CRITICAL CARE

Performance of influenza-specific triage tools in an H1N1-positive cohort: P/F ratio better predicts the need for mechanical ventilation and critical care admission[†]

B. Morton[1,*], L. Tang[2], R. Gale[3], M. Kelly[3], H. Robertson[4], M. Mogk[5], N. Robin[4] and I. Welters[2,3]

[1]Department of Clinical Sciences, Liverpool School of Tropical Medicine, Liverpool, UK, [2]Institute of Ageing and Chronic Disease, University of Liverpool, Liverpool, UK, [3]Intensive Care Unit, Royal Liverpool University Hospital, Liverpool, UK, [4]Critical Care Department, Countess of Chester Hospital, UK, and [5]MoReData GmbH, Giessen, Germany

*Corresponding author. E-mail: ben.morton@lstmed.ac.uk

Abstract

Background: Pandemic influenza presents a major threat to global health and socioeconomic well-being. Future demand for critical care may outstrip supply and force clinicians to triage patients for admission. We evaluated the Simple Triage Scoring System (STSS), Ontario Health Plan for an Influenza Epidemic (OHPIP) and Pa_{O_2}/Fi_{O_2} (P/F) ratio to determine utility in predicting need for mechanical ventilation.

Methods: We conducted a retrospective case note review of patients admitted to two centres, Royal Liverpool University Hospital and Countess of Chester Hospital, during the UK influenza pandemic of 2010–11. Demand for critical care during this period forced hospitals in Cheshire and Merseyside to implement escalation policies and increase capacity. Inclusion criteria were polymerase chain reaction–confirmed H1N1 influenza and age >18 years. Exclusion criteria were no evidence of treatment for influenza, patient not admitted to hospital or the inability to locate case notes.

Results: One hundred and one patients were included, 29 were admitted to critical care and 23 required mechanical ventilation. The P/F ratio predicted the need for mechanical ventilation with a receiver operating characteristic area under the curve (ROC AUC) of 0.885 (CI 0.817–0.952). Predictive ability was not reduced when the P/F ratio had to be estimated using the Pandharipande tool. The STSS score predicted the need for mechanical ventilation [ROC AUC 0.798 (CI 0.704–0.891)]. The reverse triage component of the OHPIP tool was a poor predictor of patient outcome.

Conclusions: The P/F ratio was a better predictor of need for mechanical ventilation than STSS. The P/F ratio is a simple and accepted determinant of hypoxaemia and should be used if secondary triaging becomes necessary during future influenza pandemics.

Key words: critical care; influenza, human; pandemics; patient admission; triage

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Editor's key points

- Severe pandemic illnesses can potentially overwhelm critical care resources and admission triage systems may be required.
- This study used data from the 2010–11 UK H1N1 influenza pandemic to compare the P/F ratio [Pa_{O_2} (mmHg)/FI_{O_2}] with two specific critical care triage tools in two UK hospitals.
- The P/F ratio performed better than the OHPIP and STSS scores in predicting the need for mechanical ventilation and critical care admission.
- The authors suggest that if critical care referral criteria are to be used a P/F ratio <300 is a suitable threshold.
- More data from different populations are required to confirm these findings.

Pandemic influenza presents a major threat to global health and socio-economic well-being,[1] therefore governments need to plan for future outbreaks to ensure that demand for critical care resources does not overwhelm supply.[2] When demand for resources is high, clinicians must triage patients to select those most likely to benefit from critical care. Two triage tools developed specifically for future pandemics are the Ontario Health Plan for an Influenza Epidemic (OHPIP)[3] and the Simple Triage Scoring System (STSS).[4]

The STSS is a secondary triage tool designed for use in the emergency department to identify patients at risk of deterioration and promote appropriate referral to critical care. The STSS is calculated using routine patient observations (respiratory rate, heart rate, blood pressure, pulse oximetry, and consciousness level) to calculate a five-component score; this does not require a detailed medical history or laboratory data (online only, Supplementary material Table 1[4]). The OHPIP is a tertiary triage tool designed for use by critical care physicians to allocate critical care resources that combines the established Sequential Organ Failure Assessment (SOFA) score[5] with a set of inclusion and exclusion criteria agreed upon by expert consensus.[3] Briefly, inclusion criteria are the need for mechanical ventilation and refractory hypotension. In addition, multiple life-limiting exclusion criteria are defined (e.g. severe trauma, cardiac arrest, metastatic malignant disease).[3] The SOFA score and inclusion and exclusion criteria are combined to give a four-part triage code: limit to medical management or palliate, admit with high priority, admit with intermediate priority, or discharge (online only, Supplementary material Table 2). The OHPIP also includes a reverse triage tool to reassess patients 48 and 120 h after critical care admission to determine whether therapy should be continued or withdrawn.

When using a triage tool, it is imperative that decision-making is transparent and equitable.[6] In the event of an influenza pandemic in the UK, measures to increase critical care capacity are first recommended, followed by implementation of the OHPIP triage tool as a second step.[2] The two stages of the OHPIP tool implementation comprise (1) application of admission triage and (2) implementation of reverse triage in the event of system saturation. However, implementation of either the OHPIP or STSS will be challenging: training will be required, there may be interuser variability, and there may be reticence to use without prior validation. A utilitarian approach to triage implementation dictates that tools should accurately predict patient outcome in order to deliver the greatest benefit to the greatest number of patients.[7] There are studies that have attempted to retrospectively correlate the OHPIP and STSS with patient outcome after the 2009 H1N1

influenza pandemic. However, these incorporated only small, unselected patient cohorts,[8–10] so only limited conclusions can be drawn about the usability and validity of these scores.

Refractory hypoxaemia is recognised as a major feature of critically ill patients with H1N1 influenza.[11] Oxygen exchange measured using the P/F ratio is routinely used in critical care as part of the diagnostic criteria for adult respiratory distress syndrome (ARDS).[12] Therefore it is a familiar tool that would require no additional training to implement as a secondary triage tool during a future influenza pandemic. Compared with the STSS, validation of the P/F ratio as a single determinant of patient outcome in influenza would potentially be a much simpler, universally understood and accepted triage tool. We used the P/F ratio as a comparator for the proposed triage tools to benchmark predictive ability.

The aim of our study was to assess the ability of the P/F ratio and OHPIP and STSS tools to predict the need for mechanical ventilation in a representative patient cohort. Determination of the utility of the proposed triage tools will help to inform clinicians and health care service providers in planning for future pandemics.

Methods

Patients

We performed a retrospective case note review of patients with confirmed H1N1 influenza during the UK influenza pandemic of 2010–11. Two centres were included in the review: the Royal Liverpool University Hospital, an inner-city tertiary care centre with >28 000 accident and emergency (A&E) department admissions per year, and the Countess of Chester Hospital, a district general hospital with >16 000 A&E admissions per year. One hundred and forty-nine patients tested positive for H1N1 influenza across the two hospital sites, 134 patients at the Royal Liverpool and 15 patients at the Countess of Chester. Patients were included if they had H1N1 influenza confirmed by polymerase chain reaction (PCR) and were age >18 years. Patients were excluded if laboratory results did not correlate with the clinical notes (e.g. no evidence of treatment for influenza), the patient was not admitted to the hospital (e.g. nasal swab sent from community) or if case notes could not be located. One hundred and one patients met the criteria for inclusion (Fig. 1). We reviewed medical case notes, laboratory results and Intensive Care National Audit and Research Centre (ICNARC) case-mix programme data for analysis. Two independent reviewers examined the records; databases were then cross-checked, with any outstanding disparities judged by the senior author. There was a need for senior arbitration in two cases. The Bristol Research Ethics Committee approved the study plan (13/LO/0609) and deemed that individual patient consent was not necessary for this study.

Triage tools

We retrospectively applied the OHPIP,[3] STSS[4] and P/F ratio based on the recorded information. For the OHPIP we used inclusion and exclusion criteria as described by Christian *et al.*[3] (online only, Supplementary material Tables 1 and 2). We applied a published tool for approximation of the P/F ratio in the absence of an arterial blood gas (log $Pa_{O_2}/FI_{O_2} = 0.48 \times 0.78 \times \log Sa_{O_2}/FI_{O_2}$).[13] In addition, we used the Richmond Agitation and Sedation Score to approximate the Glasgow Coma Scale if the patient was sedated at the point of referral.[14] We used a priori criteria to determine when the retrospective assessment should be applied. If the patient was not referred to critical care, we used their initial emergency department consultation. If the patient was referred to critical

care, we used the critical care consultation immediately prior to admission. In addition, we applied the OHPIP reassessment tool to patients who had critical care stays longer than 48 h. The hypothetical reverse triage tool output was then compared against clinical outcome measures for individual patients.

Statistical analysis

The primary outcome measure was the ability of the OHPIP and STSS tools and the P/F ratio to predict the need for mechanical ventilation. Secondary outcomes were the ability to predict the need for critical care admission and mortality. We determined that mechanical ventilation is a more objective outcome measure compared with critical care admission, as the decision to intubate and ventilate is more patient rather than institution dependent. The criteria for critical care admission may vary regionally, nationally, and internationally. Statistical analysis was performed with R (version 3.0.1; R Project for Statistical Computing, Vienna, Austria).

Descriptive data are presented as median and interquartile range (IQR; range for age). Categorical variables are given in cross-tables. Data were examined for normal distribution using normal Q-Q plots and the Shapiro–Wilk test. For non-normally distributed data, the Mann-Whitney U-test was performed to assess differences between groups. The Fisher's exact test was used to determine associations in categorical variables. For multiple comparisons, P-values were adjusted using the Bonferroni–Holm method. Receiver operating characteristic (ROC) curves were plotted to determine the ability of the selected variable to predict outcomes. We determined that an area under the curve (AUC) of 0.7 equated to a 'fair' predictor, 0.8 a 'good' predictor, and 0.9 an 'excellent' predictor.[15]

Results

We assessed the P/F ratio, STSS score, and OHPIP score in 101 patients with confirmed H1N1 influenza admitted to two UK hospitals during the winter of 2010–11. Demand for critical care during this period forced hospitals in Cheshire and Merseyside to implement 'escalation' policies, cancelling all elective surgery to increase capacity.

Twenty-three of 101 patients required mechanical ventilation (out of 29 admitted to critical care) (Table 1). Eighty-six patients
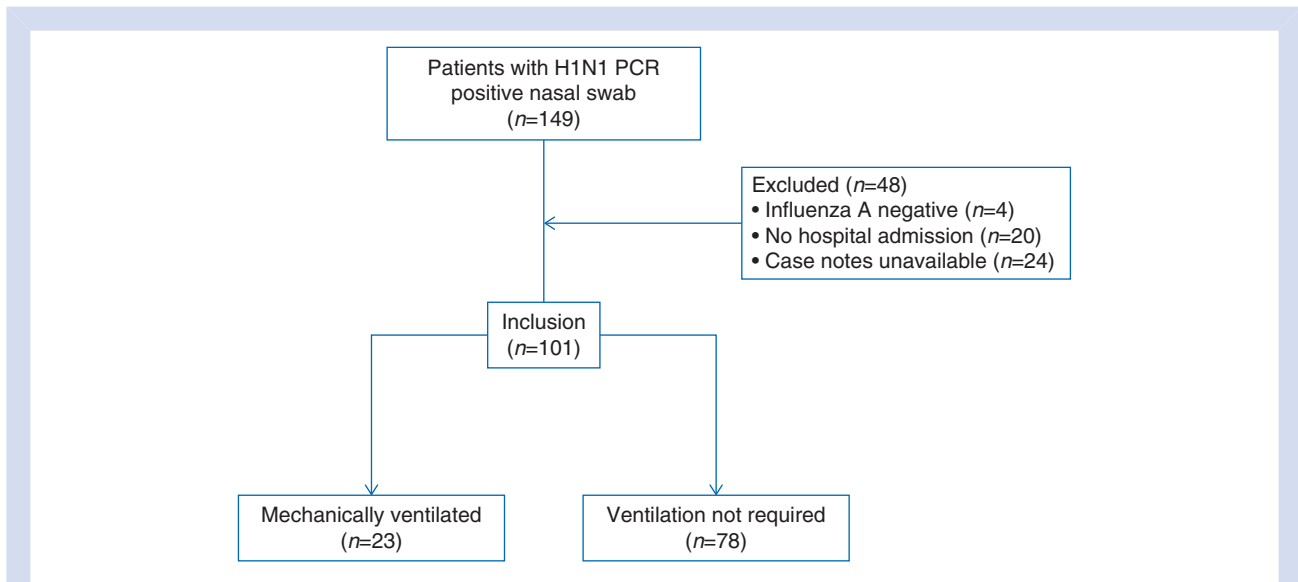

Fig 1 Consort diagram. Consort diagram demonstrates study inclusion and exclusion criteria.

Table 1 Patient demographic data. Table demonstrates demographic data for patients admitted to hospital with confirmed H1N1 influenza. P-values calculated using the Mann–Whitney U analysis. Critical care LOS and APACHE II relate to those patients admitted to intensive care. APACHE II, Acute Physiology and Chronic Health Evaluation II; IQR, interquartile range; LOS, length of stay; SOFA, Sequential Organ Failure Assessment

	Mechanical ventilation (n=23)	No mechanical ventilation (n=78)	P-value
Age, median (IQR), years	47 (18–67)	38 (17–86)	0.048
Males, n (%)	11 (47.8)	33 (42.3)	0.661
Mortality, n (%)	7 (30.4)	4 (5.1)	<0.001
Hospital LOS, median (IQR)	20 (12–30)	3 (2–7.5)	<0.001
SOFA, n (%)	4 (3–6)	2 (1–3)	<0.001
Ventilator-dependent days, median (IQR)	10 (6–18)	N/A	N/A
Critical care admission, n (%)	23 (100)	6 (7.7)	<0.001
Critical care LOS, median (IQR)	12 (7–20)	4.5 (0–11)	0.035
APACHE II, median (IQR)	16 (11–22)	16 (10–27)	<0.001

were from hospital admission areas (66 emergency department, 20 acute medical unit), 14 patients were from medical wards, and 1 patient was a critical care transfer from another hospital. Patients who required mechanical ventilation were more likely to die (mortality 30.4% *vs* 5.1%, P ≤0.001), had more severe organ impairment (median SOFA 4 *vs* 2, P≤0.001), and were older (median age 47 *vs* 38 years, P=0.048). Patients who required ventilation had more severe symptoms of respiratory distress (higher respiratory rate, lower Sa_{O_2}, lower pH, and lower P/F ratio) and a more pronounced acute phase response (lower serum albumin concentrations, higher CRP levels) (online only, Supplemental material Table 3).

The STSS scores are compared against actual patient outcomes in Table 2. Figure 2A and B demonstrate the ROC curves using the STSS for mechanical ventilation [AUC 0.798 (CI 0.704–0.891)] and critical care admission [AUC 0.816 (CI 0.727–0.904)].

The OHPIP score suggested that 19 patients should be admitted to critical care with the highest priority and 4 with intermediate priority (Table 3). Using the cut-off values 'red' and 'orange' to admit and 'blue' and 'green' to not admit, the tool predicted critical care admission with a sensitivity and specificity of 79.3% and 98.6%, respectively. With the same cut-off values, the OHPIP predicted the need for mechanical ventilation with a sensitivity of 82.6% and a specificity of 93.6%. Eleven patients met the OHPIP exclusion criteria and therefore two of this study population would have been refused admission using the tool.

The OHPIP reverse triage tool mandates re-evaluation of patients admitted to critical care at 48 and 120 h. Based on this, a recommendation is made to either withdraw critical care and palliate or continue active treatment (or discharge if the patient does not require critical care). Table 4 displays the recommendation that would have been made had the reverse triage tool been applied *vs* the actual outcome for patients.

P/F ratio [Pa_{O_2} (mmHg)/$F_{I_{O_2}}$] predicted the need for mechanical ventilation with an AUC of 0.885 (CI 0.817–0.952) (Fig. 2C) and critical care admission with an AUC of 0.885 (CI 0.807–0.964) (Fig. 2D). When no arterial blood gas sample was taken during patient assessment (30/101 patients), the P/F ratio was estimated using the previously validated Pandharipande tool.[13] Using a cut-off value P/F ratio <260, the P/F ratio predicted the need for mechanical ventilation with a sensitivity and specificity of 87.0% and 76.6%, respectively. If the Pandharipande tool was used alone, ignoring measured values, the estimated P/F ratio predicted the need for ventilation with an AUC of 0.921 (CI 0.869–0.972) and critical care admission with an AUC of 0.934 (CI 0.887–0.981). A cut-off value of P/F<280 combined the best sensitivity and specificity for mechanical ventilation (95.7% and 77.6%, respectively) (see Supplementary material Fig. 1). The SOFA score was a less useful predictor of

Table 2 Simplified Triage Scoring System (STSS) scores compared with actual patient outcomes. Table demonstrates the number of patients admitted with H1N1 influenza and their STSS scores compared with the number who were admitted, required mechanical ventilation, and survived to hospital discharge. Figures displayed as *n* (%)

STSS score	Frequency	Admitted	Ventilated	Survived
0	35	2 (5.7)	1 (2.9)	35 (100)
1	32	6 (18.8)	6 (18.8)	31 (96.9)
2	24	14 (58.3)	10 (41.7)	17 (70.8)
≥3	10	7 (70.0)	6 (60.0)	7 (70.0)
	101	29	23	90

both mechanical ventilation and critical care admission (online only, Supplementary material Fig. 2).

Discussion

Our study demonstrates that oxygen exchange (P/F ratio) better predicts the need for mechanical ventilation and critical care admission than the STSS triage tool. Patients who required mechanical ventilation were statistically more likely to present with respiratory distress and have a more pronounced acute phase reaction. The reverse triage component of the OHPIP tool was a poor predictor of patient outcome and we recommend that it should not be used in the H1N1 population. Based on our results, we recommend that the P/F ratio should be preferred to STSS as a secondary triage tool and prompt referral to critical care if the ratio is <300.

Our patient cohort broadly matches previously published work on critically ill patients with pandemic H1N1 influenza.[11 16] Patients who required mechanical ventilation and or critical care were more likely to have respiratory distress (increased respiratory rate and hypoxaemia). In our patient cohort we noted that critical care patients had decreased albumin concentrations (median 31 *vs* 38 g Litre^{-1}, P<0.001). This marker has not been reported previously as a marker of severity in pandemic influenza, although it is known that albumin levels are inversely related to mortality in acute illness.[17]

The P/F ratio was the best predictor of the need for mechanical ventilation in our patient cohort [0.885 (CI 0.817–0.952)]. In addition, there are a number of advantages to using this single parameter over the STSS. No additional training is required; it is a standard measurement used widely by emergency, respiratory, and critical care physicians; and it is part of the diagnostic criteria for ARDS.[12] An interesting finding is that estimated P/F ratios calculated using the Pandharipande equation actually had greater predictive ability than arterial blood gas values in this cohort (Supplementary material Fig. 1). Why an estimated P/F ratio should perform better than the actual value is unclear, but this finding does have potential implications: the estimation is based on a non-invasive calculation, derived from Sa_{O_2} and $F_{I_{O_2}}$, that is quick and easy to perform and may be of particular value in resource-poor geographical settings or to signpost those patients that should have arterial blood gas analysis (e.g. on handover from nurse triage to initial medical assessment). While the Pandharipande[13] formula itself is complex, its' use could be facilitated by setting up a software macro to automatically generate a P/F ratio with entry of Sa_{O_2} and $F_{I_{O_2}}$ as part of patient data management systems.

The STSS tool predicted the need for mechanical ventilation with an AUC of 0.798 (CI 0.704–0.891) in our patient cohort, less accurate than in a study by Adeniji *et al.*[10] [AUC 0.91 (CI 0.83–0.99)]. However, our cohort more accurately reflects the intended population for the triage tool: our patients were admitted to hospital during a pandemic when escalation procedures were required and our sample size was larger (101 *vs* 62 patients assessed). We found that an STSS score ≥2 was the best predictor of critical admission (sensitivity 69.6%, specificity 76.9%). Tools with AUC values >0.8 on ROC analysis are considered to be good predictors of outcome. However, when used with a specific cut-off (required for practical prospective application), the tool did not perform well, limiting utility in clinical practice.

We found that OHPIP predicted critical care admission with a positive predictive value of 95.7%, sensitivity of 75.9%, and specificity of 91.0%. Sensitivity and specificity in our cohort were higher than those reported by Guest *et al.*[8] (29% and 84%, respectively), however, they applied the tool to general case-mix
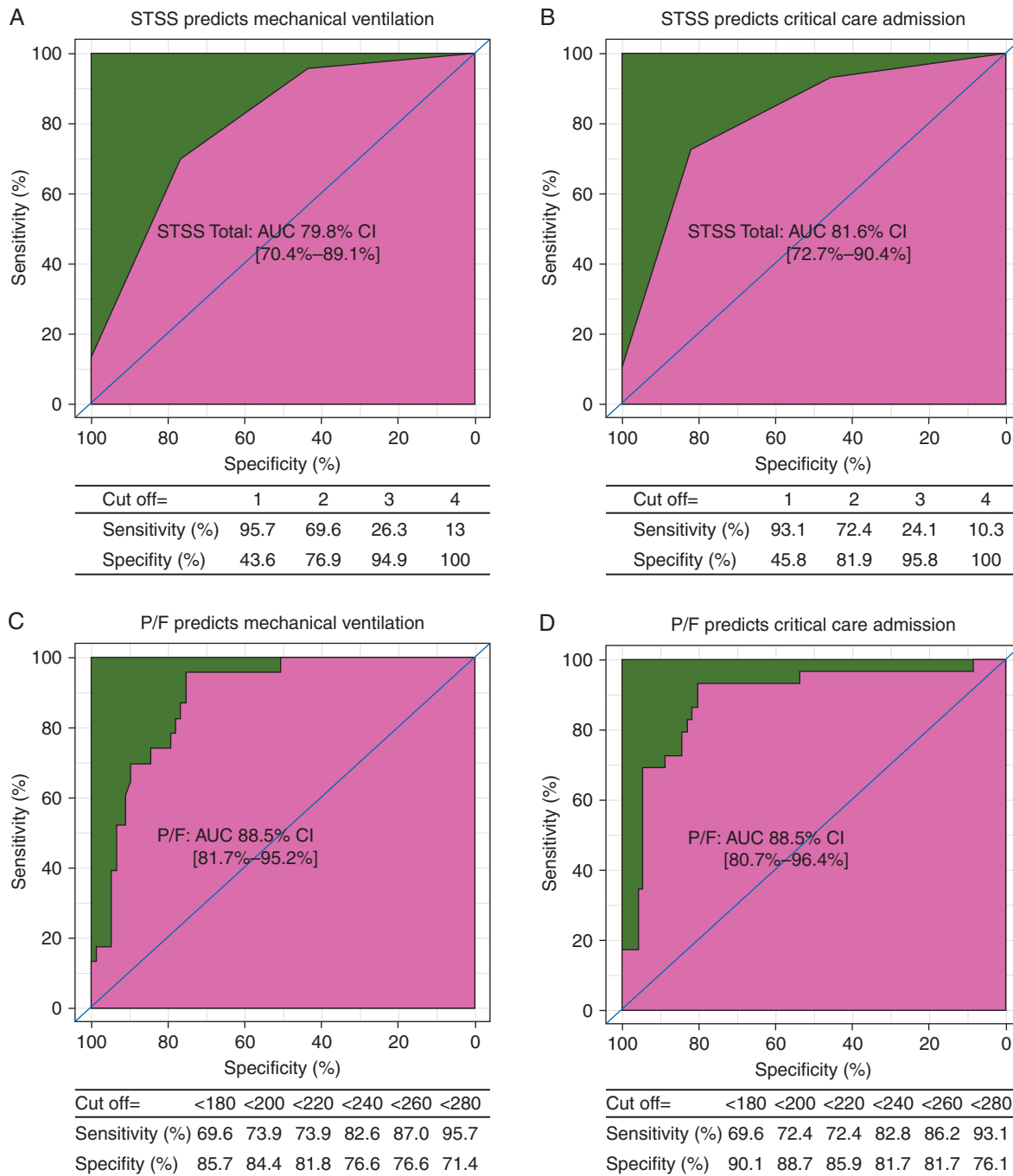
Fig 2 ROC curves for the STSS and P/F ratio in predicting the need for critical care admission and mechanical ventilation. The figure demonstrates comparisons of receiver operating characteristic curves in predicting critical care admission and the need for mechanical ventilation. (A) The ability of the STSS to predict admission to critical care. (B) The ability of the STSS to predict mechanical ventilation. (C) The ability of the P/F ratio to predict admission to critical care. (D) The ability of the P/F ratio to predict mechanical ventilation. P/F, arterial partial pressure oxygen (mmHg) divided by fractional inspired oxygen; STSS, Simplified Triage Scoring System.

intensive care admissions, not to the intended triage tool population. The OHPIP tool requires a detailed medical history to determine if exclusion criteria are met. Although we did not specifically evaluate the ease of application, a detailed medical history is required to determine exclusion criteria, some of which (e.g. spirometry) was not available, even on retrospective evaluation with full case notes. Authors of the OHPIP themselves

have stated that the 'Ontario protocol is complex, requires laboratory investigations and has not been fully evaluated'.[7] They also demonstrated that, even as experts and authors of the tool, the OHPIP is difficult to apply, with frequent disagreements between triage officers.[18]

In common with the study by Khan,[9] we found that the reverse triage component of the tool poorly predicted patient

Table 3 Ontario Health Plan for an Influenza Pandemic (OHPIP) tool recommendations compared with actual patient outcomes. The table shows the number of patients admitted with H1N1 influenza that met OHPIP criteria and compares this to the number who were admitted to critical care, those who required mechanical ventilation, and those who survived. Exclusion criteria as follows: 2, metastatic malignant disease; 3, severe irreversible neurological conditions; 5, end-stage organ failure; 1, SOFA >14. Of the 11 patients who met the criteria for exclusion (code blue), 3 died during their hospital stay, 1 died during critical care admission, and 2 were referred but refused admission

Code	OHPIP criteria	Action	Frequency	Admitted	Ventilated	Survived
Blue	Exclusion criteria met or SOFA >11	No admission	11	2	1	8
Red	SOFA ≤7 or single organ failure	Highest priority	20	19	16	13
Orange	SOFA 8–11	Intermediate priority	4	4	3	3
Green	No significant organ failure	No admission	66	4	3	66
			101	29	23	90

Table 4 Reverse triage component of the Ontario Health Plan for Influenza Pandemic (OHPIP) tool. The table demonstrates the output from the reverse triage component of the OHPIP tool. The decision to palliate is made if the SOFA score is >11 or exclusion criteria are met. Continued treatment is recommended if the SOFA score is <11 and discharge from critical care if the patient is no longer dependent on mechanical ventilation.[3] The tool is applied at 48 and 120 h. The table demonstrates the number of patients who met the criteria at each time point and the number of those patients who went on to die in hospital. STSS could not be calculated in patients who were sedated, mechanically ventilated, and required cardiovascular support. IQR, interquartile range

Decision	48 h assessment	Survived to discharge	Hospital length of stay, median (IQR)	120 h assessment	Survived to discharge	Hospital length of stay, median (IQR)
Palliate	9	7	32 (16–49)	5	4	29 (23–32)
Continue active treatment or discharge from critical care	17	12	20 (12–26)	17	13	25 (13–30)

outcome: only two of nine and one of five patients who would be recommended for palliation at 48 and 120 h assessment subsequently went on to die. We found a signal of increased critical care length of stay for those patients who would have been palliated using the reverse triage tool, but this did not reach statistical significance. Based on this, we agree with the assertion made by Khan[9] that application of the reverse triage tool would lead to inappropriate withdrawal of care.

Our study has limitations. We examined a relatively small patient cohort, although larger than previous studies.[9 10] Importantly, and unlike previous studies, we examined patients with confirmed H1N1 during a period of heightened critical care demand with escalation measures in place. The OHPIP tool was designed to be applied to all patients at critical care consultation, but our study excluded patients who were referred with alternative diagnoses; this reduces our ability to draw firm conclusions on utility. An initial aim of this study was to assess if the triage tools could predict mortality; however, the event rate (11 patients died) was low such that valid statistical analysis could not be performed in this cohort.

We pragmatically applied the tools at emergency department admission if no referral was made or upon referral to critical care. This may have introduced bias, but the median time from hospital admission to critical care referral in this cohort was 5 h, so we believe this to be minimal. Examining those patients not referred to critical care (n=72), 71 were discharged home and 1 was discharged to a rehabilitation facility, and the median hospital length of stay was 3 days (IQR 2–6). Therefore we would argue that there were no inappropriate 'non-referrals' in this cohort. Some case notes from PCR confirmed H1N1-positive patients were not available for inclusion, a common limitation of retrospective studies. We mitigated for potential differences in methods of data collection at the two hospitals with one consistent investigator (B.M.) in conjunction with separate independent investigators at each site. The transferability of our results to future influenza pandemics will depend upon the presentation of the disease: hypoxaemia was a cardinal feature of H1N1 influenza but may not be common to future outbreaks.

There are a number of ethical implications to consider when interpreting our results. The implementation of triage tools leaves the physician in conflict: on the one hand, the ethical principles of distributive justice, and on the other, legal obligations to individual patients.[19] Our recommendation to use the P/F ratio as a secondary triage tool applies to only those patients with a presumptive diagnosis of influenza, not all emergency admissions, who may present with a variety of physiological disturbances. In this context, a P/F value of <300 was 95.6% sensitive and had a 44% positive predictive value for mechanical ventilation, a useful cut-off to guide referral from emergency to critical care physicians. However, despite the great complexity of the OHPIP tool to guide critical care admission, it did not accurately replace decisions based on experience and clinical judgement in our cohort. Improper use of triage tools could lead to increased deaths and promote public mistrust of the health care system and health professionals.[20] Therefore further work is required to develop tools that can engender health professional and public trust for critical care resource allocation.

In summary, we found that the P/F ratio was a better predictor of both need for critical care admission and mechanical ventilation than the STSS. In the absence of an arterial blood gas, the P/F ratio can be accurately estimated with the Pandharipande tool[13] using simple observational data (Sa_{O_2} and Fi_{O_2}). Low oxygen exchange at critical care admission can be used to stratify risk in severe sepsis.[21] Therefore there is strong rationale for using the P/F ratio to assess the severity of H1N1 influenza, a disease characterised by refractory hypoxaemia.[11] We propose that patients with a P/F value <300 should be referred for critical care assessment. The OHPIP tool should be simplified and undergo further evaluation before it can be implemented in disaster

scenarios such as pandemic influenza. Based on our and previously published results, we believe that the reverse triage component of the OHPIP tool should not be implemented in the event of a future pandemic.

Authors' contributions

B.M.: designed the study protocol, prepared and submitted the ethical application, designed an a priori database for data collection, examined all sets of notes as an independent investigator, interpreted results, and wrote the manuscript. L.T.: contributed to the ethical application process, was an independent investigator, performed preliminary data analysis, and contributed to the preparation of the manuscript. R.G.: contributed to preparation of the study protocol and ethical documentation, was an independent investigator, and contributed to interpretation of the data. M.K.: made a significant contribution to design of the study and collected initial pilot data. H.R.: was an independent investigator, jointly developed the a priori database, and collated results at the Chester site. M.M.: performed the statistical analysis for the project. N.R.: developed the initial concept for the study, acted as a senior adjudicator at the Chester site, and contributed to preparation of the manuscript. I.W.: was the chief investigator for the study, interpreted study results, and contributed to preparation of the manuscript. All authors read and approved the final manuscript.

Supplementary material

Supplementary material is available at *British Journal of Anaesthesia* online.

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