Title: Physiological-social score (PMEWS) vs. CURB-65 to triage pandemic influenza: a comparative validation study using community-acquired pneumonia as a proxy

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Version: 2 Date: 5 December 2006

Author’s response to reviews: see over
5th December 2006

Iratxe Puebla
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Dear Ms Puebla

Re: MS3035762681191674

In response to the reviewers’ specific comments:

Capelastegui - major
1. The study is retrospective, and more than 15% of the cases were lost. 8/241 (3%) inpatient notes were missing and therefore lost to analysis for the outcomes of level II/III care and death. The 37/278 (13%) of ED presentations excluded from analysis were not because of missing notes but because data to calculate the scores was not recorded in the notes. We have amended the text and fig 2 to clarify this.

2. Mortality was high (29.2%): this fact must be accounted for. The paper needs a table showing characteristics of the patients studied.
   We have inserted table 1 with baseline demographics. Mortality was 42 of 187 admitted patients (22.5%). The reasons for this are now addressed in the discussion.

3. The physiological-social score (PMEWS) proposed by the authors did not perform well to predict mortality (AUC 0.66). This outcome (mortality) is basic to the assessment of the predictive power of severity scores for community-acquired pneumonia. We accept and have addressed in the text the lesser power of PMEWS to predict mortality. However as we explain in the text, PMEWS is not designed to be a pneumonia severity score, but a triage tool, and as such we suggest that its ability to predict need for higher level care (AUC 0.83) is of value.

4. The CURB-65 score is simple, but does not perform well to identify severe pneumonia, as is well known from other studies as well. The new rule should thus be compared with more specific scores, such as that proposed by Ewig et al and incorporated in the ATS guidelines in 2001. We did not aim to develop a new pneumonia severity score. The aim of our study was rather to assess the utility of a modified Early Warning Score in predicting requirements for care. We compared it with CURB-65 as this is currently being recommended by the British Thoracic Society as a triage tool for pandemic influenza.

5. In addition, the new rule does not add practicality or usability. I am skeptical about the practical usability of a score that uses 10 variables, 7 of which are weighted. In contrast, both the CURB-65 and CRB-65 scores are easier to apply (venipuncture to measure
serum urea in the emergency department is not problematic), and the CRB-65 score does not mandate hospital-based assessment. Early Warning Scores are widely used for inpatient monitoring and since the collection of this data we have implemented their routine use in our Emergency Department. All the data points are simple to acquire and can be done at point of contact. They are also familiar to a wide variety of medical and nursing staff, which CURB-65 and CRB-65 may not be. Although venepuncture for serum urea is, we agree, not problematic in normal circumstances, we wished to develop a tool that would be applicable in the pandemic situation with a 7-fold increase in attendances, and was not dependent on chemical pathology services which could not cope with over 1000 extra samples per day.

6. Since the study was only carried out in one hospital, how generalizable are the data? We agree that indications for admission and higher level care will always be subject to local influences (this has been well demonstrated with APACHE, SAPS and MPM). Validation of the tool on an international level, for CAP and against other patient sets, is ongoing.

7. The modification of the Medical Early Warning Score, which has been previously validated (reference 7), seems arbitrary.
We aimed to modify the tool to include acute and chronic physiological markers of poor outcome. Both SpO2(1-4), and the modified Karnofsky score have been found to predict poor outcome(5-8). Urine output was omitted on a pragmatic basis as this is unlikely to be available at point of care.

**Capelastegui – minor**
1. The tables and figures lack some formal details (explanations at the bottom of the table are missing, the number of cases used in the different analyses are not provided, acronyms need explaining, etc.), and some errors are evident (for instance, on Table 2, CURB-65=>3, sensitivity 40%, not 100%; on Table 1, the total number of cases does not coincide with the data on the text and on Figure 2).
   Table 1 (now Table 2) has been amended to clarify the number of cases analysed.
   Table 2 (now Table 3) has been corrected.

2. Figure 2 is confusing.
   Fig 2 has been amended to clarify.

3. The percentages of missing must be provided for each variable of the patients that were studied. Did you test the rule with and without missing variables? Input? Perform sensitivity analysis?
   We accept the reviewer’s comments in relation to the development of a new rule. However here we present validation of a modification to an already validated rule.

**Gemmell**
CURB-65 scoring tool should be detailed in an appendix. How will the modified MEWS be further evaluated?
Appendix 1 details the CURB-65 tool. Further evaluation is now addressed in the discussion.
References

Yours sincerely,

Kirsty Challen