ERJ Express. Published on October 10, 2013 as doi: 10.1183/09031936.00089513

Simplification of the IDSA/ATS criteria for severe community acquired pneumonia using meta-analysis and observational data

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Key Words: “IDSA/ATS”, “pneumonia”, “guidelines”, “meta analysis”, “validation”

Key findings

This analysis proposes a more simple and easy to use version of the IDSA/ATS criteria for severe community-acquired pneumonia.

Abstract

Introduction: The 2007 IDSA/ATS guidelines proposed "minor" criteria to predict ICU admission in patients with community-acquired pneumonia. These criteria were based on expert opinion. Consequently the guidelines authors asked investigators to determine whether the score could be simplified by excluding non-contributory variables.

Methods: Each IDSA/ATS minor criteria were validated using a random effects meta-analysis of 7 studies. Variables present in <5% of cases or that were non-significantly associated with mortality/ICU admission were excluded. A simplified score excluding these variables was tested for prediction of mortality and ICU admission in an established database. Prediction was assessed using the area under the receiver operator characteristic curve (AUC).

Results: Leukopaenia (<4000 cells/mm3), thrombocytopenia (<100,000 cells/mm3) and hypothermia <36°C occurred in <5% of cases. A simplified score excluding these variables performed similarly for prediction of mortality AUC 0.77 95%CI 0.73-0.81 vs 0.78 (0.74-0.82),p=0.9 and ICU admission AUC 0.85 (0.82-0.87) vs 0.85 (0.82-0.88),p=0.9. Additional predictors suggested by the IDSA/ATS were associated with mortality and ICU admission, but only incorporating acidosis <7.35 altered the AUC (0.82 95% CI 0.78-0.86,p=0.6 for mortality and 0.86 95% CI 0.82-0.88,p=0.8 for ICU admission). No improvements were statistically significant.

Conclusions: The IDSA/ATS criteria can be simplified by removing 3 infrequent variables.

INTRODUCTION

Community-acquired pneumonia (CAP) is a leading cause of death and a frequent indication for intensive care unit admissions internationally.[1] Reducing mortality from community-acquired pneumonia requires rapid identification of patients at risk and several scoring systems have been developed to identify severe community-acquired pneumonia.[2,3]

In 2007 the IDSA/ATS guidelines recommended new criteria to define severe CAP and to guide intensive care unit admission.[1] In addition to the universally accepted indications for ICU admission, requirement for mechanical ventilation or need for vasopressors, these guidelines suggested 9 minor criteria with a recommendation that patients with 3 or more criteria be considered for ICU admission.[1]

The IDSA/ATS criteria have now been validated for prediction of 30-day mortality, ICU admission and requirement for subsequent mechanical ventilation or vasopressor (MV/VS) use in several countries.[4-10]

There are, however, several outstanding questions regarding the minor criteria to address. Unlike other severity scores derived from independent predictors in multivariate analysis, the minor criteria were selected by expert opinion and its individual components have not been separately validated.[1] It has been suggested that some criteria may be stronger predictors than others, or that some criteria may be non-contributory to the score overall.[1,7,8] In addition, the 2007 guidelines specifically requested that a group of additional predictors, such as acidosis, hypoglycaemia and liver cirrhosis be tested by adding to or substituting the existing criteria to determine if they may improve its accuracy.[1]

A major problem with severity scores has been a failure to implement them in clinical practice.[11,12] Complexity of scores makes implementation more difficult and therefore scores

should be designed to contain the fewest components necessary to give accurate predictions.[13] Several scoring systems in other conditions have been successfully simplified to make them easier to use in clinical practice.[2,13]

Using a combination of meta-analysis and a large observational clinical study, this analysis aimed to improve the IDSA/ATS minor criteria by through simplification: excluding infrequent and non-contributory variables and by testing additional variables to determine if they improve the score. The study subsequently validated the resulting simplified IDSA/ATS criteria in an established observational database of patients with community-acquired pneumonia.

METHODS

The present study reports two analyses, an initial systematic review and meta-analysis evaluating the prognostic value of the individual components of the IDSA/ATS minor criteria. The second part of the analysis consists of validating simplified IDSA/ATS minor criteria in a prospective observational database.

Systematic review and meta-analysis

The systematic review and meta-analysis was conducted and is reported according to MOOSE (meta-analysis of observational studies in epidemiology) guidelines.[14]

Search Criteria

A search of PUBMED was performed using search terms:

1. ("IDSA/ATS" OR "IDSA" OR "ATS" OR "Minor criteria" OR "major criteria" OR "ICU" OR "intensive care" AND ("Pneumonia" OR "community-acquired pneumonia" OR "CAP")

The search included articles published between January 1980 and November 2012. No language criteria were applied. Full articles of all potentially appropriate abstracts were reviewed. Only peer-reviewed data was included, therefore conference abstracts were excluded. The search was repeated in EMBASE to obtain any articles missed by the original search. The search strategy was supplemented by reviewing of reference lists, bibliographies and the investigators files.

Data extraction

Two Investigators independently review abstracts to determine study eligibility. Non relevant studies were excluded based on title and abstract review only. Data abstraction was

conducted by two blinded reviewers. Where appropriate, we contacted study authors to clarify inconsistencies or to obtain unpublished data.

Study inclusion and study quality assessment

All studies were considered eligible if they fulfilled the following criteria: original publications; inclusion of consecutive/unselected patients with community acquired pneumonia; radiographic confirmation of CAP and exclusion of non-CAP diagnoses e.g. non-pneumonic exacerbation of COPD; calculation of severity score based on admission data and reported on one of the outcome measures in the study- mortality or intensive care unit admission. As previously described we used Hayden's criteria to assess quality of studies.[15]

Modification of the IDSA/ATS minor criteria

A priori, we determined that we would attempt to simplify the IDSA/ATS minor criteria by systematically excluding variables if any of the following were met: variables not significantly associated with mortality ($p>0.05$) in the pooled analysis; variables not significantly associated with ICU admission ($p>0.05$) in the pooled analysis; variables present in less than 5% of the study populations in either pooled analysis. A simplified score would therefore be developed for testing in an observational database.

The IDSA/ATS 2007 guidelines suggested additional criteria that should be tested to determine if they improve the minor criteria, these were hypoglycaemia, hyperglycaemia, metabolic acidosis, elevated lactate, liver cirrhosis, acute alcohol ingestion or alcohol withdrawal and asplenia.[1,16] The guidelines do not suggest a pre-specified cut-off for these variables and so cut-offs were identified based on the published literature (hypoglycaemia <4.4mmol/L, hyperglycaemia >14mol/L, pH <7.35, hyponatraemia <130mmol/L).[16--19] Lactate was only measured routinely in one study hospital so was excluded from this analysis

due to missing data. Where arterial blood gas results were not available they were assumed to be normal. Variables significantly associated with mortality and requirement for MV/VS, and present in >5% of the study population were added to the IDSA criteria to create a modified score.

Validation of the modified score in an observational database

The simplified scoring system was validated in the Edinburgh pneumonia study database. This was a prospective observational study of patients with community-acquired pneumonia conducted in Edinburgh, UK. The methodology of this study has been described previously.[20] As the IDSA/ATS criteria have been designed to guide ICU admission, we analysed a cohort of patients in which patients with do not attempt resuscitation orders and not for ICU orders were excluded as previously described.[4] In addition, as the minor criteria are not useful in patients already receiving mechanical ventilation or vasopressor support in the emergency department, this cohort excluded these patients (major criteria).[1]

Outcomes

In all analyses, the outcomes of interest were Intensive care unit admission, requirement for mechanical ventilation or vasopressor support (a surrogate of ICU admission) and mortality (30-day or in-hospital mortality depending on the study design).

Statistical Analysis

Meta-analysis was conducted comparing the frequency of each IDSA/ATS minor criteria in the outcome group with the frequency in those without the outcome. Odds ratios were pooled

using a Mantel-Haenszel random effects model. A random effects model was chosen due to the expected heterogeneity between studies. Statistical heterogeneity was assessed using Higgins' I^2 test.[21] In the observational database, sensitivity, specificity, positive likelihood ratio, negative likelihood ratio and area under the receiver operator characteristic curve (AUC) are presented. In interpretation of likelihood ratios it is generally held that a likelihood ratio greater than 10 and a negative likelihood ratio less than 0.1 provide strong evidence rule in or rule out a diagnosis.[22] To identify the optimal cut-off point for discrimination we used Youden's index. AUC values were compared using the method described by Hanley and McNeil.[23] Odds ratios were compared as described by Altman et al.[24]

Analyses were conducted using SPSS version 21 for windows (SPSS inc, Chicago, IL, USA) and Review manager version 5 (Cochrane collaboration).

RESULTS

The initial search retrieved 8827 publications. After exclusion of manuscripts based on abstract review alone, 30 manuscripts were potentially eligible for inclusion. After exclusion of studies that did not report data, or did not consider mortality or intensive care unit admission as an outcome, 7 studies were included in the final meta-analysis.

The size of included studies varied from 158 patients to 2413 patients. The ICU admission rate varied from 6.3% to 19.6%. All studies were observational, 3 were retrospective and 4 were prospective in design. All 7 studies were designed specifically to evaluate the IDSA/ATS criteria. 3 studies were regarded as high quality with a low risk of bias, 2 were of intermediate quality and 2 of lower quality. The characteristics of included studies are shown in Table 1.

Meta-analysis of individual components of the IDSA/ATS criteria

Individual components of the IDSA/ATS criteria were evaluated for their prediction of mortality and intensive care unit admission. Three studies reported data for both mortality and ICU admission, two studies reported data only for mortality and one study only contained data regarding ICU admission. One author responded to a request for additional data and therefore data for both mortality and ICU admission are included. Therefore, for the evaluation of mortality there were 6 studies containing valid data. These comprised 5686 patients. The most frequently positive criteria was multilobar shadowing (32.1% of patients) and the least frequent was thrombocytopenia <100,000 cells/mm^3 (3.1% of patients). The highest odds ratio was for Pa02/Fi02$\leq$250 ratio with the lowest odds ratio for hypotension. All of the individual components were significantly associated with mortality ($p<0.05$).

Significant (>50%) heterogeneity was present for all components except white cell count <4000 cells/mm^3 and thrombocytopenia <100,000 cells/mm^3. Heterogeneity was not resolved by exclusion of low quality studies or limiting studies to exclusively prospective studies.

For the prediction of ICU admission, there were 5 studies including 6240 patients. All of the variables were significantly associated with ICU admission (<0.05) for all analyses. In these studies, the most frequently positive variable was also multilobar shadowing (30.5%) with the least frequent being white cell count <4000 cells/mm^3 (2.9%). The highest odds ratio was for hypothermia <36°C with the lowest odds ratio for platelet count <100,000 cells/mm^3. There was significant heterogeneity in analyses for respiratory rate, PaO2/FiO2 ratio $\leq$ 250, confusion, urea$\geq$20 mg/dL and hypothermia <36°C. The meta-analysis results are summarised in table 2.

To determine if the different criteria were of equal or unequal weight, odds ratios for each predictor were compared using interaction tests, which allow comparison of two estimates of effect.[23] In this case, interaction tests were used to determine if there was a statistically significant increased risk of mortality or ICU admission with any one predictor over the others. Comparisons between the odds ratios demonstrated no statistically significant differences (p>0.05 for all comparisons) suggesting that the variables were not of unequal weight (table 2).

Evaluation of the additional IDSA/ATS criteria

There was a significant relationship between hypoglycaemia, hyponatraemia and acidosis with requirement for mechanical ventilation or vasopressor support. Hyponatraemia (8.5%)

and metabolic acidosis (10.5%) were relatively common predictors while all other predictors were present in less than 5% of patients.

For prediction of 30-day mortality, hypo- and hyperglycaemia, hyponatraemia, metabolic acidosis and liver cirrhosis were all significantly associated with mortality, while there was no statistically significant association with asplenia and acute alcohol withdrawal although these analyses were limited by low numbers of patients. These are shown in table 3.

Modification of the IDSA/ATS minor criteria

Based on the table above, white cell count, platelets and hypothermia contributed to less than 5% of cases in the analysis of both mortality and ICU admission. We hypothesised that exclusion of these infrequent predictors from the score would not impact its accuracy based on the area under the receiver operator characteristic curve. (Table 4)

We compared the performance of the simplified and original minor criteria in the Edinburgh dataset. This dataset has been previously described. 1062 patients were included with a median age of 63 (interquartile range 47-74), 513 (48.3%) patients were male. The 30-day mortality rate in this population was 4.5% and 6.6% required mechanical ventilation or vasopressor support.

Comparing this simplified score to the original scoring system in the Edinburgh pneumonia dataset, the performance characteristics are shown in table 4. Simplification did not affect the overall performance of the score for predicting 30-day mortality (p=0.8), requirement for MV/VS (p=0.9) or ICU admission (p=0.8).

No significant improvements in the area under the receiver operator characteristic curve were observed by incorporating any of the additional predictors (hypo- or hyperglycaemia, hyponatraemia, alcohol withdrawal, cirrhosis or asplenia). The largest improvement in the AUC was observed with the additional of acidosis (see table 5) improving the AUC for mortality from 0.78 to 0.82 but improvements were not statistically significant ($p>0.05$ for all comparisons).

In addition to showing equivalent area under the curve to the existing IDSA/ATS minor criteria, the simplified score was superior to the pneumonia severity index ($p=0.01$), the CURB65 score, $p=0.008$, CRB65, $p=0.005$ and the 2001 ATS minor criteria ($p=0.001$) for prediction of mechanical ventilation and or vasopressor support. The AUC was equivalent to those of the SMART-COP and Espana SCAP scores ($p>0.05$ for comparisons).

For prediction of mortality, there were no statistically significant differences with any of the above scores ($p>0.05$ for all comparisons)

29.6% of ICU admissions occurred between 24 hours and 72 hours of admission, representing early deterioration in ward patients. The area under the curve to identify this group of patients were: original IDSA/ATS definition 0.84 (0.79-0.89), simplified IDSA/ATS score 0.83 (0.78-0.88) and the simplified score including acidosis 0.84 (0.79-0.89).

Selecting the optimal cut-off point for the IDSA/ATS criteria

Using likelihood ratios to determine the cut-off points at which the score was most likely to be clinically useful, the analysis was first performed for requirement for MV/VS. Each of the scores demonstrated a positive likelihood ratio of greater than 10 at a cut-off of 5 criteria or more (figure 1A) indicating a very high likelihood of the score being clinically useful to

determine ICU admission. As a test to exclude the likelihood of requiring MV/VS, each set of criteria produced a likelihood ratio <0.1 using a cut-off of 1 or fewer criteria indicating that these criteria would be likely to be useful to identify patients unlikely to require ICU admission (figure 1B).

The analysis for ICU admission produced similar results, with negative likelihood ratios <0.1 at a cut-off of 1 or fewer, and positive likelihood ratio's greater than 10 associated with a cut-off of 5 or more for each of the scores. Similarly for mortality prediction, each of the scores gave a positive likelihood ratio >10 with a cut-off of 5 or greater. The negative likelihood ratio was 0.9 for the original IDSA/ATS definition using 1 or fewer criteria, and 0.8 for the modified IDSA/ATS with acidosis criteria.

Using Youden's index to identify the optimal cut-off point, 3 or more criteria were most discriminatory for both the original IDSA/ATS criteria and the modified version with acidosis. 2 or more criteria were optimal for the simplified score (figure 1C).

DISCUSSION

This study has shown that the IDSA/ATS minor criteria can be simplified by removing 3 non-contributory variables without compromising its prognostic accuracy. Removing thrombocytopenia <100,000 cells/mm^3, white cell count <4000 cells/mm^3 and hypothermia <36°C, which all occur in less than 5% of CAP cases, resulted in no significant loss of diagnostic performance but may make the score easier to use in clinical practice.

This study used both a systematic review and meta-analysis and an observational study of patients with CAP to comprehensively investigate the IDSA/ATS minor criteria. Previous studies had not validated the individual components of the IDSA/ATS criteria and had not investigated the additional criteria, such as acidosis, hyperglycaemia and hyponatraemia recommended by the guidelines authors. No previous study has investigated whether the criteria could be simplified by removing non-contributory variables.[1]

Our meta-analysis has validated the individual components of the 2007 IDSA/ATS minor criteria, showing that each of the criteria are associated with increased mortality and requirement for intensive care unit admission in CAP. The IDSA/ATS guideline committee had asked authors to investigate whether the effect of some components was greater than others, and should therefore receive more weight within the score, as is the case for some others scores such as PSI or SMART-COP.[17,25,26] Several individual studies have argued that the minor criteria are of unequal weight, for example Liapikou and colleagues found that mental confusion and leukopenia had the strongest association with mortality.[7] They could not demonstrate an association between hypotension, thrombocytopenia and multilobar involvement and mortality.[7] Phua et al found that each minor criterion was predictive of mortality and that the presence of $PaO_2/FiO_2 \leq 250$ mm Hg and confusion had the strongest association with mortality.[5] Furthermore, Guo et al showed that minor criteria of the

IDSA/ATS criteria for severe CAP were of unequal weight in predicting mortality.[8] They concluded that $PaO_2/FiO_2 \leq 250$ mm Hg, confusion and uraemia were most strongly associated with mortality, and that an association between leukopaenia, hypothermia and hypotension and mortality could not be demonstrated.[8] Our analysis suggests no predictors were significantly or consistently associated with a greater risk compared to the others showing the value of a meta-analysis approach where individual study results are conflicting.

Of the additional criteria investigated, acidosis and hypoglycaemia were most strongly associated with mortality and MV/VS but addition of these variables to the minor criteria produced little or no improvement in the AUC. Only the addition of acidosis showed some improvement in the AUC but this did not reach statistical significance. Further studies should evaluate whether addition of this parameter may improve the score.

The IDSA/ATS criteria recommended consideration of ICU admission for patients with a score of 3 or greater, but no other guidelines or manuscripts have provided guidance on how the criteria may be used in clinical practice. Based on our score performance data we can make some cautious recommendations about how this score may be used clinically. Our data suggest that patients with 0-1 criteria are at low risk of ICU admission and mortality and may be suitable for outpatient or ward level care. Patients with 2 to 4 criteria are at increased risk of ICU admission and mortality, but admitting all of this very large group of patients in level 2/level 3 care would be impractical in most healthcare settings. Therefore in this group, additional predictors, biomarkers and clinical judgement should be taken into account. In patients with 5 or more criteria (using either the original or modified scores) the risk of ICU admission and mortality is very high, and this group should be strongly recommended for level 2/level 3 care or have treatment restrictions in place if this is inappropriate.

These findings and the modified minor criteria described in this manuscript will require further independent validation studies. The IDSA/ATS guidelines will shortly be updated and policymakers may wish to consider these results in revising the minor criteria.

It is well recognised that simple scores composed of only a few variables can be equivalent to more complex scores, for example the 5 variable CURB65 score is equivalent to the 20 component pneumonia severity index for predicting 30-day mortality in CAP.[2] A major problem with severity scores has been in implementing them in busy hospital settings. For example, a survey of 536 physicians in Australia found that less than half of physicians used severity scores and that only approximately 20% of physicians could accurately calculate the PSI or CURB65 scores.[27] It is logical that more simple scores will be easier to calculate and therefore to use in clinical practice. An excellent example of a complex score being simplified is the pulmonary embolism severity index (PESI). This was developed to estimate the 30-day mortality in patients with acute pulmonary embolism. An initial complex risk stratification score containing 11 different variables each carrying a different weight was initially derived and validated.[28,29] Recognising that this was not ideal for use in a busy hospital environment, Jiménez et al proposed a simplified version of the PESI score.[13] They excluded non-contributory variables resulting in a score of only 6 variables. They then validated their simplified score in more than 17 000 patients showing it performed similarly to the more complex score.[13]

Similarly this study has demonstrated that a simplified criteria consists of respiratory rate $\geq$ 30 breaths/min, PaO_2/FiO_2 ratio $\leq$ 250, multilobar infiltrates, confusion/disorientation, uraemia (BUN level $\geq$ 20mg/dL), and systolic blood pressure <90mmHg performs similarly to the existing IDSA/ATS minor criteria.

Limitations to this study are acknowledged. There was significant heterogeneity in estimates of effect sizes in the meta-analysis resulting from different study designs and differences in patient populations. It is well recognised for example, that criteria for ICU admission in the United States are very different from those in Europe or the UK.[26] In addition, we were unable to evaluate lactate in addition to the IDSA/ATS criteria, as this was not measured in all study patients as part of the study.

In conclusion our study has simplified the IDSA/ATS criteria by removing 3 infrequent variables, resulting in a 6 point score with the same prognostic accuracy. This simplified score may be easier to remember and to implement by clinicians in a busy hospital environment.

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Funding: No specific funding was obtained for this study.

Conflict of interest statement: All authors confirm that there are no conflicts of interest in relationship to the present manuscript.

First author name	Design	Score(s) assessed	Setting and dates	N	Age (years)	ICU admission rate	Mortality rate	Study Objective/ Conclusion
Kontou (2009)	Retrospective study	IDSA/ATS criteria, PSI, CURB65	Single centre, Connecticut, USA	158	Mean age 63.1 +/- 18.8	19.6%	12.6%	Comparison of IDSA/ATS criteria to other severity scores Usefulness of IDSA/ATS in predicting severe CAP
Chalmers (2011)	Prospective observational study	IDSA/ATS, PSI, CURB65, SMART-COP, SCAP, 2001 Minor ATS criteria	Multicentre, Scotland	1062	Median 63 (IQR; 47-74)	7.6%	4.5%	Validation of minor criteria IDSA/ATS can predict requirement for ICU admission
Guo (2011)	Retrospective study	IDSA/ATS	Single centre, China	1230	Mean age 47.5 +/- 22.2	nr	16%	Weight of minor criteria SOFA scores and costs increased significantly with number of minor criteria
Fukuyama (2011)	Prospective observational study	IDSA/ATS PSI, A-DROP CURB-65 SMART-COP Espana rule	Single Centre, Okayama, Japan April 2007- May 2009	505	76 (IQR 67-83)	6.3%	6.5%	Validation of the Espana rule
Phua (2009)	Prospective observational study	IDSA/ATS	Single centre, Singapore	1242	Mean age 65.7	12.6%	14.7%	Validation of IDSA/ATS criteria
Liapikou (2009)	Prospective observational study	IDSA/ATS	Single centre, Barcelona, Spain	2102	Mean age 67 +/- 18years	11%	5.2%	Validation of IDSA/ATS criteria
Brown (2009)	Retrospective Cohort study	IDSA/ATS	Single centre, Salt lake city, USA	2413	Mean age 56.2	15.6%	3.7%	Validation of IDSA/ATS criteria

Table 1. Characteristics of included studies. Nr= not reported. IQR= interquartile range.

IDSA/ATS minor criteria	N	% positive (pooled)	Pooled Odds ratio (95% CI)	p-value	I^2
Mortality					
Respiratory rate ≥30 breaths/min	5686	1197 (21.1%)	3.03 (1.92-4.78)	<0.0001	65%
Pa02/FiO2 ratio ≤ 250	5686	1482 (26.1%)	5.62 (2.27-13.9)	0.0002	93%
Multilobar shadowing	5686	1823 (32.1%)	2.77 (1.27-6.02)	0.01	90%
Confusion	5686	897 (15.8%)	5.47 (2.81-10.7)	<0.0001	86%
Urea ≥20mg/dl	5686	1502 (26.4%)	4.76 (2.92-7.77)	<0.0001	71%
White cell count <4000 cells/mm^3	5686	202 (3.6%)	3.04 (1.98-4.65)	<0.0001	0%
Platelets <100,000 cells/mm^3	5686	175 (3.1%)	2.47 (1.46-4.18)	0.0007	19%
Hypothermia <36°C	5686	223 (3.9%)	3.06 (1.41-6.66)	0.005	61%
Hypotension	5686	788 (13.9%)	2.39 (1.35-4.22)	0.003	69%
ICU admission					
Respiratory rate ≥30 breaths/min	6240	1385 (22.2%)	4.68 (2.94-7.44)	<0.0001	81%
Pa02/FiO2 ratio ≤ 250	6240	1459 (23.4%)	5.06 (3.07-8.36)	<0.0001	83%
Multilobar shadowing	6240	1902 (30.5%)	3.25 (2.77-3.81)	<0.0001	0%
Confusion	6240	760 (12.2%)	4.78 (2.43-9.39)	<0.0001	89%
Urea ≥20mg/dl	6240	1495 (24.0%)	3.38 (2.46-4.64)	<0.0001	54%
White cell count <4000 cells/mm^3	6240	183 (2.9%)	4.21 (2.99-5.93)	<0.0001	0%
Platelets <100,000 cells/mm^3	6240	187 (3.0%)	3.12 (2.19-4.46)	<0.0001	0%
Hypothermia <36°C	6240	295 (4.7%)	5.14 (4.09-6.46)	0.004	67%
Hypotension	6240	404 (6.5%)	3.41 (2.58-4.50)	<0.0001	0%

Table 2. Meta-analysis of the relationship between individual components of the IDSA/ATS 2007 minor criteria for mortality and ICU admission. *note that the N number is different for each analysis because some studies only examined one end-point.

IDSA/ATS criteria	N (%)	% MV/VS 70	% no MV/VS-992	Odds ratio for MV/VS	p-value
Hypoglycaemia[a] (<4.4mmol/L)	46 (4.3%)	15 (21.4%)	31 (3.1%)	8.45 (4.3-16.6)	<0.0001
Hyperglycaemia (>14mmol/L)	24 (2.3%)	3 (4.3%)	21 (2.1%)	2.07 (0.60-7.12)	0.2
Hyponatraemia (<130mmol/L)	90 (8.5%)	11 (15.7%)	79 (8.0%)	2.15 (1.09-4.27)	0.02
Acidosis (pH <7.35)	112 (10.5%)	28 (40%)	84 (8.5%)	7.21 (4.25-12.2)	<0.0001
Acute alcohol ingestion/withdrawal	48 (4.5%)	2 (2.9%)	46 (4.6%)	0.60 (0.14-2.54)	0.5
Liver cirrhosis/chronic liver disease	34 (3.2%)	3 (4.3%)	31 (3.1%)	1.39 (0.41-4.66)	0.6
Asplenia	6 (0.6%)	1 (1.4%)	5 (0.5%)	2.86 (0.33-24.8)	0.3
IDSA/ATS criteria	N (%)	% 30-day mortality 48	% survivors 1014	Odds ratio 30-day mortality	p-value
Hypoglycaemia[a] (<4.4mmol/L)	46 (4.3%)	9 (18.8%)	39 (3.8%)	5.77 (2.61-12.7)	<0.0001
Hyperglycaemia (>14mmol/L)	24 (2.3%)	4 (8.3%)	20 (2.0%)	4.52 (1.48-13.8)	0.004
Hyponatraemia (<130mmol/L)	90 (8.5%)	9 (18.8%)	81 (8.0%)	2.66 (1.24-5.68)	0.009
Acidosis (pH <7.35)	112 (10.5%)	27 (56.3%)	85 (8.4%)	14.1 (7.6-25.9)	<0.0001
Acute alcohol ingestion/withdrawal	48 (4.5%)	1 (2.1%)	47 (4.6%)	0.44 (0.06-3.24)	0.4
Liver cirrhosis/chronic liver disease	34 (3.2%)	4 (8.3%)	30 (3.0%)	2.98 (1.01-8.83)	0.04
Asplenia	6 (0.6%)	1 (2.1%)	5 (0.5%)	4.29 (0.49-37.5)	0.2

Table 3. Validation of supplementary criteria for the IDSA/ATS minor criteria. [a]in non-diabetic patients.

Current IDSA/ATS criteria	**Simplified IDSA/ATS criteria**	**Modified IDSA/ATS criteria**
Respiratory rate $\geq$ 30 breaths/min	Respiratory rate $\geq$ 30 breaths/min	Respiratory rate $\geq$ 30 breaths/min
PaO_2/FiO_2 ratio $\leq$ 250	PaO_2/FiO_2 ratio $\leq$ 250	PaO_2/FiO_2 ratio $\leq$ 250
Multilobar infiltrates	Multilobar infiltrates	Multilobar infiltrates
Confusion/disorientation	Confusion/disorientation	Confusion/disorientation
Uraemia (BUN level $\geq$ 20mg/dL)	Uraemia (BUN level $\geq$ 20mg/dL)	Uraemia (BUN level $\geq$ 20mg/dL)
Leukopenia (WBC count <4000 cells/mm^3)	Systolic blood pressure <90mmHg	Systolic blood pressure <90mmHg
Thrombocytopenia (platelet count <100,000 cells/mm^3)		Acidosis
Hypothermia (core temperature <36°C)		
Hypotension requiring aggressive fluid resuscitation		
Additional criteria to consider	Additional criteria to consider	Additional criteria to consider
Hypoglycaemia	Leukopenia	Leukopenia
Acute alcoholism or alcohol withdrawal	Hypothermia	Hypothermia
Hyponatraemia	Thrombocytopenia	Thrombocytopenia
Unexplained metabolic acidosis	Hypoglycaemia	Hypoglycaemia
Elevated lactate level	Hyponatraemia	Hyponatraemia
Liver cirrhosis	Unexplained metabolic acidosis	Elevated lactate level
Asplenia	Elevated lactate level	Liver cirrhosis
	Liver cirrhosis	

Table 4. Comparison between the original and simplified IDSA/ATS minor criteria.

30-day mortality	**PLR**	**NLR**	**Sensitivity**	**Specificity**	**AUC**	**p-value**
IDSA/ATS minor criteria	2.9 (2.2-3.7)	0.52 (0.37-0.73)	58.3% (43.3-72.1%)	79.6% (76.9-82.0%)	0.78 (0.74-0.82)	N/A
Simplified IDSA/ATS minor criteria	2.7 (2.0-3.7)	0.6 (0.46-0.81)	50.0% (35.2-64.8%)	81.8% (79.2-84.1%)	0.77 (0.73-0.81)	0.9
Simplified + acidosis	3.6 (2.9-4.5)	0.36 (0.23-0.57)	70.8% (55.9-83.0%)	80.3 % (72.4-77.2%)	0.82 (0.78-0.86)	0.6
Requirement for mechanical ventilation or vasopressor support	**PLR**	**NLR**	**Sensitivity**	**Specificity**	**AUC**	**p-value**
IDSA/ATS minor criteria	4.3 (3.6-5.2)	0.26 (0.17-0.41)	78.6% (67.1-87.5%)	81.9% (79.3-84.2%)	0.85 (0.82-0.88)	N/A
Simplified IDSA/ATS minor criteria	4.2 (3.4-5.2)	0.40 (0.29-0.54)	66.7% (55.3-76.8%)	84.2% (81.8-86.4%)	0.84 (0.82-0.87)	0.9
Simplified + acidosis	4.1 (3.4-4.9)	0.32 (0.21-0.47)	74.3% (62.4%)	81.7% (79.1-84.0%)	0.86 (0.83-0.89)	0.8
Intensive care unit	**PLR**	**NLR**	**Sensitivity**	**Specificity**	**AUC**	**p-value**

admission						
IDSA/ATS minor criteria	4.2 (3.5-5.1)	0.30 (0.21-0.44)	75.3% (64.3-83.9%)	82.2% (79.6-84.5%)	0.85 (0.82-0.88)	N/A
Simplified IDSA/ATS minor criteria	4.2 (3.4-5.2)	0.38 (0.27-0.53)	68.6% (56.4-79.1%)	83.8% (81.3-86.0%)	0.85 (0.82-0.87)	0.9
Simplified + acidosis	4.1 (3.4-4.9)	0.33 (0.23-0.47)	72.8% (61.8-82.1%)	82.2 (79.6-84.5%)	0.86 (0.83-0.89)	0.8

Table 5. Comparison of performance characteristics between the original and simplified IDSA/ATS minor criteria. Abbreviations: PLR= positive likelihood ratio, NLR= negative likelihood ratio, AUC= area under the curve.

Figure legends

Figure 1. Performance characteristics of the IDSA/ATS criteria and modifications for predicting requirement for MV/VS. 1A- positive likelihood ratios for each score using a cut-off of 1 or greater, 2 or greater and so on to define severe CAP. 1B negative likelihood ratios for each score using the indicated cut-off or less to exclude severe CAP. The horizontal lines indicate the positive likelihood of 10 and negative likelihood of 0.1 which is typically held to give strong evidence to rule in or rule out a diagnosis.[22] 1C- Youdens index as a measure of overall discrimination for each cut-off. The cut-off with the highest index is the optimal cut-off in terms of sensitivity and specificity.