and had no adverse outcome

These findings will be reviewed weekly by the core research team. When appropriate, these emerging findings will be summarised to inform policy makers and practitioners during a pandemic/epidemic.

Where appropriate, only age will be treated as a continuous variable (with possible reparameterisation). All other continuous variables will be categorised on the basis of their use in existing risk scores or previous studies. This is because most continuous variables used in risk prediction have a non-linear association with adverse outcome, with increased risk at high and low values.

Cases will be excluded from analysis if we are unable to ascertain if they had adverse outcome or not. It is likely that a proportion of data for most predictor variables (especially blood results) will be missing. The most likely reason is that a measurement would not be made or test performed if it was expected to be normal. Missing data will therefore be handled in constructing scores and in multivariable analysis by assuming that all missing values are normal (i.e. score zero in the relevant risk score). A sensitivity analysis will be performed by imputing missing values (using multiple imputation) and comparing results between the three scenarios of excluding cases with missing values, treating missing values as normal and using imputed values for missing values. Further details of imputation methods will be given in a Statistical Analysis Plan.

Existing triage methods will be assessed by calculating the area under the ROC curve (c-statistic) for discriminating between cases with and without an adverse outcome (defined as death or need for support of respiratory, cardiovascular or renal function) and sensitivity and specificity at key decision-making thresholds.

The discriminant value of each clinical variable or test for adverse outcome will be assessed by calculating the c-statistic and, for dichotomous variables, the sensitivity and specificity.

New triage methods will be developed by combining potential predictors of outcome using multivariable logistic regression with Least Absolute Shrinkage and Selection Operator (LASSO) to avoid overfitting [67] The stability of derived models will be assessed using bootstrap methods with visual calibration methods [68] [69] Two new triage scores will be developed: one based on clinical variables measured at initial assessment only and the other based on all clinical variables (including blood tests and x-rays) measured in the emergency department. Integer weights will be assigned to each category of predictor variable according to the coefficient derived from a multivariable model using categorised independent predictors. This will generate a composite clinical score in which risk of adverse outcome increases with the total score.

We will conduct analysis separately for adults (age ≥16) and children. If the number of children with adverse outcomes is too low to be able to build a formal prognostic model for children, we will instead descriptively summarise the characteristics of children with and without adverse outcomes, and apply existing triage tools where their use is intended for children (e.g. The Swine Flu Hospital Pathway).

If the pandemic is severe enough to allow the cohort to be split into derivation and validation cohorts with sufficient numbers of adverse outcome we will compare new triage methods developed during the project to existing triage methods by calculating c-statistics and sensitivity/specificity at key decision-making thresholds in the second cohort.

Prehospital data analysis

We will undertake the following analyses:

1. Estimation of the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the 999 attendance decision to transport the patient to

hospital, in terms of (a) predicting adverse outcome and (b) predicting admission to hospital.

2. Descriptive analysis of the characteristics of 999 false negatives (patients with adverse outcomes who were not transported to hospital) and false positives (patients who were taken to hospital but not admitted and had no adverse outcome), in terms of patient characteristics, physiology and co-morbidities, and adverse outcome for false negatives.
3. Estimation of the sensitivity, specificity, PPV and NPV of the NHS 111 decision to send an ambulance response, in terms of (a) predicting adverse outcome, (b) predicting admission to hospital and (c) predicting transport to hospital.
4. Descriptive analysis of the characteristics of NHS 111 false negatives (patients with adverse outcomes who were advised to self-care) and false positives (patients who were provided with an ambulance response but not transported to hospital and had no adverse outcome), in terms of patient characteristics and call pathway, and adverse outcome for false negatives.
5. Univariable and multivariable analysis of the association between predictor variables recorded on the ePR and adverse outcome.
6. Evaluation of the performance of triage tools or early warning scores, such as NEWS2, that can be calculated from ePR data, including ROC analysis of the discriminant value of tools for adverse outcome.
7. Exploration of the utility of Natural Language Processing (NLP) techniques for extracting meaningful and potentially predictive clinical data from free-text data recorded within the 999 ePR data.
8. Deep learning data mining analyses to develop further predictive models for identifying false negative and false positive patients. The accuracy, sensitivity and specificity of these models will be evaluated and compared with those of logistic regression models.

Activation of the full study

In anticipation of study activation, related to COVID-19, the study protocol was amended to version 9.0 27/02/2020. Version 9.0 of the protocol amended the viral infection to be studied from influenza to all respiratory infection pandemics. The project was activated by the Department of Health and Social Care on 20/03/2020. The study was open to the enrolment of patients from greenlighted sites as of 26/03/2020. The study target of 20,000 patients was reached on 28/05/2020. The final date for patients attending an emergency department to be allowed to be enrolled in the study was on 28/05/2020.

Ethical arrangements

We have sought Research Ethics Committee (REC) approval prior to piloting and in advance of any pandemic. We have sought approval to activate the project in the event of a pandemic without a further REC review. Our previous similar project in the 2009 H1N1 pandemic was approved by the REC. The planned processes for informing patients of the project and managing data are very similar to those approved in our 2009 project. During the previous 2009 project patient identifiable information was taken to allow monitoring, data validation and GP contact. The National Information Governance Board (NIGB) gave section 251 approval to this use of identifiable patient data without consent. However the NIGB was unable to give approval to the use of patient identifiable information in the pilot

phase of this project. Since 2013, section 251 applications are reviewed by the Confidentiality Advisory Group (CAG) of the Health Research Authority.

Following revision of the protocol, we submitted a revised application to the CAG requesting section 251 approval for the following activities:

1. Staff employed by hospital and ambulances trusts who are not members of the direct care team to undertake processing of personal data, specifically pseudo-anonymisation before sending data to Sheffield CTRU. This is because it would not be possible during a pandemic for hospital and ambulance trusts to limit this activity to member of the direct care team.
2. Sharing of pseudo-anonymised data with the Sheffield CTRU (personal details removed but with a unique study identifier linking the CTRU record to the hospital or ambulance service record), on the basis that record linkage is essential to allow data queries between the CTRU and participating trusts.
3. Sharing of personal data between the participating trusts, the University of Sheffield (UoS) and NHS Digital, to allow identification of adverse outcomes and removal of records from patients who have requested exemption of their data for research purposes. Identifying adverse events is an essential outcome and due to the need to respect patient wishes regarding use of their data for research.
4. Sharing of identifiable data between Yorkshire Ambulance Service and the University of Sheffield (UoS). Patient identifiers will be used by for the purposes of linkage with outcome data held by NHS Digital and data collected from participating hospital Trusts. Further details are provided in the "Data linkage and management of linked datasets" section above.

Risks and anticipated benefits for trial participants and society

The study will not alter patient management and will simply collect routinely available data at presentation and follow-up. No additional diagnostic tests will be performed. The risks to patients involved in the study are therefore very low and principally relate to data protection and confidentiality.

The standardised form is designed to support routine clinical care and will not increase the burden on health care professionals. Approval from CAG/HRA has been granted to allow record linkage by NHS Digital using personal data and the use of a unique study identifier to allow data queries between the CTRU and participating trusts.

Patients involved in the study will potentially benefit from the use of the standardised form. This will ensure that important variables are recorded and communicated between staff providing care. The standardised form can also be used to remind staff of current guidance for management.

Future patients with suspected pandemic respiratory infections and society in general will benefit from evaluation and development of accurate triage methods that have the potential to improve clinical decision-making and ensure that patients receive the right care and health service resources are optimally used.

Informing potential trial participants of possible benefits and known risks
Posters in all participating departments will be prominently displayed advising patients of the project and providing contact details for further information. Information leaflets will be provided for staff to hand to patients with suspected pandemic respiratory infection, when possible within local infection control requirements. Leaflets and posters briefly describe the nature and purpose of the study and provides contact details for further information. If leaflets cannot be given to patients, due to infection control requirements, local staff will be asked to direct patients to the displayed posters in the ED to be informed about the study and linked to additional information.

Information about the prehospital aspects of the study has been made available online via the YAS and the University of Sheffield websites. As the data will be collected retrospectively, it is possible that data will be collected from before the study information was available online. We will seek CAG/REC approval for this.

Obtaining informed consent from participants
We will not seek patient consent to participate on the basis that the study is limited to collection of routinely available data and any delays in patient assessment would risk compromising patient care. The information leaflet outlined above will provide a tear-off slip with contact details that patients can use to inform the hospital or research team if they wish to withdraw from the study. Patients who wish to withdraw from the study will have their study records deleted. Their decision to withdraw will not be communicated to clinical staff providing further care and will not influence their subsequent management.

It is not possible to seek consent from patients identified via prehospital services (NHS 111 and ambulance services) as this data is collected retrospectively. Patients will be able to opt out of the study by contacting details available online. In addition, NHS Digital and YAS (for records on which an NHS Number was captured) will honour NHS national patient 'opt-outs' and will not supply information on these patients.

Proposed time period for retention of relevant study documentation
The original data collection form will constitute the clinical notes and be kept in each hospital according to normal practice. The database will be maintained by the Clinical Trials Unit until ten years after the end of the project.

Proposed action to comply with 'The Medicines for Human Use (Clinical Trials) Regulations 2004'.
Not applicable – this is not a clinical trial or a medicinal product of device.

Research Governance
Sheffield Teaching Hospitals NHS Foundation Trust will be the study sponsor and the project will be managed by the School of Health and Related Research (ScHARR) in the University of Sheffield. The Hospital Trust and University share a joint research office in Sheffield to facilitate management of collaborative projects such as this. The Project Management Group (PMG), consisting of the co-applicants and any appointed research staff, will manage

the study. The PMG will meet prior, during and after the pilot phase. After that meetings will be held annually until a pandemic emerges and the project is activated. During the pandemic the PMG will meet at least monthly, either in person or by teleconference. The Sheffield CTRU will manage data entry, data management of data submitted by acute Trusts.

A Steering Committee has been formed to oversee study progress. This consists of an independent Chair (Professor Tim Coats) and at least three independent members (including a relevant clinician, statistician and public/patient representative), the Chief Investigator and the Project Manager.

Project timetable and milestones:
T0: Project activated
T0 to T0+3 months: Data collection from 20,000 cases, including 200 with an adverse outcome, across 40 hospitals (see sample size section for details)
T0+3 to T0+6 months: Analysis and reporting
T0+2 to T0+5 months: Extraction of ambulance service data and NHS digital application
T0+5 to T0+13 months: Analysis and reporting of prehospital services data

Expertise:
The research team combines experts on emergency management of suspected pandemic influenza (KC, DW and AB) with expertise in paediatric emergency medicine (IM, CF), critical care (AB) and public health (AL), and the statistical expertise and research infrastructure of the Sheffield Clinical Trials Unit (SG, EL, KB).

The Team collaborated on a similar previous project during the 2009 H1N1 pandemic (HTA09/84/66). This project was completed and reported despite difficulties caused by research governance procedures and the unexpectedly mild course of the pandemic.

Steve Goodacre was Chief Investigator for HTA09/84/66 and is lead applicant for this proposal. He has undertaken many major national evaluations in emergency care, including development of clinical prediction methods. His current projects provide the necessary infrastructure to rapidly undertake the proposed research. Andrew Lee is a Senior Clinical University Teacher in Public Health who has a research interest in emergency planning and collaborated with SG, KC and DW on an NIHR Service Delivery and Organisation project involving scoping the emergency planning literature.

Kirsty Challen and Darren Walter are emergency physicians with research interests in pandemic influenza and emergency planning, and Andrew Bentley is an accredited critical care and respiratory physician. They have previously evaluated triage methods for pandemic influenza and are leading experts in this field. Ian Maconochie is a paediatric emergency physician who has evaluated paediatric early warning scores, the predictive value of clinical features in sick children and the management of febrile children.

Katie Biggs (KB) and Ellen Lee (EL) from Sheffield Clinical Trials Research Unit (CTRU) will provide CTRU oversight and statistical analysis respectively.

Carl Marincowitz (CM, Academic Clinical Lecturer in Emergency Medicine) will co-lead the prehospital study with SG. Fiona Bell (FB) and Richard Pilbery (RP) from Yorkshire Ambulance Service will provide input via the prehospital operations group, along with experts in routine data linkage (Janette Turner, JT, and Tony Stone, TS) and health informatics (Peter Bath, PB). The study managers, CM and SG also attend the PRIEST project management group and will ensure that this group is kept updated with regard to the progress of the prehospital study. The PRIEST study steering committee will provide independent oversight for the prehospital PRIEST study as part of the PRIEST project.

Patient and Public Involvement (PPI):
Enid Hirst has agreed to be the patient/public representative for the project and has reviewed the proposal. She acted as patient and public representative for our project in the 2009 pandemic and was an independent member of the study Steering Committee.

Enid Hirst was a founder member of Sheffield Emergency Care Forum (SECF) in 2010. The SECF is a patient and public representative group with a specific interest in pre-hospital, urgent and emergency care research. The forum has reviewed this proposal and provided feedback. Enid will continue to provide a link between the project and the Forum.

Enid previously spent eight years with Sheffield Community Health Council, was a lay member of the Steering Committee for NHS Direct Yorkshire and Humber, a member of Unscheduled Care Network Board in Sheffield and spent three years as a lay member of Sheffield Children's Hospital Ethics Group. She currently attends the Trauma and Emergency Care Specialty Meetings for Yorkshire and Humber and is a PPI representative for the Applied Research Collaboration (ARC) Yorkshire and Humber.

Shan Bennett has also agreed to act as a patient/public representative for the project. Shan has been a member of the SECF since 2012. Shan is a retired primary school teacher but with an interest in medical research, and a science background. Shan has experience of acting as a patient/public representative on a large number of studies including another Covid-19 related study.

Their roles will include the following:

1. Reviewing the protocol and specifically advising on ethical issues and arrangements for data protection and confidentiality
2. Reviewing the poster and information leaflet
3. Patient/public representation on the Steering Committee
4. Lay input into reporting and dissemination of findings
5. Liaison between the project and the Sheffield Emergency Care Forum

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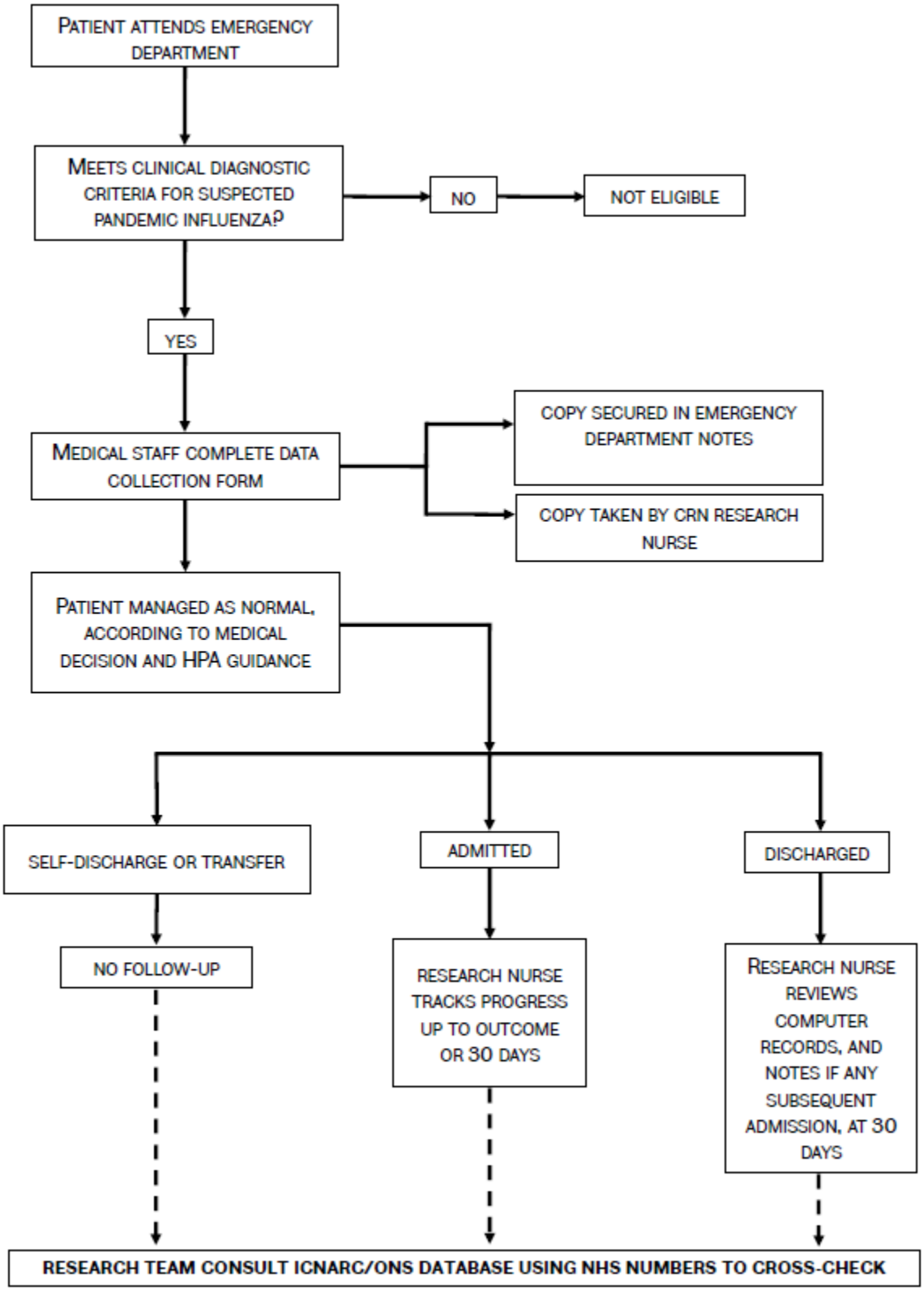
Flow diagram



Appendix I: Studies evaluating clinical predictors of adverse outcome in pandemic influenza

Author	Site	Subjects	N	Outcome	Variable	Results
Rowan (ICNARC) [10]	UK	ICU suspected H1N1 (nb only 562 confirmed)	1725	Death	Current/recent pregnancy Severe chronic organ dysfunction Immunocompromise SOFA score (per point)	HR 0.13 (0.19-0.98) p=0.048 HR 1.53 (1.16-2.02) p=0.008 HR 1.65 (1.16-2.33) p=0.005 HR 1.05 (1.02-1.08) p=0.001
Miller [13]	Utah	ICU adm age>15 PCR confirmation H1N1	47	ICU admission	Hispanic Pacific/Hawaiian BMI 30-39 BMI >39	23% v 13% popn p=0.01 26% v 1% popn p<0.001 38% v 19% popn p<0.001 36% v 3% popn p<0.001
Nguyen-van-Tam (fluCIN) [14]	UK	Hospitalised confirmed H1N1	631	Death/ICU/ HDU	Chronic lung dis (not asthma/COPD)* Obesity* Altered consciousness CXR pneumonia* CRP >100* Sa02<94% on air	OR 3.41 (1.33-8.71) p=0.010 OR 6.96 (1.46-27.28) p=0.008 OR 1.11 (1.04-1.17) p=0.001 OR 5.28 (2.95-9.47) p=0.001 OR 4.41 (2.14-9.1) p=0.001 OR 3.6 (2.17-6.27) p=0.001
ANZIC [15]	Australia/ NZ	ICU confirmed H1N1	722	ICU admission	Pregnancy BMI >35 Chronic pulm disease Maori/Pacific islander	9.1% v 1% popn 28.6% v 5.3% popn 32.7% v 13% popn 25% v 13.6% popn
Harris [16]	Australia	H1N1 confirmed	181	Hosp admission	Aboriginal/Torres Strait Pregnant Diabetes Renal disease Cardiac disease Obese	37.7% v 60.3% p=0.004 29% v 8.1% p=0.013 24.6% v 4.2% p<0.001 18% v 3.3% p=0.001 26.2% v 8.3% p=0.001 28.3% v 10% p=0.002
Santaolalla [17]	Spain	Inpatients H1N1	3025	ICU/death	Asthma COPD BMI >40 Diabetes Other metabolic disease Cardiovascular disease Chronic hepatic disease Seizures Chronic renal insufficiency	14.5% v 22.7% p<0.001 11.5% v 16.9% p<0.001 19.3% v 11.1% p<0.001 13.8% v 9.4% p<0.001 11.5% v 8.8% p=0.001 16.1% v 9.6% p<0.001 9% v 6.1% p=0.025 6.5% v 3.4% p=0.001 7.3% v 4.1% p=0.003
Cui [18]	China	Inpatient H1N1	68	Death	BMI >27	8/10 death v 14/58 alive p=0.001
Zimmerman [19]	Tel Aviv	Adults, CDC definition, PCR confirmation	191	ICU admission	SaO2 Exam lung findings CRP	Median 92% v 97% p=0.006 71% v 31% p=0.002 Median 123 v 40 p<0.001
Martin-Loeches [20]	Spain	Adults, ICU admission for respiratory failure, no pre-existing CRF, microbiological confirmation	661	Acute kidney injury	Diabetes SOFA score MODS WCC CK CRP	16.2% v 9.2% p=0.04 Mean 8.7 v 4.8 p<0.001 92.4% v 54.7% p<0.001 8.3 v 6.8 p<0.001 290 v 170 p<0.001 28 v 20 p<0.001
Echevarria-Zuno [21]	Mexico	Confirmed H1N1	6945	Death	Chronic disease Tachypnoea Cyanosis Time onset-admission (days)	OR 6.1 (2.37-15.99) OR 4.26 (2.14-8.47) OR 3.46 (1.63-7.31) OR 1.19 (1.11-1.28)
Louie [22]	US	Age<18 hospitalised H1N1	345	Death/ICU	Hispanic (v white) Pulmonary disease Cardiac disease	OR 0.4 (0.2-0.8) OR 1.6 (1.0-2.6) OR 4.3 (1.9-9.5)

					Neuro disease GI disorder Acute altered mental status	OR 2.8 (1.6-5.0) OR 2.4 (1.3-4.5) 2% v 15% p<0.001
Stein [23]	Israel	Age<18 hospitalised H1N1	478	ICU admission	Neurologic disease Cardiovasc disease Metabolic disease Tachypnoea Hypoxia CXR effusion CXR diffuse infiltrate	19% v 7.6% p=0.02 14.3% v 5.7% p=0.03 9.5% v 1.6% p=0.01 61.9% v 34.9% p=0.001 57.1% v 21.8% p<0.001 9.5% v 2.1% p=0.005 33.3% v 8.1% p<0.001
Vasoo [24]	USA	ED presentations H1N1	83	Admission ICU	History of prematurity Haemoglobinopathy Chronic neurologic disease Malignancy Tachypnoea SaO2 <92 Acute renal failure CXR infiltrate Chronic pulmonary disease History of prematurity Chronic neurologic disease Tachypnoea SaO2 <92 Acute renal failure CXR infiltrate	18.8% v 0 p=0.002 12.5% v 0 p=0.02 OR 6.9 (1.3-35.5) 9.4% v 0 p=0.054 OR 4.7 (1.7-13) 31.3% v 0 p<0.0001 15.6% v 0 p=0.007 37.9% v 0 p=0.001 OR 4.5 (1.4-14.0) OR 30 (3.2-281.8) OR 4.1 (1-17.7) OR 5.4 (1.7-17.5) OR 84.9 (9.3-772) OR 22.0 (2.3-214.2) 68.9% v 37.9 (inpts) p<0.0001
Bagdure [25]	USA	Paediatric adm H1N1	307	PICU	Neurologic disorder Immunocompromise Seizures (acute) Mental status change Hypoxia Decreased breath sounds WCC <4 CRP >mg/dl pH<7.35	38% v 19% p=0.002 3% v 9% p=0.08 15% v 3% p<0.001 20% v 2% p<0.001 76% v 58% p=0.007 48% v 30% p=0.006 13% v 26% p=0.04 82% v 57% p=0.03 75% v 27% p=0.002
Fajardo-Dolci [27]	Mexico	First 100 H1N1 confirmed deaths	100	Death	Cardiovascular disease Metabolic syndrome Diabetes Respiratory disease Hypertension	20.9% v 4.1% popn 39.5% v 14.5% popn 19.8% v 7% popn 8.1% v 0.4% popn 19.8% v 15.4% popn
Lee [28]	Hong Kong	Adults seasonal flu A/B	754	Death	Oseltamivir Male Major co-morbidity	HR 0.27 (0.13-0.55) p<0.001 HR 3.92 (1.8-8.57) p=0.001 HR 2.27 (1.02-5.09) p=0.045
Libster [29]	Argentina	Age <18 confirmed H1N1 by PCR	251	ICU admission	Asthma	OR 4.92 (1.38-17.33) p=0.002
Chien [30]	Korea	H1N1 pneumonia	96	IPPV/NIV	Pregnancy Chronic renal insufficiency SOFA	2% v 9% p=0.05 14% v 1% p = 0.04 4 v 1 p=0.000
Jain [31]	US	Confirmed H1N1	272	ICU/death	Age Neurocognitive disease Neuromuscular disease CXR pneumonia Antivirals <48h	Median 19 v 29 5% v 13% 5% v 13% 28% v 73% 45% v 23%
Tuite [32]	Canada	Confirmed H1N1	3152	Death	Age >50	OR 28.6 (7.3-111.2)
Campbell [33]	Canada	Hospital admission H1N1	1479	Death/ICU	Heart disease Diabetes	RR 2.1 (1.6-2.7) RR 2.2 (1.7-2.7)

					Immunosuppression	RR 1.5 (1.1-2.0)
Aviram [34]	Israel	ED H1N1 CXR in 24h	97	ICU/death	Bilateral opacities Multizonal opacities	60% v 15% p=0.049 60% v 6% p=0.01
Bassetti [35]	Italy	Inpatients confirmed H1N1	81	ICU/death	Neurocognitive disease COPD/asthma Pneumonia on admission	33.3% v 7% p=0.02 19.7% v 50% p=0.03 100% v 44% p=0.0008
Xi [36]	China	Adult inpatients H1N1	155	Inpatient death	Hypertension Dyspnoea at presentation	37% v 19.5% p=0.048 77.8% v 47.7% p=0.004
Pebody [37]	UK	UK national statistics (estimated case fatality rate)	440 deaths	Death	Chronic renal disease Heart disease Respiratory disease Liver disease Diabetes Immunosuppression Stroke/TIA Chronic neurological disease	RR 36.3 (20.9-63.2) RR 15.2 (9.6-24.1) RR 11.3 (7.9-16.1) RR 63.3 (38.6-103.7) RR 9.2 (5.6-14.9) RR 52.8 (36.3-76.6) RR 7.5 (2.3-23.7) RR 115.3 (84.3-157.6)
Wilking [38]	Germany	National statistics	226075	Death	Age 15-34 (ref 35-60) Age >60	OR 0.18 (0.13-0.26) OR 5.4 (3.86-7.56)
Martin-Loeches [39]	Spain	ICU adm, PCR confirmed H1N1 (also assessed 2010-11 post-pandemic)	648	Death	SOFA APACHE Age Comorbidity Heart failure Chronic renal disease Autoimmune disease Haematologic disease Respiratory coinfection	Mean 4.9 vs 8.4 p<0.001 Mean 12.53 vs 19.69 p<0.001 Mean 43.7 vs 48.4 p<0.001 69.6% vs 79.4% p=0.02 6% vs 11% p=0.03 4% vs 10% p=0.003 2.6% vs 5.7% p=0.06 3.7% vs 14.9% p<0.001 14.6% vs 23.4% p=0.01
Pereira [40]	Multiple (ESICM)	ICU adm	265	Death	SAPS III APACHE II	Mean 51 vs 60 p<0.001 Mean 25 vs 20 p<0.001
Delgado-Rodriguez [41]	Spain	Hospitalised	813	Death/ICU	Age 46-65 (ref <19) Age >65 (ref <19) Ex-smoker (note current smoker not sig) COPD DM Corticosteroids H2 blockers 2-3 comorbidities (ref 0) >3 comorbidities (ref 0)	OR 2.21 (1.09-4.71) OR 2.44 (1.03-5.83) OR 1.97 (1.07-3.52) OR 2.02 (1-3.87) OR 2.25 (1.21-4.02) OR 3.05 (1.14-7.35) OR 2.08 (1.05-6.66) OR 2.21 (1.09-4.6) OR 2.98 (1.47-6.24)
Bramley [42]	US	ICU adm	108 (plus 46 childr en)	Death	Illness to adm <2 days Asthma CXR pneumonia Treatment <2 days Sepsis syndrome	10/37 deaths vs 51/115 p =0.06 4/11 death vs 33/117 p=0.05 32/35 death vs 69/107 p<0.001 2/28 death vs 34/97 p<0.01 21/30 death vs 15/100 p<0.01
Chen [43]	Taiwan	Paediatric adm	61	Death/ICU	BMI >25 SOB CRP >3 2ary bacterial infection Infiltration on CXR Pleural effusion on CXR	3/11 w outcome vs 0/37 p=0.008 8/14 w outcome vs 8/47 p=0.008 6/12 w outcome vs 5/46 p=0.008 4/14 w outcome vs 2/47 p=0.03 6/14 w outcome vs 33/42 p=0.03 3/14 w outcome vs 0/42 p=0.02
Chen [44]	Taiwan	ED presentations (note 2007-9 all flu)	146	Hospital adm	Underlying illness SOB Headache General ache CXR positive finding	89% adm vs 69% 13% adm vs 6% 0 adm vs 5% 2% adm vs 8% 29% adm vs 15%

					WCC Neutrophil Hb	High 9% adm vs 6%, low 25 vs 19 High 25% adm vs 12%, low 11 v 9 Low 29% adm vs 20%
Kok [45]	Australia	ICU adm	173	Death (hospital)	Obesity	6% in obese vs 20% nonobese Note: nonsignificant when corrected for severity of illness
Estella [46]	Spain	Hosp adm with viral pneumonia	24	ICU adm	SaO2	96.6+/-2 ward vs 87.7 +/-5 ICU
Garnacho-Montero [47]	Spain	ICU adm H1N1	1120	Death	Age>65	32% mortality vs 22%
	Spain	ICU adm H1N1 age>65 (subgroup of above)	129	Death	Haematologic disease Immunosuppression >48h before oseltamivir	OR 5.1 (1.7-14.7) OR 3.7 (1.5-8.7) OR 2.7 (0.9-7.6)
Esterman [48]	Australia	Adm <6 months	28	Admission	Smoker in household NICU/SCBU Preterm birth Median household size	36% vs 20% population 25% vs 14.4% population 14% vs 8.2% population 5 vs 2.5 population
Dalziel [49]	International (PERN)	Children adm	265 + 265 age-matched	Severe outcome	Asthma Chronic lung disease Heart disease Renal disease Cerebral palsy Preterm birth Dyspnoea Increase/purulent sputum Seizures (acute) Irritable/drowsy Wheeze (complaint) Resp rate Heart rate SaO2 <93/supplemental O2 Chest retraction Accessory muscle use Creps Wheeze o/e Prolonged CRT Altered mental status Signs of dehydration Abnormal CXR	All OR: 2.7 (1.7-4.2) 9.8 (4.2-22.8) 6.0 (2.3-15.5) 8.0 (1.0-64.0) 34.5 (8.5-141) 4.1 (2.0-8.5) 9.9 (5.7-17.1) 11.0 (3.4-35.9) 5.6 (2.2-14.5) 2.9 (1.7-5.1) 7.0 (3.5-14.10) 0.15 (0.046-0.26) -0.19 (-0.3—0.086) 39.7 (12.6-125) 18.5 (9-38) 25.2 (10.7-59.7) 7.8 (4.1-14.8) 8.1 (4.6-14.4) 16.7 (5.2-53.4) 76.3 (10.3-564) 12.3 (4.5-33.6) 6.2 (3.1-12.5)
Capelastegui [50]	Spain	Hospitalised >18y	618	Severe complication (death, IPPV, septic shock, ARDS, "resuscitation maneuvers"	Age Male Smoker Number comorbidities Multilobar/bilateral Pneumonia Confusion Fever Dyspnoea Score: 1 pt for age>45, male, >2 comorbidities, pneumonia; 2 pt for confusion, dyspnoea	OR 2.6 (1.4-5) 46-65y, 2.8 (1.3-6) >65y OR 2.2 (1.3-3.8) 2.1 (1.1-3.9) yes, 2.2 (1.1-4.4) ex 2.9 (1.4-5.8) >2 (ref 0) 2.5 (1-5.9) 1.8 (1-3) 3.9 (1.8-8.5) 0.4 (0.2-0.8) 4.7 (2-11) AUROC 0.74 (0.68-0.8)
Lopez-Delgado [51]	Spain	ICU with respiratory failure from H1N1	60	Hospital mortality	BMI >30 Dyslipidaemia Creatinine	37% survivors vs p 0.021 18% survivor vs 8% p 0.049 108.4+/-74 survivor vs 186.4+/220 p 0.043

					Hb Platelets* pH pCO2 (mmHg) Bacterial coinfection	13+/-2 survivor vs 11.4+/-3.2 p 0.033 214 +/-101 survivor vs 113+/-82 p 0.002* 7.4+/-0.7 survivor vs 7.28+/-0.15 p<0.001 41+/-21 survivor vs 58+/-24 p0.04 10.4% survivor vs 41.6% p 0.022 *Retained in multivariate
Greenbaum [52]	US	Hospitalised 18-65y with lab-confirmed flu (not all pandemic)	9092	Mortality or ICU admission	Heavy alcohol use Chronic lung disease Asthma Cardiovasc disease Chronic metabolic disease	RR 1.34 (1.04-1.74) RR 1.35 (1.23-1.48) RR 0.85 (0.77-0.93) RR 1.12 (1.02-1.24) RR 1.29 (1.19-1.4)
		Hospitalised >65y with lab-confirmed flu (not all pandemic)	6584		Heavy alcohol use Chronic lung disease Cardiovasc disease	RR 2.47 (1.69-3.6) RR 1.51 (1.36-1.68) RR 1.41 (1.26-1.57)
Delgado-Rodriguez [53]	Spain	Hospitalised with lab-confirmed flu	1520	Mortality or ICU admission	Respiratory failure Cardiovasc disease* Cancer* Systemic steroids pre-adm* Pneumonia at adm Number organ malfunction at adm (continuous)* Alcohol >80g/day	OR 2.14 (1.12-4.08) OR 3.10 (1.89-5.09)* OR 2.61 (1.61-4.24)* OR 4.69 (2.46-8.95)* OR 1.98 (1.332-9.5) OR 3.31 (2.62-4.2)* OR 1.99 (1.09-3.64) *Retained in multivariate
Borse [54]	India	Adult ICU adm with lab-confirmed H1N1	100	Hospital mortality	No significant clinical or radiological predictors	
Mortensen [55]	California	Hospitalised/died with influenza A & asthma	170	ICU adm/death	Renal disease Infiltrates on CXR	OR 3.87 (1.08-13.87) OR 9.71 (3.93-23.99)
Semple [56]	UK	Hospitalised (FLU-CIN) >16y	1040	HDU/ICU/death	Severe resp distress Increased resp rate SaO2 <93% Resp exhaustion Severe dehydration/shock Altered consciousness Other clinical concern	OR 2.27 (1.63-3.16) OR 2.37 (1.69-3.31) OR 6.42 (4.49-9.18) OR 6.13 (2.64-14.2) OR 2.89 (2.01-4.16) OR 4.99 (2.82-8.81) OR 2.19 (1.39-4.36)
		Hospitalised (FLU-CIN) <16y	480		Severe resp distress SaO2 <93% Severe dehydration/shock Altered consciousness Other clinical concern	OR 3.16 (1.91-5.22) OR 4.95 (2.97-8.25) OR 11 (1.98-61.1) OR 6.44 (3.49-11.9) OR 2.38 (1.16-4.9)
Kusznierz [57]	Argentina	Hospitalised, lab-confirmed H1N1	242	Death	Obesity Diabetes Heart disease Hypertension Renal disease CXR consolidation Secondary bacterial inf ARDS Sepsis/shock Tamiflu <48h	4% survivors vs 40% p<0.001 6% survivors vs 19% p 0.002 6% survivors vs 19% p 0.02 16% survivors vs 38% p 0.03 4% survivors vs 11% p 0.04 75% survivors vs 38% p<0.001 0.6% survivors vs 7% p0.002 19% survivors vs 72% p <0.001 6% survivors vs 54% p<0.001 27% survivors vs 13% p0.012

Mertz [58]	Multiple	Meta-analysis (seasonal flu)	75871	Death	Obesity Cardiovascular disease Immunocompromise Endocrine disease	OR 30.10 (1.17-773.12) OR 1.97 (1.06-3.9) OR 3.81 (1.28-11.35) OR 13.92 (3.71-52.13)
				ICU admission	Chronic lung disease	OR 4.46 (1.34-14.79)
		Meta-analysis (pandemic flu)	534911	Death	<4/52 postpartum Obesity Chronic lung disease Cardiovasc disease Immunocompromise Malignancy Neuromusc disease Anaemia/haemoglobinopathy Diabetes Liver disease Metabolic disease Renal disease	OR 4.43 (1.24-15.81) OR 2.74 (1.56-4.8) OR 1.71 (1.17-2.51) OR 2.92 (1.76-4.82) OR 3.67 (1.78-7.58) OR 3.1 (2.35-4.1) OR 2.68 (1.91-3.75) OR 2.28 (1.35-3.84) OR 2.21 (1.37-3.57) OR 2 (1.32-3.04) OR 1.83 (1.19-2.79) OR 3.11 (1.54-6.28)
				ICU admission	Obesity Chronic lung disease Cardiovasc disease Neuromusc disease Diabetes Liver disease	OR 1.81 (1.48-2.22) OR 1.48 (1.19-1.83) OR 1.7 (1.39-2.08) OR 2.63 (1.83-3.79) OR 1.6 (1.32-1.94) OR 2.65 (1.44-4.88)
Morton [59]	UK	Adults admitted to hospital with PCR-confirmed H1N1 2010-11	101	Critical care admission	Simple Triage score PaO2/FiO2 ratio	AUROC 0.816 (0.72-0.9) AUROC 0.885 (0.81-0.96)
				Mechanical Ventilation	Simple Triage score PaO2/FiO2 ratio	AUROC 0.798 (0.7-0.89) AUROC 0.885 (0.82-0.95)
Garcia [60]	US	Children (<18) presenting to hospital with laboratory-confirmed H1N1 2009-10	695	Non-hospitalised vs hospitalised vs ICU	Dysnpoea Fatigue Fever Headache Myalgia Tachycardia Haematological disease Lung disease Prematurity Seizure disorder	7% vs 24% vs 55% p=0.006 8% vs 10% vs 16% p=0.004 96% vs 94% vs 84% p=0.001 26% vs 10% vs 9% p=0.003 22% vs 8% vs 5% p=0.001 5% vs 5% vs 13% p=0.006 4% vs 10% vs 8% p=0.009 2% vs 9% vs 15% p=0.001 3% vs 6% vs 16% p=0.001 1% vs 4% vs 12% p<0.001
Khandaker [61]	Australia	Children <15 admitted to hospital with laboratory-confirmed influenza	601 (506 with H1N1)	PICU admission	Neurologic disease Lung disease Bacterial coinfection	OR 2.3 (1.14-2.61) OR 3.58 (1.41-9.07) OR 6.89 (3.15-15.06)
				Mechanical ventilation	Lung disease Bacterial coinfection	OR 5.18 (1.8-14.86) OR 5.61 (2.2-14.28)

Appendix II: PRIEST Data Sources

Dataset Name and [short name]	**Source**	**Details.** **Record inclusion/exclusion criteria.** **Included direct identifiers.**	**Date range**
Ambulance Electronic Patient Record [ePR]*[1]	Yorkshire Ambulance Service NHS Trust	Information about the care of patients who receive a face-to-face contact with ambulance service. Includes: demographics; main problem; comorbidities; findings; treatments; care plan. We use this information to identify the characteristics of the patients' conditions at the time of the ambulance service contact and the care provided by the ambulance service and the disposition of the contact (e.g. care plan). We will use this information to estimate the effect of using different triage methods within the ambulance service context. Inclusion criteria: Recorded suspected or confirmed COVID19. Exclusion criteria: Identified NHS national data opt-out. Direct patient identifiers present: NHS Number, date of birth, names, postcode of residence, postcode of incident.	2020-03-26 to 2020-09-30 (inclusive)
Ambulance Computer Aided Dispatch [CAD]*[1]	Yorkshire Ambulance Service NHS Trust	Information about the prioritisation and management of calls to the ambulance service. Includes: call date and time; patient demographics; broad triage group; ambulance service urgency categorisation; transportation including location, date and time; referral to other service. We use this information to identify the ambulance service's broad triage and prioritisation of the patient contact, and the disposition of the contact (e.g. telephone only; treated on scene; conveyed to hospital; referred to other	2020-03-26 to 2020-09-30 (inclusive)

Dataset Name and [short name]	Source	Details. Record inclusion/exclusion criteria. Included direct identifiers.	Date range
		service; etc.). We primarily use this information to link patient records to identify pathways through the Emergency and Urgent Care System (e.g. NHS111, Ambulance, ED, admission to hospital). Inclusion criteria: Call belonging to included ePR record OR Call with no ambulance response but managed according to the Advanced Priority Medical Despatch triage card 36 (a pandemic triage process for patients with suspected COVID). Exclusion criteria: Identified NHS national data opt-out. Direct patient identifiers present: NHS Number, date of birth, names, postcode of residence, postcode of incident.	
NHS111 telephone service [NHS111]*[1]	Yorkshire Ambulance Service NHS Trust	Information about the management of calls made to the NHS111 telephone service. Includes: call date and time; patient demographics; symptom group; disposition; referral to other service. We use this information to identify the NHS111 telephone service's broad triage and prioritisation of the patient contact, and the disposition of the contact (e.g. telephone only; treated on scene; conveyed to hospital; referred to other service; etc.). We primarily use this information to link patient records to identify pathways through the Emergency and Urgent Care System (e.g. NHS111, Ambulance, ED, admission to hospital). NHS111 telephone triage processes changed over time and we will also investigate the impact of these changes.	2020-02-01 to 2020-09-30 (inclusive)

Dataset Name and [short name]	**Source**	**Details.** **Record inclusion/exclusion criteria.** **Included direct identifiers.**	**Date range**
		Inclusion criteria: COVID-19 related final disposition recorded. Exclusion criteria: No NHS Number recorded OR identified NHS national data opt-out. Direct patient identifiers present: NHS Number, date of birth, postcode of residence, postcode of incident.	
Emergency Department triage (baseline) and follow-up [core-PRIEST]*[1]	Participating NHS Trusts in England, Wales and Northern Ireland	Information about the care of patients at participating NHS hospital sites. Includes: demographics; past medical history; lifestyle information; clinical observations; investigations; findings; diagnoses; treatments; disposition / admission; vital status; DNR order present; inpatient care; adverse events; discharge. We use this information to identify the characteristics of the patients' conditions at the time of the Emergency Department (ED) contact and the care provided by the hospital (in ED and, potentially, subsequently as an inpatient). We will use this information to estimate the effect of using different triage methods within the ED context. Inclusion criteria: Assessing clinician in emergency department recorded suspected or confirmed pandemic infection. Direct patient identifiers present: NHS Number, date of birth, date of death.	2020-03-26 to 2020-09-30 (inclusive)
Hospital Episode Statistics: Admitted Patient Care [APC]*[1]	NHS Digital (based on data routinely supplied by hospitals providing	Information about the care of patients admitted to hospital. Includes: demographics; period of care (dates); level of care (high/intensive); diagnoses; admission and discharge details.	2020-02-01 to 2020-09-30 (inclusive)

Dataset Name and [short name]	Source	Details. Record inclusion/exclusion criteria. Included direct identifiers.	Date range
	care to patients funded by the NHS in England)	We use this data to understand what happened to patients, identifying subsequent care activity after initial COVID-related contact with pre-hospital services and/or COVID triage, potentially in a different hospital Trust (see core-PRIEST). Inclusion criteria: Patient identified in ePR, CAD, NHS111 or core-PRIEST (English Trusts only) data. Exclusion criteria: Identified NHS national data opt-out. Direct patient identifiers present: NHS Number.	
Hospital Episode Statistics: Critical Care [CC]*[1]	NHS Digital (based on data routinely supplied by hospitals providing care to patients funded by the NHS in England)	Information about the care of patients admitted to hospital who receive critical care. Includes: demographics; level, type and duration of critical care; admission and discharge (to critical care) details. We use this data to understand the severe adverse outcomes amongst the identified patient cohort, those who had a COVID-related contact with pre-hospital services and/or COVID triage, potentially in a different hospital Trust (see core-PRIEST). Inclusion criteria: Patient identified in ePR, CAD, NHS111 or core-PRIEST (English Trusts only) data. Exclusion criteria: Identified NHS national data opt-out. Direct patient identifiers present: NHS Number.	2020-02-01 to 2020-09-30 (inclusive)

Dataset Name and [short name]	**Source**	**Details.** **Record inclusion/exclusion criteria.** **Included direct identifiers.**	**Date range**
Emergency Care Dataset [ECDS]*[1]	NHS Digital (based on data routinely supplied by hospitals providing care to patients funded by the NHS in England)	Information about the care of patients who attend unscheduled or emergency care services (e.g. A&E, Minor Injury Unit; Walk-in Centre). Includes: demographics; investigations; diagnoses; treatments; acuity; disposition. Inclusion criteria: Patient identified in ePR, CAD, NHS111 or core-PRIEST (English Trusts only) data. Exclusion criteria: Identified NHS national data opt-out. We use this data to understand what happened to patients, identifying subsequent care activity after initial COVID-related contact with pre-hospital services and/or COVID triage, potentially in a different hospital Trust (see core-PRIEST). Direct patient identifiers present: NHS Number, date of birth , postcode of residence (postcode only required if 2011 census output area is unavailable).	2020-02-01 to 2020-09-30 (inclusive)
Demographics [DEMO]*[1]	NHS Digital	Basic demographic information about patients. Includes: sex, date of birth (to derive age at activity), postcode of residence (for deriving local area information, e.g. index of deprivation; rural-urban; output area classification). We use this data as a “single source of truth” (SSOT) of patient characteristics for patients in our cohort. Since we may have many records, some of which conflict, we need to select a single record and use this consistently across analyses. Age, sex, and characteristics of the area in which a person lives (e.g. deprivation) are important factors to investigate and to control for when estimating effects of different triage methods.	Record as at request date between: 2020-02-01 to 2020-09-30 (inclusive)

Dataset Name and [short name]	**Source**	**Details.** **Record inclusion/exclusion criteria.** **Included direct identifiers.**	**Date range**
		Inclusion criteria: Patient identified in ePR, CAD, NHS111 or core-PRIEST (English Trusts only) data. Exclusion criteria: Identified NHS national data opt-out. Direct patient identifiers present: Date of birth, postcode of residence (postcode only required if 2011 census output area is unavailable).	
Death Registration [DR]*[1]	NHS Digital (data provided by Office for National Statistics [ONS] based on data provided by register offices)	Information about registered deaths. Includes: date of death; category of place of death; causes of death. We use this data to understand if a patient in our identified cohort died and whether their death was related to COVID19. Inclusion criteria: Patient identified in ePR, CAD, NHS111 or core-PRIEST (English Trusts only) data. Exclusion criteria: Identified NHS national data opt-out. Direct patient identifiers present: Date of death.	2020-02-01 to 2020-09-30 (inclusive)
General Practice Extraction Service (GPES) Data for Pandemic Planning and Research [GDPPR]*[1]	NHS Digital (based on data extracted from GP records in England)	Information about risk factors / comorbidities (e.g. smoking status, previous diagnosis of diabetes). Risk factors and comorbidities are important factors to investigate and to control for when estimating effects of different triage methods. Inclusion criteria: Patient identified in ePR, CAD, NHS111 or core-PRIEST (English Trusts only) data.	All records up to 2020-09-30 (inclusive)

Dataset Name and [short name]	**Source**	**Details.** **Record inclusion/exclusion criteria.** **Included direct identifiers.**	**Date range**
		Exclusion criteria: Dissented from secondary use of GP patient identifiable data OR identified NHS national data opt-out. Direct patient identifiers present: NHS Number	
Pseudonymised Unique Property Reference Number (UPRN) and property classification [PUPRN]*[1,2]	NHS England (based on patient registration data from GP practices in England)	Pseudonymised UPRN (such that University of Sheffield can identify patients who live in the same property, within the cohort, but cannot identify the property itself) and property classification of each patient's place of residence (e.g. "Care / Nursing Home", "Prison", "House In Multiple Occupation"). This data allows us to identify a patients' residential setting and the impact this may have had on patients' care. This also allows us to more correctly estimate overall effects in the possible circumstance that many patients from a single (or few) care/nursing homes suffered severe adverse outcomes. Inclusion criteria: Patient identified in ePR, CAD, NHS111 or core-PRIEST (English Trusts only) data. Exclusion criteria: NHS national data opt-out. **Direct patient identifiers present:** NHS Number.	As at date of extraction from NHS England data store, between 2020-08-01 and 2020-09-30 (inclusive)

* Legal basis for disclosure of confidential patient information:
[1] NHS Act 2006 - section 251 .
[2] The data held by NHS England does not represent confidential patient information (CPI). However, identifying that a subset of it belongs to our specific cohort, via sharing of NHS Numbers belonging to the cohort by the University of Sheffield to NHS England, does mean that the subset represents CPI.

Appendix III: NHS Digital Data items

ECDS	Demographics	HES Admitted Patient Care	HES Critical Care	ONS Death Registrations
Patient pseudo-ID Arrival date & Time Arrival mode Ambulance Incident number Ambulance organisation Attendance category Provider and site identifiers Department type Patient age Patient ethnicity Acuity Chief complaint Comorbidities Diagnoses Investigations Treatments Decision to admit Referral (service type) Discharge status Discharge destination Conclusion + Departure dates & times Census Output Area, 2011	Patient pseudo-ID NHS Number Date of birth Current postcode [or Census Output Area, 2011, if available]	Patient pseudo-ID Admitted date and time Admission method Admission source Patient age Patient ethnicity Primary diagnosis Secondary diagnoses Discharge date Discharge method Discharge destination Hospital provider spell number SUS spell ID Episode start date Episode end date Episode order Provider and site identifiers Patient classification Main speciality Treatment speciality Care level (general/specialist) Census Output Area, 2011	Patient pseudo-ID Admitted date and time Provider and site identifiers Unit function (type/specialism) Unit configuration (level 2/3) Admission source Admission type Basic respiratory support days Advanced respiratory support days Basic cardiovascular support days Advanced cardiovascular support days Renal support days Critical care level 2 days Critical care level days Discharge date Discharge status Discharge destination	Patient pseudo-ID Date of Death Place of Death (type) Underlying cause of death Cause of death (all) mentions