The University Of Sheffield.

PAndemic INfluenza Triage in the Emergency Department

The *PaInTED* Study

Health Services Research Section, School of Health and Related Research

Protocol

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PAndemic INfluenza Triage in the Emergency Department: The PAINTED Study

Research objectives

1. To determine the discriminant value of currently available emergency department triage methods for predicting severe illness or death in patients presenting with suspected pandemic influenza
2. To determine the independent predictive value of presenting clinical characteristics and routine tests for severe illness or death in patients presenting with suspected pandemic influenza
3. To determine whether the discriminant value of emergency department triage can be improved by developing two new triage methods based upon (a) presenting clinical characteristics alone and (b) presenting clinical characteristics, electrocardiogram (ECG), chest X-ray and routine blood test results

Existing research

The United Kingdom (UK) influenza pandemic contingency plan predicts around 750,000 excess emergency department attendances and 82,500 excess hospitalisations during a pandemic [1]. Given that there is likely to be significant staff absence it will be impractical for all patients fully to be assessed by a senior clinician. If, as is likely, interpandemic levels of care cannot be offered during a pandemic, methods of triage and resource allocation will have to be fair, robust and reproducible [2].

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.

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. The level of risk used to trigger these decisions need not necessarily be fixed or determined in advance. Indeed, it is likely that decision-making thresholds could change during the course of a pandemic as the balance between resource availability and demand changes. Triage methods that use a risk prediction score to determine the need for hospital care may therefore be more useful than a triage rule that classifies patients into admission and discharge categories.

Current Health Protection Agency (HPA) guidance, supported by the British Thoracic Society and British Infection Society, recommends the use of the CURB-

65 pneumonia score [3]. This score uses five variables (confusion, urea level, respiratory rate, blood pressure and age) to generate a score between zero and five. More recent Department of Health guidelines on surge capacity in a pandemic also considered use of a physiological-social score (Pandemic Modified Early Warning Score (PMEWS)) [4]. This score uses physiological variables, age, social factors, chronic disease and performance status to generate a score between zero and seven. The most recent national guidance, specific to H1N1 (swine), includes a new swine flu hospital pathway for emergency department management with seven criteria, any one of which predicts increased risk and the need for hospital assessment [5].

Existing literature shows CURB-65 to perform reasonably well as a mortality predictor in an emergency department population with community-acquired pneumonia (area under the Receiver-Operator Curve (AUROC) 0.76) [6] but less well in predicting the need for high-level care (AUROC 0.69 [7] and 0.64 [8]). The physiological-social score considered by the Department of Health (PMEWS) is not a particularly good mortality predictor in community-acquired pneumonia (used as a proxy for pandemic influenza), with AUROC 0.66 but performed much better predicting requirement for higher level care (AUROC 0.83) [8] and has shown promise when used in the prehospital setting to determine need for emergency department attendance (AUROC 0.71 [9] and 0.8 (personal communication J Gray Feb 2009)). The most recently issued national guidelines appear to have been developed by expert consensus and have as yet undergone no validation in the appropriate patient populations.

To our knowledge there have been no studies evaluating any of these triage methods in patients with suspected pandemic influenza and no studies to develop a risk prediction score in the emergency department population with suspected pandemic influenza.

We are not aware of any studies currently planned or underway to test or develop emergency department triage methods in the current pandemic. ICNARC have been commissioned to undertake a swine flu triage project (SwiFT) for admitted patients referred to critical care. SwiFT involves modelling to identify which of those patients who would usually be admitted to critical care may be refused admission at the height of the pandemic (once all surge capacity measures have been instituted) - i.e. both those with a very high likelihood of death despite critical care and those that may be expected to survive without critical care.

Our project and SwiFT will be examining different triage decisions and different patient groups and are clearly separate projects. We will be collaborating with INCARC to ensure that our research is synergistic and does not involve any unnecessary duplication of work.

Research methods

We will undertake a prospective cohort study of patients presenting to the emergency department with suspected pandemic influenza. Emergency department staff will be provided with a standardised form for assessing such cases that will double as clinical notes and study data collection form. It will include the elements of the CURB-65 score, the physiological-social score, the swine flu hospital pathway and any other measures that could be routinely recorded in the emergency department (co-morbidities, physiological observations, routine blood tests, ECG and chest x-ray). We will also record details of any pre-presentation anti-viral medication, antibiotics and immunisation status (once available). Research staff will then follow patients up until 30 days after attendance by hospital record review and, if appropriate, general practitioner contact to identify patient outcomes.

Planned Intervention

We will evaluate triage methods used to determine whether a patient with suspected pandemic influenza should be admitted to hospital or not, and whether they should be admitted to intensive or high dependency care. These will include the CURB-65 score, the physiological-social score and the swine flu hospital pathway. We will also develop two new 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 current Department of Health guidance.

Planned inclusion/exclusion criteria

We will include all adults and children presenting the emergency department of the participating hospitals with suspected pandemic influenza during the peak

of the pandemic. Patients will be eligible for inclusion if they meet the current clinical diagnostic criteria of (1) fever (pyrexia ≥38°C) or a history of fever and (2) influenza-like illness (two or more of cough, sore throat, rhinorrhoea, limb or joint pain, headache, vomiting or diarrhoea) or severe and/or life-threatening illness suggestive of an infectious process; or if they meet any future clinical diagnostic criteria recommended by the Department of Health. The assessing clinician will determine eligibility and complete the data collection form if the patient is considered to have suspected pandemic influenza. We will not attempt to retrospectively apply the clinical diagnostic criteria and exclude patients who appear to have been inappropriately included. Patients will only be excluded if they request exclusion from the study.

Ethical arrangements

We are seeking fast track Research Ethics Committee (REC) and National Information Governance Board (NIGB) approval. Application forms for both are completed and ready to send as soon as a funding decision is made.

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.

Data will be abstracted from the collection form and hospital notes by researchers working with an honorary contract from the hospital Trust or researcher passport recognised by the Trust. This researcher will keep a record of all patients who withdraw from the project but will not communicate details to other staff. He/she will enter anonymised data onto a secure online database provided by the Clinical Trials Unit at the University of Sheffield. The research team in general will only have access to anonymised data on the secure database.

Patients involved in the study will potentially benefit from the use of the standardised patient assessment 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 influenza 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 details of a named contact for further information. Information leaflets will be available that briefly describe the nature and purpose of the study and details of a named contact for further information. Copies of the data collection form will also be provided to allow

patients to see what data are being collected. We will issue press releases and use media contacts in Sheffield and Manchester to publicise the project and maximise public awareness.

Obtaining informed consent from participants

We will not be seeking 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.

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. A copy of the data collection form will be retained by the researcher in a secure location in each hospital. These will be destroyed six months after the end of the project. The anonymised database will be maintained by the Clinical Trials Unit until ten years after the end of the project.

Proposed sample size

The sample size will ultimately depend upon the size and severity of the pandemic, but combining our data collection method with clinical case documentation will ensure that data are collected for most cases. We plan to collect data during the pandemic at four hospitals in Sheffield and Manchester covering a population of over 1 million. We are piloting data collection now so that it can start as soon as funding is approved and ethical and regulatory requirements are satisfied.

Department of Health estimates of a 25% clinical attack rate and illustrative case hospitalisation and case fatality rates of 0.55% and 0.37% respectively suggest that a pandemic may lead to 12,500 emergency department attendances, 1400 hospitalisations and 900 excess deaths in our population [1]. If half of these occur while we are collecting data then around 6000 cases with 600 positive outcomes will be available for analysis.

We will split the database for analysis into two datasets of equal size, one for developing new scores and testing existing scores, and one for comparing the new and existing scores. To develop a new triage method we need around 10 events per parameter tested in the model, so 200 positive cases would allow us to test 20 parameters. A sample size of 283 positive cases ensures a power of 80% 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 [10].

Statistical analysis

Existing triage methods: CURB-65, the physiological-social score and the swine flu clinical pathway will be assessed by calculating the area under the ROC curve (c-statistic) for discriminating between cases with and without a positive outcome (defined as death or need for support of respiratory, cardiovascular or renal function) and sensitivity and specificity at key decision-making thresholds.

New triage methods: As outlined above, we will develop two new triage scores: one based on initial assessment only and the other based on all emergency department data. We will test the association of each potential clinical predictor variable with outcome and then undertake logistic regression to identify independent predictors of outcome. The strongest independent predictors of outcome will then be combined to form a new triage score. Continuous predictor variables will be divided into categories on the basis of the relationship of the variable with outcome. Integer weights will be assigned to each category of predictor variable according to the coefficient derived from a multivariate model using categorised independent predictors. This will generate a composite clinical score in which risk of positive outcome increases with the total score.

The data set will be split randomly into two equal sets. The first set will be used to compare the c-statistic of existing scores and derive the two new scores. The second set will be used to compare the c-statistic of the two new scores to that of the best existing score.

Proposed outcome measures

Patients will be followed up by researcher review of case note and hospital computer record review up to 30 days after emergency department presentation. If they die or require respiratory, cardiovascular or renal support they will be defined as having a positive outcome. If they survive to 30 days without requiring respiratory, cardiovascular or renal support they will be defined as having a negative outcome. If a severe pandemic leads to hospital resources being overwhelmed we will categorise patients as having a positive outcome if they were deemed to have needed respiratory, cardiovascular or renal support but were denied this due to lack of resources. We will record whether they are treated with antiviral agents or antibiotics and the length and location of any hospital stay. We will also record details of any hospital readmissions and adverse events (defined as any potential or actual threat to the patient's wellbeing) that occur during 30-day follow-up.

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 canulation

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.

Outcome assessment will be based primarily on researcher review of hospital computer records and case notes. If there is no evidence in these of a positive outcome the patient will be recorded as having a negative outcome. If outcome is uncertain (for example, if the patient is transferred to another hospital or leaves hospital against medical advice) the researcher will contact the patient's general practitioner for clarification. This means that there will be a small risk of misclassification if the patient dies or attends another hospital after discharge home, but we believe the resource implications of attempting to identify such cases does not justify the small potential risk of bias.

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 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.

Research Governance

The University of Sheffield will be the study sponsor. The Project Management Group (PMG), consisting of the co-applicants and the appointed research staff, will manage the study. The PMG will meet monthly by teleconference or in person to oversee study progress.

Time constraints mean that we will not be able to convene a formal Steering Committee to review the protocol, meet regularly and fulfil all the normal functions. However, we will ask an independent statistician, clinician and layperson to form a Steering Committee that will provide independent advice and monitor progress by email or telephone.

Project timetable and milestones

We have already prepared ethics and NIGB applications, and are currently piloting the data collection forms. We will be able to start the project as soon as a funding decision is made. Research staff have been identified and can start work on the project at short notice.

	Aug	Sep	Oct	Nov	Dec	Jan
PROCESSES						
Ethics, NIGB and governance	X					
Data collection		X	X	X		
Follow-up			X	X	X	
Data analysis					X	X
Reporting and dissemination						X
STAFFING						
Project manager	X	X	X	X	X	X
Clerical assistant	X	X	X	X	X	X
Database manager	X	X	X	X	X	
Researchers		X	X	X	X	

Expertise

The research team combines the leading experts on emergency management of suspected pandemic influenza (KC, DW and AB) with the statistical expertise and research infrastructure of the Medical Care Research Unit (SG, JN, MC and RW). We also have public health input from MS who is currently on secondment with the Health Protection Agency.

The proposal builds on an existing collaboration developed as part of the MRC-funded DAVROS study (Development and validation of risk-adjusted outcomes for systems of emergency care). For the DAVROS study we have collected presenting data from over 10,000 patients admitted to hospital with a medical emergency and then followed them up to determine their 30-day outcomes. This has involved establishing processes for using routine data without patient consent, including data management and data protection, which have been approved by the Research Ethics Committee and NIGB, and used effectively without significant problems. DAVROS was undertaken to develop a risk-adjustment method but is now also being used by KC, SG and JN to develop a clinical triage tool for emergency medical admissions. Our proposal will apply the data collection and analysis methods used in DAVROS to the specific problem of suspected pandemic influenza.

David Harrison, from the Intensive Care National Audit and Research Centre (ICNARC), has agreed to be a collaborator on the project. He is currently working with us on the DAVROS study. We will draw upon his expertise in risk prediction and ensure that our project works synergistically alongside pandemic influenza research currently being undertaken by ICNARC.

Specific details of the collaborating units:
The Medical Care Research Unit, Sheffield: Steve Goodacre and Jon Nicholl have undertaken many major national evaluations in emergency care, including development of clinical prediction methods. Current projects provide the necessary infrastructure to rapidly undertake the proposed research. Richard Wilson is currently managing the DAVROS study and has developed extensive expertise in data collection, management and protection in observation studies using routine data sources without patient consent.

University Hospital of South Manchester NHS Trust: Kirsty Challen and Darren Walter are emergency physicians 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.

Department of Public Health, Sheffield: Mark Strong is a public health specialist who is currently on secondment with the Health Protection Agency.

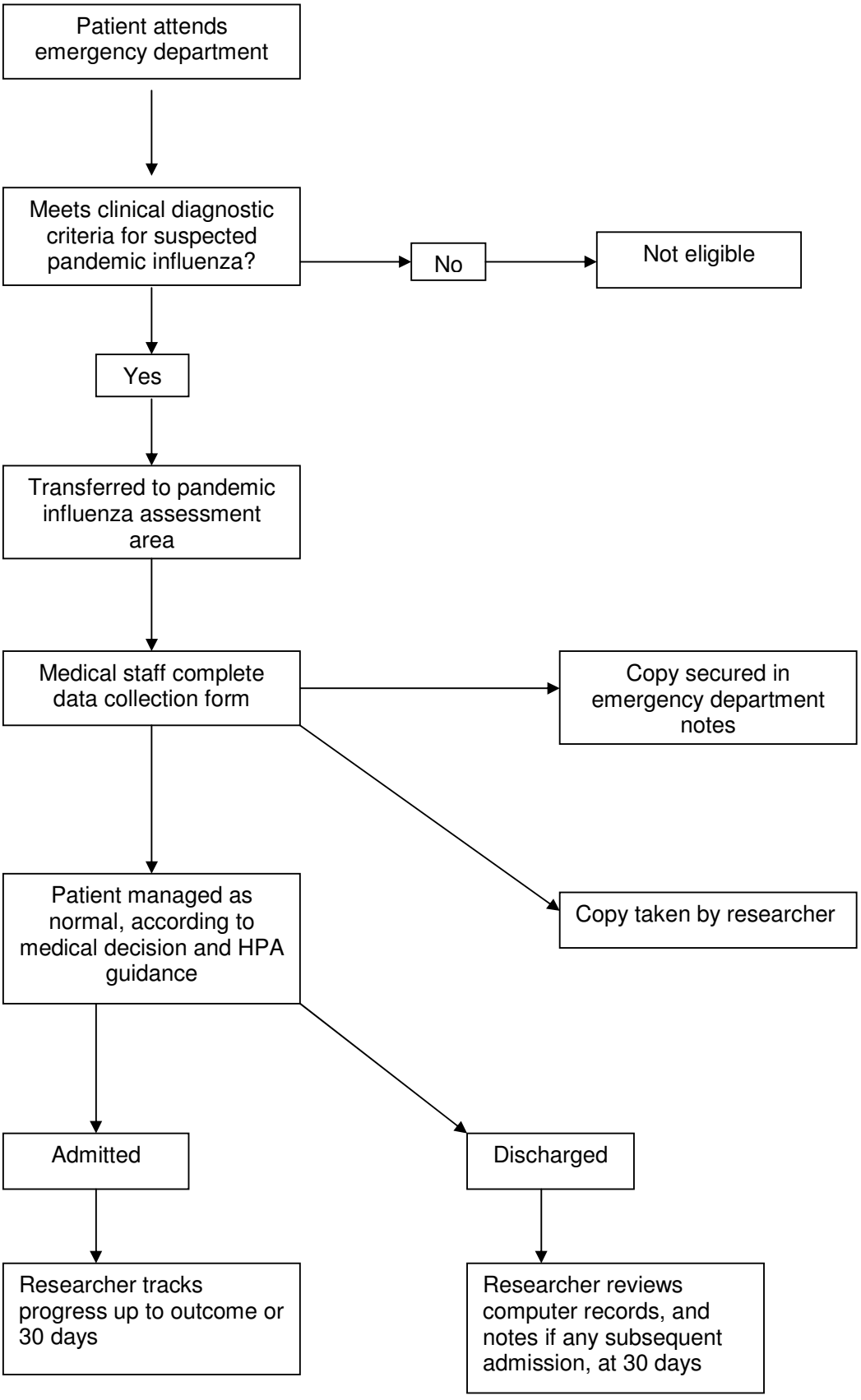
The Sheffield Clinical Trials Unit: Mike Campbell is an experienced medical statistician with expertise in development and validation of clinical prediction rules.

Service Users
Enid Hirst has agreed to be the patient/public representative for the project and has reviewed the proposal. She has acted as a user representative for many previous health service research projects undertaken by our group, including being a lay member of the Steering Committee of the DAVROS study.

Enid previously spent eight years with Sheffield Community Health Council, was a lay member of the Steering Committee for NHS Direct Yorkshire and Humber, was a member of Unscheduled Care Network Board in Sheffield, spent three years with Sheffield Children's Hospital Patient Forum, and has attended Trust Board meetings at Sheffield Children's Hospital for many years as an observer for the Community Health Council and then the Patient Forum. She is now a member of Sheffield LINks (Local Involvement Network), a lay member of the Out of Hours Accreditation Group, is on the Dental Services Joint Planning Group for Sheffield, is a patient representative for the Group looking into Dentally Anxious Patients, and is a patient representative on the new Critical Care/Emergency Medicine Priority Group.

Her role 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

Flow diagram



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