ELECTRONIC SUPPLEMENTARY MATERIAL
APPENDIX A

DEFINITIONS:

Pneumonia:

Definite pulmonary infection (requires 1 & 2 to be satisfied): [1]

1.New or progressive pulmonary infiltrate on chest X-ray

AND

(a) Positive pleural fluid or blood cultures for the same organism in the tracheal aspirate

or

(b) Radiological cavitation and no evidence of a non-infective cause

or

(c) Histopathological demonstration of pneumonia or necrosis (transbronchial biopsy or autopsy)

or

(d)

(i)New fever evidenced by a rise in core body temperature (>1°C and >38.3 °C) compared with the previous 24 hour period AND

(ii)New leucocytosis evidenced by a >25% increase in circulating leucocytes compared with the previous 24 hour period AND

(iii) Purulent tracheal aspirate AND

(iv) No evidence of a non-infective cause AND

(v) No evidence of extrapulmonary infection

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while Probable Pulmonary Infection was defined as:

1. New or progressive pulmonary infiltrate on chest X-ray

AND

2. Two of the following three (with no evidence of a non-infective cause)

(a) Purulent tracheal aspirate

(b) A rise in core body temperature (>1 °C and >38.3 °C)

(c) >25% increase in circulating leucocytes

Hospital-Acquired Pneumonia (HAP) was defined as a pulmonary infection in non-mechanically ventilated patients, which was not incubating at the time of admission, and occurring 48 hours or more after admission [2].

Ventilator-Associated Pneumonia (VAP) was defined as a pulmonary infection arising in ≥ 48 hours after endotracheal intubation with no evidence of pneumonia at the time of intubation or the diagnosis of a new pulmonary infection if the initial admission to ICU was for pneumonia [2].

Very Early-onset VAP (VE-VAP) was defined as pulmonary infection arising within 48 hours of intubation, and that was not incubating at the time of intubation [3].

Early-onset VAP was defined as VAP with onset more than 48 hours but less than five days after intubation [2].

Late-onset VAP was defined as VAP with onset five or more days after intubation [4].

Severity of Infection

Severity of sepsis: Severity is defined as sepsis /severe sepsis / septic shock following the ACCP/SCCM 1992 conference. To qualify for severe sepsis, new/worsening organ dysfunction (OD) other than the lung must be present, and related to the episode of pneumonia [5].

Definite etiology: a microorganism isolated in a patient with suspicion of pneumonia from blood or respiratory sample and judged as definite by the attending physician. Cultures with normal flora, *S. epidemidis* or coagulase-negative, and Candida species were considered to be non-pathogenic; these cultures and those that showed no growth were classified as negative cultures for purposes of analysis.

Organ dysfunction was defined according to SOFA score definitions [6].

Contribution of pneumonia to death was defined according to attending physician that consider whether pneumonia is: 1) directly related with death; 2) contributing factor for death or; 3) unrelated with the fatal outcome.

Comorbidities definitions:

Non-metastatic cancer: Could include regional lymph nodes

Chronic Renal Failure: Chronic renal supportive therapy (ie chronic haemodialysis/ haemofiltration/ peritoneal dialysis) for irreversible renal disease or history of chronic renal insufficiency associated with clinical adverse effects (usually Creatinine > 300 umol/l)

COPD: Chronic obstructive pulmonary disease, chronic bronchitis and or emphysema requiring prescribed treatment

Chronic respiratory failure: permanent shortness of breath on light activity, due to pulmonary (chronic restrictive or obstructive) disease. The subject is unable to work, climb stairs or perform household duties. Documented chronic hypoxaemia, hypercarbia, secondary polycythaemia, severe pulmonary hypertension (mean PAP > 40 mmHg) or requirement for chronic respiratory support (eg home O2 therapy)

Chronic Heart Failure: Fatigue, dyspnea or angina at either rest or a minimum level of activity. The subject cannot stand-alone, walk slowly or dress without symptoms (ie NYHA class IV).

Cirrhosis: Diagnosed by either biopsy taken prior to or during ICU admission, or clinical features such as portal hypertension, presence of oesophageal/gastric varices (demonstrated by surgery, imaging or endoscopy), or the demonstration of retrograde splenic-venous flow by ultrasound, or history of variceal bleeding, or episodes of acute hepatic failure/encephalopathy/coma.

Alcoholism: Alcohol intake that exceeds the social drinking custom (usually regular intake of more than 80 grams of alcohol/day for at lest 6 months prior to ICU admission) and responsible for clinical adverse effects such as logorrhea, encephalopathy, neurological disorder, nutritional disorder, cirrhosis.

Homelessness: No fixed address for 6 months prior to ICU admission

Drug Abuse: Drug addiction with intravenous drugs (opioids and derivatives) for at least 6 months prior to ICU admission.

Diabetes Mellitus: Requiring daily insulin therapy

Solid organ transplant: liver/heart/lung/kidney still requiring immunosuppression

Immunosuppression: can be associated with the following:

- known daily corticosteroid therapy with greater than or equal to a total daily dose equivalent to 1 mg/kg or greater than 40 mg/day of oral prednisolone for at least 7 consecutive days within one month prior to study entry
- clinically suspected or known to have Acquired Immunodeficiency Syndrome (AIDS) as defined by the Centre for Disease Control
- granulocyte count less than 1 X 10^9/l due to a cause other than severe sepsis (eg metastatic or haematological malignancies or chemotherapy)
- immunosuppressant therapy (eg due to an organ or bone marrow transplant)

McCabe's Classification of Chronic Disease [7]

Each of the above co-mobidities, if present, should be coded according to this classification:

1. Non-fatal underlying disease or no underlying disease
   (All patients other than the ones categorised below)
2. "Ultimately fatal (<5 years) underlying disease
   Examples: bone marrow aplasia, chronic leukaemia, and myeloproliferative

Syndrome, myeloma, malignant lymphoma less than stage IV, transplantation of heart, lung, bone marrow, pancreas or liver, cancer without metastasis, portal hypertension, cardiac insufficiency (NYHA III), chronic respiratory insufficiency with oxygen therapy, chronic haemodialysis, AIDS classification IV, A, B or E.

3. “Rapidly fatal (<1 year) underlying disease

   Examples: acute leukaemia, primitive or blastic transformation of chronic myeloid leukaemia, malignant lymphoma or Hodgkin’s disease stage IV, metastatic cancer, hepatic failure with encephalopathy, ischaemic or nonobstructive cardiac failure NYHA IV, rapidly progressive respiratory failure, AIDS classification IV, C or D or HIV encephalopathy

Median and interquartile range days of antibiotic by antibiotic or antibiotic class.

Antibiotic	**Median**	**IQR**
Colistin	11	8-15
Carbapenems	8	4.25-11
Linezolid	8	4-11
Fluoroquinolones	7	4-10
Piperacillin/tazobactam	7	4-10
Non- AP cephalosporins	6	2-8
AP cephalosporins	6	3-10
Glycopeptides	6	3-10
Aminoglycosides	5	3-9

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