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Disease characteristics and management of hospitalized adolescents and adults with Community-Acquired Pneumonia in China

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**Disease characteristics and management of hospitalized adolescents and adults
with Community-Acquired Pneumonia in China**

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Abstract

Objectives: To describe the clinical characteristics and management of patients hospitalized with CAP in China.

Design: This was a multicenter, retrospective, observational study.

Setting: 13 teaching hospitals in northern, central and southern China from 1 January 2014 to 31 December 2014

Participants: Information on hospitalized patients aged ≥ 14 years with radiographically-confirmed pneumonia with illness onset in the community was collected using standard case report forms.

Primary and secondary outcome measures: Resource use for CAP management.

Results: Of 14,793 patients screened, 6,056 with radiographically-confirmed CAP were included in the final analysis. Low mortality risk patients with a CURB-65 score 0-1 and PSI risk class I-II accounted for 73.2% (4434/5812) and 54.8% (2034/3710) of CAP patients respectively. 21.8% (1157/6056) patients had already achieved clinical stability on admission. 29.2% (1132/3880) patients without pseudomonas infection risk factors received antimicrobial over-treatment regimens. The median length of stay in hospital was 10 days. The median duration between clinical stability to discharge was 5.0 days with 30-day mortality of 4.2%.

Conclusions: These data demonstrated overuse of health resources in CAP management, indicating that there is the potential for improvement and substantial savings to health-care systems in China.

Strengths and limitations of this study

- This is the largest multi-center study to investigate demographic characteristics, severity and microbiological testing, empirical antimicrobial treatment, duration of hospitalization and 30-day mortality among adults and adolescents hospitalized with CAP in mainland China, including adolescents and adults of all ages admitted to general hospital wards or ICUs from the participating centers, patients who were critically ill, aged >90 years, and/or immunosuppressed.
- The participating hospital sites are teaching hospitals in seven cities in three provinces, and may not be representative of CAP in smaller, rural hospitals.
- The majority of patients are adult CAP patients, our findings do not apply to children hospitalized with CAP.

Background

Community acquired pneumonia (CAP) is one of the most common infectious syndromes and is a leading cause of death worldwide [1-2]. In Europe, the reported rate of CAP ranges from 1.6 to 9 cases per 1,000 in the general adult population per year [3-5]. Despite advances in medical technology and global economic development, CAP-associated mortality remains high (e.g., 20.9/100,000 in the United States and 12.7/100,000 in Canada) [2,6]. Patients hospitalized in intensive care units for CAP have mortality in excess of 20% for immunocompetent patients and closer to 30% for those immunocompromised [7]. In Japan and Korea, the 30-day mortality of patients hospitalized with CAP is about 4-6% [8-9].

Although mainland China has nearly 19% of the world's population, there are limited data on CAP management and disease burden in China during the last ten years. According to a household interview survey published in the China Health and Family Planning Statistical Yearbook (2013), the two-week prevalence of pneumonia in China was estimated to be 11/1,000, and the direct cost due to bacterial pneumonia was about 320 million RMB (approximately \$46.4 million) [10]. In 2015, CAP-China, a multicenter clinical network, was founded with the support of National Key Technology Support Program from Ministry of Science and Technology (2015BAI12B11) to provide data on CAP for clinical researchers and healthcare policy makers in China.

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4 A multicenter retrospective study of all hospitalized CAP patients from 13 centers in
5
6 northern, central and southern China among CAP-China members was implemented
7
8 in 2015 (Clinicaltrial Registration No. NCT02489578). To our knowledge, this is the
9
10 largest multi-center study to investigate demographic characteristics, severity and
11
12 microbiological testing, empirical antimicrobial treatment, duration of hospitalization
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14 and 30-day mortality among adults and adolescents hospitalized with CAP in
15
16 mainland China.
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20 21 **Methods**

22 23 **Study Design and Population**

24
25 Data were collected from 13 hospitals in Northern (Beijing), Central (Yantai, Qindao,
26
27 Weifang, Zibo, Rizhao cities in Shandong Province) and Southern (Kunming City in
28
29 Yunan Province) China. A listing of participating centers can be found in Appendix 1.
30
31 All patients admitted to the 13 hospitals during 1 January 2014 through 31 December
32
33 2014 with the relevant disease codes of pneumonia or pulmonary infection in the
34
35 World Health Organization International Classification of Diseases 10th revision
36
37 (ICD-10, Appendix 2) were eligible. Data on all eligible patients identified in
38
39 screening were retrieved from the Hospital Information System (HIS) in each center.
40
41 Trained physicians reviewed the medical case history and collected data on 786
42
43 variables for each patient. Chest radiographs and computerized tomography (CT)
44
45 scans for each patient were reviewed by pulmonary physicians and radiologists in
46
47 each center. Two-leveled review process was performed for data collection and entry.
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49 The CAP case definition includes (1) illness onset in the community; (2) chest
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4 radiograph or CT scan showing infiltration or interstitial changes, with or without
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6 pleural effusion; (3) any one of pneumonia clinical manifestations: (a) recent cough,
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8 sputum or aggravation of respiratory symptoms, the emergence of purulent sputum,
9
10 with or without chest pain; (b) fever (temperature $\geq 37.3^{\circ}\text{C}$) or hypothermia
11
12 (temperature $< 36^{\circ}\text{C}$); (c) signs of pulmonary consolidation and (or) moist crackles;
13
14 or (d) WBC $> 10 \times 10^9/\text{L}$, or $< 4 \times 10^9/\text{L}$, with or without neutrophil predominance.

15
16 Patients were excluded if (1) age < 14 years; (2) pneumonia onset ≥ 48 hours after
17
18 admission; (3) lung infiltrate or interstitial changes which were interpreted as lung
19
20 cancer, pulmonary tuberculosis, non-infectious interstitial lung diseases, pulmonary
21
22 edema, atelectasis, pulmonary embolism, pulmonary eosinophil infiltration,
23
24 pulmonary vasculitis; (4) HIV positive; (5) re-admission within 72 hours after
25
26 discharge.

27
28 The study design was approved by the Ethics committee of China-Japan Friendship
29
30 Hospital (No. 2015-86). Given the retrospective nature of the study, the Ethics
31
32 committee determined that informed consent was not necessary.

33 34 35 36 37 38 39 40 41 42 **Quality control of the study**

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44 Key investigators, including clinicians, statisticians, microbiologists and radiologists
45
46 worked together to draft the protocol and created a single formatted case report form
47
48 (CRF) that was utilized by all centers. Before study initiation, all investigators from
49
50 the thirteen centers received training on the protocol, screening process, definition of
51
52 underlying diseases and formatted CRF (Appendix file 3). After data were collected,
53
54 the CRF was reviewed by a trained researcher to ensure its completeness and data
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4 quality. A second review was performed independently by a trained team of
5
6 physicians in each center before being entering in duplicate into a computerized
7
8 database.
9

10 11 **Data Collection:**

12 A total of 786 variables were included in the formatted CRF, including:
13

14 (1) Demographic data: age, gender, ID number, source of admission, types of medical
15 insurance;
16

17 (2) Underlying diseases: chronic lung, heart, renal and liver diseases, diabetes, solid
18 organ cancers, immunocompromised status, such as leukemia and lymphoma,
19 chemotherapy or radiation within six months, bone marrow and solid organ
20 transplantation, splenectomy. Definition of underlying diseases is listed in Appendix
21 file 4.
22

23 (3) Factors for acquisition or prevention of CAP: pregnancy, postpartum within six
24 months, current smoking history, excessive drinking, exposure to day care center
25 children, bed-ridden longer than two months, chronic receipt of corticosteroids
26 (dosage equivalent prednisolone $\geq 10\text{mg/d}$ for more than 30 days), statin use, *S.*
27 *pneumoniae* or Influenza vaccination within one year.
28

29 (4) Clinical manifestations, clinical signs: recorded on the day of admission, on the 4th
30 hospital day, change of antibiotics within 14 days of admission, and the day of
31 discharge or death. Laboratory and radiological findings were also recorded if such
32 tests were repeated by attending physicians. Pneumonia disease severity scores (PSI
33 /CURB-65) were also recorded.
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4 (5) Microbiological examination: Gram stain and culture of sputum within 48 hours,
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6 blood culture within 48 hours, urinary antigen testing, BALF and pleural fluid culture
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8 within one week after admission, serum antibody (including IgM and IgG) for
9
10 atypical pathogens (*Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, *Legionella*
11
12 *pneumophila*) and respiratory virus, real-time PCR testing for atypical pathogens and
13
14 respiratory viruses.
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18 (6) Antimicrobial treatment before admission and change of antimicrobials during
19
20 hospitalization. Use of corticosteroids, vasopressors, mechanical ventilation,
21
22 Continuous renal replacement therapy (CRRT) and extracorporeal membrane
23
24 oxygenation (ECMO) were also recorded.
25
26

27
28 (7) Clinical stability was defined as satisfying all of the following: temperature ≤ 37.8
29
30 $^{\circ}\text{C}$ more than 24 hours without use of antipyretic medications; resting heart rate ≤ 100
31
32 beats/min; respiratory rate ≤ 24 breaths/ minute; systolic blood pressure ≥ 90 mmHg;
33
34 SpO₂ $\geq 90\%$ on room air; ability to maintain oral intake; normal mental status^[12].
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37
38 (8) Over-treatment was defined as: (i) use of antipseudomonal β -lactams or
39
40 β -lactams+ fluoroquinolones in patients aged < 65 years without risk factors for
41
42 pseudomonal infection; (ii) use of (antipseudomonal or not) β -lactams+ fluoroquinolones
43
44 in patients aged ≥ 65 years without risk factors for pseudomonal infection and not in an
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46 ICU^[13].
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50 (9) Risk factors for pseudomonal infection was defined as chronic airway disease
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52 (bronchiectasis and COPD), immunocompromised status and at least one risk factor
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54 for HCAP as defined by the 2008 IDSA/ATS adult CAP guidelines. ^[11,13-16].
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4 (10) Empirical antimicrobial regimens recommended by Chinese CAP guidelines
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6 were showed in Appendix 8.
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8 **Microbiology testing**

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11 The conditions that a pathogen was defined as the definite or probable etiology based
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13 on were showed in Appendix 6.
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15 **Statistical analysis**

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17 No formal sample size calculations were performed because of the retrospective
18
19 descriptive study design. All data were analyzed by descriptive statistics with SPSS19.
20
21 Measurement data were tested for normality by Kolmogorov-Smirnov. Measurement
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23 data of normal distribution was reported as mean \pm standard deviation. Measurement
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25 data of non-normal distribution was reported as median. The χ^2 test statistics were
26
27 used for 30-day mortality subgroup analysis. A P-value of <0.05 was considered
28
29 statistically significant.
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36 **Results**

37 **Screening Process**

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39 A total of 14,793 patients were screened to meet the inclusion and exclusion criteria
40
41 for CAP and 6,056 patients were included in the final analysis (Appendix Figure 1).
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46 **Epidemiological characteristics**

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48 The proportions of male and female patients were similar. The median age was 65
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50 years, range 14-103 years. Prevalent co-morbidities included hypertension (35.3%),
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52 coronary heart disease (19.8%), diabetes (15.8%), cerebrovascular diseases (15.2%)
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54 and COPD (13.7%) . 15.4% of CAP patients had at least one health care associated
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4 pneumonia (HCAP) risk factor (according to IDSA/ATS HAP/HCAP guideline
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6 published in 2007 ^[7]). 45.6% patients received antibiotics before admission.
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9 A substantial proportion of admitted patients had relatively mild disease as indicated
10
11 by the following: i) CURB-65 score ^[17] 0-1 accounted for 76.3%, ii) PSI risk class
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13 ^[18] I-II accounted for 54.8%; iii) Shorr Score ^[19] 0-1 accounts for 98.7%; and iv)
14
15 Aliberti Score low risk ^[20] group in 88.9%; v) only 12.1% (274/2260) patients had
16
17 procalcitonin (PCT) more than 2 ng/ml; vi) as many as 65.2% (3854/5915) patients
18
19 had normal peripheral leukocyte counts (4,000-10,000/ul). Most importantly, 21.8%
20
21 patients had met criteria for clinical stability at hospital admission ^[12]. (Table 1-2)
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23

24 25 26 **Clinical and radiological features**

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28 Clinical and radiological features on admission are shown in Table 2. Cough, sputum,
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30 shortness of breath and fever were the most common. 64.3% patients had multi-lobar
31
32 infiltrates and 20.8% of patients had pleural effusion.
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35 36 37 **Microbiological testing**

38
39 75.9% patients had some type of microbiologic testing. 63.7% of patients had a
40
41 sputum culture obtained within 48 hours of admission, although only 20.7% of
42
43 patients were able to produce a sputum culture of acceptable quality. The proportion
44
45 of patients with blood culture, BALF culture, and pleural effusion culture were 10.7%,
46
47 9.3% and 2.0% respectively. Only 0.1% of patients had a urinary antigen test sent to
48
49 evaluate for *Legionella pneumophila*, and 2.6% had urinary antigen testing for
50
51 *Streptococcus pneumoniae*. (Table 3)
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57 Of all patients, serological testing for antibodies to *Mycoplasma pneumoniae* was only
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4 performed on a single serum specimen for IgM (31%) and IgG antibodies (13.6%).
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6 Similarly, serological testing on a single serum specimen was done for *Chlamydia*
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8 *pneumoniae* IgM antibody in 22.2% of patients and for IgM antibodies to *Legionella*
9
10 *pneumophila* and respiratory viruses in 11%. No convalescent serum specimens were
11
12 collected for serological testing for any pathogens, limiting interpretation of serology
13
14 results for a single serum specimen.
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17
18 A definite or probable pathogen was identified only in 12.9% of patients (782/6,056):
19
20 only bacteria in 86.7% (678/782), only atypical pathogens in 0.9% (7/782), only
21
22 viruses in 8.6% (67/782), bacteria and viruses in 3.3% (26/782), viruses and atypical
23
24 pathogens in 0.6% (5/782). The most common five pathogens identified were
25
26 *Pseudomonas aeruginosa* 26.9% (210/782), *Klebsiella pneumoniae* 17.4% (136/782),
27
28 *Escherichia coli* 8.8% (69/782), *Acinetobacter* 8.4% (66/782) and influenza A virus
29
30 7.2% (56/782). (Appendix 6)
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36 **Empiric antimicrobial regimens**

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38 β -lactams (received by 72.4% of patients) and fluoroquinolones (received by 42.2%)
39
40 were the most common classes of antibiotics that were administered empirically. In
41
42 patients without pseudomonal infection risk factors, 24.4% (471/1928) patients aged
43
44 <65 years received empiric antibiotic regimens including antipseudomonal β -lactams,
45
46 and 15.9% (306/1928) patients aged <65 years received β -lactams + fluoroquinolones;
47
48 20.8% (355/1708) patients aged ≥ 65 years and not in ICU received β -lactams
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50 (antipseudomonal or not) + fluoroquinolones combined regimens. The total percentage
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52 of patients who received over-treatment with empiric antibiotics was 29.2%
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(1132/3880). (Table 4)

Clinical outcomes

Clinical outcomes are shown in Table 5. Overall, 6.5% of patients were admitted to an ICU, and 2.8% required invasive mechanical ventilation. Vasopressors were administered to 3.5% of patients, and 27.5% received corticosteroids during the hospitalization. The 30-day mortality was 4.2%. The median duration of hospitalization was 10 days. The median duration from admission to clinical stability was 4 days, and from clinical stability to discharge was 5 days. The median duration of ICU hospitalization was 8 days. The top five causes of death were severe pneumonia/multi-organ dysfunction syndrome (MODS) 66.9% (172/257), cardiac failure 3.1% (8/257), stroke 1.9% (5/257), acute myocardial infarction 1.9% (5/257), and gastrointestinal hemorrhage 1.9% (5/257).

Appendix 7 shows the results of sub-group analysis of 30-day mortality. Fatality increased with age and there was a jump up at 16.0% among those aged ≥ 90 years. Mortality was similar between male and female patients (4.9% vs 3.5%). Mortality in patients was $>10\%$ in patients with organ/bone marrow transplantation, immunosuppressive therapy, long-term oral corticosteroids use, chemotherapy/radiology within 6 months and splenectomy. Mortality in patients admitted to an ICU was 25.3%.

Discussion

This study represents the largest, multicenter, retrospective cohort study on the etiologies and outcomes in adolescents and adults with CAP in China. In this study,

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4 we found that admission of patients with low mortality risk, overuse of antibiotics and
5
6 unnecessary serological testing for *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*,
7
8 *Legionella pneumophila* and respiratory viruses, were the main challenges of CAP
9
10 management.

11
12 We identified four major categories of overuse of health care resources in CAP
13
14 management in China:
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17
18 (1) A large number of low-risk patients were admitted to the hospitals. Guidelines for
19
20 CAP management in China and the U.S. recommend that decisions for hospitalization
21
22 should be based on illness severity [11,13]. It was estimated that over \$8 billion dollars
23
24 are spent in CAP treatment every year in the U.S, and the cost for inpatient CAP
25
26 management is 25-30 times more than for outpatient CAP management [22-24].
27
28 Therefore, admission of low mortality risk CAP patients results in major unnecessary
29
30 cost expenditures. Moreover, outpatients usually return to their baseline activity levels
31
32 much sooner than inpatients, and enjoyed a higher quality of life [25-26]. Finally,
33
34 hospitalization is associated with the risk of nosocomial infections, potentially caused
35
36 by high virulent and multidrug-resistant organisms [27]. Admission of low-risk CAP
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38 patients was also observed in a recent large U.S. study [28], so it may not be unique to
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40 China.
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50 (2) Length of stay in hospital was unnecessarily long. CAP guidelines recommended
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52 that patients should be discharged as soon as they achieve clinical stability and have
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54 no other active medical problems. Keeping patients in hospital and observing them
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56 while receiving oral antibiotic therapy, or waiting for normalization of all clinical
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4 parameters are not indicated and are associated with increased costs and potentially
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6 with in-hospital adverse events ^[27,29-30]. We observed that CAP patients were
7
8 discharged a median of 5 days after achieving clinical stability, and 22% met clinical
9
10 stability criteria at admission. Given the median LOS of 10 days for all CAP patients,
11
12 discharging CAP patients once they achieved clinical stability would lead to
13
14 cost-savings of approximately half of the total hospitalization expenses.
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18
19 (3) 29.1% patients without risk factors for *Pseudomonas* infection received
20
21 over-treatment with empiric antimicrobial regimens. Antipseudomonal β -lactams
22
23 (17.0%) or β -lactams + quinolones (12.1%) were the most common empiric regimens
24
25 for over-treatment. This may be due to overestimation of illness severity, clinician
26
27 unfamiliarity with CAP guidelines, or lack of microbiologic diagnostic testing.
28
29 Moreover, we found quinolones use in more than 40% of CAP patients. The U.S.
30
31 Food and Drug Administration (FDA) has released warnings of potential adverse
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33 effects of fluoroquinolones, such as Q-T prolongation, tendon injury, psychiatric
34
35 disorder, etc ^[31-33]. As second-line anti-tuberculosis drugs, fluoroquinolones can also
36
37 affect the diagnosis of tuberculosis and induce drug-resistance ^[34-35].
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45 (4) Unnecessary serological testing was performed. We observed that many patients
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47 had an acute serum specimen collected for IgG serology testing for atypical bacteria
48
49 and respiratory viruses without a convalescent serum specimen obtained for paired
50
51 serological testing. Furthermore, many patients had testing for IgM antibodies for a
52
53 variety of respiratory pathogens, but elevation of IgM antibodies with a low-normal
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55 IgG titer is uncommon during acute illness ^[36-38]. Similarly, although a low IgM
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4 antibody level with a high IgG titer would be suggestive of past infection, the
5
6 performance characteristics of these assays may not be reliable. A follow-up
7
8 convalescent serum specimen to document changes in IgG and IgM antibody levels is
9
10 generally required for diagnosis ^[39-40]. Thus, the value of antibody testing on a single
11
12 acute serum specimen to determine the etiology of CAP is questionable. The costs of
13
14 more frequent use of PCR testing on lower respiratory specimens may be partially
15
16 offset by not performing serological testing in CAP patients.
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21 Although we identified substantial over-use of health-care resources, the outcome of
22
23 patients hospitalized with CAP in China was not ideal. Although the 30-day mortality
24
25 was low (4.2%), this should be interpreted in the context that approximately 70% had
26
27 mild CAP as indicated by pneumonia scoring indices. Mortality for CAP patients with
28
29 a CURB-65 score of ≥ 2 (15.8%) or PSI risk \geq III risk class (9.1%) were higher than
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31 what has been reported in developed countries, especially in critically ill patients with
32
33 a CURB-65 score of 3-5 and PSI risk IV-V class ^[41-42].
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40 The strengths of this study, in contrast to some past epidemiological investigations ^[21],
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42 included data on bacterial isolates obtained in current clinical practice,
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44 microbiologic testing ordered, and antimicrobials administered, according to Chinese
45
46 standards-of-care, and the study population included adolescents and adults of all ages
47
48 admitted to general hospital wards or ICUs from the participating centers to reduce
49
50 selection bias. We also included patients who were critically ill, aged >90 years, with
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52 risk factors for HCAP, and/or immunosuppressed (e.g., cancer, chronic corticosteroid
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4 use or receipt of other immunosuppressive agents, splenectomy, etc., excluding HIV
5
6 infection).

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9 This study had several limitations. First, given the retrospective study design, it is
10 possible that selection bias was present and the study population may not have been
11 representative of all CAP patients admitted to the 13 participating sites. Secondly, the
12 participating hospital sites were teaching hospitals in seven cities in three provinces,
13 and were not selected to be representative of CAP hospital management in China,
14 especially in smaller, rural hospitals. Third, this study reports on CAP management
15 during 2014; analysis of multiple years of data can allow assessment of changes in
16 CAP management. Fourth, there was no standardization of CAP admission or
17 discharge criteria and this may have varied among hospitals. We realize that
18 admission of clinically stable patients or those in low-risk mortality groups, and
19 prolonged hospitalization despite achieving clinical stability may be based upon social
20 rather than clinical factors, such as lack of available family support, older age, mental
21 illness and drug abuse, etc ^[30,43]. Fifth, the use of sputum to detect bacterial etiologies
22 of CAP may represented identification of colonization rather than infection. Sixth,
23 45.6% of CAP patients received antibiotics before hospital admission and before
24 specimen collection, and this likely reduced the detection of some bacterial infections,
25 such as *Streptococcus pneumoniae*. Therefore, the bacterial pathogens identified in
26 this study may not be representative of all bacterial causes of CAP in the source
27 patient populations for this study. Finally, while we included adolescents, the majority
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3 of patients were adult CAP patients, and our findings do not apply to children
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6 hospitalized with CAP.
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11 In conclusion, we characterized adolescents and adults hospitalized for CAP in China
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13 and identified several problems suggesting the over-use of healthcare resources in
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15 CAP management. This suggests that education and training of clinicians on current
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17 CAP guidelines in China are needed to improve clinical management and could also
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19 result in substantial cost-saving in healthcare expenditures for CAP patients. The
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21 multi-center hospital network can serve as a platform for conducting intervention
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23 studies for hospitalized CAP patients in the future, utilizing the baseline data from this
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25 observational study.
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Table 1: Demographic characteristics and underlying diseases

Items	Cases (%)
Male	3245 (53.6)
Age (years, median, IQR)	65 (53-78)
14~64	2925 (48.3)
65~74	1134 (18.7)
75~89	1810 (29.9)
≥90	187 (3.1)
Source of admission (n=6051)	
From Out-patient Department	4355 (72.0)
From Emergency Room	1640 (27.1)
Transfer from other hospital	56 (0.9)
Days from illness onset to admission (n=6054, median, IQR)	6·0 (11.0)
Patients who received antibiotics before admission	2759 (45.6)
β-lactams	1031 (37.4)
Fluoroquinolones	596 (21.6)
Macrolides	174 (6.3)
β-lactams+ fluoroquinolones	459 (16.7)
β-lactams+ macrolides	216 (7.8)
Others	283 (10.3)
Systemic glucocorticosteroids use before admission	283 (4.7)
Underlying Diseases	
Hypertension	2136 (35.3)
Coronary Heart Disease	1202 (19.8)
Diabetes	955 (15.8)
Cerebrovascular Diseases	921 (15.2)
COPD	827 (13.7)
Bronchiectasis	652 (10.8)
Asthma	351 (5.8)
Malignant solid tumors	309 (5.10)
Chronic renal diseases	222 (3.8)
Congestive Heart Failure	211 (3.5)
Connective Tissue Diseases	171 (2.8)
Chronic Hepatic Diseases	96 (1.6)

Immunocompromised Status	
Long-term oral Corticosteroid use	100 (1.7)
Chemotherapy/Radiotherapy within 6 months	71 (1.2)
Hematological neoplasms	54 (0.9)
Immunosuppressive therapy	52 (0.9)
Organ/Bone Marrow Transplantation	13 (0.2)
Splenectomy	8 (0.1)
Smoking status	
Current smokers	1038 (17.1)
Ex-smokers	608 (10.0)
Alcoholism	424 (7.0)
Risk factors for aspiration	384 (6.3)
History of CAP within one year	391 (6.5)
History of vaccination	
Influenza vaccine within 1 year	12 (0.2)
<i>Streptococcus pneumoniae</i> vaccine within 5 years	8 (0.1)
Risk factors for HCAP according to IDSA/ATS criteria	
Hospitalized in an acute care hospital for two or more days within 90 days	454 (7.5)
Received recent intravenous antibiotic therapy, chemotherapy, or wound care within the past 30 days	696 (11.5)
Attended a hospital or hemodialysis clinic	41 (0.7)
Residence in a nursing home or long-term care facility	19 (0.3)
CURB-65 score (n=5812)	
0	2185 (37.6)
1	2249 (38.7)
2	1036 (17.8)
3	288 (5.0)
4	52 (0.9)
5	2 (0.0)
PSI risk class (n=3710)	
□	1147 (30.9)
□	887 (23.9)
□	746 (20.1)
□	709 (11.7)

□	221 (6.0)
Shorr Score (n=5865)	
0	5106 (87.1)
1	685 (11.7)
2	71 (1.2)
3	3 (0.0)
4	0 (0.0)
Aliberti Score (n=6056)	
Low risk group	5386 (88.9)
High risk group	670 (11.1)
Clinical stability on admission (n=5311)	1157 (21.8)

COPD: chronic obstructive pulmonary disease; HCAP: healthcare associated pneumonia; IDSA/ATS: Infectious Diseases Society America/American Thoracic Society. PSI: pneumonia severity index. Clinical stability was defined as satisfying the following at the same time: temperature ≤ 37.8 °C more than 24 hours; heart rate ≤ 100 beats/min in resting state; breathing rate ≤ 24 breaths/minute; systolic blood pressure ≥ 90 mmHg; SpO₂ $\geq 90\%$ on room air; ability to maintain oral intake; normal mental status.

Table 2: Clinical and radiological features on admission

Items	Cases (%)
Fever ($T \geq 38^{\circ}\text{C}$, n=6052)	2905 (48.0)
Hypothermia ($T < 36^{\circ}\text{C}$, n=6052)	51 (0.8)
Cough	5389 (89.0)
Sputum	4928 (81.4)
Shortness of breath	2191 (36.2)
Chest pain	732 (12.1)
Decrease of consciousness	308 (5.1)
Chest signs	
Moist rales	3033 (50.1)
Dry rales	1436 (23.7)
Edema of lower limbs	616 (10.2)
Cyanosis	565 (9.3)
SBP < 90 mmHg	537 (8.9)
Radiology	
Infiltrate more than two lobes	3894 (64.3)
Plural effusion	1148 (20.8)
Cavitation	237 (3.9)
WBC (mm^{-3} , n=5915)	
>10,000	1692 (28.6)
<4,000	369 (6.2)
4,000~10,000	3854 (65.2)
BUN $> 7.0 \text{ mmol} \cdot \text{L}^{-1}$ (n=5819)	1222 (21.0)
PH < 7.30 (n=3456)	90 (2.6)
$\text{PaO}_2/\text{FiO}_2 < 300 \text{ mmHg}$ (n=3453)	1348 (39.0)
PCT ($\text{ng} \cdot \text{ml}^{-1}$, n=2260)	
$\text{PCT} \leq 0.25$	1350 (59.7)
$0.25 < \text{PCT} < 1$	506 (22.4)
$1 \leq \text{PCT} < 2$	130 (5.8)
$\text{PCT} \geq 2$	274 (12.1)

SBP: systolic blood pressure; WBC: white blood cell count; BUN: blood urea nitrogen; Scr: serum creatinine; PH: potential of hydrogen; $\text{PaO}_2/\text{FiO}_2$: arterial pressure of oxygen/fraction of inspiration oxygen; PCT: procalcitonin.

Table 3: Microbiological examination for CAP

Items	Cases (%)
Any Microbiological examination	4596 (75.9)
Microbiological examination for bacterial	4210 (69.5)
Microbiological examination for atypical etiology	2045 (33.8)
Microbiological examination for virus	2137 (34.2)
Bacterial or fungal Culture	
Qualified sputum culture*	1126 (18.6)
Blood culture **	645 (10.7)
BALF culture* ⁺	565 (9.3)
Pleural effusion culture**	122 (2.0)
Antibody-Based Assays on acute serum	
<i>Mycoplasma pneumoniae</i>	IgM: 1878 (31.0) IgG: 822 (13.6)
<i>Chlamydia pneumoniae</i>	IgM: 1342 (22.2) IgG: 223 (3.7)
<i>Legionella pneumoniae</i>	IgM: 665 (11.0) IgG: 230 (3.8)
Adenovirus	IgM: 665 (11.0) IgG: 0 (0.0)
Respiratory syncytial virus	IgM: 664 (11.0) IgG: 0 (0.0)
Influenza A virus	IgM: 664 (11.0) IgG: 0 (0.0)
Influenza B virus	IgM: 661 (10.9) IgG: 0 (0.0)
Parainfluenza virus	IgM: 664 (11.0) IgG: 0 (0.0)
Nucleic Acid-Based Molecular Diagnostics	
From sputum	324(5.4)
Time Interval [¶] (days, median, IQR)	12.0 (15.5)
From BALF ⁺	22 (0.4)

Time Interval¶(days, median, IQR)	15.0 (15.5)
<i>Mycoplasma pneumoniae</i>	337 (5.6)
<i>Chlamydia</i> spp	337 (5.6)
<i>Legionella</i> spp	337 (5.6)
Influenza A virus	337 (5.6)
Influenza B virus	337 (5.6)
Other respiratory virus#	337 (5.6)
Antigen test	
<i>Streptococcus pneumoniae</i>	159 (2.6)
<i>Legionella</i> spp	49 (0.8)
Influenza A virus	116 (1.9)
Influenza B virus	30 (0.5)

*: within 48hr after admission

**:within one week after admission

¶: days from illness onset to testings

parainfluenza virus (PIV) types 1, 2, 3 and 4, rhinovirus (HRV), enterovirus (EV), coronavirus (hCoV) types 229E, NL63, OC43 and HKU1, parapneumovirus (hMPV), and adenovirus (AdV), bocavirus

†: bronchoalveolar lavage fluid

Table 4: Empirical antimicrobial regimen for CAP patients (n=5942)*

Empirical antimicrobials (%)	Without risk factors for <i>P.seudomonas</i> infection (n=3880)				With risk factors for <i>P.seudomonas</i> infection (n=2062)
	age<65yr and not in ICU (n=1849)	age<65yr and in ICU (n=79)	age≥65yr and not in ICU (n=1708)	age≥65yr and in ICU (n=145)	
β-lactams (antipseudomonal)	183 (4.7) [#]	21 (0.5) [#]	411 (10.6)	58 (1.5)	574 (27.8)
β-lactams	333 (8.6)	9 (0.2)	487 (12.6)	20 (0.5)	394 (19.1)
Fluoroquinolones	509 (13.1)	10 (0.3)	275 (7.1)	6 (0.2)	288 (14.0)
Macrolides	20 (0.5)	0 (0.0)	17 (0.4)	0 (0.0)	15 (0.7)
β-lactams (antipseudomonal)	204 (5.3) [#]	13 (0.3) [#]	189 (4.9) [#]	30 (0.8)	256 (12.4)
+ fluoroquinolones					
β-lactams+ fluoroquinolones	303 (7.8) [#]	3 (0.1) [#]	166 (4.3) [#]	9 (0.2)	191 (9.3)
β-lactams+ macrolides	161 (4.1)	2 (0.1)	64 (1.6)	2 (0.1)	60 (2.9)
β-lactams (antipseudomonal)	50 (1.3) [#]	0 (0.0%) [#]	45 (1.2%)	2 (0.1%)	62 (3.0%)
+ macrolides					
Fluoroquinolones + macrolides	24 (0.6)	0 (0.0)	11 (0.3)	0 (0.0)	7 (0.3)
Others	108 (2.8)	22 (0.6)	90 (2.3)	23 (0.6)	215 (10.4)

*: data on empirical antimicrobial regimens in 114 patients were missing.

[#]Overtreatment was defined as: 1) use of antipseudomonal β-lactams or β-lactams+ fluoroquinolones in patients aged <65yr without risk factors for *P.seudomonas* infection; 2) use of (antipseudomonal or not) β-lactams+ fluoroquinolones in patients aged > 65yr without risk factors for *P.seudomonas* infection and not in ICU ^[13].

- Risk factors for *P.seudomonas* infection was defined as chronic airway disease (bronchiectasis or COPD), immunocompromised status and HCAP according to IDSA/ATS criteria ^[13].

Table 5: Supportive treatment and clinical outcomes of patients with CAP

Items	Cases (%)
ICU admission	391 (6.5)
Mechanical ventilation	
Non-invasive ventilation	304 (5.0)
Invasive ventilation in ICU	136 (2.2)
Invasive ventilation not in ICU	35 (0.6)
Vasopressor use	214 (3.5)
CRRT	18 (0.3)
ECMO	3 (0.0)
Systemic glucocorticosteroids use after diagnosis of CAP	1664 (27.5)
ICU patients who received systemic glucocorticoids	173 (10.4)
Patients on invasive mechanical ventilation who received systemic glucocorticoids	87 (5.2)
Patients on non-invasive mechanical ventilation who received systemic glucocorticoids	175 (10.5)
30-day mortality	257 (4.2)
Length of stay in Hospital (days, median, IQR)	10.0 (8.0-14.0)
Days between admission-clinical stability (median, n=5278, IQR)	4.0 (1.0-10.0)
Days between clinical stability-discharge (median, n=5311, IQR)	5.0 (1.0-9.0)
Length of stay in ICU (days, median, n=373,IQR)	8.0 (4.0-16.0)
Treatment failure within 14 days	459 (7.6)
Needs non-invasive ventilation	180 (3.0)
Needs invasive ventilation	161 (2.7)
Needs vasopressors	144 (2.4)
Death	168 (2.8)
Direct causes of death	
Severe pneumonia/MODS	172 (66.9)
Heart failure	8 (3.1)
Stroke	5 (1.9)
Acute myocardial infarction	5 (1.9)
Hemorrhage of digestive tract	5 (1.9)

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Acute renal failure	3 (1.2)
Arrhythmia	3 (1.2)
Accident aspiration	2 (0.8)
Others	54 (21.0)

ICU: intensive care unit; CRRT: continuous renal replacement therapy; ECMO: extracorporeal membrane oxygenation; MODS: multiple organ dysfunction syndrome; DIC: disseminated intravascular coagulation.

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Appendix 1: Details of Participating centers

Name of the hospital	Province, city	2 nd and 3 rd level hospital	Teaching Hospital	Beds	Staff of Clinical Microbiology Lab
Beijing Chao-Yang Hospital Affiliated to Capital Medical University	Beijing	3 rd	Yes	1400	11
Beijing Jishuitan Hospital 4 th Medical College of Peking University	Beijing	3 rd	Yes	1500	10
Beijing Luhe Hospital Affiliated to Capital Medical University	Beijing	3 rd	Yes	1042	5
Qingdao Municipal Hospital	ShanDong, Qingdao	3 rd	Yes	1200	4
Qilu Hospital Of Shandong University(Qindao)	ShanDong, Jinan	3 rd	Yes	1200	6
Beijing Huimin Hospital	Beijing	2 nd	Yes	500	2
Linzi District People's Hospital	ShanDong, Zibo	2 nd	Yes	1200	5
The 2 nd Hospital of Beijing Corps, Chinese Armed Police Forces	Beijing	3 rd	Yes	450	2
China-Japan Friendship Hospital	Beijing	3 rd	Yes	1610	9
Yan'an Hospital Affiliated to Kunming Medical University	Kunming, Yan'an	3 rd	Yes	1302	4

Yantai Yuhuangding Hospital	Shangdong, Yantai	3 rd	Yes	3000	6
Rizhao Chinese Medical Hospital Affiliated to Shandong Chinese Medical University	Shangdong, Rizhao	3 rd	Yes	1212	8
Weifang NO.2 People's Hospital	Shangdong, Weifang	3 rd	Yes	1006	8

Definition of 2nd and 3rd level hospital in China:

The 2nd level hospital was defined as a hospital providing medical, prevention, health care and rehabilitation services to multiple communities (with a radius of population more than 100,000 peoples); the 3rd level hospital was defined as a hospital providing medical service to the whole country beyond cities and provinces, with comprehensive medical, teaching and research ability.

Appendix 2: ICD-10

Influenza with pneumonia, other influenza virus identified	J10.0
Influenza with pneumonia, virus not identified	J11.0
Virus pneumonia, not elsewhere classified	J12
Adenoviral pneumonia	J12.0
Respiratory syncytial virus pneumonia	J12.1
Parainfluenza virus pneumonia	J12.2
Other virus pneumonia	J12.8
Viral pneumonia, unspecified	J12.9
Pneumonia due to <i>Streptococcus pneumoniae</i>	J13
Pneumonia due to <i>Haemophilus influenzae</i>	J14
Bacterial pneumonia, not elsewhere classified	J15
Pneumonia due to <i>Klebsiella pneumoniae</i>	J15.0
Pneumonia due to <i>Pseudomonas spp.</i>	J15.1
Pneumonia due to <i>Staphylococcus</i>	J15.2
Pneumonia due to <i>Streptococcus spp.</i> , group B	J15.3
Pneumonia due to other <i>streptococci</i>	J15.4
Pneumonia due to <i>Escherichia coli</i>	J15.5
Pneumonia due to other aerobic Gram-negative bacteria	J15.6
Pneumonia due to <i>Mycoplasma pneumoniae</i>	J15.7
Other bacterial pneumonia	J15.8

Bacterial pneumonia, unspecified	J15.9
Pneumonia due to other infectious organisms, not elsewhere classified	J16
Chlamydia pneumonia	J16.0
Pneumonia due to other specified infectious organisms	J16.8
Pneumonia due to other specified infectious organism	J16.8
Pneumonia in diseases classified elsewhere	J17*
Pneumonia in bacterial diseases classified elsewhere	J17.0*
Pneumonia in viral diseases classified elsewhere	J17.1*
Pneumonia in mycoses	J17.2*
Pneumonia in other diseases classified elsewhere	J17.8*
Pulmonary mycobacterial infection	A31.0
Pulmonary actinomycosis	A42.0
Pulmonary nocardiosis	A43.0
Legionnaires' disease	A48.1
Varicella pneumonia	B01.2+
Measles complicated by pneumonia	B05.1+
Cytomegaloviral pneumonitis	B25.0+
Pulmonary candidiasis	B37.1
Acute pulmonary coccidioidomycosis	B38.0
Acute pulmonary histoplasmosis capsulati	B39.0
Acute pulmonary blastomycosis	B40.0

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Pulmonary paracoccidioidomycosis	B41.0
Pulmonary sporotrichosis	B42.0+
Invasive pulmonary aspergillosis	B44.0
Other pulmonary aspergillosis	B44.1
Pulmonary cryptococcosis	B45.0
Pulmonary mucormycosis	B46.0
Pneumonia, organism unspecified	J18
Bronchopneumonia, unspecified organism	J18.0
Lobar pneumonia, unspecified	J18.1
Hypostatic, pneumonia, unspecified	J18.2
Other pneumonia, organism unspecified	J18.8
Pneumonia, unspecified	J18.9

Appendix 3: Case Report Form Of Patients Hospitalized With CAP/HCAP

Code:	R-
Name:	Gender: <input type="radio"/> Male <input type="radio"/> Female
Age: ____years old	Nationality: <input type="radio"/> Han <input type="radio"/> Others
Height: ____cm	Weight: __ kg
ID Number:	
Date Of Admission: ____Y ____M ____D	
Case Number :	ID Number:
Admission Form:	<input type="radio"/> Outpatience <input type="radio"/> Emergency <input type="radio"/> Transfers
Tel:	Cell Phone:
Provider Payments: <input type="radio"/> Social Medical Insurance <input type="radio"/> New Rural Cooperative Medical System <input type="radio"/> Medical Services At State Expense <input type="radio"/> Commercial Medical Insurance <input type="radio"/> Self-paying <input type="radio"/> Others	

Study Director: Bin Cao

Team Members: Liang Chen、 Hu Li、 Meng Liu、 Xiudi Han、 Xiaoli Zhu 、 Bo Liu、 Jinxiang Wang、 Xuexin Yao、 Chunxiao Zhang、 Shujing Shi、 Fei Zhou、 Chunxue Xue、 Yanli Li、 Donghao Yu
(Beijing Chao-Yang Hospital 001; Beijing Jishuitan Hospital 002; Beijing Luhe Hospital 003; Qingdao Municipal Hospital 004; Qilu Hospital Of Shandong University(Qindao) 005; Beijing Huimin Hospital 006; Linzi District People's Hospital 007; The 2nd Hospital of Beijing Corps, Chinese Armed Police Forces 008; China-Japan Friendship Hospital 009; Yan'an Hospital Affiliated to Kunming Medical University 010)

Inclusion Criteria:

1. Age ≥ 14 years old
2. Onset in community
3. Chest X-ray or CT scan showing infiltration or interstitial changes, with or without pleural effusion
4. Any one of pneumonia clinical manifestations, including:
 - (a) Recent cough, sputum or aggravation of respiratory symptoms, the emergence of purulent sputum, with or without chest pain;
 - (b) Fever (temperature $\geq 37.3^{\circ}\text{C}$) or hypothermia (temperature $< 36^{\circ}\text{C}$);
 - (c) Signs of pulmonary consolidation and (or) moist rales;
 - (d) $\text{WBC} > 10 \times 10^9/\text{L}$, or $< 4 \times 10^9/\text{L}$, with or without nucleus left.

Meet criteria 1,2 ,3 and anyone of criteria 4

Exclusion Criteria:

1. Lung infiltrate or interstitial changes which can be interpreted as lung cancer, pulmonary tuberculosis, non-infectious interstitial lung diseases, pulmonary edema, atelectasis, pulmonary embolism, pulmonary eosinophil infiltration, pulmonary vasculitis;
2. HIV positive
3. Readmission within 72 hours after discharging.

Part 1: Baseline Characteristics

Underlying Disease	
COPD <input type="radio"/> Y <input type="radio"/> N	Asthma <input type="radio"/> Y <input type="radio"/> N
Bronchiectasis <input type="radio"/> Y <input type="radio"/> N	Malignancy <input type="radio"/> Y <input type="radio"/> N
Sleep Apnea Syndrome <input type="radio"/> Y <input type="radio"/> N	Congestive Heart Failure <input type="radio"/> Y <input type="radio"/> N
Coronary Heart Disease <input type="radio"/> Y <input type="radio"/> N	Hypertention <input type="radio"/> Y <input type="radio"/> N
Peripheral Vascular Diseases <input type="radio"/> Y <input type="radio"/> N	Diabetes Mellitus <input type="radio"/> Y <input type="radio"/> N
Cerebrovascular Disease <input type="radio"/> Y <input type="radio"/> N	Autoimmune Diseases ^a <input type="radio"/> Y <input type="radio"/> N
Chronic Viral Hepatitis <input type="radio"/> Y <input type="radio"/> N	Cirrhosis <input type="radio"/> Y <input type="radio"/> N
Hematological Malignancy <input type="radio"/> Y <input type="radio"/> N	Organ /bone Marrow Transplantation <input type="radio"/> Y <input type="radio"/> N
Immunosuppressive Therapy ^b <input type="radio"/> Y <input type="radio"/> N	Chemotherapy/Radiotherapy Within 6 Months <input type="radio"/> Y <input type="radio"/> N
Chronic Renal Diseases <input type="radio"/> Y <input type="radio"/> N	Splenectomy <input type="radio"/> Y <input type="radio"/> N

Note: a.SLE, Sjogren's syndrome, rheumatoid arthritis, polymyositis / dermatomyositis, systemic vasculitis, ankylosing spondylitis, inflammatory bowel disease, hyperthyroidism, etc;; b.Anti-rejection drugs

With The Following Situation	
Pregnancy	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown; If Y, Pregnancy__weeks.
Within 6 months after delivery	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown; If Y, __weeks after delivery
Smoking	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Former Smoker <input type="radio"/> Unknown If Y, Smoked For__years, __cigarettes/day; If Former Smoker, Smoked For__years, __cigarettes/day ,GivenUp For__years
Alcoholism ^a	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown
Risk factors for inhalation ^b	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown
Contact Children In Day-care Center	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown
Bed Ridden (≥2months)	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown
Long-term inhaled Corticosteroid use ^d	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown
Long-term oral Corticosteroid use ^c	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown; If Y, Name Of Corticosteroid: _____,

	Dose __mg/day, For __days
Oral Statin Drugs	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown
History Of CAP Within One Year	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown
Influenza Vaccine Within 1 Year	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown
<i>Streptococcus pneumoniae</i> Vaccine Within 5 Years	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown

Note: **a:** drinking more than 5 bottles of beer (500ml / bottle) or half a catty liquor once in 2 weeks; or drinking more than 2.5 bottles of beer (500ml / bottle) or 2 ounce of white spirit per day for more than five years; **b:** Inhalation risk factors included choking, drowning, nasal, pseudobulbar palsy, dementia, coma, poisoning, Parkinson's disease, etc; **c:** Long-term oral corticosteroids was defined as: oral prednisone ≥ 10 mg / d or equivalent doses of other corticosteroids for more than 3 weeks; **d:** Long-term inhaled corticosteroids was defined as: inhaled corticosteroid for more than 30 days, the daily dose wasn't limited.

Risk Factors Of Health-Care Acquired Pneumonia	
Hospitalization For 2d Or More In The Preceding 90 Days	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown
Home Infusion Therapy (Including Antibiotics) Or Home Wound Care In 30 Days	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown
Chronic dialysis within 30 Days	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown
Residence In A Nursing Home Or Extended Care Facility	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown

Part 2: Data of This Hospitalization

1. Signs And Symptoms

History Of Present Illness	
Clinical Manifestation	
Date Of Illness Onset : ____Y ____M ____D	
Fever? (T\geq37.3 °C)	<input type="radio"/> Y <input type="radio"/> N; If Y, Tmax: ____°C
Hypothermia? (T<36°C)	<input type="radio"/> Y <input type="radio"/> N; If Y, Tmin: ____°C
Cough?	<input type="radio"/> Y <input type="radio"/> N
Sputum?	<input type="radio"/> Y <input type="radio"/> N; If Y, <input type="radio"/> Yellow Phlegm <input type="radio"/> White Phlegm <input type="radio"/> Bloody Sputum <input type="radio"/> Unknown
Chest Pain?	<input type="radio"/> Y <input type="radio"/> N
Shortness Of Breath?	<input type="radio"/> Y <input type="radio"/> N
Sore Throat Or Rhinorrhea	<input type="radio"/> Y <input type="radio"/> N
Chill/Shiver	<input type="radio"/> Y <input type="radio"/> N
Exhaustion/	<input type="radio"/> Y <input type="radio"/> N

Muscle And Joint Aches//Headache	
Darrhea?	<input type="radio"/> Y <input type="radio"/> N
Familial Aggregation (2 Epidemiological Related People Suffered From Pneumonia In Two Weeks) ?	<input type="radio"/> Y <input type="radio"/> N
Physical Examination (The Worst Value Of The Day On Admission)	
Tmax, °C	
Tmin, °C	
HR, beats/min	
RR, breaths/min	
BP(Systolic Pressure / Diastolic Pressure), mmHg	
Disorder Of Consciousness?	<input type="radio"/> Y <input type="radio"/> N
Cyanosis?	<input type="radio"/> Y <input type="radio"/> N
Physical Signs Of Lung:	Moist rales <input type="radio"/> Y <input type="radio"/> N Dry rales <input type="radio"/> Y <input type="radio"/> N
Edema Of Legs?	<input type="radio"/> Y <input type="radio"/> N; If Y, Asymmetric Edema Of Legs? <input type="radio"/> Y <input type="radio"/> N

3.Pre-hospital Medical Data Y N

Radiology		
Chest X-ray <input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown Date of Examination: ___Y___M___D	Site Of Pneumonia	<input type="radio"/> Bilateral Lung <input type="radio"/> Unilateral Lung
	Site Of Pneumonia	<input type="radio"/> Superior Lobe Of Right Lung <input type="radio"/> Middle Lobe Of Right Lung <input type="radio"/> Inferior Lobe Of Right Lung <input type="radio"/> Superior Lobe Of Left Lung <input type="radio"/> Inferior Lobe Of Left Lung <input type="radio"/> Unknown
	Plural effusion	<input type="radio"/> N <input type="radio"/> Left <input type="radio"/> Right <input type="radio"/> Bilateral
	Cavity	<input type="radio"/> Y <input type="radio"/> N
	consolidation	<input type="radio"/> Y <input type="radio"/> N
	Interstitial Change	<input type="radio"/> Y <input type="radio"/> N
Lung CT <input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown Date of Examination: ___Y___M___D	Infiltration	<input type="radio"/> Y <input type="radio"/> N
	Alveolar Infiltration	<input type="radio"/> Superior Lobe Of Right Lung <input type="radio"/> Middle Lobe Of Right Lung <input type="radio"/> Inferior Lobe Of Right Lung <input type="radio"/> Superior Lobe Of Left Lung <input type="radio"/> Inferior Lobe Of Left Lung <input type="radio"/> Bilateral Diffuse Infiltration <input type="radio"/> Unilateral Diffuse iInfiltration

	Plural effusion	<input type="radio"/> N <input type="radio"/> Left <input type="radio"/> Right <input type="radio"/> Bilateral
	Cavity	<input type="radio"/> Y <input type="radio"/> N
	consolidation	<input type="radio"/> Y <input type="radio"/> N
	Abscesses	<input type="radio"/> Y <input type="radio"/> N
	Patchy Shadow	<input type="radio"/> Y <input type="radio"/> N
	Interstitial change	<input type="radio"/> Y <input type="radio"/> N
Microbiological Examination		
Microbiological Examination Before Admission <input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown		
If Y: Date Of Specimen Collection: ____Y__M__D Specimen Type: <input type="radio"/> Sputum <input type="radio"/> Blood <input type="radio"/> BALF <input type="radio"/> Asopharyngeal Swab <input type="radio"/> Endotracheal Aspirate <input type="radio"/> Plural Effusion <input type="radio"/> Urine Microbiological Examination Results: _____		
Treatment Before Admission		
Antimicrobials Before Admission <input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown		
Drug name (Generic Name And Trade Name)	Route Of Administration	Drug Regime n
eg: Ceftriaxone (罗氏芬)	<input checked="" type="radio"/> Intravenous <input type="radio"/> Oral	2.0g , Qd
	<input type="radio"/> Intravenous <input type="radio"/> Oral	
	<input type="radio"/> Intravenous <input type="radio"/> Oral	
	<input type="radio"/> Intravenous <input type="radio"/> Oral	
	<input type="radio"/> Intravenous <input type="radio"/> Oral	
Antiviral Drug Use Before Admission <input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown		
	<input type="radio"/> Intravenous <input type="radio"/> Oral	
	<input type="radio"/> Inhalation	
	<input type="radio"/> Intravenous <input type="radio"/> Oral	
	<input type="radio"/> inhalation	
Corticosteroid Use Before Admission <input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown		
	<input type="radio"/> Intravenous <input type="radio"/> Oral	
	<input type="radio"/> inhalation	
	<input type="radio"/> Intravenous <input type="radio"/> Oral	
	<input type="radio"/> inhalation	
Vasopressor Use Before Admission <input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown		
If Y, Start Time: _____		Terminal Time: _____
Invasive Ventilation Before Admission <input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown		
If Y, Start Time: _____		Terminal Time: _____

Note: b. Vasopressors: Norepinephrine, Dopamine, Dobutamine, Metaraminol, adrenaline

4. Laboratory Examination In 24hr On Admission

Category	Item	Value	Unit
Blood Routine	WBC		*10 ⁹ /L
	Neu		*10 ⁹ /L
	Lym		*10 ⁹ /L
	HGB		g/L
	HCT		%
	PLT		*10 ⁹ /L
Biochemistry	ALB		g/L
	LDH		U/L
	AST		U/L
	ALT		U/L
	ALP		U/L
	TBIL		umol/L
	DBIL		umol/L
	CK		U/L
	BUN		mmol/L
	Cr		mmol/L
	Glu		mmol/L
	K		mmol/L
	Na		mmol/L
	Serum Detection	ESR	
CRP			mg/dL
PCT			ng/ml
D-dimer			ng/ml
PT			s
APTT			s
INR			
BNP			pg/ml
Ferritin		ug/l	

5. Blood Gas Analysis, Radiology and Ultrasonography After Admission

Category	Item	Value
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The Worst Value In 24hr On Admission)	Blood gas analysis	Oxygen Therapy* <input type="radio"/> Y <input type="radio"/> N		<input type="radio"/> Oxygen Inhalation Through Nasal Tube___L/min <input type="radio"/> Oxygen Inhalation Through Venturi Mask_____% <input type="radio"/> Oxygen Inhalation Through Oxygen Masks_L/min <input type="radio"/> Non-invasive Ventilation <input type="radio"/> Invasive Ventilation <input type="radio"/> Unknowen
		FiO ₂		
		pH		
		PO ₂ (mmHg)		
		PCO ₂ (mmHg)		
		SaO ₂		
		Actual Bicarbonate (mmol/l)		
		Lac (mmol/l)		
In 24hr On Admission)	Radiology	Chest X-ray <input type="radio"/> Y <input type="radio"/> N	Alveolar Infiltration	<input type="radio"/> Superior Lobe Of Right Lung <input type="radio"/> Middle Lobe Of Right Lung <input type="radio"/> Inferior Lobe Of Right Lung <input type="radio"/> Superior Lobe Of Left Lung <input type="radio"/> Inferior Lobe Of Left Lung <input type="radio"/> Bilateral Diffuse Infiltration <input type="radio"/> Unilateral Diffuse Infiltration
			Plural effusion	<input type="radio"/> N <input type="radio"/> Left <input type="radio"/> Right <input type="radio"/> Bilateral
			Cavity	<input type="radio"/> Y <input type="radio"/> N
			consolidation	<input type="radio"/> Y <input type="radio"/> N
			Patchy Shadow	<input type="radio"/> Y <input type="radio"/> N
			Interstitial Change	<input type="radio"/> Y <input type="radio"/> N
		Lung CT <input type="radio"/> Y <input type="radio"/> N	Alveolar Infiltration	<input type="radio"/> Superior Lobe Of Right Lung <input type="radio"/> Middle Lobe Of Right Lung <input type="radio"/> Inferior Lobe Of Right Lung <input type="radio"/> Superior Lobe Of Left Lung <input type="radio"/> Inferior Lobe Of Left Lung <input type="radio"/> Bilateral Diffuse Infiltration <input type="radio"/> Unilateral Diffuse Infiltration
			Plural effusion	<input type="radio"/> N <input type="radio"/> Left <input type="radio"/> Right <input type="radio"/> Bilateral
			Cavity	<input type="radio"/> Y <input type="radio"/> N
			consolidation	<input type="radio"/> Y <input type="radio"/> N
			Patchy Shadow	<input type="radio"/> Y <input type="radio"/> N

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		Interstitial Change	<input type="radio"/> Y <input type="radio"/> N
		Alveolar Infiltration	<input type="radio"/> Superior Lobe Of Right Lung <input type="radio"/> Middle Lobe Of Right Lung <input type="radio"/> Inferior Lobe Of Right Lung <input type="radio"/> Superior Lobe Of Left Lung <input type="radio"/> Inferior Lobe Of Left Lung <input type="radio"/> Bilateral Diffuse Infiltration <input type="radio"/> Unilateral Diffuse Infiltration
Ultrasonography	Lower Limb Vascular Ultrasound Exam	Venous Thrombosis	<input type="radio"/> N <input type="radio"/> Left <input type="radio"/> Right <input type="radio"/> Bilateral <input type="radio"/> Unexamined

Note: The Worst Value Of Blood Gas Analysis And FiO2 At That Time.

For peer review only

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4 **6.Keep Detailed Records Of The Following Time Points,And Write down The Code In The First Row Of The Table:**

- 5 ①The 4th day (The Day On Admission Is The 1st Day); ②The day of changing Antibiotics in 14 days After Admission; ③The 14th day after Admission ;
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7 ④The Day Of Discharging
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Category	Item(Unit)	The Reason and The Date					
Vital Signs	Disorder Of Consciousness						
	Tmax (°C)						
	Tmin(°C)						
	HR (beats/min)						
	RR (breaths/min)						
	BP(/ mmHg)						
Symptoms 1. Exacerbation 2. Alleviation 3. No-change	Cough						
	Sputum						
	Chest Pain						
	Shortness Of Breath						
	Moist Rales						
	Dry Rales						
Blood Routine	WBC (*10^9/L)						
	Neu (*10^9/L)						
	Lym (*10^9/L)						
	HGB (g/L)						
	HCT (%)						
	PLT (*10^9/L)						
Biochemistry	ALB (g/L)						
	LDH (U/L)						
	AST (U/L)						
	ALT (U/L)						
	ALP (U/L)						
	TBIL (umol/L)						
	DBIL (umol/L)						
	CK (U/L)						
	CTNI (ng/ml)						
	BUN (mmol/L)						
Cr (mmol/L)							

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Note: a. Direct Microscopy of sputum is not included

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7. Treatment During Hospitalization

Antibiotics Use <input type="radio"/> Y <input type="radio"/> N				
Drug Name (Generic Name And Trade Name)	Route Of Administration	Drug Regimen	Start Time	Terminal Ttime
eg: Ceftriaxone (罗氏芬)	<input checked="" type="radio"/> Intravenous <input type="radio"/> Oral	2.0g, Qd	2014-3-2	2014-4-5
	<input type="radio"/> Intravenous <input type="radio"/> Oral			
	<input type="radio"/> Intravenous <input type="radio"/> Oral			
	<input type="radio"/> Intravenous <input type="radio"/> Oral			
	<input type="radio"/> Intravenous <input type="radio"/> Oral			
	<input type="radio"/> Intravenous <input type="radio"/> Oral			
	<input type="radio"/> Intravenous <input type="radio"/> Oral			
	<input type="radio"/> Intravenous <input type="radio"/> Oral			
Antiviral Drugs Use <input type="radio"/> Y <input type="radio"/> N				
Drug name (Generic Name And Trade Name)	Route Of Administration	Drug Regimen	Start Time	Terminal Time
	<input type="radio"/> Intravenous <input type="radio"/> Oral <input type="radio"/> Inhalation			
	<input type="radio"/> Intravenous <input type="radio"/> Oral <input type="radio"/> Inhalation			
	<input type="radio"/> Intravenous <input type="radio"/> Oral <input type="radio"/> Inhalation			
Glucocorticoids Use <input type="radio"/> Y <input type="radio"/> N				
Drug name (Generic Name And Trade Name)	Route Of Administration	Drug Regimen	Start Time	Terminal Time
	<input type="radio"/> Intravenous <input type="radio"/> Oral <input type="radio"/> Inhalation			
	<input type="radio"/> Intravenous <input type="radio"/> Oral <input type="radio"/> Inhalation			
Vasopressors Use <input type="radio"/> Y <input type="radio"/> N				
Drug Name	Route Of Administration	Drug Regimen	Start Time	Terminal Ttime
Immunoregulation Drugs (Including Intravenous Immunoglobulin , Thymosins) <input type="radio"/> Y <input type="radio"/> N				
Drug Name	Route of administration	Drug Regimen	Start time	Terminal time

Alternative/ Supportive Treatment			
Item	Use	Start Time	Terminal Time
Continuous Venous-venous Hemofiltration	<input type="radio"/> Y <input type="radio"/> N		
Extracorporeal Membrane Oxygenation (ECMO)	<input type="radio"/> Y <input type="radio"/> N		
Non-invasive Ventilation	<input type="radio"/> Y <input type="radio"/> N		
Invasive Ventilation	<input type="radio"/> Y <input type="radio"/> N		

8. Measurement Of T Lymphocyte Subsets

Date of specimen collection: Y M D

T lymphocyte subsets	CD4		/ml
	CD8		/ml
	CD4%		
	CD8%		
	NK		/ml
	NKT		/ml
	CD4/CD8		

Note: Without Time Limitation

9. Microbiological Examination

(1). Microbiological Examination In 48hrs After Admission Y N

Microbiological Examination For Sputum Or eEndotracheal aAspiration	
Date Of Specimen Collection: <u> </u> Y <u> </u> M <u> </u> D	
Item	Results
Direct Microscopy	<input type="radio"/> Good Quality Sputum (> 25 leukocytes and < 10 epithelial cells per × 100 magnification field) <input type="radio"/> Not Good Quality Sputum <input type="radio"/> Unknown
	<input type="radio"/> G+ Cocci <input type="radio"/> G+ Bacillus <input type="radio"/> G- Cocci <input type="radio"/> G- Bacillus <input type="radio"/> Positive Acid-fast Stain <input type="radio"/> None

Bacteria Culture	<input type="checkbox"/> Streptococcus pneumoniae <input type="checkbox"/> Moraxella catarrhalis <input type="checkbox"/> Haemophilus influenzae <input type="checkbox"/> Staphylococcus aureus <input type="checkbox"/> Pseudomonas aeruginosa <input type="checkbox"/> Klebsiella pneumoniae <input type="checkbox"/> Enterobacter cloacae <input type="checkbox"/> Proteus spp <input type="checkbox"/> Acinetobacter spp <input type="checkbox"/> Serratia marcescens <input type="checkbox"/> Stenotrophomonas maltophilia <input type="checkbox"/> Enterobacter aerogenes <input type="checkbox"/> Escherichia coli <input type="checkbox"/> Enterococcus faecalis <input type="checkbox"/> Enterococcus faecium <input type="checkbox"/> Others: ____ <input type="checkbox"/> None Or Normal oropharyngeal flora
	Drug Resistant Bacteria <input type="checkbox"/> Methicillin Resistance Staphylococcus aureus (MRSA) <input type="checkbox"/> Vancomycin-resistant Enterococcus Bacteria producing ESBLs: <input type="checkbox"/> Escherichia coli <input type="checkbox"/> Klebsiella pneumoniae <input type="checkbox"/> Enterobacter cloacae <input type="checkbox"/> Serratia marcescens non - fermentative bacteria.: <input type="checkbox"/> Acinetobacter baumannii <input type="checkbox"/> Pseudomonas aeruginosa <input type="checkbox"/> Others: ____ If Streptococcus pneumoniae , MIC for penicillin ____ug/ml; <input type="checkbox"/> Not detected If MRSA, MIC for Vancomycin ____ug/ml; <input type="checkbox"/> Not detected
Direct Microscopy	<input type="checkbox"/> Fungal Spore <input type="checkbox"/> Fungal Hyphae <input type="checkbox"/> Cryptococcus neoformans <input type="checkbox"/> None
Fungi Culture	<input type="checkbox"/> Sporangium Fumigatus <input type="checkbox"/> Aspergillus flavus <input type="checkbox"/> Aspergillus terreus <input type="checkbox"/> Mucor Mucedo <input type="checkbox"/> Candida Spp <input type="checkbox"/> Cryptococcus Neoformans <input type="checkbox"/> Undetected <input type="checkbox"/> Others: ____
Nucleic Acid Test For Respiratory Virus	<input type="checkbox"/> Influenza A H1N1 <input type="checkbox"/> Avian influenza H7N9 <input type="checkbox"/> Influenza A H2N3 <input type="checkbox"/> Influenza A H5N1 <input type="checkbox"/> Nontypeable Influenza A <input type="checkbox"/> Influenza B <input type="checkbox"/> Adenovirus <input type="checkbox"/> Parainfluenza virus 1 <input type="checkbox"/> Parainfluenza virus 2 <input type="checkbox"/> Parainfluenza virus 3 <input type="checkbox"/> Parainfluenza virus 4 <input type="checkbox"/> Respiratory syncytial virus A <input type="checkbox"/> Rhinovirus <input type="checkbox"/> Respiratory syncytial virus B <input type="checkbox"/> Coronavirus OC43HKU1 <input type="checkbox"/> Enterovirus <input type="checkbox"/> Coronavirus 229ENL63 <input type="checkbox"/> Herpes simplex virus <input type="checkbox"/> Bocavirus <input type="checkbox"/> Cytomegalovirus <input type="checkbox"/> EB virus <input type="checkbox"/> MERS-CoV

Nucleic Acid Test For Atypical Etiology	<input type="radio"/> Mycoplasma pneumoniae <input type="radio"/> Chlamydia pneumoniae <input type="radio"/> Legionella spp
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(2).Microbiological Examination For BALF? Y N

Microbiological examination for BALF (Within One Week After Admission)	
Date Of Specimen Collection: <u> </u> <u> </u> <u> </u> <u> </u> <u> </u> <u> </u>	
Item	Results
Direct Microscopy	<input type="radio"/> G+ Cocci <input type="radio"/> G+ Bacillus <input type="radio"/> G- Cocci <input type="radio"/> G- Bacillus <input type="radio"/> Positive Acid-fast Stain <input type="radio"/> None
Bacteria Culture	<input type="radio"/> Streptococcus pneumoniae <input type="radio"/> Moraxella catarrhalis <input type="radio"/> Haemophilus influenzae <input type="radio"/> staphylococcus aureus <input type="radio"/> Pseudomonas aeruginosa <input type="radio"/> Klebsiella pneumoniae <input type="radio"/> Enterobacter cloacae <input type="radio"/> Proteus spp <input type="radio"/> Acinetobacter spp <input type="radio"/> Serratia marcescens <input type="radio"/> Stenotrophomonas maltophilia <input type="radio"/> Enterobacter aerogenes <input type="radio"/> Escherichia coli <input type="radio"/> Enterococcus faecalis <input type="radio"/> Enterococcus faecium <input type="radio"/> Others: ____ <input type="radio"/> None Or Normal oropharyngeal flora
	Drug Resistant Bacteria
	<input type="radio"/> Methicillin Resistance Staphylococcus aureus (MRSA) <input type="radio"/> Vancomycin-resistant Enterococcus Bacteria producing ESBLs: <input type="radio"/> Escherichia coli <input type="radio"/> Klebsiella pneumoniae <input type="radio"/> Enterobacter cloacae <input type="radio"/> Serratia marcescens non - fermentative bacteria.: <input type="radio"/> Acinetobacter baumannii <input type="radio"/> Pseudomonas aeruginosa <input type="radio"/> Others: ____
	If Streptococcus pneumoniae , MIC for penicillin ____ug/ml; <input type="radio"/> Not Detected
	If MRSA, MIC for Vancomycin ____ug/ml; <input type="radio"/> Not Detected
Direct Microscopy	<input type="radio"/> Fungal Spore <input type="radio"/> Fungal Hyphae <input type="radio"/> Cryptococcus neoformans <input type="radio"/> None

Fungi Culture	<input type="radio"/> <i>Spergillus Fumigatus</i> <input type="radio"/> <i>Aspergillus terreus</i> <input type="radio"/> <i>Candida Spp</i> <input type="radio"/> Undetected	<input type="radio"/> <i>Aspergillus flavus</i> <input type="radio"/> <i>Mucor Mucedo</i> <input type="radio"/> <i>Cryptococcus Neoformans</i> <input type="radio"/> Others: ____
Nucleic Acid For Respiratory Virus	<input type="radio"/> Influenza A H1N1 <input type="radio"/> Influenza A H2N3 <input type="radio"/> Nontypeable Influenza A <input type="radio"/> Adenovirus <input type="radio"/> Parainfluenza virus 2 <input type="radio"/> Parainfluenza virus 4 <input type="radio"/> Rhinovirus <input type="radio"/> Coronavirus OC43HKU1 <input type="radio"/> Coronavirus 229ENL63 <input type="radio"/> Bocavirus <input type="radio"/> EB virus	<input type="radio"/> Avian influenza H7N9 <input type="radio"/> Influenza A H5N1 <input type="radio"/> Influenza B <input type="radio"/> Parainfluenza virus 1 <input type="radio"/> Parainfluenza virus 3 <input type="radio"/> Respiratory syncytial virus A <input type="radio"/> Respiratory syncytial virus B <input type="radio"/> Enterovirus <input type="radio"/> Herpes simplex virus <input type="radio"/> Cytomegalovirus <input type="radio"/> MERS-CoV
Nucleic Acid Test For Atypical Etiology	<input type="radio"/> <i>Mycoplasma pneumoniae</i> <input type="radio"/> <i>Legionella spp</i>	<input type="radio"/> <i>Chlamydia pneumoniae</i>

(3). Blood Culture In One Week After Admission? Y N

Blood Culture (In One Week After Admission)		
Date Of Specimen Collection: <u> </u> <u> </u> <u> </u>		
Item	Results	
Bacteria Culture	<input type="radio"/> <i>Staphylococcus aureus</i> <input type="radio"/> <i>Haemophilus influenzae</i> <input type="radio"/> <i>Klebsiella pneumoniae</i> <input type="radio"/> <i>Proteus spp</i> <input type="radio"/> <i>Serratia marcescens</i> <input type="radio"/> <i>Enterobacter aerogenes</i> <input type="radio"/> <i>Enterococcus faecalis</i> <input type="radio"/> Others: ____	<input type="radio"/> <i>Moraxella catarrhalis</i> <input type="radio"/> <i>Pseudomonas aeruginosa</i> <input type="radio"/> <i>Enterobacter cloacae</i> <input type="radio"/> <i>Acinetobacter spp</i> <input type="radio"/> <i>Stenotrophomonas maltophilia</i> <input type="radio"/> <i>Escherichia coli</i> <input type="radio"/> <i>Enterococcus faecium</i> <input type="radio"/> None or normal oropharyngeal flora
	Drug Resistant Bacteria	
	<input type="radio"/> Methicillin resistance staphylococcus aureus (MRSA) <input type="radio"/> Vancomycin-resistant Enterococcus Bacteria producing ESBLs: <input type="radio"/> <i>Escherichia coli</i> <input type="radio"/> <i>Enterobacter cloacae</i> non - fermentative bacteria.: <input type="radio"/> <i>Acinetobacter baumannii</i> <input type="radio"/> <i>Klebsiella pneumoniae</i> <input type="radio"/> <i>Serratia marcescens</i> <input type="radio"/> <i>Pseudomonas aeruginosa</i> <input type="radio"/> Others: ____	

	If Streptococcus pneumoniae , MIC for penicillin___ug/ml; <input type="radio"/> Not Detected	
	If MRSA, MIC for Vancomycin___ug/ml; <input type="radio"/> Not Detected	
Fungi Culture	<input type="radio"/> Candidiasis albicans <input type="radio"/> Candida tropicalis <input type="radio"/> Candida parapsilosis <input type="radio"/> Aspergillus fumigatus <input type="radio"/> Aspergillus terreus <input type="radio"/> Undetected	<input type="radio"/> Candida krusei <input type="radio"/> Candida glabrata <input type="radio"/> Cryptococcus neoformans <input type="radio"/> Aspergillus flavus <input type="radio"/> Mucor Mucedo <input type="radio"/> Others: ___

(4)、Pleural Effusion? Y N

Pleural Effusion Test? Y N

Microbiological Examination For Pleural Effusion (Without Time Limitation)	
Date of Specimen collection: <u> </u> Y <u> </u> M <u> </u> D	
Pleural Effusion Routine	
Total Cell Count: <u> </u> ×10 ⁶ /L; Multinuclear Cell: <u> </u> ×10 ⁶ /L; Mononuclear Cells: <u> </u> ×10 ⁶ /L	
Pleural Effusion Biochemistry	
LDH: <u> </u> U/L; ADA: <u> </u> U/L; Pr: <u> </u> g/L Glu: <u> </u> mmol/L Cl: <u> </u> mmol/L	
Item	Results
Bacteria Culture	<input type="radio"/> Staphylococcus aureus <input type="radio"/> Moraxella catarrhalis <input type="radio"/> Haemophilus influenzae <input type="radio"/> Pseudomonas aeruginosa <input type="radio"/> Klebsiella pneumoniae <input type="radio"/> Enterobacter cloacae <input type="radio"/> Proteus spp <input type="radio"/> Acinetobacter spp <input type="radio"/> Serratia marcescens <input type="radio"/> Stenotrophomonas maltophilia <input type="radio"/> Enterobacter aerogenes <input type="radio"/> Escherichia coli <input type="radio"/> Enterococcus faecalis <input type="radio"/> Enterococcus faecium <input type="radio"/> Others: _____ <input type="radio"/> None or Normal Oropharyngeal Flora
	Drug Resistant Bacteria <input type="radio"/> Methicillin resistance staphylococcus aureus (MRSA) <input type="radio"/> Vancomycin-resistant Enterococcus Bacteria producing ESBLs: <input type="radio"/> Escherichia coli <input type="radio"/> Klebsiella pneumoniae <input type="radio"/> Enterobacter cloacae <input type="radio"/> Serratia marcescens non - fermentative bacteria.: <input type="radio"/> Acinetobacter baumannii <input type="radio"/> Pseudomonas aeruginosa <input type="radio"/> Others: ___
Fungi Culture	<input type="radio"/> Candidiasis albicans <input type="radio"/> Candida krusei <input type="radio"/> Candida tropicalis <input type="radio"/> Candida glabrata

<input type="radio"/> Candida parapsilosis <input type="radio"/> Aspergillus fumigatus <input type="radio"/> Aspergillus terreus <input type="radio"/> Undetected	<input type="radio"/> Cryptococcus neoformans <input type="radio"/> Aspergillus flavus <input type="radio"/> Mucor Mucedo <input type="radio"/> Others: _
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(5)、Antigen Test In 48hr After Admission? Y N

Urinary antigen (in 48hr after admission)	
Date of specimen collection: <u> </u> Y <u> </u> M <u> </u> D	
Urinary Antigen For <i>Legionella</i> <i>spp</i>	<input type="radio"/> Positive <input type="radio"/> Negative <input type="radio"/> Undetected
Urinary Antigen For <i>Streptococcus pneumoniae</i>	<input type="radio"/> Positive <input type="radio"/> Negative <input type="radio"/> Undetected
Throat Swab Aantigen Test (In 48hr After Admission)	
Date Of Specimen Collection: <u> </u> Y <u> </u> M <u> </u> D	
Respiratory Syncytial Virus Antigen Test	<input type="radio"/> Positive <input type="radio"/> Negative <input type="radio"/> Undetected
Influenza A Antigen Test	<input type="radio"/> Positive <input type="radio"/> Negative <input type="radio"/> Undetected
Influenza B Antigen Test	<input type="radio"/> Positive <input type="radio"/> Negative <input type="radio"/> Undetected

(6)、Antibody Test? a) Y N

b) If Y, Titer Of Antibody In Paired Serum? Y, Interval days

N

Antibody Test (Without Time Limitation)	
Date Of Specimen Collection: <u> </u> Y <u> </u> M <u> </u> D	
<input type="radio"/> IgM for <i>Mycoplasmal pneumonia</i>	<input type="radio"/> IgM for Influenza A
<input type="radio"/> IgG for <i>Mycoplasmal pneumonia</i>	<input type="radio"/> IgM for Parainfluenza
<input type="radio"/> IgM for <i>Chlamydia spp</i>	<input type="radio"/> IgM for Q fever
<input type="radio"/> IgG for <i>Chlamydia spp.</i>	<input type="radio"/> IgM for Adenovirus
<input type="radio"/> IgM for <i>Legionella spp</i>	<input type="radio"/> IgM for Respiratory syncytial virus
<input type="radio"/> IgG for <i>Legionella spp</i>	<input type="radio"/> IgM for Parainfluenza 1,2,3

10. Outcomes

(1).Treatment Failure Within 14 Days

Treatment Failure Within 14 Days (Multiple choices)	
(The Value Of The 1 st Day On Admission As The Baseline Data)	
1.Needs Invasive Ventilation	<input type="radio"/> Y <input type="radio"/> N
2.Needs Non-invasive Ventilation	<input type="radio"/> Y <input type="radio"/> N
3.Needs Vasopressors	<input type="radio"/> Y <input type="radio"/> N
4.Death	<input type="radio"/> Y <input type="radio"/> N
The Reasons For Treatment Failure	
1.CAP Progression	Pneumonia Progression <input type="radio"/> Y <input type="radio"/> N
2.CAP Complications	Pyothorax <input type="radio"/> Y <input type="radio"/> N
	Endocarditis <input type="radio"/> Y <input type="radio"/> N
	Meningitis <input type="radio"/> Y <input type="radio"/> N
	Others: _____
3.Severe Sepsis Due To CAP	ARDS <input type="radio"/> Y <input type="radio"/> N
	Sepsis <input type="radio"/> Y <input type="radio"/> N
	Hepatic Failure <input type="radio"/> Y <input type="radio"/> N
	Renal Ffailure <input type="radio"/> Y <input type="radio"/> N
	Clotting Disorders, <input type="radio"/> Y <input type="radio"/> N
	Encephalopathy <input type="radio"/> Y <input type="radio"/> N
Others: _____	
4.Complications Or Underlying Disease Deterioration	Pulmonary Embolism <input type="radio"/> Y <input type="radio"/> N
	Myocardial Infarction <input type="radio"/> Y <input type="radio"/> N
	Arrhythmia <input type="radio"/> Y <input type="radio"/> N
	Gastrointestinal Bleeding <input type="radio"/> Y <input type="radio"/> N
	Congestive Heart Failure <input type="radio"/> Y <input type="radio"/> N
	COPD <input type="radio"/> Y <input type="radio"/> N
	Diabetes Mellitus <input type="radio"/> Y <input type="radio"/> N
	Nephropathy <input type="radio"/> Y <input type="radio"/> N
Others: _____	
5.Complications Due To Treatment	Hemopneumothorax <input type="radio"/> Y <input type="radio"/> N
	Allergic To Antibiotics <input type="radio"/> Y <input type="radio"/> N
	HAP/VAP <input type="radio"/> Y <input type="radio"/> N
	Vascular Catheter Infection <input type="radio"/> Y <input type="radio"/> N
	C. Difficile Infection <input type="radio"/> Y <input type="radio"/> N
	Iatrogenic Urinary Tract Infection <input type="radio"/> Y <input type="radio"/> N
Others: _____	
6.Unknown	<input type="radio"/> Y <input type="radio"/> N

(2). Complications During Hospitalization

Complications During Hospitalization	
Complications (Multiple Choices)	<input type="radio"/> Y <input type="radio"/> N
Respiratory Failure <input type="radio"/> Y <input type="radio"/> N	ARDS <input type="radio"/> Y <input type="radio"/> N
Heart Failure <input type="radio"/> Y <input type="radio"/> N	Acute Myocardial Infarction <input type="radio"/> Y <input type="radio"/> N
Acute Liver Failure <input type="radio"/> Y <input type="radio"/> N	Acute Renal Failure <input type="radio"/> Y <input type="radio"/> N
Septic Shock <input type="radio"/> Y <input type="radio"/> N	Stroke <input type="radio"/> Y <input type="radio"/> N
DIC <input type="radio"/> Y <input type="radio"/> N	Antibiotic Associated Diarrhea <input type="radio"/> Y <input type="radio"/> N
Arrhythmia <input type="radio"/> Y <input type="radio"/> N	MODS <input type="radio"/> Y <input type="radio"/> N
Pulmonary Embolism <input type="radio"/> Y <input type="radio"/> N	Deep Venous Thrombosis <input type="radio"/> Y <input type="radio"/> N
Ventilator Associated Pneumonia <input type="radio"/> Y <input type="radio"/> N	Gastrointestinal Bleeding <input type="radio"/> Y <input type="radio"/> N
Invasive Aspergillosis <input type="radio"/> Y <input type="radio"/> N	Mediastinal Emphysema <input type="radio"/> Y <input type="radio"/> N
Pneumothorax <input type="radio"/> Y <input type="radio"/> N	Nosocomial Bloodstream Infection <input type="radio"/> Y <input type="radio"/> N
Others <input type="radio"/> Y <input type="radio"/> N	If Y: _____

(3). Outcomes

Clinical Stability Before Discharge	<input type="radio"/> Y <input type="radio"/> N If Y, the date of clinical stability ____Y____M____D. Meet the following seven criteria: Temperature <37.8°C for more than 24hr; Heart rate ≤100 beats/min ; Respiratory rate ≤24 breaths/min ;Systolic blood pressure ≥90 mm Hg ; Arterial oxygen saturation ≥90% or pO ₂ ≥ 60 mm Hg on room air ; Ability to maintain oral intake; Normal mental status.
Admitted to RICU/ICU?	<input type="radio"/> Y <input type="radio"/> N If Y, The Date Of Admitted To RICU/ICU: ____Y____M____D The Date Of Transfer From RICU/ICU: ____Y____M____D
Discharging	The Date Of Discharging ____Y____M____D Outcome <input type="radio"/> Improvement <input type="radio"/> Against-advice discharge <input type="radio"/> Death If death, The Death Date ____Y____M____D
Direct Cause Of Death (only one choice)	<input type="radio"/> Severe Pneumonia <input type="radio"/> Respiratory Failure <input type="radio"/> Shock <input type="radio"/> Heart Failure <input type="radio"/> Acute Myocardial Infarction

	<input type="checkbox"/> Acute renal Failure	<input type="checkbox"/> Hepatic failure
	<input type="checkbox"/> DIC	<input type="checkbox"/> Stroke
	<input type="checkbox"/> Gastrointestinal Bleeding	<input type="checkbox"/> Others: _____

10. Cost And Economy Data

Total Expenses _____ Yuan:

Drugs Cost: _____ Yuan , Antimicrobials Cost _____ Yuan

Laboratory Testing Expenses: _____ Yuan

Bed Charge: _____ Yuan

Health Care Worker Labor Cost: _____ Yuan

Appendix 4: Definition of underlying diseases

- 1) Long-term smoking was defined as: cigarette smokers of 10 cigarettes/d during at least the previous year;
- 2) Alcoholism was defined as: drinking more than 5 bottles of beer (500ml / bottle) or half a catty liquor once in 2 weeks; or drinking more than 2.5 bottles of beer (500ml / bottle) or 2 ounce of white spirit per day for more than five years;
- 3) Long-term oral corticosteroids was defined as: oral prednisone $\geq 10\text{mg} / \text{d}$ or equivalent doses of other corticosteroids for more than 3 weeks ^[1].
- 4) Long-term inhaled corticosteroids was defined as: inhaled corticosteroid for more than 30 days, the daily dose wasn't limited;
- 5) COPD was defined as: persistent airflow limitation, $\text{FEV1} / \text{FVC} < 70\%$ post bronchodilator;
- 6) Asthma was defined by the history of respiratory symptoms such as wheeze, cough that varied over time and intensity, together with variable respiratory airway limitation;
- 7) Hypertension was defined as systolic blood pressure $\geq 140\text{mmHg}$ and /or diastolic blood pressure $\geq 90\text{mmHg}$ in resting status;
- 8) Coronary heart disease included angina pectoris, myocardial infarction, ischemic cardiomyopathy;
- 9) Chronic congestive heart failure was defined as cardiomegaly and ejection fraction $\leq 40\%$;
- 10) Cerebrovascular diseases included transient ischemic attack, cerebral hemorrhage, subarachnoid hemorrhage, cerebral infarction, etc;

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4 11) Diabetes mellitus: included diabetes mellitus type 1 and diabetes mellitus type 2,
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6 not included impaired glucose tolerance and impaired fasting glycaemia;
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9 12) Chronic liver disease included chronic viral hepatitis, chronic alcoholic liver
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11 disease, chronic fatty liver disease, etc;
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13 13) Chronic kidney disease included diabetic nephropathy, hypertensive renal damage,
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15 chronic glomerulonephritis, chronic pyelonephritis, lupus nephritis, IgA nephropathy,
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17 nephrotic syndrome, hereditary kidney disease, etc;
18
19 14) Connective Tissue Diseases include SLE, Sjogren's syndrome, rheumatoid arthritis,
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21 polymyositis / dermatomyositis, systemic vasculitis, ankylosing spondylitis,
22
23 inflammatory bowel disease, hyperthyroidism, etc;
24
25
26 15) Organ transplantation or bone marrow transplantation included solid organ
27
28 transplanting, such as liver transplantation, kidney transplantation, lung
29
30 transplantation or pancreas transplantation, etc and bone marrow transplantation;
31
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33 16) Aspiration risk factors included choking, drowning, nasal, pseudobulbar palsy,
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35 dementia, coma, poisoning, Parkinson's disease, etc.
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38 17) Immunosuppressive therapy: was defined as systematic glucocorticosteroid (such as
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40 prednisone ≥ 10 mg/d for more than 3 weeks in the last month); cyclosporine or
41
42 azathioprine use within 3 months, and methotrexate use ≥ 12.5 mg/week within 3
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44 months; biological modifiers such as etanercept and infliximab within 3 weeks.
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48 18) Immunocompromised status included chemotherapy/radiotherapy within 6 months,
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50 immunosuppressive therapy, organ/bone marrow transplantation, splenectomy,
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52 hematological neoplasms ^[2].
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4 19) Risk factors for pseudomonal infection was defined as chronic airway disease
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6 (bronchiectasis or COPD), immunocompromised status and HCAP risk factors
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8 according to IDSA/ATS criteria [3-7] .
9

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11 20) Overtreatment was defined as: i) use of antipseudomonal β -lactams or β -lactams+
12
13 fluoquinolones in patients aged <65yr without risk factors for pseudomonal infection; i
14
15 i) use of (antipseudomonal or not) β -lactams+ fluoquinolones in patients aged \geq 65yr
16
17 without risk factors for pseudomonal infection and not in ICU ^[3].
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55 **Appendix 5: Definition of microbiological criteria of CAP:**

56 **Definite**, if one of the following criteria was met:

- 57 4. Positive urinary antigen for *Legionella pneumophila* (LP, Binax Now L
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3 pneumophila urinary antigen test; Trinity Biotech, Bray, Ireland);
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5 5. Positive urinary antigen for *Streptococcus pneumoniae* (Binax Now *S pneumoniae*
6 urinary antigen test; Emergo Europe, The Netherlands);
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9 6. Positive bacterial culture from blood or plural fluid except for coagulase negative
10 *Staphylococcus spp.*
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13 7. Paired sera with a fourfold or more increase in the titers of antibodies to
14 *Mycoplasma pneumoniae* (MP), *Chlamydia pneumoniae*, *L pneumophila* or
15 respiratory viruses (Influenza A and B, Parainfluenza, Adenovirus, Respiratory
16 syncytial virus). Or Serum IgM antibody (MIF) $\geq 1:16$ for *Chlamydia pneumoniae*.
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21 **Probable**, if one of the following criteria was met:

- 22 a. Detection of respiratory virus in sputum/bronchoalveolar lavage (BALF)/throat
23 swabs by Realtime-PCR (Zhijiang, Shanghai, China) according to manufacturer's
24 instructions, including respiratory syncytial virus (RSV) types A and B, influenza
25 virus (IFV) types A and B, parainfluenza virus (PIV) types 1, 2, 3 and 4, rhinovirus
26 (HRV), enterovirus (EV), coronavirus (hCoV) types 229E, NL63, OC43 and
27 HKU1, parapneumovirus (hMPV), and adenovirus (AdV), bocavirus;
28
29 b. Bacteria isolated from purulent sputum (defined as an adequate quality sputum
30 sample with > 25 leukocytes and < 10 epithelial cells per $\times 100$ magnification field)
31 with compatible findings of Gram staining;
32
33 c. Detection of *Mycoplasma pneumoniae* (MP), *Chlamydia pneumoniae* or *L*
34 *pneumophila* in sputum/BALF/throat swabs by Realtime-PCR (Zhijiang,
35 Shanghai, China)
36
37 d. Positive antigen for Influenza A/B (AlereTM, Clearview Exact Influenza A& B)
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39 e. Serum IgM antibody positive for *Mycoplasma pneumoniae* (MP), or Serum IgG
40 antibody (MIF) $\geq 1:512$ for *Chlamydia pneumoniae*.
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Appendix 6: CAP patients with definite and probable microbiological diagnosis

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Etiology	Without risk factors for pseudomonal infection (n=409)				With risk factors for pseudomonal infection (n=373)	Total (n=782)
	age<65yr and not in ICU (n=182)	age<65yr and in ICU (n=29)	age≥65yr and not in ICU (n=162)	age≥65yr and in ICU (n=36)		
Bacterial	146 (83.9%)	19 (4.6%)	144 (3.2%)	35 (8.6%)	31 (8.3%)	704 (90.0%)
<i>Pseudomonas aeruginosa</i>	27	0	31	6	146	210
<i>Klebsiella pneumoniae</i>	30	9	27	10	60	136
<i>E. coli</i>	15	1	17	2	34	69
<i>Acinetobacter</i>	13	3	20	3	27	66
<i>Staphylococcus aureus</i>	7	3	10	7	26	53
<i>Enterobacter cloacae</i>	9	1	8	3	17	38
<i>Streptococcus pneumoniae</i>	9	1	5	1	11	27
<i>Stenotrophomonas</i>	8	1	10	2	6	27
<i>Enterococcus faecalis</i>	5	0	3	0	13	21
<i>Enterococcus faecium</i>	3	0	1	0	5	9
others	20	3	18	7	40	88
Atypical etiology	7 (1.7%)	5 (1.2%)	3 (0.7%)	0 (0.0%)	0 (0.0%)	12 (1.5%)
<i>Mycoplasma pneumoniae</i>	6	0	1	0	0	7
<i>Legionella pneumoniae</i>	0	1	2	0	0	3
<i>Chlamydia pneumoniae</i>	0	1	0	0	0	1
Virus	36 (8.8%)	15 (3.7%)	23 (5.6%)	2 (0.5%)	22 (5.9%)	98 (12.5%)
Influenza A virus	25	8	14	1	10	58
Rhinovirus	3	2	2	0	2	9
Influenza B virus	0	0	4	1	3	8
Adenovirus	6	1	0	0	0	7
Respiratory syncytial virus	1	0	0	0	0	1
Human metapneumovirus	0	0	1	0	0	1
Cytomegalovirus	1	1	0	0	3	5
Bacterials+viruses	4 (1.0%)	5 (1.2%)	7 (1.7%)	1 (0.2%)	9 (2.4%)	26 (3.3%)
Viruses+atypical pathogens	2 (0.5%)	2 (0.5%)	1 (0.2%)	0 (0.0%)	0 (0.0%)	5 (0.6%)

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Appendix 7: Sub-group analysis of 30-day mortality

Severity of illness	30-day mortality	P value
CURB-65		<0.001
0'	25 (1.0%)	
1'	65 (2.9%)	
2'	96 (10.4%)	
3'	50 (32.5%)	
4'	6 (30.0%)	
5'	1 (50.0%)	
PSI risk class		<0.001
I	8 (0.7%)	
II	10 (1.1%)	
III	23 (3.0%)	
IV	70 (10.3%)	
V	59 (30.6%)	
Age		<0.001
14~64 ys	54 (1.8%)	
65~74 ys	49 (4.3%)	
75~89 ys	124 (6.9%)	
≥90 ys	30 (16.0%)	
Gender		0.005
Male	160 (4.9%)	
Female	97 (3.5%)	
Underlying Diseases		
None of any underlying disease	19 (0.3%)	
Organ/Bone marrow Transplantation	3 (23.1%)	<0.001
Immunosuppressive therapy	9 (17.3%)	<0.001
Chemotherapy/Radiology within 6 months	12 (16.9%)	<0.001

Hematological neoplasms	8 (14.8%)	<0.001
Chronic Renal diseases	32 (14.4%)	<0.001
Long-term oral corticosteroids use	14 (14.0%)	<0.001
Chronic congestive heart failure	23 (10.9%)	<0.001
Cerebrovascular Diseases	93 (10.1%)	<0.001
Malignant solid tumors	29 (9.4%)	<0.001
Coronary Heart Diseases	83 (6.9%)	<0.001
Diabetes	57 (6.0%)	<0.001
Hypertension	124 (5.8%)	<0.001
Connective Tissue Diseases	9 (5.3%)	0.001
Chronic Liver diseases	5 (5.2%)	0.009
COPD	38 (4.6%)	<0.001
Asthma	8 (2.5%)	0.126
Bronchiectasis	10 (1.5%)	0.536
ICU admission		
Yes	99 (25.3%)	<0.001
No	158 (2.8%)	
Systemic glucocorticosteroids use in admission		
Yes	97 (5.8%)	<0.001
No	160 (3.6%)	

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Appendix 8 Empirical antimicrobial regimens according to Chinese CAP guideline

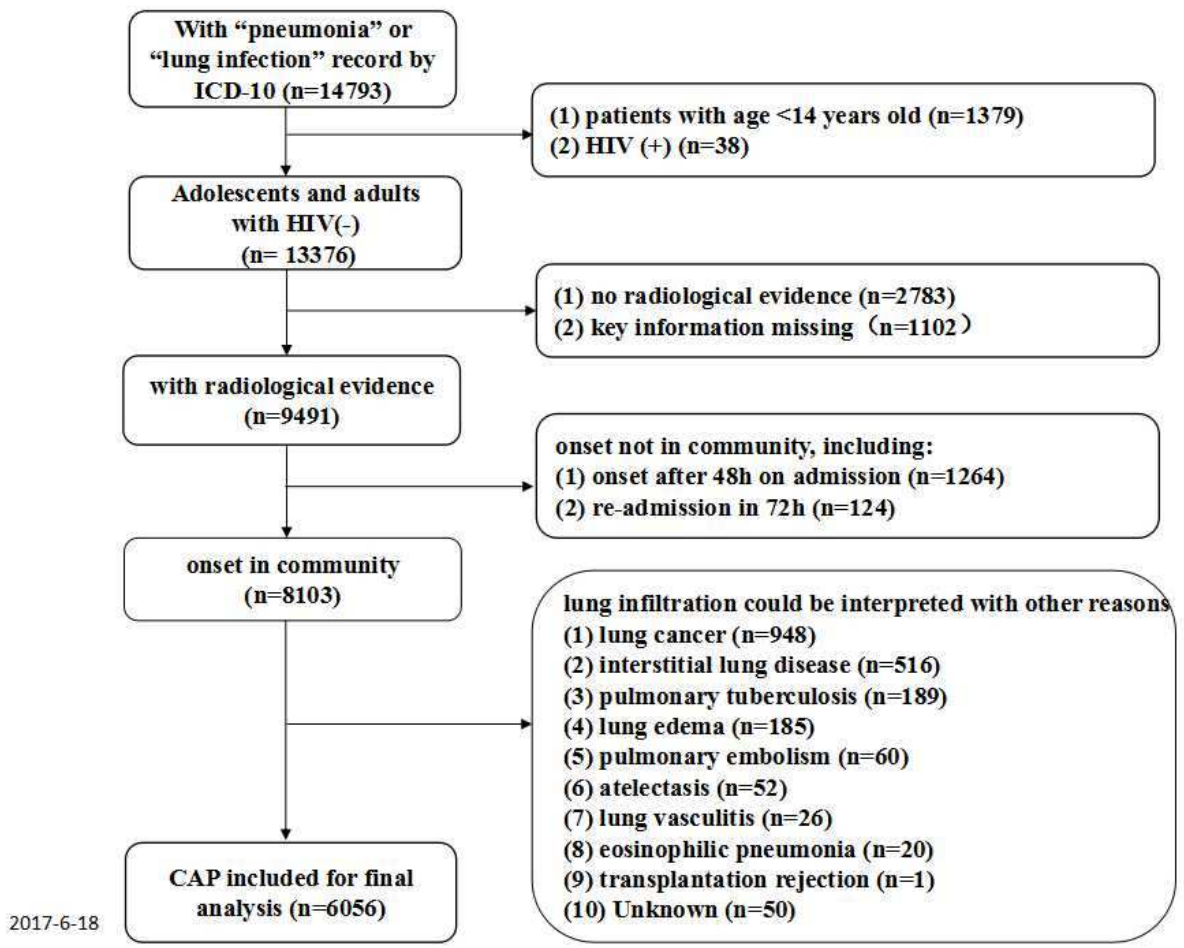
Populations	Common pathogens	Anti-infective agents for initial empirical therapy	Comment
Outpatient treatment (Oral administration is recommended)			
Young adults without underlying disease(s)	<i>S. pneumoniae</i> , <i>M. pneumoniae</i> , <i>H. influenzae</i> , <i>C. pneumoniae</i> , influenza virus, adenovirus, <i>M. catarrhalis</i>	(1) Aminopenicillins, penicillins-β-lactamase-inhibitor combinations; (2) I or II generation cephalosporins; (3) doxycycline or minocycline; (4) respiratory quinolones; (5) macrolides	(1) Differentiate among bacterial pneumonia, <i>Mycoplasma</i> , <i>Chlamydia</i> and viral pneumonia based on clinical characteristics; (2) Mild pneumonia caused by <i>Mycoplasma</i> , <i>Chlamydia</i> , and virus is usually self-limited
Patients with underlying disease(s) or elderly patients (age ≥ 65 years)	<i>S. pneumoniae</i> , <i>H. influenzae</i> , <i>Enterobacteriaceae</i> such as <i>K. pneumoniae</i> , <i>C. pneumoniae</i> , influenza virus, RSV, <i>M. catarrhalis</i>	(1) Penicillins-β-lactamase-inhibitor combinations; (2) II or III generation cephalosporins (oral); (3) respiratory quinolones; (4) penicillins-lactamase-inhibitor combinations, II generation cephalosporins, III generation cephalosporins combined with doxycycline or minocycline or macrolides	Monotherapy with doxycycline or minocycline or macrolides is not recommended in patients with risk factors of resistant <i>S. pneumoniae</i> (1), such as age > 65 years, underlying diseases (chronic cardiac, pulmonary, or renal diseases, diabetes mellitus, and immunosuppression), alcoholism, and β-lactams treatment within 3 months.
Inpatient treatment, non-ICU (Intravenous or oral administration)			

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Young adults without underlying disease(s)	<i>S. pneumoniae</i> , <i>H. influenzae</i> , <i>M. catarrhalis</i> , <i>S. aureus</i> , <i>M. pneumoniae</i> , <i>C. pneumoniae</i> , influenza virus, adenovirus, other respiratory tract viruses	(1) Penicillin G, aminopenicillins, penicillins-β-lactamase-inhibitor combinations; (2) II or III generation cephalosporins, cephamycins, oxacephems; (3) the above drugs combined with doxycycline, minocycline or macrolides; (4) respiratory quinolones; (5) macrolides	(1) Only 1.9% the <i>S. pneumoniae</i> isolates from adult CAP are resistant to intravenous penicillins in China. The percentage of intermediate strains is only about 9%. Intravenous penicillins are still effective in hospitalized patients infected with penicillin-intermediate <i>S. pneumoniae</i> when increasing the dosage (23, 161); (2) When atypical pathogens are suspected, doxycycline or minocycline or respiratory quinolones are preferred. Macrolides can be used in regions with lower resistance rate to mycoplasma
Patients with underlying disease(s) or elderly patients (age ≥ 65 years)	<i>S. pneumoniae</i> , <i>H. influenzae</i> , <i>Enterobacteriaceae</i> such as <i>K. pneumoniae</i> , influenza virus, RSV, <i>M. catarrhalis</i> , anaerobic bacteria, <i>Legionella</i>	(1) Penicillins-β-lactamase-inhibitor combinations; (2) III generation cephalosporins or their enzyme-inhibitor combinations, carbapenems such as cephamycins, oxacephems, ertapenem; (3) monotherapy of the above drugs or in combination with macrolides; (4) respiratory quinolones	(1) <i>Enterobacteriaceae</i> infection must be considered in patients with underlying disease(s) and elderly patients. The patients must be further evaluated for the risk of infection with ESBLs-producing <i>Enterobacteriaceae</i> ; (2) Elderly patients should be monitored for the risk factors of aspiration
Requirement for ICU admission (Intravenous administration is recommended)			
Young adults without underlying disease(s)	<i>S. pneumoniae</i> , <i>S. aureus</i> , influenza virus, adenovirus, <i>Legionella</i>	(1) Penicillins-β-lactamase-inhibitor combinations, III generation cephalosporins, cephamycins, oxacephems, ertapenem combined with macrolides; (2) respiratory quinolones	(1) <i>S. pneumoniae</i> is the most common pathogen. The other pathogens such as <i>S. aureus</i> , <i>Legionella</i> , influenza virus should also be considered (1, 2, 162-166); (2) During influenza seasons, attention must be paid to influenza viral infections. Combination with neuraminidase inhibitors should be considered. Attention should be paid to secondary <i>S. aureus</i> infection (167). The agents active against MRSA can be used in combination if necessary

<p>Patients with underlying disease(s) or elderly patients (age ≥ 65 years)</p>	<p><i>S. pneumoniae</i>, <i>Legionella</i>, <i>Enterobacteriaceae</i> such as <i>K. pneumoniae</i>, <i>S. aureus</i>, anaerobic bacteria, influenza virus, RSV</p>	<p>(1) Penicillins-β-lactamase-inhibitor combinations, III generation cephalosporins or in combination with beta-lactamase inhibitors, carbapenems such as ertapenem combined with macrolides; (2) penicillins-β-lactamase-inhibitor combinations, III generation cephalosporins or in combination with beta-lactamase inhibitors, carbapenems such as ertapenem combined with respiratory quinolones</p>	<p>(1) Evaluate the risk of infection with ESBLs-producing <i>Enterobacteriaceae</i>; (2) Physicians should be aware of the risk factors for aspiration and antimicrobial coverage of relevant pathogens</p>
<p>CAP with risk factors for <i>P. aeruginosa</i> infection and requirement for inpatient treatment or ICU admission (Intravenous administration is recommended)</p>			
<p>Patients with structural lung disease</p>	<p><i>P. aeruginosa</i>, <i>S. pneumoniae</i>, <i>Legionella</i>, <i>Enterobacteriaceae</i> such as <i>K. pneumoniae</i>, <i>S. aureus</i>, anaerobic bacteria, influenza virus, RSV virus</p>	<p>(1) β-lactams with antipseudomonal activity; (2) quinolones with antipseudomonal activity; (3) β-lactams with antipseudomonal activity combined with quinolones or aminoglycosides with antipseudomonal activity; (4) combination of β-lactams, aminoglycosides and quinolones with antipseudomonal activity</p>	<p>Risk factors include: (1) airway <i>P. aeruginosa</i> colonization; (2) repeated doses of antibacterial drugs or glucocorticoids due to chronic airway disease. Combination therapy is recommended for patients with severe CAP or proven antimicrobial resistance</p>

Appendix Figure 1 Patient screening algorithm for hospitalized CAP



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Disease characteristics and management of hospitalized adolescents and adults with Community-Acquired Pneumonia in China : a retrospective multicenter survey

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Keywords:	disease characteristics, management, Community-Acquired Pneumonia, China

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Disease characteristics and management of hospitalized adolescents and adults with Community-Acquired Pneumonia in China: a retrospective multicenter survey

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Abstract

Objectives To describe the clinical characteristics and management of patients hospitalized with CAP in China.

Design This was a multicenter, retrospective, observational study.

Setting 13 teaching hospitals in northern, central and southern China from 1 January 2014 to 31 December 2014

Participants Information on hospitalized patients aged ≥ 14 years with radiographically-confirmed pneumonia with illness onset in the community was collected using standard case report forms.

Primary and secondary outcome measures Resource use for CAP management.

Results Of 14,793 patients screened, 5828 with radiographically-confirmed CAP were included in the final analysis. Low mortality risk patients with a CURB-65 score 0-1 and PSI risk class I-II accounted for 81.2% (4434/5594) and 56.4% (2034/3609) of CAP patients respectively. 21.7% (1111/5130) patients had already achieved clinical stability on admission. 40.9% (1575/3852) patients without pseudomonal infection risk factors received antimicrobial over-treatment regimens. The median length of stay in hospital was 11 days. The median duration between clinical stability to discharge was 5.0 days with 30-day mortality of 4.2%.

Conclusions These data demonstrated overuse of health resources in CAP management, indicating that there is the potential for improvement and substantial savings to health-care systems in China.

Strengths and limitations of this study

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- This is the largest multi-center study to investigate demographic characteristics, severity and microbiological testing, empirical antimicrobial treatment, duration of hospitalization and 30-day mortality among adults and adolescents hospitalized with CAP in mainland China, including adolescents and adults of all ages admitted to general hospital wards or ICUs from the participating centers, patients who were critically ill and aged >90 years.
 - The participating hospital sites are teaching hospitals in seven cities in three provinces, and may not be representative of CAP in smaller, rural hospitals.
 - The majority of patients are adult CAP patients, our findings do not apply to children hospitalized with CAP.

29 **Background**

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Community acquired pneumonia (CAP) is one of the most common infectious syndromes and is a leading cause of death worldwide.^{1,2} In Europe, the reported rate of CAP ranges from 1.6 to 9 cases per 1,000 in the general adult population per year.³
^{4 5} Despite advances in medical technology and global economic development, CAP-associated mortality remains high (e.g., 20.9/100,000 in the United States and 12.7/100,000 in Canada).^{2,6} Patients hospitalized in intensive care units for CAP have mortality in excess of 20% for immunocompetent patients and closer to 30% for those immunocompromised.⁷ In Japan and Korea, the 30-day mortality of patients hospitalized with CAP is about 4-6%.^{8,9}

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Although mainland China has nearly 19% of the world's population, there are limited data on CAP management and disease burden in China during the last ten

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4 years. According to a household interview survey published in the China Health and
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6 Family Planning Statistical Yearbook (2013), the two-week prevalence of pneumonia
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8 in China was estimated to be 11/1,000, and the direct cost due to bacterial pneumonia
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10 was about 320 million RMB (approximately \$46.4 million).¹⁰ In 2015, CAP-China, a
11
12 multicenter clinical network, was founded with the support of National Key
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14 Technology Support Program from Ministry of Science and Technology
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16 (2015BAI12B11) to provide data on CAP for clinical researchers and healthcare
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18 policy makers in China.
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24 A multicenter retrospective study of all hospitalized CAP patients from 13 centers
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26 in northern, central and southern China among CAP-China members was
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28 implemented in 2015 (Clinicaltrial Registration No.NCT02489578). To our
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30 knowledge, this is the largest multi-center study to investigate demographic
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32 characteristics, severity and microbiological testing, empirical antimicrobial treatment,
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34 duration of hospitalization and 30-day mortality among adults and adolescents
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36 hospitalized with CAP in mainland China.
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41 **Methods**

42 **Study Design and Population**

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44 Data were collected from 13 hospitals in Northern (Beijing), Central (Yantai, Qindao,
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46 Weifang, Zibo, Rizhao cities in Shandong Province) and Southern (Kunming City in
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48 Yunan Province) China. A listing of participating centers can be found in Appendix 1.
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50 All patients admitted to the 13 hospitals during 1 January 2014 through 31 December
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52 2014 with the relevant disease codes of pneumonia or pulmonary infection in the
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4 World Health Organization International Classification of Diseases 10th revision
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6 (ICD-10, Appendix 2) were eligible. Data on all eligible patients identified in
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8 screening were retrieved from the Hospital Information System (HIS) in each center.
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10
11 Trained physicians reviewed the medical case history and collected data on 786
12
13 variables for each patient. Chest radiographs and computerized tomography (CT)
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15 scans for each patient were reviewed by pulmonary physicians and radiologists in
16
17 each center. Two-leveled review process was performed for data collection and entry.
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21 The CAP case definition includes (1) illness onset in the community(defined as
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23 community acquired infection among those who have not been hospitalized during
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25 recent 28 days)¹¹; (2) chest radiograph or CT scan showing infiltrate or interstitial
26
27 changes, with or without pleural effusion; (3) any one of pneumonia clinical
28
29 manifestations: (a) recent cough, sputum or aggravation of respiratory symptoms, the
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31 emergence of purulent sputum, with or without chest pain; (b) fever (defined as
32
33 axillary temperature $\geq 37.3^{\circ}\text{C}$)¹² or hypothermia (axillary temperature $< 36^{\circ}\text{C}$); (c)
34
35 signs of pulmonary consolidation and (or) moist crackles; or (d) WBC $> 10 \times 10^9/\text{L}$, or
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37 $< 4 \times 10^9/\text{L}$, with or without neutrophil predominance.
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44 Patients were excluded if (1) age < 14 years; (2) pneumonia onset ≥ 48 hours after
45
46 admission; (3) lung infiltrate or interstitial changes which were interpreted as lung
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48 cancer, pulmonary tuberculosis, non-infectious interstitial lung diseases, pulmonary
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50 edema, atelectasis, pulmonary embolism, pulmonary eosinophil infiltrate, pulmonary
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52 vasculitis; (4) immunocompromised status; (5) re-admission within 72 hours after
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54 discharge.
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4 The study design was approved by the Ethics committee of China-Japan Friendship
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6 Hospital (No.2015-86). Given the retrospective nature of the study, the Ethics
7
8 committee determined that informed consent was not necessary.
9

10 11 **Quality control of the study**

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13 Key investigators, including clinicians, statisticians, microbiologists and radiologists
14
15 worked together to draft the protocol and created a single formatted case report form
16
17 (CRF) that was utilized by all centers. Before study initiation, all investigators from
18
19 the thirteen centers received training on the protocol, screening process, definition of
20
21 underlying diseases and formatted CRF (Appendix file 3). After data were collected,
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23 the CRF was reviewed by a trained researcher to ensure its completeness and data
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25 quality. A second review was performed independently by a trained team of
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27 physicians in each center before being entering in duplicate into a computerized
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29 database.
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35 36 **Data Collection:**

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38 A total of 786 variables were included in the formatted CRF, including:

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41 (1) Demographic data: age, gender, ID number, source of admission, types of medical
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43 insurance;
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45
46 (2) Underlying diseases: chronic lung, heart, renal and liver diseases, diabetes,
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48 hypertension, solid organ cancers. Definition of underlying diseases is listed in
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50 Appendix file 4.
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53 (3) Factors for acquisition or prevention of CAP: pregnancy, postpartum within six
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55 months, current smoking history, excessive drinking, exposure to day care center
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4 children, bed-ridden longer than two months, chronic receipt of corticosteroids
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6 (dosage equivalent prednisolone $\geq 10\text{mg/d}$ for more than 30 days), statin use, *S.*
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8 *pneumonia* or Influenza vaccination within one year.

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10
11 (4) Clinical manifestations, clinical signs: recorded on the day of admission, on the 4th
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13 hospital day, change of antibiotics within 14 days of admission, and the day of
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15 discharge or death. Laboratory and radiological findings were also recorded if such
16
17 tests were repeated by attending physicians. Pneumonia disease severity scores (PSI
18
19 /CURB-65) were also recorded.
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23 (5) Microbiological examination: Gram stain and culture of sputum within 48 hours,
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25 blood culture within 48 hours, BALF and pleural fluid culture within one week after
26
27 admission, serum antibody (including IgM and IgG) for atypical pathogens
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29 (*Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, *Legionella pneumophila*).
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31 Urinary antigen testing was performed for *Streptococcus pneumoniae* and *Legionella*
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33 *spp.* Real-time PCR testing was done for respiratory virus and atypical pathogens with
34
35 sputum and BALF. Nasopharyngeal (NP) swab was used for antigen testing for
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37 Influenza A and Influenza B. Aspirate was not routinely used for antigen testing.
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41 (6) Antimicrobial treatment before admission and change of antimicrobials during
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43 hospitalization. Use of corticosteroids, vasopressors, mechanical ventilation,
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45 Continuous renal replacement therapy (CRRT) and extracorporeal membrane
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47 oxygenation (ECMO) were also recorded.
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51 (7) Clinical stability was defined as satisfying all of the following: axillary
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53 temperature ≤ 37.8 °C more than 24 hours without use of antipyretic medications;
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4 resting heart rate ≤ 100 beats/min; respiratory rate ≤ 24 breaths/ minute; systolic blood
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6 pressure ≥ 90 mmHg; SpO₂ $\geq 90\%$ on room air; ability to maintain oral intake; normal
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8 mental status.¹³
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11 (8) Over-treatment was defined as: i) use of antipseudomonal β -lactams or β -lactams+
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13 fluoquinolones in hospitalized (not in ICU) patients without risk factors for
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15 pseudomonal infection; ii) use of β -lactams (antipseudomonal or not)+ fluoquinolones
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17 in ICU patients aged < 65 yr without risk factors for pseudomonas infection; iii) use of
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19 anti-MRSA drugs in hospitalized (not in ICU) patients.¹⁴
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23 (9) Risk factors for pseudomonal infection was defined as chronic airway disease
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25 (bronchiectasis and COPD) and at least one risk factor for HCAP as defined by the
26
27 2005 IDSA/ATS adult CAP guidelines.^{14 15 16 17 18}
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31 (10) Empirical antimicrobial regimens recommended by Chinese CAP guidelines
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33 were showed in Appendix 5.
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36 **Microbiology testing**

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38 The conditions that a pathogen was defined as the definite or probable etiology based
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40 on were showed in Appendix 6.
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43 **Statistical analysis**

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45 No formal sample size calculations were performed because of the retrospective
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47 descriptive study design. All data were analyzed by descriptive statistics with SPSS19.
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49 Measurement data were tested for normality by Kolmogorov-Smirnov. Measurement
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51 data of normal distribution was reported as mean \pm standard deviation. Measurement
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53 data of non-normal distribution was reported as median. The χ^2 test statistics were
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4 used for 30-day mortality subgroup analysis. A P-value of <0.05 was considered
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6 statistically significant.
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8 **Results**

9 **Screening Process**

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11 A total of 14,793 patients were screened to meet the inclusion and exclusion criteria
12
13 for CAP and 5828 patients were included in the final analysis (Appendix Figure 1).
14
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16 **Epidemiological characteristics**

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18 The proportions of male and female patients were similar. The median age was 65
19
20 years, range 14-103 years. Prevalent co-morbidities included hypertension (35.2%),
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22 coronary heart disease (20.0%), diabetes (15.7%), cerebrovascular diseases (15.3%)
23
24 and COPD (13.7%). 14.9% of CAP patients had at least one healthcare associated
25
26 pneumonia (HCAP) risk factor (according to IDSA/ATS HAP/HCAP guideline
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28 published in 2005¹⁵). 45.7% patients received antibiotics before admission.
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31
32 A substantial proportion of admitted patients had relatively mild disease as
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34 indicated by the following: i) CURB-65 score¹⁹ 0-1 accounted for 81.2%, ii) PSI risk
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36 class²⁰ I-II accounted for 56.3%; iii) Shorr Score²¹ 0-1 accounts for 99.6%; and iv)
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38 Aliberti Score²² low riskgroup in 89.7%; v) only 12.0% (261/2172) patients had
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40 procalcitonin (PCT) more than 2 ng/ml; vi) as many as 65.7% (3741/5698) patients
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42 had normal peripheral leukocyte counts (4,000-10,000/ul). Most importantly, 21.7%
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44 patients had met criteria for clinical stability at hospital admission.¹³ (Table 1-2)
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Table 1: Demographic characteristics and underlying diseases

Items	Cases (%)
Male	3117 (53.5)
Age (years, median, IQR)	65 (53-78)
14~64	2802 (48.1)
65~74	1081 (18.5)
75~89	1760 (30.2)
≥90	185 (3.2)
Source of admission (n=5823)	
From Out-patient Department	4183 (71.8)
From Emergency Room	1588 (27.3)
Transfer from other hospital	52 (0.9)
Days from illness onset to admission (n=5826, median, IQR)	6.0 (3.0-14.0)
Patients who received antibiotics before admission	2664 (45.7)
β-lactams	1015 (38.1)
Fluoroquinolones	586 (22.0)
Macrolides	170 (6.4)
β-lactams+ fluoroquinolones	413 (15.5)
β-lactams+ macrolides	201 (7.5)
Others	279 (10.5)
Systemic glucocorticosteroids use before admission	250 (4.3)
Underlying Diseases	4219 (72.4)
Hypertension	2053 (35.2)
Coronary Heart Disease	1163 (20.0)
Diabetes	913 (15.7)
Cerebrovascular Diseases	890 (15.3)
COPD	801 (13.7)
Bronchiectasis	629 (10.8)
Asthma	339 (5.8)
Malignant solid tumors	254 (4.4)
Congestive Heart Failure	202 (3.5)
Chronic renal diseases	201 (3.4)
Connective Tissue Diseases	110 (1.9)
Chronic Hepatic Diseases	90 (1.5)

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4	Smoking status	
5	Current smokers	1009 (17.3)
6	Ex-smokers	590 (10.1)
7	Alcoholism	407 (7.0)
8	Risk factors for aspiration*	377 (6.5)
9	History of CAP within one year	368 (6.3)
10	History of vaccination	
11	Influenza vaccine within 1 year	12 (0.2)
12	<i>Streptococcus pneumoniae</i> vaccine within 5 years	8 (0.1)
13	Risk factors for HCAP according to IDSA/ATS criteria	868 (14.9)
14	Hospitalized in an acute care hospital for two or more days	404 (6.9)
15	within 90 days	
16	Received recent intravenous antibiotic therapy, chemotherapy,	656 (11.3)
17	or wound care within the past 30 days	
18	Attended a hospital or hemodialysis clinic	36 (0.6)
19	Residence in a nursing home or long-term care facility	19 (0.3)
20	CURB-65 score (n=5594)	
21	0	2343 (41.9)
22	1	2199 (39.3)
23	2	884 (15.8)
24	3	147 (2.6)
25	4	20 (0.4)
26	5	1 (0.0)
27	PSI risk class (n=3609)	
28	I	1130 (31.3)
29	II	904 (25.0)
30	III	748 (20.7)
31	IV	646 (17.9)
32	V	181 (5.0)
33	Shorr Score (n=5650)	
34	0	5084 (90.0)
35	1	541 (9.6)
36	2	23 (0.4)
37	3	2 (0.0)
38	4	0 (0.0)
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Aliberti Score (n=5828)	
Low risk group	5226 (89.7)
High risk group	602 (10.3)
Clinical stability on admission § (n=5130)	1111 (21.7)

COPD: chronic obstructive pulmonary disease; HCAP: healthcare associated pneumonia; IDSA/ATS: Infectious Diseases Society America/American Thoracic Society. PSI: pneumonia severity index. *Risk factors for aspiration included choking, drowning, nasal, pseudobulbar palsy, dementia, coma, poisoning, Parkinson's disease.

§ Clinical stability was defined as satisfying the following at the same time: axillary temperature ≤ 37.8 °C more than 24 hours; heart rate ≤ 100 beats/min in resting state; breathing rate ≤ 24 breaths/minute; systolic blood pressure ≥ 90 mmHg; SpO₂ $\geq 90\%$ on room air; ability to maintain oral intake; normal mental status.

Table 2: Clinical and radiological features on admission

Items	Cases (%)
Axillary Temperature ≥ 38 °C (n=5826)	2783 (47.8)
Axillary Temperature < 36 °C (n=5793)	44 (0.8)
Cough	5192 (89.1)
Sputum	4751 (81.5)
Shortness of breath	2116 (36.3)
Chest pain	709 (12.2)
Decrease of consciousness	294 (5.0)
Chest signs	
Moist rales	2919 (50.1)
Dry rales	1387 (23.8)
Edema of lower limbs	592 (10.2)
Cyanosis	547 (9.4)
SBP < 90 mmHg	45 (0.8)
Radiology	
Infiltrate more than two lobes	3776 (64.8)
Plural effusion	1205 (20.7)
Cavitation	228 (3.9)
WBC (mm^{-3} , n=5698)	

>10,000	1626 (28.5)
<4,000	331 (5.8)
4,000~10,000	3741 (65.7)
BUN >7.0 mmol·L ⁻¹ (n=5601)	1166 (20.8)
PH <7.30 (n=3330)	87 (2.6)
PaO ₂ /FiO ₂ <300 mmHg (n=3327)	1196 (35.9)
PCT (ng·ml ⁻¹ , n=2172)	
PCT≤0.25	1307 (60.2)
0.25<PCT<1	479 (22.1)
1≤PCT<2	125 (5.8)
PCT≥2	261 (12.0)

SBP: systolic blood pressure; WBC: white blood cell count; BUN: blood urea nitrogen; Scr: serum creatinine; PH: potential of hydrogen; PaO₂/FiO₂: arterial pressure of oxygen/fraction of inspiration oxygen; PCT:procalcitonin.

Clinical and radiological features

Clinical and radiological features on admission are shown in Table 2. Cough, sputum, shortness of breath and fever were the most common. 64.8% patients had multi-lobar infiltrates and 20.7% of patients had pleural effusion.

Microbiological testing

75.0% patients had some types of microbiologic testing. 68.9% of patients had a sputum culture obtained within 48 hours of admission, although only 18.5% of patients were able to produce a sputum culture of acceptable quality. The proportion of patients with blood culture, BALF culture, and pleural effusion culture were 10.3%, 9.1% and 1.9% respectively. Only 0.8% of patients had a urinary antigen test sent to evaluate for *Legionella pneumophila*, and 2.6% had urinary antigen testing for *Streptococcus pneumoniae*. (Table 3)

Table 3: Microbiological examination for CAP

Items	Cases (%)
Any Microbiological examination	4371 (75.0)
Microbiological examination for bacterial	4015 (68.9)
Microbiological examination for atypical etiology	1983 (34.0)
Microbiological examination for virus	2014 (34.6)
Bacterial or fungal Culture	4015 (68.9)
Qualified sputum culture*	1078 (18.5)
Blood culture **	602 (10.3)
BALF culture* ⁺	532 (9.1)
Pleural effusion culture**	108 (1.9)
Antibody-Based Assays on acute serum	
<i>Mycoplasma pneumoniae</i>	IgM: 1821 (31.2)
	IgG: 794 (13.6)
<i>Chlamydia pneumoniae</i>	IgM: 1294 (22.2)
	IgG: 220 (3.8)
<i>Legionella pneumoniae</i>	IgM: 645 (11.1)
	IgG: 227 (3.9)
Adenovirus	IgM: 644 (11.1)
	IgG: 0 (0.0)
Respiratory syncytial virus	IgM: 643 (11.0)
	IgG: 0 (0.0)
Influenza A virus	IgM: 643 (11.0)
	IgG: 0 (0.0)
Influenza B virus	IgM: 640 (11.0)
	IgG: 0 (0.0)
Parainfluenza virus	IgM: 643 (11.0)
	IgG: 0 (0.0)
Nucleic Acid-Based Molecular Diagnostics	
From sputum	297(5.1)
Time Interval [¶] (days, median, IQR)	9.0 (6.0-16.0)
From BALF ⁺	19 (0.3)

Time Interval [¶] (days, median, IQR)	13.0 (9.0-24.0)
<i>Mycoplasma pneumoniae</i>	270 (4.6)
<i>Chlamydia</i> spp	270 (4.6)
<i>Legionella</i> spp	270 (4.6)
Influenza A virus	270 (4.6)
Influenza B virus	270 (4.6)
Other respiratory virus [#]	270 (4.6)
Urinary Antigen test	
<i>Streptococcus pneumoniae</i>	150 (2.6)
<i>Legionella</i> spp	47 (0.8)
Nasopharyngeal swab antigen testing	
Influenza A virus	41 (0.7)
Influenza B virus	21 (0.4)

*: within 48hr after admission

** :within one week after admission

[¶]: days from illness onset to testings

[#]parainfluenza virus (PIV) types 1, 2, 3 and 4, rhinovirus (HRV), enterovirus (EV), coronavirus (hCoV) types 229E, NL63, OC43 and HKU1, parapneumovirus (hMPV), and adenovirus (AdV), bocavirus

⁺**BALF**: bronchoalveolar lavage fluid

Of all patients, serological testing for antibodies to *Mycoplasma pneumoniae* was only performed on a single serum specimen for IgM (31.2%) and IgG antibodies (13.6%). Similarly, serological testing on a single serum specimen was done for *Chlamydia pneumoniae* IgM antibody in 22.2% of patients and for IgM antibodies to *Legionella pneumophila* and respiratory viruses in 11.1%. No convalescent serum specimens were collected for serological testing for any pathogens, limiting interpretation of serology results for a single serum specimen.

A definite or probable pathogen was identified only in 12.7% of patients (738/5828): only bacteria in 87.1% (643/738), only atypical pathogens in 0.9% (7/738), only viruses in 8.5% (63/738), bacteria and viruses in 2.7% (20/738), viruses and atypical pathogens in 0.7% (5/738). The most common five pathogens identified were *Pseudomonas aeruginosa* 26.7% (197/738), *Klebsiella pneumoniae* 17.6% (130/738), *Escherichia coli* 8.9% (66/738), *Acinetobacter* 8.4% (62/738) and influenza A virus 7.3% (54/738). (Appendix 7)

Empiric antimicrobial regimens

β -lactams (received by 72.7% of patients) and fluoroquinolones (received by 42.2%) were the most common classes of antibiotics that were administered empirically. In patients (not in ICU) without pseudomonal infection risk factors, 27.8% (1070/3852) patients received empiric antibiotic regimens including antipseudomonal β -lactams, and 12.1% (468/3852) patients received β -lactams + fluoroquinolones; 0.4% (16/3852) patients aged <65 years and not in ICU received β -lactams (antipseudomonal or not) + fluoroquinolones combined regimens. Overall, 40.9% (1575/3852) patients without pseudomonal infection risk factors received antimicrobial over-treatment regimens. (Table 4)

Table 4: Empirical antimicrobial regimen for CAP patients (n=5716)*

Empirical antimicrobials (%)	Without risk factors for <i>P.seudomonas</i> infection (n=3852)				With risk factors for <i>P.seudomonas</i> infection (n=1864)
	age<65yr and not in ICU (n=1881)	age<65yr and in ICU (n=79)	age≥65yr and not in ICU (n=1742)	age≥65yr and in ICU (n=150)	

β-lactams (antipseudomonal)	178 (4.6) [#]	21 (0.5)	407 (10.6) [#]	58 (1.5)	541 (29.0)
β-lactams	331 (8.6)	9 (0.2)	482 (12.5)	20 (0.5)	345 (18.5)
Fluoroquinolones	502 (13.0)	10 (0.3)	273 (7.1)	6 (0.2)	252 (13.5)
Macrolides	20 (0.5)	0 (0.0)	17 (0.4)	0 (0.0)	10 (0.5)
β-lactams (antipseudomonal) + fluoroquinolones	201 (5.2) [#]	13 (0.3) [#]	189 (4.9) [#]	30 (0.8)	238 (12.8)
β-lactams+	302 (7.8) [#]	3 (0.1) [#]	166 (4.3) [#]	9 (0.2)	177 (9.5)
fluoroquinolones					
β-lactams+	160 (4.2)	2 (0.1)	64 (1.7)	2 (0.1)	55 (3.0)
macrolides					
β-lactams (antipseudomonal) + macrolides	50 (1.3) [#]	0 (0.0)	45 (1.2) [#]	2 (0.1)	58 (3.1)
Fluoroquinolones + macrolides	24 (0.6)	0 (0.0)	11 (0.3)	0 (0.0)	6 (0.3)
anti-MRSA drugs	9 (0.2) [#]	8 (0.2)	12 (0.3) [#]	6 (0.2)	29 (1.6)
Others	104 (2.7)	13 (0.3)	76 (2.0)	17 (0.4)	153 (8.2)

*: data on empirical antimicrobial regimens in 112 patients were missing.

[#]Overtreatment was defined as: i) use of antipseudomonal β-lactams or β-lactams+ fluoroquinolones in hospitalized (not in ICU) patients without risk factors for pseudomonal infection; ii) use of β-lactams (antipseudomonal or not)+ fluoroquinolones in ICU patients aged < 65yr without risk factors for pseudomonas infection; iii) use of anti-MRSA drugs in hospitalized (not in ICU) patients.¹⁴

- Risk factors for *P.seudomonas* infection was defined as chronic airway disease (bronchiectasis or COPD) and HCAP according to IDSA/ATS criteria.¹⁵

Clinical outcomes

Clinical outcomes are shown in Table 5. Overall, 6.3% of patients were admitted to an ICU, and 2.7% required invasive mechanical ventilation. Vasopressors were administered to 3.4% of patients, and 26.4% received corticosteroids during the hospitalization. The 30-day mortality was 4.2%. The median duration of hospitalization was 11 days. The median duration from admission to clinical stability

was 4 days, and from clinical stability to discharge was 5 days. The median duration of ICU hospitalization was 8 days. The top five causes of death were severe pneumonia/multi-organ dysfunction syndrome (MODS) 69.1% (170/246), cardiac failure 2.8% (7/246), acute myocardial infarction 2.0% (5/246), stroke 1.6% (4/246) and gastrointestinal hemorrhage 1.6% (4/246).

Table 5: Supportive treatment and clinical outcomes of patients with CAP

Items	Cases (%)
ICU admission	367 (6.3)
Mechanical ventilation	
Non-invasive ventilation	286 (4.9)
Invasive ventilation in ICU	123 (2.1)
Invasive ventilation not in ICU	33 (0.6)
Vasopressor use	197 (3.4)
CRRT	16 (0.3)
ECMO	3 (0.1)
Systemic glucocorticosteroids use after diagnosis of CAP	1540 (26.4)
ICU patients who received systemic glucocorticoids	154 (2.6)
Patients on invasive mechanical ventilation who received systemic glucocorticoids	75 (1.3)
Patients on non-invasive mechanical ventilation who received systemic glucocorticoids	158 (2.7)
30-day mortality	246 (4.2)
Length of stay in Hospital (days, median, IQR)	11.0 (5.0-24.0)
Days between admission-clinical stability (median, n=5130, IQR)	4.0 (1.0-10.0)
Days between clinical stability-discharge (median, n=5130, IQR)	5.0 (1.0-9.0)
Length of stay in ICU (days, median, n=350, IQR)	8.0 (4.0-16.0)
Treatment failure within 14 days	427 (7.3)
Needs non-invasive ventilation	169 (2.9)
Needs invasive ventilation	145 (2.5)

Needs vasopressors	130 (2.2)
Death	147 (2.5)
Direct causes of death	
Severe pneumonia/MODS	170 (69.1)
Heart failure	7 (2.8)
Acute myocardial infarction	5 (2.0)
Stroke	4 (1.6)
Hemorrhage of digestive tract	4 (1.6)
Acute renal failure	2 (0.8)
Arrhythmia	2 (0.8)
Accident aspiration	1 (0.4)
Others	51 (20.7)

ICU: intensive care unit; CRRT: continuous renal replacement therapy; ECMO: extracorporeal membrane oxygenation; MODS: multiple organ dysfunction syndrome; DIC: disseminated intravascular coagulation.

Appendix 8 shows the results of sub-group analysis of 30-day mortality. Fatality increased with age. Mortality was similar between male and female patients (4.9% vs 3.5%). Mortality in patients admitted to an ICU was 15.3%.

Discussion

This study represents the largest, multicenter, retrospective cohort study on the etiologies and outcomes in adolescents and adults with CAP in China. In this study, we found that admission of patients with low mortality risk, overuse of antibiotics and incorrect serological testing for *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, *Legionella pneumophila* and respiratory viruses, were the main challenges of CAP management.

We identified four major categories of overuse of health care resources in CAP management in China:

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4 (1) A large number of low-risk patients were admitted to the hospitals. Guidelines
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6 for CAP management in China and the U.S. recommend that decisions for
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8 hospitalization should be based on illness severity.^{14 23} It was estimated that over \$8
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10 billion dollars are spent in CAP treatment every year in the U.S, and the cost for
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12 inpatient CAP management is 25-30 times more than for outpatient CAP
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14 management.^{24 25 26} Therefore, admission of low mortality risk CAP patients results in
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16 major unnecessary cost expenditures. Moreover, outpatients usually return to their
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18 baseline activity levels much sooner than inpatients, and enjoyed a higher quality of
19
20 life.^{27 28} Finally, hospitalization is associated with the risk of nosocomial infections,
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22 potentially caused by high virulent and multidrug-resistant organisms.²⁹ Admission of
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24 low-risk CAP patients was also observed in a recent large U.S. study,¹¹ so it may not
25
26 be unique to China. However, there are many other factors that play an important role
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28 in deciding the need for hospitalization such as comorbidities, lack of available family
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30 support, older age, mental illness and drug abuse, etc.^{30 31}

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39 (2) Length of stay in hospital was unnecessarily long. CAP guidelines
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41 recommended that patients should be discharged as soon as they achieve clinical
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43 stability and have no other active medical problems. Keeping patients in hospital and
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45 observing them while receiving oral antibiotic therapy, or waiting for normalization of
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47 all clinical parameters are not indicated and are associated with increased costs and
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49 potentially with in-hospital adverse events.^{13 29 30} We observed that CAP patients were
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51 discharged a median of 5 days after achieving clinical stability, and 22% met clinical
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53 stability criteria at admission. Given the median LOS of 11 days for all CAP patients,
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4 discharging CAP patients once they achieved clinical stability would lead to
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6 cost-savings of approximately half of the total hospitalization expenses. Similarly, the
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8 length of stay in hospital may be influenced by other social factors.
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11 (3) 40.9% patients without risk factors for *Pseudomonal* infection received
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13 over-treatment with empiric antimicrobial regimens. Antipseudomonal β -lactams
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15 (28.2%) or β -lactams + quinolones (12.2%) were the most common empiric regimens
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17 for over-treatment. This may be due to overestimation of illness severity, clinician
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19 unfamiliarity with CAP guidelines, or lack of microbiologic diagnostic testing.
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21 Moreover, we found quinolones use in more than 40% of CAP patients. The U.S.
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23 Food and Drug Administration (FDA) has released warnings of potential adverse
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25 effects of fluoroquinolones, such as Q-T prolongation, tendon injury, psychiatric
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27 disorder, etc.^{32 33 34} As second-line anti-tuberculosis drugs, fluoroquinolones can also
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29 affect the diagnosis of tuberculosis and induce drug-resistance.^{35 36}
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38 (4) Incorrect serological testing was performed. We observed that many patients
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40 had an acute serum specimen collected for IgG serology testing for atypical bacteria
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42 and respiratory viruses without a convalescent serum specimen obtained for paired
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44 serological testing. Furthermore, many patients had testing for IgM antibodies for a
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46 variety of respiratory pathogens, but elevation of IgM antibodies with a low-normal
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48 IgG titer is uncommon during acute illness.^{37 38 39} Paired serology for virus and atypical
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50 pathogens is recommended for epidemiological purpose. A follow-up convalescent
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52 serum specimen to document changes in IgG and IgM antibody levels is generally
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54 required for diagnosis.^{40 41} Thus, the value of antibody testing on a single acute serum
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specimen to determine the etiology of CAP is questionable. The costs of more frequent use of PCR testing on lower respiratory specimens may be partially offset by not performing serological testing in CAP patients.

The strengths of this study, in contrast to some past epidemiological investigations,⁴² included data on bacterial isolates obtained in current clinical practice, microbiologic testing ordered, and antimicrobials administered, according to Chinese standards-of-care, and the study population included adolescents and adults of all ages admitted to general hospital wards or ICUs from the participating centers to reduce selection bias. We also included patients who were critically ill, aged >90 years and with risk factors for HCAP.

This study had several limitations. First, given the retrospective study design, it is possible that selection bias was present and the study population may not have been representative of all CAP patients admitted to the 13 participating sites. Secondly, the participating hospital sites were teaching hospitals in seven cities in three provinces, and were not selected to be representative of CAP hospital management in China, especially in smaller, rural hospitals. Third, this study reports on CAP management during 2014; analysis of multiple years of data can allow assessment of changes in CAP management. Fourth, 45.7% of CAP patients received antibiotics before hospital admission and before specimen collection, which may reduce the detection of some bacterial infections, such as *Streptococcus pneumoniae*. Urinary antigen testing for *Streptococcus pneumoniae* was performed only in 2.6% of total population. Therefore, the bacterial pathogens identified in this study may not be representative of all

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3 bacterial causes of CAP in the source patient populations for this study. Finally, while
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5
6 we included adolescents, the majority of patients were adult CAP patients, and our
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9 findings do not apply to children hospitalized with CAP.

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11 In conclusion, we characterized adolescents and adults hospitalized for CAP in
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13 China and identified several problems suggesting the over-use of healthcare resources
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15 in CAP management. This suggests that education and training of clinicians on
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17 current CAP guidelines in China are needed to improve clinical management and
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19 could also result in substantial cost-saving in healthcare expenditures for CAP
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21 patients. The multi-center hospital network can serve as a platform for conducting
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23 intervention studies for hospitalized CAP patients in the future, utilizing the baseline
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25 data from this observational study.
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9
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11
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27
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35 **Data sharing statement** No additional data available
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For peer review only

Appendix 1: Details of Participating centers

Name of the hospital	Province, city	2 nd and 3 rd level hospital	Teaching Hospital	Beds	Staff of Clinical Microbiology Lab
Beijing Chao-Yang Hospital Affiliated to Capital Medical University	Beijing	3 rd	Yes	1400	11
Beijing Jishuitan Hospital 4 th Medical College of Peking University	Beijing	3 rd	Yes	1500	10
Beijing Luhe Hospital Affiliated to Capital Medical University	Beijing	3 rd	Yes	1042	5
Qingdao Municipal Hospital	ShanDong, Qingdao	3 rd	Yes	1200	4
Qilu Hospital Of Shandong University(Qindao)	ShanDong, Jinan	3 rd	Yes	1200	6
Beijing Huimin Hospital	Beijing	2 nd	Yes	500	2
Linzi District People's Hospital	ShanDong, Zibo	2 nd	Yes	1200	5
The 2 nd Hospital of Beijing Corps, Chinese Armed Police Forces	Beijing	3 rd	Yes	450	2
China-Japan Friendship Hospital	Beijing	3 rd	Yes	1610	9
Yan'an Hospital Affiliated to Kunming Medical University	Kunming, Yan'an	3 rd	Yes	1302	4

Yantai Yuhuangding Hospital	Shangdong, Yantai	3 rd	Yes	3000	6
Rizhao Chinese Medical Hospital Affiliated to Shandong Chinese Medical University	Shangdong, Rizhao	3 rd	Yes	1212	8
Weifang NO.2 People's Hospital	Shangdong, Weifang	3 rd	Yes	1006	8

Definition of 2nd and 3rd level hospital in China:

The 2nd level hospital was defined as a hospital providing medical, prevention, health care and rehabilitation services to multiple communities (with a radius of population more than 100,000 peoples); the 3rd level hospital was defined as a hospital providing medical service to the whole country beyond cities and provinces, with comprehensive medical, teaching and research ability.

Appendix 2: ICD-10

Influenza with pneumonia, other influenza virus identified	J10.0
Influenza with pneumonia, virus not identified	J11.0
Virus pneumonia, not elsewhere classified	J12
Adenoviral pneumonia	J12.0
Respiratory syncytial virus pneumonia	J12.1
Parainfluenza virus pneumonia	J12.2
Other virus pneumonia	J12.8
Viral pneumonia, unspecified	J12.9
Pneumonia due to <i>Streptococcus pneumoniae</i>	J13
Pneumonia due to <i>Haemophilus influenzae</i>	J14
Bacterial pneumonia, not elsewhere classified	J15
Pneumonia due to <i>Klebsiella pneumoniae</i>	J15.0
Pneumonia due to <i>Pseudomonas spp.</i>	J15.1
Pneumonia due to <i>Staphylococcus</i>	J15.2
Pneumonia due to <i>Streptococcus spp.</i> , group B	J15.3
Pneumonia due to other <i>streptococci</i>	J15.4
Pneumonia due to <i>Escherichia coli</i>	J15.5
Pneumonia due to other aerobic Gram-negative bacteria	J15.6
Pneumonia due to <i>Mycoplasma pneumoniae</i>	J15.7
Other bacterial pneumonia	J15.8

Bacterial pneumonia, unspecified	J15.9
Pneumonia due to other infectious organisms, not elsewhere classified	J16
Chlamydia pneumonia	J16.0
Pneumonia due to other specified infectious organisms	J16.8
Pneumonia due to other specified infectious organism	J16.8
Pneumonia in diseases classified elsewhere	J17*
Pneumonia in bacterial diseases classified elsewhere	J17.0*
Pneumonia in viral diseases classified elsewhere	J17.1*
Pneumonia in mycoses	J17.2*
Pneumonia in other diseases classified elsewhere	J17.8*
Pulmonary mycobacterial infection	A31.0
Pulmonary actinomycosis	A42.0
Pulmonary nocardiosis	A43.0
Legionnaires' disease	A48.1
Varicella pneumonia	B01.2+
Measles complicated by pneumonia	B05.1+
Cytomegaloviral pneumonitis	B25.0+
Pulmonary candidiasis	B37.1
Acute pulmonary coccidioidomycosis	B38.0
Acute pulmonary histoplasmosis capsulati	B39.0
Acute pulmonary blastomycosis	B40.0

Pulmonary paracoccidioidomycosis	B41.0
Pulmonary sporotrichosis	B42.0+
Invasive pulmonary aspergillosis	B44.0
Other pulmonary aspergillosis	B44.1
Pulmonary cryptococcosis	B45.0
Pulmonary mucormycosis	B46.0
Pneumonia, organism unspecified	J18
Bronchopneumonia, unspecified organism	J18.0
Lobar pneumonia, unspecified	J18.1
Hypostatic, pneumonia, unspecified	J18.2
Other pneumonia, organism unspecified	J18.8
Pneumonia, unspecified	J18.9

Appendix 3: Case Report Form Of Patients Hospitalized With CAP/HCAP

Code:	R-
Name:	Gender: <input type="radio"/> Male <input type="radio"/> Female
Age: _____years old	Nationality: <input type="radio"/> Han <input type="radio"/> Others
Height: _____cm	Weight: ____ kg
ID Number:	
Date Of Admission: ____Y____M____D	
Case Number :	ID Number:
Admission Form:	<input type="radio"/> Outpatience <input type="radio"/> Emergency <input type="radio"/> Transfers
Tel:	Cell Phone:
Provider Payments: <input type="radio"/> Social Medical Insurance <input type="radio"/> New Rural Cooperative Medical System <input type="radio"/> Medical Services At State Expense <input type="radio"/> Commercial Medical Insurance <input type="radio"/> Self-paying <input type="radio"/> Others	

Study Director: Bin Cao

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 Xuexin Yao、Chunxiao Zhang、Shujing Shi、Fei Zhou、Chunxue Xue、Yanli Li、Donghao Yu
 (Beijing Chao-Yang Hospital 001; Beijing Jishuitan Hospital 002; Beijing Luhe Hospital 003; Qingdao
 Municipal Hospital 004; Qilu Hospital Of Shandong University(Qindao) 005; Beijing Huimin Hospital
 006; Linzi District People's Hospital 007; The 2nd Hospital of Beijing Corps, Chinese Armed Police
 Forces 008; China-Japan Friendship Hospital 009; Yan'an Hospital Affiliated to Kunming Medical
 University 010)

Inclusion Criteria:

1. Age ≥ 14 years old
2. Onset in community
3. Chest X-ray or CT scan showing infiltration or interstitial changes, with or without pleural effusion
4. Any one of pneumonia clinical manifestations, including:
 - (a) Recent cough, sputum or aggravation of respiratory symptoms, the emergence of purulent sputum, with or without chest pain;
 - (b) Fever (axillary temperature $\geq 37.3^{\circ}\text{C}$) or hypothermia (axillary temperature $< 36^{\circ}\text{C}$);
 - (c) Signs of pulmonary consolidation and (or) moist rales;
 - (d) $\text{WBC} > 10 \times 10^9/\text{L}$, or $< 4 \times 10^9/\text{L}$, with or without nucleus left.

Meet criteria 1,2 ,3 and anyone of criteria 4

Exclusion Criteria:

1. Lung infiltrate or interstitial changes which can be interpreted as lung cancer, pulmonary tuberculosis, non-infectious interstitial lung diseases, pulmonary edema, atelectasis, pulmonary embolism, pulmonary eosinophil infiltration, pulmonary vasculitis;
2. HIV positive
3. Readmission within 72 hours after discharging.

Part 1: Baseline Characteristics

Underlying Disease	
COPD <input type="radio"/> Y <input type="radio"/> N	Asthma <input type="radio"/> Y <input type="radio"/> N
Bronchiectasis <input type="radio"/> Y <input type="radio"/> N	Malignancy <input type="radio"/> Y <input type="radio"/> N
Sleep Apnea Syndrome <input type="radio"/> Y <input type="radio"/> N	Congestive Heart Failure <input type="radio"/> Y <input type="radio"/> N
Coronary Heart Disease <input type="radio"/> Y <input type="radio"/> N	Hypertention <input type="radio"/> Y <input type="radio"/> N
Peripheral Vascular Diseases <input type="radio"/> Y <input type="radio"/> N	Diabetes Mellitus <input type="radio"/> Y <input type="radio"/> N
Cerebrovascular Disease <input type="radio"/> Y <input type="radio"/> N	Autoimmune Diseases ^a <input type="radio"/> Y <input type="radio"/> N
Chronic Viral Hepatitis <input type="radio"/> Y <input type="radio"/> N	Cirrhosis <input type="radio"/> Y <input type="radio"/> N
Hematological Malignancy <input type="radio"/> Y <input type="radio"/> N	Organ /bone Marrow Transplantation <input type="radio"/> Y <input type="radio"/> N
Immunosuppressive Therapy ^b <input type="radio"/> Y <input type="radio"/> N	Chemotherapy/Radiotherapy Within 6 Months <input type="radio"/> Y <input type="radio"/> N
Chronic Renal Diseases <input type="radio"/> Y <input type="radio"/> N	Splenectomy <input type="radio"/> Y <input type="radio"/> N

Note: ^aSLE, Sjogren's syndrome, rheumatoid arthritis, polymyositis / dermatomyositis, systemic vasculitis, ankylosing spondylitis, inflammatory bowel disease, hyperthyroidism, etc;; ^b.Anti-rejection drugs

With The Following Situation	
Pregnancy	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown; If Y, Pregnancy ___ weeks.
Within 6 months after delivery	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown; If Y, ___ weeks after delivery
Smoking	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Former Smoker <input type="radio"/> Unknown If Y, Smoked For ___ years, ___ cigarettes/day; If Former Smoker, Smoked For ___ years, ___ cigarettes/day ,GivenUp For ___ years
Alcoholism ^a	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown
Risk factors for inhalation ^b	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown
Contact Children In Day-care Center	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown
Bed Ridden (≥2months)	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown
Long-term inhaled Corticosteroid use ^d	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown
Long-term oral Corticosteroid use ^c	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown; If Y, Name Of Corticosteroid: _____,

	Dose __mg/day, For ____ days
Oral Statin Drugs	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown
History Of CAP Within One Year	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown
Influenza Vaccine Within 1 Year	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown
<i>Streptococcus pneumoniae</i> Vaccine Within 5 Years	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown

Note: **a:** drinking more than 5 bottles of beer (500ml / bottle) or half a catty liquor once in 2 weeks; or drinking more than 2.5 bottles of beer (500ml / bottle) or 2 ounce of white spirit per day for more than five years; **b:** Inhalation risk factors included choking, drowning, nasal feeding, pseudobulbar palsy, dementia, coma, poisoning, Parkinson's disease; **c:** Long-term oral corticosteroids was defined as: oral prednisone ≥ 10 mg / d or equivalent doses of other corticosteroids for more than 3 weeks; **d:** Long-term inhaled corticosteroids was defined as: inhaled corticosteroid for more than 30 days, the daily dose wasn't limited.

Risk Factors Of Health-Care Acquired Pneumonia	
Hospitalization For 2d Or More In The Preceding 90 Days	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown
Home Infusion Therapy (Including Antibiotics) Or Home Wound Care In 30 Days	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown
Chronic dialysis within 30 Days	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown
Residence In A Nursing Home Or Extended Care Facility	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown

Part 2: Data of This Hospitalization

1. Signs And Symptoms

History Of Present Illness	
Clinical Manifestation	
Date Of Illness Onset : ____Y ____M ____D	
Fever? (T \geq 37.3 °C)	<input type="radio"/> Y <input type="radio"/> N; If Y, Tmax: ____°C
Hypothermia? (T<36°C)	<input type="radio"/> Y <input type="radio"/> N; If Y, Tmin: ____°C
Cough?	<input type="radio"/> Y <input type="radio"/> N
Sputum?	<input type="radio"/> Y <input type="radio"/> N; If Y, <input type="radio"/> Yellow Phlegm <input type="radio"/> White Phlegm <input type="radio"/> Bloody Sputum <input type="radio"/> Unknown
Chest Pain?	<input type="radio"/> Y <input type="radio"/> N
Shortness Of Breath?	<input type="radio"/> Y <input type="radio"/> N
Sore Throat Or Rhinorrhea	<input type="radio"/> Y <input type="radio"/> N
Chill/Shiver	<input type="radio"/> Y <input type="radio"/> N
Exhaustion/	<input type="radio"/> Y <input type="radio"/> N

Muscle And Joint Aches//Headache	
Darrhea?	<input type="radio"/> Y <input type="radio"/> N
Familial Aggregation (2 Epidemiological Related People Suffered From Pneumonia In Two Weeks) ?	<input type="radio"/> Y <input type="radio"/> N
Physical Examination (The Worst Value Of The Day On Admission)	
Tmax, °C	
Tmin, °C	
HR, beats/min	
RR, breaths/min	
BP(Systolic Pressure / Diastolic Pressure), mmHg	
Disorder Of Consciousness?	<input type="radio"/> Y <input type="radio"/> N
Cyanosis?	<input type="radio"/> Y <input type="radio"/> N
Physical Signs Of Lung:	Moist rales <input type="radio"/> Y <input type="radio"/> N Dry rales <input type="radio"/> Y <input type="radio"/> N
Edema Of Legs?	<input type="radio"/> Y <input type="radio"/> N; If Y, Asymmetric Edema Of Legs? <input type="radio"/> Y <input type="radio"/> N

3.Pre-hospital Medical Data Y N

Radiology		
Chest X-ray <input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown Date of Examination: ___Y___M___D	Site Of Pneumonia	<input type="radio"/> Bilateral Lung <input type="radio"/> Unilateral Lung
	Site Of Pneumonia	<input type="radio"/> Superior Lobe Of Right Lung <input type="radio"/> Middle Lobe Of Right Lung <input type="radio"/> Inferior Lobe Of Right Lung <input type="radio"/> Superior Lobe Of Left Lung <input type="radio"/> Inferior Lobe Of Left Lung <input type="radio"/> Unknown
	Plural effusion	<input type="radio"/> N <input type="radio"/> Left <input type="radio"/> Right <input type="radio"/> Bilateral
	Cavity	<input type="radio"/> Y <input type="radio"/> N
	consolidation	<input type="radio"/> Y <input type="radio"/> N
	Interstitial Change	<input type="radio"/> Y <input type="radio"/> N
Lung CT <input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown Date of Examination: ___Y___M___D	Infiltration	<input type="radio"/> Y <input type="radio"/> N
	Alveolar Infiltration	<input type="radio"/> Superior Lobe Of Right Lung <input type="radio"/> Middle Lobe Of Right Lung <input type="radio"/> Inferior Lobe Of Right Lung <input type="radio"/> Superior Lobe Of Left Lung <input type="radio"/> Inferior Lobe Of Left Lung <input type="radio"/> Bilateral Diffuse Infiltration <input type="radio"/> Unilateral Diffuse iInfiltration

	Plural effusion	<input type="radio"/> N <input type="radio"/> Left <input type="radio"/> Right <input type="radio"/> Bilateral
	Cavity	<input type="radio"/> Y <input type="radio"/> N
	consolidation	<input type="radio"/> Y <input type="radio"/> N
	Abscesses	<input type="radio"/> Y <input type="radio"/> N
	Patchy Shadow	<input type="radio"/> Y <input type="radio"/> N
	Interstitial change	<input type="radio"/> Y <input type="radio"/> N
Microbiological Examination		
Microbiological Examination Before Admission <input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown		
If Y: Date Of Specimen Collection: ____Y____M____D Specimen Type: <input type="radio"/> Sputum <input type="radio"/> Blood <input type="radio"/> BALF <input type="radio"/> Asopharyngeal Swab <input type="radio"/> Endotracheal Aspirate <input type="radio"/> Plural Effusion <input type="radio"/> Urine Microbiological Examination Results: _____		
Treatment Before Admission		
Antimicrobials Before Admission <input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown		
Drug name (Generic Name And Trade Name)	Route Of Administration	Drug Regime n
eg: Ceftriaxone (罗氏芬)	<input checked="" type="radio"/> Intravenous <input type="radio"/> Oral	2.0g , Qd
	<input type="radio"/> Intravenous <input type="radio"/> Oral	
	<input type="radio"/> Intravenous <input type="radio"/> Oral	
	<input type="radio"/> Intravenous <input type="radio"/> Oral	
	<input type="radio"/> Intravenous <input type="radio"/> Oral	
Antiviral Drug Use Before Admission <input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown		
	<input type="radio"/> Intravenous <input type="radio"/> Oral	
	<input type="radio"/> Inhalation	
	<input type="radio"/> Intravenous <input type="radio"/> Oral	
	<input type="radio"/> inhalation	
Corticosteroid Use Before Admission <input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown		
	<input type="radio"/> Intravenous <input type="radio"/> Oral	
	<input type="radio"/> inhalation	
	<input type="radio"/> Intravenous <input type="radio"/> Oral	
	<input type="radio"/> inhalation	
Vasopressor Use Before Admission <input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown		
If Y, Start Time: _____		Terminal Time: _____
Invasive Ventilation Before Admission <input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown		
If Y, Start Time: _____		Terminal Time: _____

Note: b. Vasopressors: Norepinephrine, Dopamine, Dobutamine, Metaraminol, adrenaline

4. Laboratory Examination In 24hr On Admission

Category	Item	Value	Unit
Blood Routine	WBC		*10 ⁹ /L
	Neu		*10 ⁹ /L
	Lym		*10 ⁹ /L
	HGB		g/L
	HCT		%
	PLT		*10 ⁹ /L
Biochemistry	ALB		g/L
	LDH		U/L
	AST		U/L
	ALT		U/L
	ALP		U/L
	TBIL		umol/L
	DBIL		umol/L
	CK		U/L
	BUN		mmol/L
	Cr		mmol/L
	Glu		mmol/L
	K		mmol/L
	Na		mmol/L
	Serum Detection	ESR	
CRP			mg/dL
PCT			ng/ml
D-dimer			ng/ml
PT			s
APTT			s
INR			
BNP			pg/ml
Ferritin			ug/l

5. Blood Gas Analysis, Radiology and Ultrasonography After Admission

Category	Item	Value
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Blood gas analysis (The Worst Value In 24hr On Admission)	Oxygen Therapy ※ <input type="radio"/> Y <input type="radio"/> N	<input type="radio"/> Oxygen Inhalation Through Nasal Tube____L/min <input type="radio"/> Oxygen Inhalation Through Venturi Mask_____% <input type="radio"/> Oxygen Inhalation Through Oxygen Masks__L/min <input type="radio"/> Non-invasive Ventilation <input type="radio"/> Invasive Ventilation <input type="radio"/> Unknowen	
	FiO ₂		
	pH		
	PO ₂ (mmHg)		
	PCO ₂ (mmHg)		
	SaO ₂		
	Actual Bicarbonate (mmol/l)		
Lac (mmol/l)			
Radiology (In 24hr On Admission)	Chest X-ray <input type="radio"/> Y <input type="radio"/> N	Alveolar Infiltration	<input type="radio"/> Superior Lobe Of Right Lung <input type="radio"/> Middle Lobe Of Right Lung <input type="radio"/> Inferior Lobe Of Right Lung <input type="radio"/> Superior Lobe Of Left Lung <input type="radio"/> Inferior Lobe Of Left Lung <input type="radio"/> Bilateral Diffuse Infiltration <input type="radio"/> Unilateral Diffuse Infiltration
		Plural effusion	<input type="radio"/> N <input type="radio"/> Left <input type="radio"/> Right <input type="radio"/> Bilateral
		Cavity	<input type="radio"/> Y <input type="radio"/> N
		consolidation	<input type="radio"/> Y <input type="radio"/> N
		Patchy Shadow	<input type="radio"/> Y <input type="radio"/> N
	Lung CT <input type="radio"/> Y <input type="radio"/> N	Alveolar Infiltration	<input type="radio"/> Superior Lobe Of Right Lung <input type="radio"/> Middle Lobe Of Right Lung <input type="radio"/> Inferior Lobe Of Right Lung <input type="radio"/> Superior Lobe Of Left Lung <input type="radio"/> Inferior Lobe Of Left Lung <input type="radio"/> Bilateral Diffuse Infiltration <input type="radio"/> Unilateral Diffuse Infiltration
		Plural effusion	<input type="radio"/> N <input type="radio"/> Left <input type="radio"/> Right <input type="radio"/> Bilateral
		Cavity	<input type="radio"/> Y <input type="radio"/> N
		consolidation	<input type="radio"/> Y <input type="radio"/> N
		Patchy Shadow	<input type="radio"/> Y <input type="radio"/> N

		Interstitial Change	<input type="radio"/> Y <input type="radio"/> N
		Alveolar Infiltration	<input type="radio"/> Superior Lobe Of Right Lung <input type="radio"/> Middle Lobe Of Right Lung <input type="radio"/> Inferior Lobe Of Right Lung <input type="radio"/> Superior Lobe Of Left Lung <input type="radio"/> Inferior Lobe Of Left Lung <input type="radio"/> Bilateral Diffuse Infiltration <input type="radio"/> Unilateral Diffuse Infiltration
Ultrasonography	Lower Limb Vascular Ultrasound Exam	Venous Thrombosis	<input type="radio"/> N <input type="radio"/> Left <input type="radio"/> Right <input type="radio"/> Bilateral <input type="radio"/> Unexamined

Note※The Worst Value Of Blood Gas Analysis And FiO2 At That Time.

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6.Keep Detailed Records Of The Following Time Points,And Write down The Code In The First Row Of The Table:

- ①The 4th day (The Day On Admission Is The 1st Day);
- ②The day of changing Antibiotics in 14 days After Admission;
- ③The 14th day after Admission ;
- ④The Day Of Discharging

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Category	Item(Unit)	BMJ Open	The Reason and The Date					
Vital Signs	Disorder Of Consciousness							
	Tmax (°C)							
	Tmin(°C)							
	HR (beats/min)							
	RR (breaths/min)							
	BP(/ mmHg)							
Symptoms 1. Exacerbation 2. Alleviation 3. No-change	Cough							
	Sputum							
	Chest Pain							
	Shortness Of Breath							
	Moist Rales							
	Dry Rales							
Blood Routine	WBC (*10⁹/L)							
	Neu (*10⁹/L)							
	Lym (*10⁹/L)							
	HGB (g/L)							
	HCT (%)							
	PLT (*10⁹/L)							
Biochemistry	ALB (g/L)							
	LDH (U/L)							
	AST (U/L)							
	ALT (U/L)							
	ALP (U/L)							
	TBIL (umol/L)							
	DBIL (umol/L)							
	CK (U/L)							
	CTNI (ng/ml)							
	BUN (mmol/L)							
	Cr (mmol/L)							

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Note: a. Direct Microscopy of sputum is not included

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7.Treatment During Hospitalization

Antibiotics Use <input type="radio"/> Y <input type="radio"/> N				
Drug Name (Generic Name And Trade Name)	Route Of Administration	Drug Regimen	Start Time	Terminal Ttime
eg: Ceftriaxone (罗氏芬)	<input checked="" type="radio"/> Intravenous <input type="radio"/> Oral	2.0g, Qd	2014-3-2	2014-4-5
	<input type="radio"/> Intravenous <input type="radio"/> Oral			
	<input type="radio"/> Intravenous <input type="radio"/> Oral			
	<input type="radio"/> Intravenous <input type="radio"/> Oral			
	<input type="radio"/> Intravenous <input type="radio"/> Oral			
	<input type="radio"/> Intravenous <input type="radio"/> Oral			
	<input type="radio"/> Intravenous <input type="radio"/> Oral			
Antiviral Drugs Use <input type="radio"/> Y <input type="radio"/> N				
Drug name (Generic Name And Trade Name)	Route Of Administration	Drug Regimen	Start Time	Terminal Time
	<input type="radio"/> Intravenous <input type="radio"/> Oral <input type="radio"/> Inhalation			
	<input type="radio"/> Intravenous <input type="radio"/> Oral <input type="radio"/> Inhalation			
	<input type="radio"/> Intravenous <input type="radio"/> Oral <input type="radio"/> Inhalation			
Glucocorticoids Use <input type="radio"/> Y <input type="radio"/> N				
Drug name (Generic Name And Trade Name)	Route Of Administration	Drug Regimen	Start Time	Terminal Time
	<input type="radio"/> Intravenous <input type="radio"/> Oral <input type="radio"/> Inhalation			
	<input type="radio"/> Intravenous <input type="radio"/> Oral <input type="radio"/> Inhalation			
Vasopressors Use <input type="radio"/> Y <input type="radio"/> N				
Drug Name	Route Of Administration	Drug Regimen	Start Time	Terminal Ttime
Immunoregulation Drugs (Including Intravenous Immunoglobulin , Thymosins) <input type="radio"/> Y <input type="radio"/> N				
Drug Name	Route of administration	Drug Regimen	Start time	Terminal time

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Alternative/ Supportive Treatment			
Item	Use	Start Time	Terminal Time
Continuous Venous-venous Hemofiltration	<input type="radio"/> Y <input type="radio"/> N		
Extracorporeal Membrane Oxygenation (ECMO)	<input type="radio"/> Y <input type="radio"/> N		
Non-invasive Ventilation	<input type="radio"/> Y <input type="radio"/> N		
Invasive Ventilation	<input type="radio"/> Y <input type="radio"/> N		

8. Measurement Of T Lymphocyte Subsets

Date of specimen collection: ___Y ___M ___D

T lymphocyte subsets	CD4		/ml
	CD8		/ml
	CD4%		
	CD8%		
	NK		/ml
	NKT		/ml
	CD4/CD8		

Note: Without Time Limitation

9. Microbiological Examination

(1). Microbiological Examination In 48hrs After Admission Y N

Microbiological Examination For Sputum Or eEndotracheal aAspiration	
Date Of Specimen Collection: ___Y___M___D	
Item	Results
Direct Microscopy	<input type="radio"/> Good Quality Sputum (> 25 leukocytes and < 10 epithelial cells per × 100 magnification field) <input type="radio"/> Not Good Quality Sputum <input type="radio"/> Unknown
	<input type="radio"/> G+ Cocci <input type="radio"/> G+ Bacillus <input type="radio"/> G- Cocci <input type="radio"/> G- Bacillus <input type="radio"/> Positive Acid-fast Stain <input type="radio"/> None

<p>Bacteria Culture</p>	<ul style="list-style-type: none"> ○Streptococcus pneumoniae ○Haemophilus influenzae ○Pseudomonas aeruginosa ○Enterobacter cloacae ○Acinetobacter spp ○Stenotrophomonas maltophilia ○Escherichia coli ○Enterococcus faecium ○None Or Normal oropharyngeal flora 	<ul style="list-style-type: none"> ○Moraxella catarrhalis ○staphylococcus aureus ○Klebsiella pneumoniae ○Proteus spp ○Serratia marcescens ○Enterobacter aerogenes ○Enterococcus faecalis ○Others: _____
	<p>Drug Resistant Bacteria</p> <ul style="list-style-type: none"> ○Methicillin Resistance Staphylococcus aureus (MRSA) ○Vancomycin-resistant Enterococcus <p>Bacteria producing ESBLs:</p> <ul style="list-style-type: none"> ○Escherichia coli ○Enterobacter cloacae <p>non - fermentative bacteria.:</p> <ul style="list-style-type: none"> ○Acinetobacter baumannii ○Others: _____ 	
	<p>If Streptococcus pneumoniae , MIC for penicillin_____ug/ml;</p> <ul style="list-style-type: none"> ○Not detected 	
	<p>If MRSA, MIC for Vancomycin_____ug/ml;</p> <ul style="list-style-type: none"> ○Not detected 	
<p>Direct Microscopy</p>	<ul style="list-style-type: none"> ○Fungal Spore ○Cryptococcus neoformans 	<ul style="list-style-type: none"> ○Fungal Hyphae ○None
<p>Fungi Culture</p>	<ul style="list-style-type: none"> ○Spergillus Fumigatus ○Aspergillus terreus ○Candida Spp ○Undetected 	<ul style="list-style-type: none"> ○Aspergillusflavus ○Mucor Mucedo ○Cryptococcus Neoformans ○Others: _____
<p>Nucleic Acid Test For Respiratory Virus</p>	<ul style="list-style-type: none"> ○Influenza A H1N1 ○Influenza A H2N3 ○Nontypeable Influenza A ○Adenovirus ○Parainfluenza virus2 ○Parainfluenza virus 4 ○Rhinovirus ○Coronavirus OC43HKU1 ○Coronavirus 229ENL63 ○Bocavirus ○EB virus 	<ul style="list-style-type: none"> ○Avian influenza H7N9 ○Influenza A H5N1 ○Influenza B ○Parainfluenza virus 1 ○Parainfluenza virus 3 ○Respiratory syncytial virus A ○Respiratory syncytial virus B ○Enterovirus ○Herpes simplex virus ○Cytomegalovirus ○MERS-CoV

Nucleic Acid Test For Atypical Etiology	<input type="radio"/> Mycoplasma pneumoniae <input type="radio"/> Legionella spp	<input type="radio"/> Chlamydia pneumoniae
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(2).Microbiological Examination For BALF? Y N

Microbiological examination for BALF (Within One Week After Admission)	
Date Of Specimen Collection: <u> </u> Y <u> </u> M <u> </u> D	
Item	Results
Direct Microscopy	<input type="radio"/> G+ Cocci <input type="radio"/> G+ Bacillus <input type="radio"/> G- Cocci <input type="radio"/> G- Bacillus <input type="radio"/> Positive Acid-fast Stain <input type="radio"/> None
Bacteria Culture	<input type="radio"/> Streptococcus pneumoniae <input type="radio"/> Moraxella catarrhalis <input type="radio"/> Haemophilus influenzae <input type="radio"/> staphylococcus aureus <input type="radio"/> Pseudomonas aeruginosa <input type="radio"/> Klebsiella pneumoniae <input type="radio"/> Enterobacter cloacae <input type="radio"/> Proteus spp <input type="radio"/> Acinetobacter spp <input type="radio"/> Serratia marcescens <input type="radio"/> Stenotrophomonas maltophilia <input type="radio"/> Enterobacter aerogenes <input type="radio"/> Escherichia coli <input type="radio"/> Enterococcus faecalis <input type="radio"/> Enterococcus faecium <input type="radio"/> Others: <u> </u> <input type="radio"/> None Or Normal oropharyngeal flora
	Drug Resistant Bacteria
	<input type="radio"/> Methicillin Resistance Staphylococcus aureus (MRSA) <input type="radio"/> Vancomycin-resistant Enterococcus
	Bacteria producing ESBLs:
	<input type="radio"/> Escherichia coli <input type="radio"/> Klebsiella pneumoniae <input type="radio"/> Enterobacter cloacae <input type="radio"/> Serratia marcescens
	non - fermentative bacteria.:
	<input type="radio"/> Acinetobacter baumannii <input type="radio"/> Pseudomonas aeruginosa <input type="radio"/> Others: <u> </u>
	If Streptococcus pneumoniae , MIC for penicillin <u> </u> ug/ml;
	<input type="radio"/> Not Detected
	If MRSA, MIC for Vancomycin <u> </u> ug/ml;
	<input type="radio"/> Not Detected
Direct Microscopy	<input type="radio"/> Fungal Spore <input type="radio"/> Fungal Hyphae <input type="radio"/> Cryptococcus neoformans <input type="radio"/> None

	If <i>Streptococcus pneumoniae</i> , MIC for penicillin ___ug/ml; <input type="radio"/> Not Detected	
	If MRSA, MIC for Vancomycin ___ug/ml; <input type="radio"/> Not Detected	
Fungi Culture	<input type="radio"/> <i>Candidiasis albicans</i> <input type="radio"/> <i>Candida tropicalis</i> <input type="radio"/> <i>Candida parapsilosis</i> <input type="radio"/> <i>Aspergillus fumigatus</i> <input type="radio"/> <i>Aspergillus terreus</i> <input type="radio"/> Undetected	<input type="radio"/> <i>Candida krusei</i> <input type="radio"/> <i>Candida glabrata</i> <input type="radio"/> <i>Cryptococcus neoformans</i> <input type="radio"/> <i>Aspergillus flavus</i> <input type="radio"/> <i>Mucor Mucedo</i> <input type="radio"/> Others: ____

(4)、Pleural Effusion? Y N

Pleural Effusion Test? Y N

Microbiological Examination For Pleural Effusion (Without Time Limitation)	
Date of Specimen collection: <u> </u> Y <u> </u> M <u> </u> D	
Pleural Effusion Routine	
Total Cell Count: ___×10 ⁶ /L; Multinuclear Cell: ___×10 ⁶ /L; Mononuclear Cells: ___×10 ⁶ /L	
Pleural Effusion Biochemistry	
LDH: ___U/L; ADA: ___U/L; Pr: ___g/L Glu: ___mmol/L Cl: ___mmol/L	
Item	Results
Bacteria Culture	<input type="radio"/> <i>Staphylococcus aureus</i> <input type="radio"/> <i>Moraxella catarrhalis</i> <input type="radio"/> <i>Haemophilus influenzae</i> <input type="radio"/> <i>Pseudomonas aeruginosa</i> <input type="radio"/> <i>Klebsiella pneumoniae</i> <input type="radio"/> <i>Enterobacter cloacae</i> <input type="radio"/> <i>Proteus spp</i> <input type="radio"/> <i>Acinetobacter spp</i> <input type="radio"/> <i>Serratia marcescens</i> <input type="radio"/> <i>Stenotrophomonas maltophilia</i> <input type="radio"/> <i>Enterobacter aerogenes</i> <input type="radio"/> <i>Escherichia coli</i> <input type="radio"/> <i>Enterococcus faecalis</i> <input type="radio"/> <i>Enterococcus faecium</i> <input type="radio"/> Others: _____ <input type="radio"/> None or Normal Oropharyngeal Flora
	Drug Resistant Bacteria <input type="radio"/> Methicillin resistance staphylococcus aureus (MRSA) <input type="radio"/> Vancomycin-resistant Enterococcus Bacteria producing ESBLs: <input type="radio"/> <i>Escherichia coli</i> <input type="radio"/> <i>Klebsiella pneumoniae</i> <input type="radio"/> <i>Enterobacter cloacae</i> <input type="radio"/> <i>Serratia marcescens</i> non - fermentative bacteria.: <input type="radio"/> <i>Acinetobacter baumannii</i> <input type="radio"/> <i>Pseudomonas aeruginosa</i> <input type="radio"/> Others: ____
Fungi Culture	<input type="radio"/> <i>Candidiasis albicans</i> <input type="radio"/> <i>Candida krusei</i> <input type="radio"/> <i>Candida tropicalis</i> <input type="radio"/> <i>Candida glabrata</i>

<input type="radio"/> Candida parapsilosis <input type="radio"/> Aspergillus fumigatus <input type="radio"/> Aspergillus terreus <input type="radio"/> Undetected	<input type="radio"/> Cryptococcus neoformans <input type="radio"/> Aspergillus flavus <input type="radio"/> Mucor Mucedo <input type="radio"/> Others: _
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(5)、Antigen Test In 48hr After Admission? Y N

Urinary antigen (in 48hr after admission)			
Date of specimen collection: <u> </u> Y <u> </u> M <u> </u> D			
Urinary Antigen For <i>Legionella</i> <i>spp</i>	<input type="radio"/> Positive	<input type="radio"/> Negative	<input type="radio"/> Undetected
Urinary Antigen For <i>Streptococcus pneumoniae</i>	<input type="radio"/> Positive	<input type="radio"/> Negative	<input type="radio"/> Undetected
Throat Swab Aantigen Test (In 48hr After Admission)			
Date Of Specimen Collection: <u> </u> Y <u> </u> M <u> </u> D			
Respiratory Syncytial Virus Antigen Test	<input type="radio"/> Positive	<input type="radio"/> Negative	<input type="radio"/> Undetected
Influenza A Antigen Test	<input type="radio"/> Positive	<input type="radio"/> Negative	<input type="radio"/> Undetected
Influenza B Antigen Test	<input type="radio"/> Positive	<input type="radio"/> Negative	<input type="radio"/> Undetected

(6)、Antibody Test? a) Y N

b) If Y, Titer Of Antibody In Paired Serum? Y, Interval days

N

Antibody Test (Without Time Limitation)	
Date Of Specimen Collection: <u> </u> Y <u> </u> M <u> </u> D	
<input type="radio"/> IgM for <i>Mycoplasmal pneumonia</i>	<input type="radio"/> IgM for Influenza A
<input type="radio"/> IgG for <i>Mycoplasmal pneumonia</i>	<input type="radio"/> IgM for Parainfluenza
<input type="radio"/> IgM for <i>Chlamydia spp</i>	<input type="radio"/> IgM for Q fever
<input type="radio"/> IgG for <i>Chlamydia spp.</i>	<input type="radio"/> IgM for Adenovirus
<input type="radio"/> IgM for <i>Legionella spp</i>	<input type="radio"/> IgM for Respiratory syncytial virus
<input type="radio"/> IgG for <i>Legionella spp</i>	<input type="radio"/> IgM for Parainfluenza 1,2,3

10、 Outcomes

(1).Treatment Failure Within 14 Days

Treatment Failure Within 14 Days (Multiple choices)		
(The Value Of The 1 st Day On Admission As The Baseline Data)		
1.Needs Invasive Ventilation	○Y ○N	
2.Needs Non-invasive Ventilation	○Y ○N	
3.Needs Vasopressors	○Y ○N	
4.Death	○Y ○N	
The Reasons For Treatment Failure		
1.CAP Progression	Pneumonia Progression	○Y ○N
2.CAP Complications	Pyothorax	○Y ○N
	Endocarditis	○Y ○N
	Meningitis	○Y ○N
	Others: _____	
3.Severe Sepsis Due To CAP	ARDS	○Y ○N
	Sepsis	○Y ○N
	Hepatic Failure	○Y ○N
	Renal Ffailure	○Y ○N
	Clotting Disorders,	○Y ○N
	Encephalopathy	○Y ○N
Others: _____		
4.Complications Or Underlying Disease Deterioration	Pulmonary Embolism	○Y ○N
	Myocardial Infarction	○Y ○N
	Arrhythmia	○Y ○N
	Gastrointestinal Bleeding	○Y ○N
	Congestive Heart Failure	○Y ○N
	COPD	○Y ○N
	Diabetes Mellitus	○Y ○N
	Nephropathy	○Y ○N
Others: _____		
5.Complications Due To Treatment	Hemopneumothorax	○Y ○N
	Allergic To Antibiotics	○Y ○N
	HAP/VAP	○Y ○N
	Vascular Catheter Infection	○Y ○N
	C. Difficile Infection	○Y ○N
	Iatrogenic Urinary Tract Infection	○Y ○N
Others: _____		
6.Unknown	○Y ○N	

(2). Complications During Hospitalization

Complications During Hospitalization	
Complications (Multiple Choices)	○Y ○N
Respiratory Failure ○Y ○N	ARDS ○Y ○N
Heart Failure ○Y ○N	Acute Myocardial Infarction ○Y ○N
Acute Liver Failure ○Y ○N	AcuteRenal Failure ○Y ○N
Septic Shock ○Y ○N	Stroke ○Y ○N
DIC ○Y ○N	Antibiotic Associated Diarrhea ○Y ○N
Arrhythmia ○Y ○N	MODS ○Y ○N
Pulmonary Embolism ○Y ○N	Deep Venous Thrombosis ○Y ○N
Ventilator Associated Pneumonia ○Y ○N	Gastrointestinal Bleeding ○Y ○N
Invasive Aspergillosis ○Y ○N	Mediastinal Emphysema ○Y ○N
Pneumothorax ○Y ○N	Nosocomial Bloodstream Infection ○Y ○N
Others ○Y ○N	If Y: _____

(3) . Outcomes

Clinical Stability Before Discharge	○Y ○N If Y, the date of clinical stability ____ Y ____ M ____ D. Meet the following seven criteria: Temperature<37.8°C for more than 24hr; Heart rate ≤100 beats/min ; Respiratory rate ≤24 breaths/min ;Systolic blood pressure ≥90 mm Hg ; Arterial oxygen saturation ≥90% or pO2 ≥ 60 mm Hg on room air ; Ability to maintain oral intake; Normal mental status.
Admitted to RICU/ICU?	○Y ○N If Y, The Date Of Admitted To RICU/ICU: ____ Y ____ M ____ D The Date Of Transfer From RICU/ICU: ____ Y ____ M ____ D
Discharging	The Date Of Discharging ____ Y ____ M ____ D Outcome ○Improvement ○Against-advice discharge ○Death If death, The Death Date ____ Y ____ M ____ D
Direct Cause Of Death (only one choice)	○Severe Pneumonia ○Respiratory Failure ○Shock○Heart Failure ○Acute Myocardial Infarction

	○Acute renal Failure	○Hepatic failure
	○DIC	○Stroke
	○Gastrointestinal Bleeding	○Others: _____

10. Cost And Economy Data

Total Expenses _____ Yuan:

Drugs Cost: _____ Yuan , Antimicrobials Cost _____ Yuan

Laboratory Testing Expenses: _____ Yuan

Bed Charge: _____ Yuan

Health Care Worker Labor Cost: _____ Yuan

Appendix 4: Definition of underlying diseases

- 1) Long-term smoking was defined as: cigarette smokers of 10 cigarettes/d during at least the previous year;
- 2) Alcoholism was defined as: drinking more than 5 bottles of beer (500ml / bottle) or half a catty liquor once in 2 weeks; or drinking more than 2.5 bottles of beer (500ml / bottle) or 2 ounce of white spirit per day for more than five years;
- 3) Long-term oral corticosteroids was defined as: oral prednisone $\geq 10\text{mg} / \text{d}$ or equivalent doses of other corticosteroids for more than 3 weeks.¹
- 4) Long-term inhaled corticosteroids was defined as: inhaled corticosteroid for more than 30 days, the daily dose wasn't limited;
- 5) COPD was defined as: persistent airflow limitation, $\text{FEV}_1 / \text{FVC} < 70\%$ post bronchodilator;
- 6) Asthma was defined by the history of respiratory symptoms such as wheeze, cough that varied over time and intensity, together with variable respiratory airway limitation;
- 7) Hypertension was defined as systolic blood pressure $\geq 140\text{mmHg}$ and /or diastolic blood pressure $\geq 90\text{mmHg}$ in resting status;
- 8) Coronary heart disease included angina pectoris, myocardial infarction, ischemic cardiomyopathy;
- 9) Chronic congestive heart failure was defined as cardiomegaly and ejection fraction $\leq 40\%$;

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4 10) Cerebrovascular diseases included transient ischemic attack, cerebral hemorrhage,
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6 subarachnoid hemorrhage, cerebral infarction, etc;
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10 11) Diabetes mellitus: included diabetes mellitus type 1 and diabetes mellitus type 2,
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12 not included impaired glucose tolerance and impaired fasting glycaemia;
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14 12) Chronic liver disease included chronic viral hepatitis, chronic alcoholic liver
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16 disease, chronic fatty liver disease, etc;
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19 13) Chronic kidney disease included diabetic nephropathy, hypertensive renal damage,
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21 chronic glomerulonephritis, chronic pyelonephritis, lupus nephritis, IgA nephropathy,
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23 nephrotic syndrome, hereditary kidney disease, etc;
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26 14) Connective Tissue Diseases include SLE, Sjogren's syndrome, rheumatoid
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28 arthritis, polymyositis / dermatomyositis, systemic vasculitis, ankylosing spondylitis,
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30 inflammatory bowel disease, hyperthyroidism, etc;
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33 15) Organ transplantation or bone marrow transplantation included solid organ
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35 transplanting, such as liver transplantation, kidney transplantation, lung
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37 transplantation or pancreas transplantation, etc and bone marrow transplantation;
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40 16) Aspiration risk factors included choking, drowning, nasal, pseudobulbar palsy,
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42 dementia, coma, poisoning, Parkinson's disease.
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45 17) Immunosuppressive therapy: was defined as systematic glucocorticosteroid (such
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47 as prednisone ≥ 10 mg/d for more than 3 weeks in the last month); cyclosporine or
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49 azathioprine use within 3 months, and methotrexate use ≥ 12.5 mg/week within 3
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51 months; biological modifiers such as etanercept and infliximab within 3 weeks.
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4 18) Immunocompromised status included HIV(+), chemotherapy/radiotherapy within
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6 6 months, immunosuppressive therapy, organ/bone marrow transplantation,
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8 splenectomy, hematological neoplasms.²
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11 19) Risk factors for pseudomonal infection was defined as chronic airway disease
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13 (bronchiectasis or COPD) and HCAP risk factors according to IDSA/ATS criteria.³⁻⁷
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17 20) Overtreatment was defined as: i) use of antipseudomonal β -lactams or β -lactams+
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19 fluoquinolones in hospitalized (not in ICU) patients without risk factors for
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21 pseudomonal infection; i i) use of β -lactams(antipseudomonal or not)+ fluoquinolones
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23 in ICU patients aged < 65yr without risk factors for pseudomonas infection; iii) use of
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25 anti-MRSA drugs in hospitalized (not in ICU) patients.³
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Appendix 5 Empirical antimicrobial regimens according to Chinese CAP guideline

Populations	Common pathogens	Anti-infective agents for initial empirical therapy	Comment
Outpatient treatment (Oral administration is recommended)			
Young adults without underlying disease(s)	<i>S. pneumoniae</i> , <i>M. pneumoniae</i> , <i>H. influenzae</i> , <i>C. pneumoniae</i> , influenza virus, adenovirus, <i>M. catarrhalis</i>	(1) Aminopenicillins, penicillins-β-lactamase-inhibitor combinations; (2) I or II generation cephalosporins; (3) doxycycline or minocycline; (4) respiratory quinolones; (5) macrolides	(1) Differentiate among bacterial pneumonia, <i>Mycoplasma</i> , <i>Chlamydia</i> and viral pneumonia based on clinical characteristics; (2) Mild pneumonia caused by <i>Mycoplasma</i> , <i>Chlamydia</i> , and virus is usually self-limited
Patients with underlying disease(s) or elderly patients (age ≥ 65 years)	<i>S. pneumoniae</i> , <i>H. influenzae</i> , <i>Enterobacteriaceae</i> such as <i>K. pneumoniae</i> , <i>C. pneumoniae</i> , influenza virus, RSV, <i>M. catarrhalis</i>	(1) Penicillins-β-lactamase-inhibitor combinations; (2) II or III generation cephalosporins (oral); (3) respiratory quinolones; (4) penicillins-lactamase-inhibitor combinations, II generation cephalosporins, III generation cephalosporins combined with doxycycline or minocycline or macrolides	Monotherapy with doxycycline or minocycline or macrolides is not recommended in patients with risk factors of resistant <i>S. pneumoniae</i> (1), such as age ≥ 65 years, underlying diseases (chronic cardiac, pulmonary, or renal diseases, diabetes mellitus, and immunosuppression), alcoholism, and β-lactams treatment within 3 months.
Inpatient treatment, non-ICU (Intravenous or oral administration)			

Young adults without underlying disease(s)	<i>S. pneumoniae</i> , <i>H. influenzae</i> , <i>M. catarrhalis</i> , <i>S. aureus</i> , <i>M. pneumoniae</i> , <i>C. pneumoniae</i> , influenza virus, adenovirus, other respiratory tract viruses	(1) Penicillin G, aminopenicillins, penicillins- β -lactamase-inhibitor combinations; (2) II or III generation cephalosporins, cephamycins, oxacephems; (3) the above drugs combined with doxycycline, minocycline or macrolides; (4) respiratory quinolones; (5) macrolides	(1) Only 1.9% of the <i>S. pneumoniae</i> isolates from adult CAP are resistant to intravenous penicillins in China. The percentage of intermediate strains is only about 9%. Intravenous penicillins are still effective in hospitalized patients infected with penicillin-intermediate <i>S. pneumoniae</i> when increasing the dosage (23, 161); (2) When atypical pathogens are suspected, doxycycline or minocycline or respiratory quinolones are preferred. Macrolides can be used in regions with lower resistance rate to mycoplasma
Patients with underlying disease(s) or elderly patients (age \geq 65 years)	<i>S. pneumoniae</i> , <i>H. influenzae</i> , <i>Enterobacteriaceae</i> such as <i>K. pneumoniae</i> , influenza virus, RSV, <i>M. catarrhalis</i> , anaerobic bacteria, <i>Legionella</i>	(1) Penicillins- β -lactamase-inhibitor combinations; (2) III generation cephalosporins or their enzyme-inhibitor combinations, carbapenems such as cephamycins, oxacephems, ertapenem; (3) monotherapy of the above drugs or in combination with macrolides; (4) respiratory quinolones	(1) <i>Enterobacteriaceae</i> infection must be considered in patients with underlying disease(s) and elderly patients. The patients must be further evaluated for the risk of infection with ESBLs-producing <i>Enterobacteriaceae</i> ; (2) Elderly patients should be monitored for the risk factors of aspiration
Requirement for ICU admission (Intravenous administration is recommended)			
Young adults without underlying disease(s)	<i>S. pneumoniae</i> , <i>S. aureus</i> , influenza virus, adenovirus, <i>Legionella</i>	(1) Penicillins- β -lactamase-inhibitor combinations, III generation cephalosporins, cephamycins, oxacephems, ertapenem combined with macrolides; (2) respiratory quinolones	(1) <i>S. pneumoniae</i> is the most common pathogen. The other pathogens such as <i>S. aureus</i> , <i>Legionella</i> , influenza virus should also be considered (1, 2, 162-166); (2) During influenza seasons, attention must be paid to influenza viral infections. Combination with neuraminidase inhibitors should be considered. Attention should be paid to secondary <i>S. aureus</i> infection (167). The agents active against MRSA can be used in combination if necessary

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<p>Patients with underlying disease(s) or elderly patients (age ≥ 65 years)</p>	<p><i>S. pneumoniae</i>, <i>Legionella</i>, <i>Enterobacteriaceae</i> such as <i>K. pneumoniae</i>, <i>S. aureus</i>, anaerobic bacteria, influenza virus, RSV</p>	<p>(1) Penicillins-β-lactamase-inhibitor combinations, III generation cephalosporins or in combination with beta-lactamase inhibitors, carbapenems such as ertapenem combined with macrolides; (2) penicillins-β-lactamase-inhibitor combinations, III generation cephalosporins or in combination with beta-lactamase inhibitors, carbapenems such as ertapenem combined with respiratory quinolones</p>	<p>(1) Evaluate the risk of infection with ESBLs-producing <i>Enterobacteriaceae</i>; (2) Physicians should be aware of the risk factors for aspiration and antimicrobial coverage of relevant pathogens</p>
<p>CAP with risk factors for <i>P. aeruginosa</i> infection and requirement for inpatient treatment or ICU admission (Intravenous administration is recommended)</p>			
<p>Patients with structural lung disease</p>	<p><i>P. aeruginosa</i>, <i>S. pneumoniae</i>, <i>Legionella</i>, <i>Enterobacteriaceae</i> such as <i>K. pneumoniae</i>, <i>S. aureus</i>, anaerobic bacteria, influenza virus, RSV virus</p>	<p>(1) β-lactams with antipseudomonal activity; (2) quinolones with antipseudomonal activity; (3) β-lactams with antipseudomonal activity combined with quinolones or aminoglycosides with antipseudomonal activity; (4) combination of β-lactams, aminoglycosides and quinolones with antipseudomonal activity</p>	<p>Risk factors include: (1) airway <i>P. aeruginosa</i> colonization; (2) repeated doses of antibacterial drugs or glucocorticoids due to chronic airway disease. Combination therapy is recommended for patients with severe CAP or proven antimicrobial resistance</p>

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Appendix 6: Definition of microbiological criteria of CAP:

Definite, if one of the following criteria was met:

4. Positive urinary antigen for *Legionella pneumophila* (LP, Binax Now L pneumophila urinary antigen test; Trinity Biotech, Bray, Ireland);
5. Positive urinary antigen for *Streptococcus pneumoniae* (Binax Now S pneumoniae urinary antigen test; Emergo Europe, The Netherlands);
6. Positive bacterial culture from blood or plural fluid except for coagulase negative *Staphylococcus spp.*
7. Paired sera with a fourfold or more increase in the titers of antibodies to *Mycoplasma pneumoniae* (MP), *Chlamydia pneumoniae*, *L pneumophila* or respiratory viruses (Influenza A and B, Parainfluenza, Adenovirus, Respiratory syncytial virus). Or Serum IgM antibody (MIF) \geq 1:16 for *Chlamydia pneumoniae*.

Probable, if one of the following criteria was met:

- a. Detection of respiratory virus in sputum/bronchoalveolar lavage (BALF)/throat swabs by Realtime-PCR (Zhijiang, Shanghai, China) according to manufacturer's instructions, including respiratory syncytial virus (RSV) types A and B, influenza virus (IFV) types A and B, parainfluenza virus (PIV) types 1, 2, 3 and 4, rhinovirus (HRV), enterovirus (EV), coronavirus (hCoV) types 229E, NL63, OC43 and HKU1, parapneumovirus (hMPV), and adenovirus (AdV), bocavirus;
- b. Bacteria isolated from purulent sputum (defined as an adequate quality sputum sample with > 25 leukocytes and < 10 epithelial cells per $\times 100$ magnification field) with compatible findings of Gram staining;
- c. Detection of *Mycoplasma pneumoniae* (MP), *Chlamydia pneumoniae* or *L pneumophila* in sputum/BALF/throat swabs by Realtime-PCR (Zhijiang, Shanghai, China)
- d. Positive antigen for Influenza A/B (Alere™, Clearview Exact Influenza A& B)

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4 e. Serum IgM antibody positive for *Mycoplasma pneumoniae* (MP), or Serum IgG
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6 antibody (MIF) \geq 1:512 for *Chlamydia pneumoniae*.
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For peer review only

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5 **Appendix 7: CAP patients with definite and probable microbiological diagnosis**
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Etiology	Without risk factors for pseudomonal infection (n=409)				With risk factors for pseudomonal infection (n=329)	Total (n=738)
	age<65yr and not in ICU (n=182)	age<65yr and in ICU (n=29)	age≥65yr and not in ICU (n=162)	age≥65yr and in ICU (n=36)		
Bacterial	142 (19.2%)	14 (1.9%)	137 (18.6%)	34 (4.6%)	316 (42.8%)	643 (87.1%)
<i>Pseudomonas aeruginosa</i>	27	0	31	6	133	197
<i>Klebsiella pneumoniae</i>	30	9	27	10	54	130
<i>E. coli</i>	15	1	17	2	31	66
<i>Acinetobacter</i>	13	3	20	3	23	62
<i>Staphylococcus aureus</i>	7	3	10	7	24	51
<i>Enterobacter cloacae</i>	9	1	8	3	17	38
<i>Streptococcus pneumoniae</i>	9	1	5	1	9	25
<i>Stenotrophomonas</i>	8	1	10	2	4	25
<i>Enterococcus faecalis</i>	5	0	3	0	9	17
<i>Enterococcus faecium</i>	3	0	1	0	5	9
others	20	3	18	7	35	83
Atypical etiology	5 (0.7%)	0 (0.0%)	2 (0.3%)	0 (0.0%)	0 (0.0%)	7 (0.9%)
<i>Mycoplasma pneumoniae</i>	6	0	1	0	0	7
<i>Legionella pneumoniae</i>	0	1	2	0	0	3
<i>Chlamydia pneumoniae</i>	0	1	0	0	0	1
Virus	30 (4.1%)	8 (1.1%)	15 (2.0%)	1 (0.1%)	9 (1.2%)	63 (8.5%)
Influenza A virus	25	8	14	1	6	54
Rhinovirus	3	2	2	0	1	8
Influenza B virus	0	0	4	1	3	8
Adenovirus	6	1	0	0	0	7
Respiratory syncytial virus	1	0	0	0	0	1
Human metapneumovirus	0	0	1	0	0	1
Cytomegalovirus	1	1	0	0	0	2
Bacterials+viruses	4 (0.5%)	5 (0.7%)	6 (0.8%)	1 (0.1%)	4 (0.5%)	20 (2.7%)
Viruses+atypical pathogens	2 (0.3%)	2 (0.3%)	1 (0.1%)	0 (0.0%)	0 (0.0%)	5 (0.7%)

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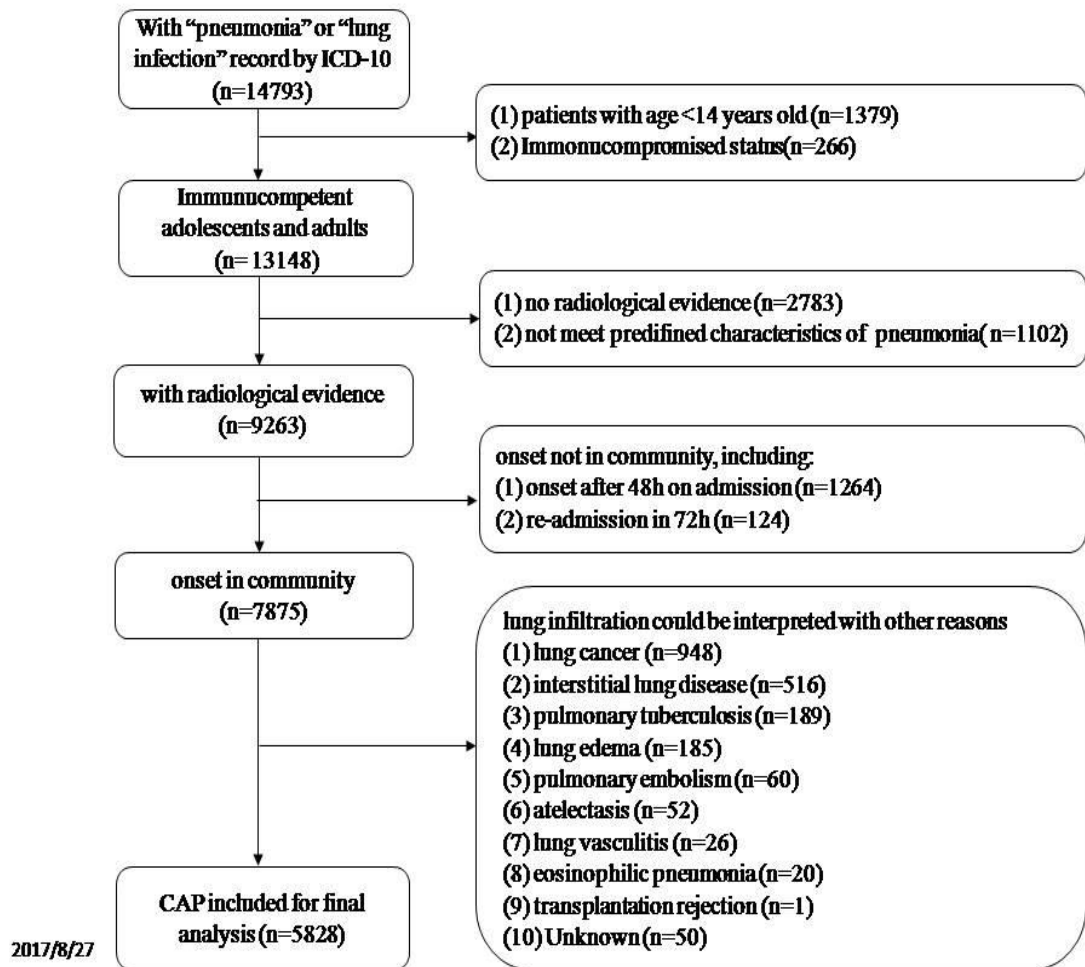
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Appendix 8: Sub-group analysis of 30-day mortality

Item	30-day mortality	P value
Severity of illness		
CURB-65		<0.001
0'	63 (2.7%)	
1'	93 (4.2%)	
2'	64 (7.2%)	
3'	15 (10.2%)	
4'	1 (5.0%)	
5'	1 (100.0%)	
PSI risk class		<0.001
I	26 (2.3%)	
II	27 (3.0%)	
III	24 (3.2%)	
IV	45 (7.0%)	
V	22 (12.2%)	
Age		>0.05
14~64 ys	108 (3.9%)	
65~74 ys	44 (4.1%)	
75~89 ys	81 (4.6%)	
≥90 ys	13 (7.0%)	
Gender		>0.05
Male	144 (4.6%)	
Female	102 (3.8%)	
Underlying Diseases		
None of any underlying disease	47 (2.9%)	
Chronic congestive heart failure	14 (6.9%)	<0.001

COPD	51 (6.4%)	<0.001
Malignant solid tumors	15 (5.9%)	<0.001
Chronic Renal diseases	11 (5.5%)	<0.001
Cerebrovascular Diseases	42 (4.7%)	<0.001
Connective Tissue Diseases	5 (4.5%)	0.003
Coronary Heart Diseases	50 (4.3%)	<0.001
Bronchiectasis	27 (4.3%)	<0.001
Hypertension	87 (4.2%)	<0.001
Asthma	14 (4.1%)	<0.001
Diabetes	36 (3.9%)	<0.001
Chronic Liver diseases	2 (2.2%)	>0.05
ICU admission		
Yes	56 (15.3%)	<0.001
No	190 (3.5%)	
Systemic glucocorticosteroids use in admission		
Yes	87 (5.6%)	<0.001
No	159 (3.7%)	

Appendix Figure 1 Patient screening algorithm for hospitalized CAP



STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (Page 1) (b) Provide in the abstract an informative and balanced summary of what was done and what was found (Page 3-4)
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported (Page 4-5)
Objectives	3	State specific objectives, including any prespecified hypotheses (Page 5)
Methods		
Study design	4	Present key elements of study design early in the paper (Page 6)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection (Page 6-9)
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants (Page 6-7) (b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable (Page 7-10)
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group (Page 6- 7)
Bias	9	Describe any efforts to address potential sources of bias (Page 7)
Study size	10	Explain how the study size was arrived at (Page 9)
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why (Page 9-10)
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (Page 9-10) (b) Describe any methods used to examine subgroups and interactions (Page 9-10) (c) Explain how missing data were addressed (Page 9) (d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy (Page 9-10) (e) Describe any sensitivity analyses (Page 9-10)

Continued on next page

Results

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (Page 10) (b) Give reasons for non-participation at each stage (Page 10, Appendix figure 1) (c) Consider use of a flow diagram (Appendix figure 1)
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (Page 10-11) (b) Indicate number of participants with missing data for each variable of interest (Table 1-5) (c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time <i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure <i>Cross-sectional study</i> —Report numbers of outcome events or summary measures (Page 10-15)
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (Page 10-15) (b) Report category boundaries when continuous variables were categorized (Page 11) (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses (Appendix 8)

Discussion

Key results	18	Summarise key results with reference to study objectives (Page 20-23)
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias (Page 23-24)
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence (Page 20- 23)
Generalisability	21	Discuss the generalisability (external validity) of the study results (Page 24)

Other information

Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based (Page 25)
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*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

Disease characteristics and management of hospitalized adolescents and adults with Community-Acquired Pneumonia in China : a retrospective multicenter survey

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Secondary Subject Heading:	Medical management
Keywords:	disease characteristics, management, community-acquired pneumonia, China

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4 **Disease characteristics and management of hospitalized adolescents and adults**
5 **with Community-Acquired Pneumonia in China: a retrospective multicenter**
6 **survey**
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56
57 **Abstract**
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Objectives To describe the clinical characteristics and management of patients hospitalized with CAP in China.

Design This was a multicenter, retrospective, observational study.

Setting 13 teaching hospitals in northern, central and southern China from 1 January 2014 to 31 December 2014

Participants Information on hospitalized patients aged ≥ 14 years with radiographically-confirmed pneumonia with illness onset in the community was collected using standard case report forms.

Primary and secondary outcome measures Resource use for CAP management.

Results Of 14,793 patients screened, 5828 with radiographically-confirmed CAP were included in the final analysis. Low mortality risk patients with a CURB-65 score 0-1 and PSI risk class I-II accounted for 81.2% (4434/5594) and 56.4% (2034/3609) CAP patients respectively. 21.7% (1111/5130) patients had already achieved clinical stability on admission. A definite or probable pathogen was identified only in 12.7% (738/5828) patients. 40.9% (1575/3852) patients without pseudomonas infection risk factors received antimicrobial over-treatment regimens. The median duration between clinical stability to discharge was 5.0 days with 30-day mortality of 4.2%.

Conclusions These data demonstrated overuse of health resources in CAP management, indicating that there is potential for improvement and substantial savings to health-care systems in China.

Strengths and limitations of this study

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- This is the largest multi-center study to investigate demographic characteristics, severity and microbiological testing, empirical antimicrobial treatment, duration of hospitalization and 30-day mortality among adults and adolescents hospitalized with CAP in mainland China, including adolescents and adults of all ages admitted to general hospital wards or ICUs from the participating centers, patients who were critically ill and aged >90 years.
 - The participating hospital sites are teaching hospitals in seven cities in three provinces, and may not be representative of CAP in smaller, rural hospitals.
 - The majority of patients are adult CAP patients, so our findings do not apply to children hospitalized with CAP.

29 **Background**

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Community acquired pneumonia (CAP) is one of the most common infectious syndromes and is a leading cause of death worldwide.^{1,2} In Europe, the reported rate of CAP ranges from 1.6 to 9 cases per 1,000 in the general adult population per year.³
^{4 5} Despite advances in medical technology and global economic development, CAP-associated mortality remains high (e.g., 20.9/100,000 in the United States and 12.7/100,000 in Canada).^{2,6} Patients hospitalized in intensive care units for CAP have mortality in excess of 20% for immunocompetent patients and closer to 30% for those immunocompromised.⁷ In Japan and Korea, the 30-day mortality of patients hospitalized with CAP is about 4-6%.^{8,9}

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Although mainland China has nearly 19% of the world's population, there are limited data on CAP management and disease burden in China during the last ten

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4 years. According to a household interview survey published in the China Health and
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6 Family Planning Statistical Yearbook (2013), the two-week prevalence of pneumonia
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8 in China was estimated to be 11/1,000, and the direct cost due to bacterial pneumonia
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10 was about 320 million RMB (approximately \$46.4 million).¹⁰ In 2015, CAP-China, a
11
12 multicenter clinical network, was founded with the support of National Key
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14 Technology Support Program from Ministry of Science and Technology
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16 (2015BAI12B11) to provide data on CAP for clinical researchers and healthcare
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18 policy makers in China.
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24 A multicenter retrospective study of all hospitalized CAP patients from 13 centers
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26 in northern, central and southern China among CAP-China members was
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28 implemented in 2015 (Clinicaltrial Registration No.NCT02489578). To our
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30 knowledge, this is the largest multi-center study to investigate demographic
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32 characteristics, severity and microbiological testing, empirical antimicrobial treatment,
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34 duration of hospitalization and 30-day mortality among adults and adolescents
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36 hospitalized with CAP in mainland China.
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41 **Methods**

42 **Study Design and Population**

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44 Data were collected from 13 hospitals in Northern (Beijing), Central (Yantai, Qindao,
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46 Weifang, Zibo, Rizhao cities in Shandong Province) and Southern (Kunming City in
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48 Yunan Province) China. A listing of participating centers can be found in Appendix 1.
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50 All patients admitted to the 13 hospitals during 1 January 2014 through 31 December
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52 2014 with the relevant disease codes of pneumonia or pulmonary infection in the
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4 World Health Organization International Classification of Diseases 10th revision
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6 (ICD-10, Appendix 2) were eligible. Data on all eligible patients identified in
7
8 screening were retrieved from the Hospital Information System (HIS) in each center.
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10 Trained physicians reviewed the medical case history and collected data on 786
11
12 variables for each patient. Chest radiographs and computerized tomography (CT)
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14 scans for each patient were reviewed by pulmonary physicians and radiologists in
15
16 each center. Two-leveled review process was performed for data collection and entry.
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21 The CAP case definition includes (1) illness onset in the community(defined as
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23 community acquired infection among those who have not been hospitalized during
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25 recent 28 days)¹¹; (2) chest radiograph or CT scan showing infiltrate or interstitial
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27 changes, with or without pleural effusion; (3) any one of pneumonia clinical
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29 manifestations: (a) recent cough, sputum or aggravation of respiratory symptoms, the
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31 emergence of purulent sputum, with or without chest pain; (b) fever (defined as
32
33 axillary temperature $\geq 37.3^{\circ}\text{C}$)¹² or hypothermia (axillary temperature $< 36^{\circ}\text{C}$); (c)
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35 signs of pulmonary consolidation and (or) moist crackles; or (d) WBC $> 10 \times 10^9/\text{L}$, or
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37 $< 4 \times 10^9/\text{L}$, with or without neutrophil predominance.
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44 Patients were excluded if (1) age < 14 years; (2) pneumonia onset ≥ 48 hours after
45
46 admission; (3) lung infiltrate or interstitial changes which were interpreted as lung
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48 cancer, pulmonary tuberculosis, non-infectious interstitial lung diseases, pulmonary
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50 edema, atelectasis, pulmonary embolism, pulmonary eosinophil infiltrate, pulmonary
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52 vasculitis; (4) immunocompromised status (including HIV(+),
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54 chemotherapy/radiotherapy within 6 months, immunosuppressive therapy, organ/bone
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4 marrow transplantation, splenectomy, hematological neoplasms); (5) re-admission
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6 within 72 hours after discharge.
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9 The study design was approved by the Ethics committee of China-Japan Friendship
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11 Hospital (No.2015-86). Given the retrospective nature of the study, the Ethics
12
13 Committee determined that informed consent was not necessary.
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15 16 **Quality control of the study**

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18 Key investigators, including clinicians, statisticians, microbiologists and radiologists
19
20 worked together to draft the protocol and created a single formatted case report form
21
22 (CRF) that was utilized by all centers. Before study initiation, all investigators from
23
24 the thirteen centers received training on the protocol, screening process, definition of
25
26 underlying diseases and formatted CRF (Appendix file 3). After data were collected,
27
28 the CRF was reviewed by a trained researcher to ensure its completeness and data
29
30 quality. A second review was performed independently by a trained team of
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32 physicians in each center before being entering in duplicate into a computerized
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34 database.
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40 41 **Data Collection:**

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43 A total of 786 variables were included in the formatted CRF, including:

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45 (1) Demographic data: age, gender, ID number, source of admission, types of medical
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47 insurance;
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51 (2) Underlying diseases: chronic lung, heart, renal and liver diseases, diabetes,
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53 hypertension, solid organ cancers. Definition of underlying diseases is listed in
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55 Appendix file 4.
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4 (3) Factors for acquisition or prevention of CAP: pregnancy, postpartum within six
5
6 months, current smoking history, excessive drinking, exposure to day care center
7
8 children, bed-ridden longer than two months, chronic receipt of corticosteroids
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10 (dosage equivalent prednisolone ≥ 10 mg/d for more than 30 days), statin use, *S.*
11
12 *pneumonia* or Influenza vaccination within one year.

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15
16 (4) Clinical manifestations, clinical signs: recorded on the day of admission, on the 4th
17
18 hospital day, change of antibiotics within 14 days of admission, and the day of
19
20 discharge or death. Laboratory and radiological findings were also recorded if such
21
22 tests were repeated by attending physicians. Pneumonia disease severity scores (PSI
23
24 /CURB-65) were also recorded.

25
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28 (5) Microbiological examination: Gram stain and culture of sputum within 48 hours,
29
30 blood culture within 48 hours, BALF and pleural fluid culture within one week after
31
32 admission, serum antibody (including IgM and IgG) for atypical pathogens
33
34 (*Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, *Legionella pneumophila*).
35
36 Urinary antigen testing was performed for *Streptococcus pneumonia* and *Legionella*
37
38 *spp.* Real-time PCR testing was done for respiratory virus and atypical pathogens with
39
40 sputum and BALF. Nasopharyngeal (NP) swab was used for antigen testing for
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42 Influenza A and Influenza B. Aspirate was not routinely used for antigen testing.
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49 (6) Antimicrobial treatment before admission and change of antimicrobials during
50
51 hospitalization. Use of corticosteroids, vasopressors, mechanical ventilation,
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53 Continuous renal replacement therapy (CRRT) and extracorporeal membrane
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55 oxygenation (ECMO) were also recorded.
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4 (7) Clinical stability was defined as satisfying all of the following: axillary
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6 temperature ≤ 37.8 °C more than 24 hours without use of antipyretic medications;
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8 resting heart rate ≤ 100 beats/min; respiratory rate ≤ 24 breaths/ minute; systolic blood
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10 pressure ≥ 90 mmHg; SpO₂ $\geq 90\%$ on room air; ability to maintain oral intake; normal
11
12 mental status.¹³

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16 (8) Over-treatment was defined as: i) use of antipseudomonal β -lactams or β -lactams+
17
18 fluoroquinolones in hospitalized (not in ICU) patients without risk factors for
19
20 pseudomonal infection; ii) use of β -lactams (antipseudomonal or not)+
21
22 fluoroquinolones in ICU patients aged < 65 yr without risk factors for pseudomonas
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24 infection; iii) use of anti-MRSA drugs in hospitalized (not in ICU) patients (Use of
25
26 anti-MRSA drugs in ICU patients with MRSA risk after influenza virus infection was
27
28 considered adequate).¹⁴

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30
31 (9) Risk factors for pseudomonal infection was defined as chronic airway disease
32
33 (bronchiectasis and COPD) and at least one risk factor for HCAP as defined by the
34
35 2005 IDSA/ATS adult CAP guidelines.^{14 15 16 17 18}

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37 (10) Empirical antimicrobial regimens recommended by Chinese CAP guidelines
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39 were showed in Appendix 5.

40 41 42 43 44 45 46 **Microbiology testing**

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48 The conditions that a pathogen was defined as the definite or probable etiology based
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50 on were showed in Appendix 6.

51 52 53 54 **Statistical analysis**

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56 No formal sample size calculations were performed because of the retrospective
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4 descriptive study design. All data were analyzed by descriptive statistics with SPSS19.
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6 Measurement data were tested for normality by Kolmogorov-Smirnov. Measurement
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8 data of normal distribution was reported as mean \pm standard deviation. Measurement
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10 data of non-normal distribution was reported as median. The χ^2 test statistics were
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12 used for 30-day mortality subgroup analysis. A P-value of <0.05 was considered
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14 statistically significant.
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18 19 **Results**

20 21 **Screening Process**

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23 A total of 14,793 patients were screened to meet the inclusion and exclusion criteria
24
25 for CAP and 5828 patients were included in the final analysis (Appendix Figure 1).
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28 29 **Epidemiological characteristics**

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31 The proportions of male and female patients were similar. The median age was 65
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33 years, range 14-103 years. Prevalent co-morbidities included hypertension (35.2%),
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35 coronary heart disease (20.0%), diabetes (15.7%), cerebrovascular diseases (15.3%)
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37 and COPD (13.7%). 14.9% of CAP patients had at least one healthcare associated
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39 pneumonia (HCAP) risk factor (according to IDSA/ATS HAP/HCAP guideline
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41 published in 2005¹⁵). 45.7% patients received antibiotics before admission.
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46 A substantial proportion of admitted patients had relatively mild disease as
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48 indicated by the following: i) CURB-65 score¹⁹ 0-1 accounted for 81.2%, ii) PSI risk
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50 class²⁰ I-II accounted for 56.3%; iii) Shorr Score²¹ 0-1 accounts for 99.6%; and iv)
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52 Aliberti Score²² low riskgroup in 89.7%; v) only 12.0% (261/2172) patients had
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54 procalcitonin (PCT) more than 2 ng/ml; vi) as many as 65.7% (3741/5698) patients
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had normal peripheral leukocyte counts (4,000-10,000/ul). Most importantly, 21.7% patients had met criteria for clinical stability at hospital admission.¹³ (Table 1-2)

Table 1: Demographic characteristics and underlying diseases

Items	Cases (%)
Male	3117 (53.5)
Age (years, median, IQR)	65 (53-78)
14~64	2802 (48.1)
65~74	1081 (18.5)
75~89	1760 (30.2)
≥90	185 (3.2)
Source of admission (n=5823)	
From Out-patient Department	4183 (71.8)
From Emergency Room	1588 (27.3)
Transfer from other hospital	52 (0.9)
Days from illness onset to admission (n=5826, median, IQR)	6.0 (3.0-14.0)
Patients who received antibiotics before admission	2664 (45.7)
β-lactams	1015 (38.1)
Fluoroquinolones	586 (22.0)
Macrolides	170 (6.4)
β-lactams+ fluoroquinolones	413 (15.5)
β-lactams+ macrolides	201 (7.5)
Others	279 (10.5)
Systemic glucocorticosteroids use before admission	250 (4.3)
Underlying Diseases	4219 (72.4)
Hypertension	2053 (35.2)
Coronary Heart Disease	1163 (20.0)
Diabetes	913 (15.7)
Cerebrovascular Diseases	890 (15.3)
COPD	801 (13.7)
Bronchiectasis	629 (10.8)
Asthma	339 (5.8)
Malignant solid tumors	254 (4.4)
Congestive Heart Failure	202 (3.5)

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3		
4	Chronic renal diseases	201 (3.4)
5	Connective Tissue Diseases	110 (1.9)
6	Chronic Hepatic Diseases	90 (1.5)
7		
8	Smoking status	
9		
10	Current smokers	1009 (17.3)
11	Ex-smokers	590 (10.1)
12		
13	Alcoholism	407 (7.0)
14		
15	Risk factors for aspiration*	377 (6.5)
16	History of CAP within one year	368 (6.3)
17		
18	History of vaccination	
19		
20	Influenza vaccine within 1 year	12 (0.2)
21	<i>Streptococcus pneumoniae</i> vaccine within 5 years	8 (0.1)
22		
23	Risk factors for HCAP according to IDSA/ATS criteria	868 (14.9)
24	Hospitalized in an acute care hospital for two or more days	404 (6.9)
25	within 90 days	
26		
27	Received recent intravenous antibiotic therapy, chemotherapy,	656 (11.3)
28	or wound care within the past 30 days	
29		
30	Attended a hospital or hemodialysis clinic	36 (0.6)
31	Residence in a nursing home or long-term care facility	19 (0.3)
32		
33	CURB-65 score (n=5594)	
34	0	2343 (41.9)
35	1	2199 (39.3)
36	2	884 (15.8)
37	3	147 (2.6)
38	4	20 (0.4)
39	5	1 (0.0)
40		
41		
42		
43		
44	PSI risk class (n=3609)	
45	I	1130 (31.3)
46	II	904 (25.0)
47	III	748 (20.7)
48	IV	646 (17.9)
49	V	181 (5.0)
50		
51		
52		
53		
54	Shorr Score (n=5650)	
55	0	5084 (90.0)
56	1	541 (9.6)
57		
58		
59		
60		

2	23 (0.4)
3	2 (0.0)
4	0 (0.0)
Aliberti Score (n=5828)	
Low risk group	5226 (89.7)
High risk group	602 (10.3)
Clinical stability on admission § (n=5130)	1111 (21.7)

COPD: chronic obstructive pulmonary disease; HCAP: healthcare associated pneumonia; IDSA/ATS: Infectious Diseases Society America/American Thoracic Society. PSI: pneumonia severity index. *Risk factors for aspiration included choking, drowning, nasal feeding, pseudobulbar palsy, dementia, coma, poisoning, Parkinson's disease.

§ Clinical stability was defined as satisfying the following at the same time: axillary temperature ≤ 37.8 °C more than 24 hours; heart rate ≤ 100 beats/min in resting state; breathing rate ≤ 24 breaths/minute; systolic blood pressure ≥ 90 mmHg; SpO₂ $\geq 90\%$ on room air; ability to maintain oral intake; normal mental status.

Table 2: Clinical and radiological features on admission

Items	Cases (%)
Axillary Temperature ≥ 38 °C (n=5826)	2783 (47.8)
Axillary Temperature < 36 °C (n=5793)	44 (0.8)
Cough	5192 (89.1)
Sputum	4751 (81.5)
Shortness of breath	2116 (36.3)
Chest pain	709 (12.2)
Decrease of consciousness	294 (5.0)
Chest signs	
Moist rales	2919 (50.1)
Dry rales	1387 (23.8)
Edema of lower limbs	592 (10.2)
Cyanosis	547 (9.4)
SBP < 90 mmHg	45 (0.8)
Radiology	
Infiltrate more than two lobes	3776 (64.8)

Plural effusion	1205 (20.7)
Cavitation	228 (3.9)
WBC (mm^{-3} , n=5698)	
>10,000	1626 (28.5)
<4,000	331 (5.8)
4,000~10,000	3741 (65.7)
BUN $>7.0 \text{ mmol}\cdot\text{L}^{-1}$ (n=5601)	1166 (20.8)
PH <7.30 (n=3330)	87 (2.6)
$\text{PaO}_2/\text{FiO}_2 < 300 \text{ mmHg}$ (n=3327)	1196 (35.9)
PCT ($\text{ng}\cdot\text{ml}^{-1}$, n=2172)	
$\text{PCT} \leq 0.25$	1307 (60.2)
$0.25 < \text{PCT} < 1$	479 (22.1)
$1 \leq \text{PCT} < 2$	125 (5.8)
$\text{PCT} \geq 2$	261 (12.0)

SBP: systolic blood pressure; WBC: white blood cell count; BUN: blood urea nitrogen; Scr: serum creatinine; PH: potential of hydrogen; $\text{PaO}_2/\text{FiO}_2$: arterial pressure of oxygen/fraction of inspiration oxygen; PCT: procalcitonin.

Clinical and radiological features

Clinical and radiological features on admission are shown in Table 2. Cough, sputum, shortness of breath and fever were the most common. 64.8% patients had multi-lobar infiltrates and 20.7% of patients had pleural effusion.

Microbiological testing

75.0% patients had some types of microbiologic testing. 68.9% of patients had a sputum culture obtained within 48 hours of admission, although only 18.5% of patients were able to produce a sputum culture of acceptable quality. The proportion of patients with blood culture, BALF culture, and pleural effusion culture were 10.3%, 9.1% and 1.9% respectively. Only 0.8% of patients had a urinary antigen test sent to

evaluate for *Legionella pneumophila*, and 2.6% had urinary antigen testing for *Streptococcus pneumoniae*. (Table 3)

Table 3: Microbiological examination for CAP

Items	Cases (%)
Any Microbiological examination	4371 (75.0)
Microbiological examination for bacterial	4015 (68.9)
Microbiological examination for atypical etiology	1983 (34.0)
Microbiological examination for virus	2014 (34.6)
Bacterial or fungal Culture	4015 (68.9)
Qualified sputum culture*	1078 (18.5)
Blood culture **	602 (10.3)
BALF culture* ⁺	532 (9.1)
Pleural effusion culture**	108 (1.9)
Antibody-Based Assays on acute serum	
<i>Mycoplasma pneumoniae</i>	IgM: 1821 (31.2) IgG: 794 (13.6)
<i>Chlamydia pneumoniae</i>	IgM: 1294 (22.2) IgG: 220 (3.8)
<i>Legionella pneumophila</i>	IgM: 645 (11.1) IgG: 227 (3.9)
Adenovirus	IgM: 644 (11.1) IgG: 0 (0.0)
Respiratory syncytial virus	IgM: 643 (11.0) IgG: 0 (0.0)
Influenza A virus	IgM: 643 (11.0) IgG: 0 (0.0)
Influenza B virus	IgM: 640 (11.0) IgG: 0 (0.0)
Parainfluenza virus	IgM: 643 (11.0) IgG: 0 (0.0)
Nucleic Acid-Based Molecular Diagnostics	
From sputum	297(5.1)
Time Interval¶(days, median, IQR)	9.0 (6.0-16.0)
From BALF ⁺	19 (0.3)
Time Interval¶(days, median, IQR)	13.0 (9.0-24.0)

<i>Mycoplasma pneumoniae</i>	270 (4.6)
<i>Chlamydia</i> spp	270 (4.6)
<i>Legionella</i> spp	270 (4.6)
Influenza A virus	270 (4.6)
Influenza B virus	270 (4.6)
Other respiratory virus#	270 (4.6)
Urinary Antigen test	
<i>Streptococcus pneumoniae</i>	150 (2.6)
<i>Legionella</i> spp	47 (0.8)
Nasopharyngeal swab antigen testing	
Influenza A virus	41 (0.7)
Influenza B virus	21 (0.4)

*: within 48hr after admission

** :within one week after admission

¶: days from illness onset to testing

#parainfluenza virus (PIV) types 1, 2, 3 and 4, rhinovirus (HRV), enterovirus (EV), coronavirus (hCoV) types 229E, NL63, OC43 and HKU1, parapneumovirus (hMPV), and adenovirus (AdV), bocavirus

⁺**BALF**: bronchoalveolar lavage fluid

Of all patients, serological testing for antibodies to *Mycoplasma pneumoniae* was only performed on a single serum specimen for IgM (31.2%) and IgG antibodies (13.6%). Similarly, serological testing on a single serum specimen was done for *Chlamydia pneumoniae* IgM antibody in 22.2% of patients and for IgM antibodies to *Legionella pneumophila* and respiratory viruses in 11.1%. No convalescent serum specimens were collected for serological testing for any pathogens, limiting interpretation of serology results for a single serum specimen.

A definite or probable pathogen was identified only in 12.7% of patients

(738/5828): only bacteria in 87.1% (643/738), only atypical pathogens in 0.9% (7/738), only viruses in 8.5% (63/738), bacteria and viruses in 2.7% (20/738), viruses and atypical pathogens in 0.7% (5/738). The most common five pathogens identified were *Pseudomonas aeruginosa* 26.7% (197/738), *Klebsiella pneumoniae* 17.6% (130/738), *Escherichia coli* 8.9% (66/738), *Acinetobacter* 8.4% (62/738) and influenza A virus 7.3% (54/738). (Appendix 7)

Empiric antimicrobial regimens

β -lactams (received by 72.7% of patients) and fluoroquinolones (received by 42.2%) were the most common classes of antibiotics that were administered empirically. In patients (not in ICU) without pseudomonal infection risk factors, 27.8% (1070/3852) patients received empiric antibiotic regimens including antipseudomonal β -lactams, and 12.1% (468/3852) patients received β -lactams + fluoroquinolones; 0.4% (16/3852) patients aged <65 years and not in ICU received β -lactams (antipseudomonal or not) + fluoroquinolones combined regimens. Overall, 40.9% (1575/3852) patients without pseudomonal infection risk factors received antimicrobial over-treatment regimens. (Table 4)

Table 4: Empirical antimicrobial regimen for CAP patients (n=5716)*

Empirical antimicrobials (%)	Without risk factors for <i>P. seudomonas</i> infection (n=3852)				With risk factors for <i>P. seudomonas</i> infection (n=1864)
	age<65yr and not in ICU (n=1881)	age<65yr and in ICU (n=79)	age≥65yr and not in ICU (n=1742)	age≥65yr and in ICU (n=150)	
β -lactams (antipseudomonal)	178 (4.6) [#]	21 (0.5)	407 (10.6) [#]	58 (1.5)	541 (29.0)

β-lactams	331 (8.6)	9 (0.2)	482 (12.5)	20 (0.5)	345 (18.5)
Fluoroquinolones	502 (13.0)	10 (0.3)	273 (7.1)	6 (0.2)	252 (13.5)
Macrolides	20 (0.5)	0 (0.0)	17 (0.4)	0 (0.0)	10 (0.5)
β-lactams (antipseudomonal) + fluoroquinolones	201 (5.2) [#]	13 (0.3) [#]	189 (4.9) [#]	30 (0.8)	238 (12.8)
β-lactams+ fluoroquinolones	302 (7.8) [#]	3 (0.1) [#]	166 (4.3) [#]	9 (0.2)	177 (9.5)
β-lactams+ macrolides	160 (4.2)	2 (0.1)	64 (1.7)	2 (0.1)	55 (3.0)
β-lactams (antipseudomonal) + macrolides	50 (1.3) [#]	0 (0.0)	45 (1.2) [#]	2 (0.1)	58 (3.1)
Fluoroquinolones + macrolides	24 (0.6)	0 (0.0)	11 (0.3)	0 (0.0)	6 (0.3)
anti-MRSA drugs	9 (0.2) [#]	8 (0.2)	12 (0.3) [#]	6 (0.2)	29 (1.6)
Others	104 (2.7)	13 (0.3)	76 (2.0)	17 (0.4)	153 (8.2)

*: data on empirical antimicrobial regimens in 112 patients were missing.

[#]Overtreatment was defined as: i) use of antipseudomonal β-lactams or β-lactams+ fluoroquinolones in hospitalized (not in ICU) patients without risk factors for pseudomonal infection; ii) use of β-lactams (antipseudomonal or not)+ fluoroquinolones in ICU patients aged < 65yr without risk factors for pseudomonal infection; iii) use of anti-MRSA drugs in hospitalized (not in ICU) patients (Use of anti-MRSA drugs in ICU patients with MRSA risk after influenza virus infection was considered adequate).¹⁴

- Risk factors for *P.seudomonal* infection was defined as chronic airway disease (bronchiectasis or COPD) or HCAP according to IDSA/ATS criteria.¹⁵

Clinical outcomes

Clinical outcomes are shown in Table 5. Overall, 6.3% of patients were admitted to an ICU, and 2.7% required invasive mechanical ventilation. Vasopressors were administered to 3.4% of patients, and 26.4% received corticosteroids during the hospitalization. The 30-day mortality was 4.2%. The median duration of hospitalization was 11 days. The median duration from admission to clinical stability

was 4 days, and from clinical stability to discharge was 5 days. The median duration of ICU hospitalization was 8 days. The top five causes of death were severe pneumonia/multi-organ dysfunction syndrome (MODS) 69.1% (170/246), cardiac failure 2.8% (7/246), acute myocardial infarction 2.0% (5/246), stroke 1.6% (4/246) and gastrointestinal hemorrhage 1.6% (4/246).

Table 5: Supportive treatment and clinical outcomes of patients with CAP

Items	Cases (%)
ICU admission	367 (6.3)
Mechanical ventilation	
Non-invasive ventilation	286 (4.9)
Invasive ventilation in ICU	123 (2.1)
Invasive ventilation not in ICU	33 (0.6)
Vasopressor use	197 (3.4)
CRRT	16 (0.3)
ECMO	3 (0.1)
Systemic glucocorticosteroids use after diagnosis of CAP	1540 (26.4)
ICU patients who received systemic glucocorticoids	154 (2.6)
Patients on invasive mechanical ventilation who received systemic glucocorticoids	75 (1.3)
Patients on non-invasive mechanical ventilation who received systemic glucocorticoids	158 (2.7)
30-day mortality	246 (4.2)
Length of stay in Hospital (days, median,IQR)	11.0 (5.0-24.0)
Days between admission-clinical stability (median, n=5130,IQR)	4.0 (1.0-10.0)
Days between clinical stability-discharge (median, n=5130,IQR)	5.0 (1.0-9.0)
Length of stay in ICU (days, median, n=350,IQR)	8.0 (4.0-16.0)
Treatment failure within 14 days	427 (7.3)
Needs non-invasive ventilation	169 (2.9)
Needs invasive ventilation	145 (2.5)

Needs vasopressors	130 (2.2)
Death	147 (2.5)
Direct causes of death	
Severe pneumonia/MODS	170 (69.1)
Heart failure	7 (2.8)
Acute myocardial infarction	5 (2.0)
Stroke	4 (1.6)
Hemorrhage of digestive tract	4 (1.6)
Acute renal failure	2 (0.8)
Arrhythmia	2 (0.8)
Accident aspiration	1 (0.4)
Others	51 (20.7)

ICU: intensive care unit; CRRT: continuous renal replacement therapy; ECMO: extracorporeal membrane oxygenation; MODS: multiple organ dysfunction syndrome; DIC: disseminated intravascular coagulation.

Appendix 8 shows the results of sub-group analysis of 30-day mortality. Fatality increased with age. Mortality was similar between male and female patients (4.9% vs 3.5%). Mortality in patients admitted to an ICU was 15.3%.

Discussion

This study represents the largest, multicenter, retrospective cohort study on the etiologies and outcomes in adolescents and adults with CAP in China. In this study, we found that admission of patients with low mortality risk, inadequate microbiological diagnostic tests, overuse of antibiotics and incorrect serological testing for *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, *Legionella pneumophila* and respiratory viruses, were the main challenges of CAP management.

We identified four major categories of overuse of health care resources in CAP management in China:

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4 (1) A large number of low-risk patients were admitted to the hospitals. Guidelines
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6 for CAP management in China and the U.S. recommend that decisions for
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8 hospitalization should be based on illness severity.^{14 23} It was estimated that over \$8
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10 billion dollars are spent in CAP treatment every year in the U.S, and the cost for
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12 inpatient CAP management is 25-30 times more than for outpatient CAP
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14 management.^{24 25 26} Therefore, admission of low mortality risk CAP patients results in
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16 major unnecessary cost expenditures. Moreover, outpatients usually return to their
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18 baseline activity levels much sooner than inpatients, and enjoyed a higher quality of
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20 life.^{27 28} Finally, hospitalization is associated with the risk of nosocomial infections,
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22 potentially caused by high virulent and multidrug-resistant organisms.²⁹ Admission of
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24 low-risk CAP patients was also observed in a recent large U.S. study,¹¹ so it may not
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26 be unique to China. However, there are many other factors that play an important role
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28 in deciding the need for hospitalization such as comorbidities, lack of available family
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30 support, older age, mental illness and drug abuse, etc.^{30 31}

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39 (2) Length of stay in hospital was unnecessarily long. CAP guidelines recommend
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41 that patients should be discharged as soon as they achieve clinical stability and have
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43 no other active medical problems. Keeping patients in hospital and observing them
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45 while receiving oral antibiotic therapy, or waiting for normalization of all clinical
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47 parameters are not indicated and are associated with increased costs and potentially
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49 with in-hospital adverse events.^{13 29 30} We observed that CAP patients were discharged
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51 a median of 5 days after achieving clinical stability, and 22% met clinical stability
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53 criteria at admission. Given the median LOS of 11 days for all CAP patients,
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4 discharging CAP patients once they achieved clinical stability would lead to
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6 cost-savings of approximately half of the total hospitalization expenses. Similarly, the
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8 length of stay in hospital may be influenced by other social factors.
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11 (3) 40.9% patients without risk factors for *Pseudomonas* infection received
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13 over-treatment with empiric antimicrobial regimens. Antipseudomonal β -lactams
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15 (28.2%) or β -lactams + quinolones (12.2%) were the most common empiric regimens
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17 for over-treatment. This may be due to overestimation of illness severity, clinicians
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19 unfamiliarity with CAP guidelines, or lack of microbiologic diagnostic testing.
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21 Moreover, we found quinolones use in more than 40% of CAP patients. The U.S.
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23 Food and Drug Administration (FDA) has released warnings of potential adverse
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25 effects of fluoroquinolones, such as Q-T prolongation, tendon injury, psychiatric
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27 disorder, etc.^{32 33 34} As second-line anti-tuberculosis drugs, fluoroquinolones can also
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29 affect the diagnosis of tuberculosis and induce drug-resistance.^{35 36}
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38 (4) Incorrect serological testing was performed. We observed that many patients
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40 had an acute serum specimen collected for IgG serology testing for atypical bacteria
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42 and respiratory viruses without a convalescent serum specimen obtained for paired
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44 serological testing. Furthermore, many patients had testing for IgM antibodies for a
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46 variety of respiratory pathogens, but elevation of IgM antibodies with a low-normal
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48 IgG titer is uncommon during acute illness.^{37 38 39} Paired serology for virus and atypical
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50 pathogens is recommended for epidemiological purpose. A follow-up convalescent
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52 serum specimen to document changes in IgG and IgM antibody levels is generally
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54 required for diagnosis.^{40 41} Thus, the value of antibody testing on a single acute serum
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specimen to determine the etiology of CAP is questionable. The costs of more frequent use of PCR testing on lower respiratory specimens may be partially offset by not performing serological testing in CAP patients.

The strengths of this study, in contrast to some past epidemiological investigations,⁴² included data on bacterial isolates obtained in current clinical practice, microbiologic testing ordered, and antimicrobials administered, according to Chinese standards-of-care, and the study population included adolescents and adults of all ages admitted to general hospital wards or ICUs from the participating centers to reduce selection bias. We also included patients who were critically ill, aged >90 years and with risk factors for HCAP.

This study had several limitations. First, given the retrospective study design, it is possible that selection bias was present and the study population may not have been representative of all CAP patients admitted to the 13 participating sites. Secondly, the participating hospital sites were teaching hospitals in seven cities in three provinces, and were not selected to be representative of CAP hospital management in China, especially in smaller, rural hospitals. Third, this study reports on CAP management during 2014; analysis of multiple years of data can allow assessment of changes in CAP management. Fourth, 45.7% of CAP patients received antibiotics before hospital admission and before specimen collection, which may reduce the detection of some bacterial infections, such as *Streptococcus pneumoniae*. The low number of tests performed (good quality sputum, blood cultures, urine antigens, polymerase chain reaction) limit the knowledge of the true etiology of CAP in the study. Therefore, the

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4 bacterial pathogens identified in this study may not be representative of all bacterial
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6 causes of CAP in the source patient populations for this study. Finally, while we
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8 included adolescents, the majority of patients were adult CAP patients, and our
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10 findings do not apply to children hospitalized with CAP.
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14 In conclusion, we characterized adolescents and adults hospitalized for CAP in
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16 China and identified several problems suggesting the over-use of healthcare resources
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18 in CAP management. This suggests that education and training of clinicians on
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20 current CAP guidelines in China are needed to improve clinical management and
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22 could also result in substantial cost-saving in healthcare expenditures for CAP
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24 patients. The multi-center hospital network can serve as a platform for conducting
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26 intervention studies for hospitalized CAP patients in the future, utilizing the baseline
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28 data from this observational study.
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Appendix 1: Details of Participating centers

Name of the hospital	Province, city	2 nd and 3 rd level hospital	Teaching Hospital	Beds	Staff of Clinical Microbiology Lab
Beijing Chao-Yang Hospital Affiliated to Capital Medical University	Beijing	3 rd	Yes	1400	11
Beijing Jishuitan Hospital 4 th Medical College of Peking University	Beijing	3 rd	Yes	1500	10
Beijing Luhe Hospital Affiliated to Capital Medical University	Beijing	3 rd	Yes	1042	5
Qingdao Municipal Hospital	ShanDong, Qingdao	3 rd	Yes	1200	4
Qilu Hospital Of Shandong University(Qindao)	ShanDong, Jinan	3 rd	Yes	1200	6
Beijing Huimin Hospital	Beijing	2 nd	Yes	500	2
Linzi District People's Hospital	ShanDong, Zibo	2 nd	Yes	1200	5
The 2 nd Hospital of Beijing Corps, Chinese Armed Police Forces	Beijing	3 rd	Yes	450	2
China-Japan Friendship Hospital	Beijing	3 rd	Yes	1610	9
Yan'an Hospital Affiliated to Kunming Medical University	Kunming, Yan'an	3 rd	Yes	1302	4

Yantai Yuhuangding Hospital	Shangdong, Yantai	3 rd	Yes	3000	6
Rizhao Chinese Medical Hospital Affiliated to Shandong Chinese Medical University	Shangdong, Rizhao	3 rd	Yes	1212	8
Weifang NO.2 People's Hospital	Shangdong, Weifang	3 rd	Yes	1006	8

Definition of 2nd and 3rd level hospital in China:

The 2nd level hospital was defined as a hospital providing medical, prevention, health care and rehabilitation services to multiple communities (with a radius of population more than 100,000 peoples); the 3rd level hospital was defined as a hospital providing medical service to the whole country beyond cities and provinces, with comprehensive medical, teaching and research ability.

Appendix 2: ICD-10

Influenza with pneumonia, other influenza virus identified	J10.0
Influenza with pneumonia, virus not identified	J11.0
Virus pneumonia, not elsewhere classified	J12
Adenoviral pneumonia	J12.0
Respiratory syncytial virus pneumonia	J12.1
Parainfluenza virus pneumonia	J12.2
Other virus pneumonia	J12.8
Viral pneumonia,unspecified	J12.9
Pneumonia due to <i>Streptococcus pneumoniae</i>	J13
Pneumonia due to <i>Haemophilus influenzae</i>	J14
Bacterial pneumonia, not elsewhere classified	J15
Pneumonia due to <i>Klebsiella pneumoniae</i>	J15.0
Pneumonia due to <i>Pseudomonas spp.</i>	J15.1
Pneumonia due to <i>Staphylococcus</i>	J15.2
Pneumonia due to <i>Streptococcus spp.</i> , group B	J15.3
Pneumonia due to other <i>streptococci</i>	J15.4
Pneumonia due to <i>Escherichia coli</i>	J15.5
Pneumonia due to other aerobic Gram-negative bacteria	J15.6
Pneumonia due to <i>Mycoplasma pneumoniae</i>	J15.7
Other bacterial pneumonia	J15.8

Bacterial pneumonia, unspecified	J15.9
Pneumonia due to other infectious organisms, not elsewhere classified	J16
Chlamydia pneumonia	J16.0
Pneumonia due to other specified infectious organisms	J16.8
Pneumonia due to other specified infectious organism	J16.8
Pneumonia in diseases classified elsewhere	J17*
Pneumonia in bacterial diseases classified elsewhere	J17.0*
Pneumonia in viral diseases classified elsewhere	J17.1*
Pneumonia in mycoses	J17.2*
Pneumonia in other diseases classified elsewhere	J17.8*
Pulmonary mycobacterial infection	A31.0
Pulmonary actinomycosis	A42.0
Pulmonary nocardiosis	A43.0
Legionnaires' disease	A48.1
Varicella pneumonia	B01.2+
Measles complicated by pneumonia	B05.1+
Cytomegaloviral pneumonitis	B25.0+
Pulmonary candidiasis	B37.1
Acute pulmonary coccidioidomycosis	B38.0
Acute pulmonary histoplasmosis capsulati	B39.0
Acute pulmonary blastomycosis	B40.0

Pulmonary paracoccidioidomycosis	B41.0
Pulmonary sporotrichosis	B42.0+
Invasive pulmonary aspergillosis	B44.0
Other pulmonary aspergillosis	B44.1
Pulmonary cryptococcosis	B45.0
Pulmonary mucormycosis	B46.0
Pneumonia, organism unspecified	J18
Bronchopneumonia, unspecified organism	J18.0
Lobar pneumonia, unspecified	J18.1
Hypostatic, pneumonia, unspecified	J18.2
Other pneumonia, organism unspecified	J18.8
Pneumonia, unspecified	J18.9

Appendix 3: Case Report Form Of Patients Hospitalized With CAP/HCAP

Code:	R-
Name:	Gender: <input type="radio"/> Male <input type="radio"/> Female
Age: _____years old	Nationality: <input type="radio"/> Han <input type="radio"/> Others
Height: _____cm	Weight: ____ kg
ID Number:	
Date Of Admission: ____Y____M____D	
Case Number :	ID Number:
Admission Form:	<input type="radio"/> Outpatience <input type="radio"/> Emergency <input type="radio"/> Transfers
Tel:	Cell Phone:
Provider Payments: <input type="radio"/> Social Medical Insurance <input type="radio"/> New Rural Cooperative Medical System <input type="radio"/> Medical Services At State Expense <input type="radio"/> Commercial Medical Insurance <input type="radio"/> Self-paying <input type="radio"/> Others	

Study Director: Bin Cao

Team Members: Liang Chen、Hu Li、Meng Liu、Xiudi Han、Xiaoli Zhu 、Bo Liu、Jinxiang Wang、
 Xuexin Yao、Chunxiao Zhang、Shujing Shi、Fei Zhou、Chunxue Xue、Yanli Li、Donghao Yu
 (Beijing Chao-Yang Hospital 001; Beijing Jishuitan Hospital 002; Beijing Luhe Hospital 003; Qingdao
 Municipal Hospital 004; Qilu Hospital Of Shandong University(Qindao) 005; Beijing Huimin Hospital
 006; Linzi District People's Hospital 007; The 2nd Hospital of Beijing Corps, Chinese Armed Police
 Forces 008; China-Japan Friendship Hospital 009; Yan'an Hospital Affiliated to Kunming Medical
 University 010)

Inclusion Criteria:

1. Age ≥ 14 years old
2. Onset in community
3. Chest X-ray or CT scan showing infiltration or interstitial changes, with or without pleural effusion
4. Any one of pneumonia clinical manifestations, including:
 - (a) Recent cough, sputum or aggravation of respiratory symptoms, the emergence of purulent sputum, with or without chest pain;
 - (b) Fever (axillary temperature $\geq 37.3^{\circ}\text{C}$) or hypothermia (axillary temperature $< 36^{\circ}\text{C}$);
 - (c) Signs of pulmonary consolidation and (or) moist rales;
 - (d) $\text{WBC} > 10 \times 10^9/\text{L}$, or $< 4 \times 10^9/\text{L}$, with or without nucleus left.

Meet criteria 1,2 ,3 and anyone of criteria 4

Exclusion Criteria:

1. Lung infiltrate or interstitial changes which can be interpreted as lung cancer, pulmonary tuberculosis, non-infectious interstitial lung diseases, pulmonary edema, atelectasis, pulmonary embolism, pulmonary eosinophil infiltration, pulmonary vasculitis;
2. HIV positive
3. Readmission within 72 hours after discharging.

Part 1: Baseline Characteristics

Underlying Disease	
COPD <input type="radio"/> Y <input type="radio"/> N	Asthma <input type="radio"/> Y <input type="radio"/> N
Bronchiectasis <input type="radio"/> Y <input type="radio"/> N	Malignancy <input type="radio"/> Y <input type="radio"/> N
Sleep Apnea Syndrome <input type="radio"/> Y <input type="radio"/> N	Congestive Heart Failure <input type="radio"/> Y <input type="radio"/> N
Coronary Heart Disease <input type="radio"/> Y <input type="radio"/> N	Hypertention <input type="radio"/> Y <input type="radio"/> N
Peripheral Vascular Diseases <input type="radio"/> Y <input type="radio"/> N	Diabetes Mellitus <input type="radio"/> Y <input type="radio"/> N
Cerebrovascular Disease <input type="radio"/> Y <input type="radio"/> N	Autoimmune Diseases ^a <input type="radio"/> Y <input type="radio"/> N
Chronic Viral Hepatitis <input type="radio"/> Y <input type="radio"/> N	Cirrhosis <input type="radio"/> Y <input type="radio"/> N
Hematological Malignancy <input type="radio"/> Y <input type="radio"/> N	Organ /bone Marrow Transplantation <input type="radio"/> Y <input type="radio"/> N
Immunosuppressive Therapy ^b <input type="radio"/> Y <input type="radio"/> N	Chemotherapy/Radiotherapy Within 6 Months <input type="radio"/> Y <input type="radio"/> N
Chronic Renal Diseases <input type="radio"/> Y <input type="radio"/> N	Splenectomy <input type="radio"/> Y <input type="radio"/> N

Note: aSLE, Sjogren's syndrome, rheumatoid arthritis, polymyositis / dermatomyositis, systemic vasculitis, ankylosing spondylitis, inflammatory bowel disease, hyperthyroidism, etc;; b.Anti-rejection drugs

With The Following Situation	
Pregnancy	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown; If Y, Pregnancy__weeks.
Within 6 months after delivery	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown; If Y, __weeks after delivery
Smoking	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Former Smoker <input type="radio"/> Unknown If Y, Smoked For__years, __cigarettes/day; If Former Smoker, Smoked For__years, __cigarettes/day ,GivenUp For____years
Alcoholism ^a	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown
Risk factors for inhalation ^b	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown
Contact Children In Day-care Center	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown
Bed Ridden (≥2months)	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown
Long-term inhaled Corticosteroid use ^d	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown
Long-term oral Corticosteroid use ^c	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown; If Y, Name Of Corticosteroid: _____,

	Dose __mg/day, For ____ days
Oral Statin Drugs	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown
History Of CAP Within One Year	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown
Influenza Vaccine Within 1 Year	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown
<i>Streptococcus pneumoniae</i> Vaccine Within 5 Years	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown

Note: **a:** drinking more than 5 bottles of beer (500ml / bottle) or half a catty liquor once in 2 weeks; or drinking more than 2.5 bottles of beer (500ml / bottle) or 2 ounce of white spirit per day for more than five years; **b:** Inhalation risk factors included choking, drowning, nasal feeding, pseudobulbar palsy, dementia, coma, poisoning, Parkinson's disease; **c:** Long-term oral corticosteroids was defined as: oral prednisone ≥ 10 mg / d or equivalent doses of other corticosteroids for more than 3 weeks; **d:** Long-term inhaled corticosteroids was defined as: inhaled corticosteroid for more than 30 days, the daily dose wasn't limited.

Risk Factors Of Health-Care Acquired Pneumonia	
Hospitalization For 2d Or More In The Preceding 90 Days	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown
Home Infusion Therapy (Including Antibiotics) Or Home Wound Care In 30 Days	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown
Chronic dialysis within 30 Days	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown
Residence In A Nursing Home Or Extended Care Facility	<input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown

Part 2: Data of This Hospitalization

1. Signs And Symptoms

History Of Present Illness	
Clinical Manifestation	
Date Of Illness Onset : ____Y ____M ____D	
Fever? (T \geq 37.3 °C)	<input type="radio"/> Y <input type="radio"/> N; If Y, Tmax: ____°C
Hypothermia? (T<36°C)	<input type="radio"/> Y <input type="radio"/> N; If Y, Tmin: ____°C
Cough?	<input type="radio"/> Y <input type="radio"/> N
Sputum?	<input type="radio"/> Y <input type="radio"/> N; If Y, <input type="radio"/> Yellow Phlegm <input type="radio"/> White Phlegm <input type="radio"/> Bloody Sputum <input type="radio"/> Unknown
Chest Pain?	<input type="radio"/> Y <input type="radio"/> N
Shortness Of Breath?	<input type="radio"/> Y <input type="radio"/> N
Sore Throat Or Rhinorrhea	<input type="radio"/> Y <input type="radio"/> N
Chill/Shiver	<input type="radio"/> Y <input type="radio"/> N
Exhaustion/	<input type="radio"/> Y <input type="radio"/> N

Muscle And Joint Aches//Headache	
Darrhea?	<input type="radio"/> Y <input type="radio"/> N
Familial Aggregation (2 Epidemiological Related People Suffered From Pneumonia In Two Weeks) ?	<input type="radio"/> Y <input type="radio"/> N
Physical Examination (The Worst Value Of The Day On Admission)	
Tmax, °C	
Tmin, °C	
HR, beats/min	
RR, breaths/min	
BP(Systolic Pressure / Diastolic Pressure), mmHg	
Disorder Of Consciousness?	<input type="radio"/> Y <input type="radio"/> N
Cyanosis?	<input type="radio"/> Y <input type="radio"/> N
Physical Signs Of Lung:	Moist rales <input type="radio"/> Y <input type="radio"/> N Dry rales <input type="radio"/> Y <input type="radio"/> N
Edema Of Legs?	<input type="radio"/> Y <input type="radio"/> N; If Y, Asymmetric Edema Of Legs? <input type="radio"/> Y <input type="radio"/> N

3.Pre-hospital Medical Data Y N

Radiology		
Chest X-ray <input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown Date of Examination: ___Y___M___D	Site Of Pneumonia	<input type="radio"/> Bilateral Lung <input type="radio"/> Unilateral Lung
	Site Of Pneumonia	<input type="radio"/> Superior Lobe Of Right Lung <input type="radio"/> Middle Lobe Of Right Lung <input type="radio"/> Inferior Lobe Of Right Lung <input type="radio"/> Superior Lobe Of Left Lung <input type="radio"/> Inferior Lobe Of Left Lung <input type="radio"/> Unknown
	Plural effusion	<input type="radio"/> N <input type="radio"/> Left <input type="radio"/> Right <input type="radio"/> Bilateral
	Cavity	<input type="radio"/> Y <input type="radio"/> N
	consolidation	<input type="radio"/> Y <input type="radio"/> N
	Interstitial Change	<input type="radio"/> Y <input type="radio"/> N
Lung CT <input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown Date of Examination: ___Y___M___D	Infiltration	<input type="radio"/> Y <input type="radio"/> N
	Alveolar Infiltration	<input type="radio"/> Superior Lobe Of Right Lung <input type="radio"/> Middle Lobe Of Right Lung <input type="radio"/> Inferior Lobe Of Right Lung <input type="radio"/> Superior Lobe Of Left Lung <input type="radio"/> Inferior Lobe Of Left Lung <input type="radio"/> Bilateral Diffuse Infiltration <input type="radio"/> Unilateral Diffuse iInfiltration

	Plural effusion	<input type="radio"/> N <input type="radio"/> Left <input type="radio"/> Right <input type="radio"/> Bilateral
	Cavity	<input type="radio"/> Y <input type="radio"/> N
	consolidation	<input type="radio"/> Y <input type="radio"/> N
	Abscesses	<input type="radio"/> Y <input type="radio"/> N
	Patchy Shadow	<input type="radio"/> Y <input type="radio"/> N
	Interstitial change	<input type="radio"/> Y <input type="radio"/> N
Microbiological Examination		
Microbiological Examination Before Admission <input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown		
If Y: Date Of Specimen Collection: ____Y____M____D Specimen Type: <input type="radio"/> Sputum <input type="radio"/> Blood <input type="radio"/> BALF <input type="radio"/> Asopharyngeal Swab <input type="radio"/> Endotracheal Aspirate <input type="radio"/> Plural Effusion <input type="radio"/> Urine Microbiological Examination Results: _____		
Treatment Before Admission		
Antimicrobials Before Admission <input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown		
Drug name (Generic Name And Trade Name)	Route Of Administration	Drug Regime n
eg: Ceftriaxone (罗氏芬)	<input checked="" type="radio"/> Intravenous <input type="radio"/> Oral	2.0g , Qd
	<input type="radio"/> Intravenous <input type="radio"/> Oral	
	<input type="radio"/> Intravenous <input type="radio"/> Oral	
	<input type="radio"/> Intravenous <input type="radio"/> Oral	
	<input type="radio"/> Intravenous <input type="radio"/> Oral	
Antiviral Drug Use Before Admission <input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown		
	<input type="radio"/> Intravenous <input type="radio"/> Oral	
	<input type="radio"/> Inhalation	
	<input type="radio"/> Intravenous <input type="radio"/> Oral	
	<input type="radio"/> inhalation	
Corticosteroid Use Before Admission <input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown		
	<input type="radio"/> Intravenous <input type="radio"/> Oral	
	<input type="radio"/> inhalation	
	<input type="radio"/> Intravenous <input type="radio"/> Oral	
	<input type="radio"/> inhalation	
Vasopressor Use Before Admission <input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown		
If Y, Start Time: _____		Terminal Time: _____
Invasive Ventilation Before Admission <input type="radio"/> Y <input type="radio"/> N <input type="radio"/> Unknown		
If Y, Start Time: _____		Terminal Time: _____

Note: b. Vasopressors: Norepinephrine, Dopamine, Dobutamine, Metaraminol, adrenaline

4. Laboratory Examination In 24hr On Admission

Category	Item	Value	Unit
Blood Routine	WBC		*10 ⁹ /L
	Neu		*10 ⁹ /L
	Lym		*10 ⁹ /L
	HGB		g/L
	HCT		%
	PLT		*10 ⁹ /L
Biochemistry	ALB		g/L
	LDH		U/L
	AST		U/L
	ALT		U/L
	ALP		U/L
	TBIL		umol/L
	DBIL		umol/L
	CK		U/L
	BUN		mmol/L
	Cr		mmol/L
	Glu		mmol/L
	K		mmol/L
	Na		mmol/L
	Serum Detection	ESR	
CRP			mg/dL
PCT			ng/ml
D-dimer			ng/ml
PT			s
APTT			s
INR			
BNP			pg/ml
Ferritin			ug/l

5. Blood Gas Analysis, Radiology and Ultrasonography After Admission

Category	Item	Value
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Blood gas analysis (The Worst Value In 24hr On Admission)	Oxygen Therapy ※ <input type="radio"/> Y <input type="radio"/> N	<input type="radio"/> Oxygen Inhalation Through Nasal Tube____L/min <input type="radio"/> Oxygen Inhalation Through Venturi Mask_____% <input type="radio"/> Oxygen Inhalation Through Oxygen Masks__L/min <input type="radio"/> Non-invasive Ventilation <input type="radio"/> Invasive Ventilation <input type="radio"/> Unknowen	
	FiO ₂		
	pH		
	PO ₂ (mmHg)		
	PCO ₂ (mmHg)		
	SaO ₂		
	Actual Bicarbonate (mmol/l)		
Lac (mmol/l)			
Radiology (In 24hr On Admission)	Chest X-ray <input type="radio"/> Y <input type="radio"/> N	Alveolar Infiltration	<input type="radio"/> Superior Lobe Of Right Lung <input type="radio"/> Middle Lobe Of Right Lung <input type="radio"/> Inferior Lobe Of Right Lung <input type="radio"/> Superior Lobe Of Left Lung <input type="radio"/> Inferior Lobe Of Left Lung <input type="radio"/> Bilateral Diffuse Infiltration <input type="radio"/> Unilateral Diffuse Infiltration
		Plural effusion	<input type="radio"/> N <input type="radio"/> Left <input type="radio"/> Right <input type="radio"/> Bilateral
		Cavity	<input type="radio"/> Y <input type="radio"/> N
		consolidation	<input type="radio"/> Y <input type="radio"/> N
		Patchy Shadow	<input type="radio"/> Y <input type="radio"/> N
	Lung CT <input type="radio"/> Y <input type="radio"/> N	Alveolar Infiltration	<input type="radio"/> Superior Lobe Of Right Lung <input type="radio"/> Middle Lobe Of Right Lung <input type="radio"/> Inferior Lobe Of Right Lung <input type="radio"/> Superior Lobe Of Left Lung <input type="radio"/> Inferior Lobe Of Left Lung <input type="radio"/> Bilateral Diffuse Infiltration <input type="radio"/> Unilateral Diffuse Infiltration
		Plural effusion	<input type="radio"/> N <input type="radio"/> Left <input type="radio"/> Right <input type="radio"/> Bilateral
		Cavity	<input type="radio"/> Y <input type="radio"/> N
		consolidation	<input type="radio"/> Y <input type="radio"/> N
		Patchy Shadow	<input type="radio"/> Y <input type="radio"/> N

		Interstitial Change	<input type="radio"/> Y <input type="radio"/> N
		Alveolar Infiltration	<input type="radio"/> Superior Lobe Of Right Lung <input type="radio"/> Middle Lobe Of Right Lung <input type="radio"/> Inferior Lobe Of Right Lung <input type="radio"/> Superior Lobe Of Left Lung <input type="radio"/> Inferior Lobe Of Left Lung <input type="radio"/> Bilateral Diffuse Infiltration <input type="radio"/> Unilateral Diffuse Infiltration
Ultrasonography	Lower Limb Vascular Ultrasound Exam	Venous Thrombosis	<input type="radio"/> N <input type="radio"/> Left <input type="radio"/> Right <input type="radio"/> Bilateral <input type="radio"/> Unexamined

Note※The Worst Value Of Blood Gas Analysis And FiO2 At That Time.

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6.Keep Detailed Records Of The Following Time Points,And Write down The Code In The First Row Of The Table:

- ①The 4th day (The Day On Admission Is The 1st Day);
- ②The day of changing Antibiotics in 14 days After Admission;
- ③The 14th day after Admission ;
- ④The Day Of Discharging

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Category	Item(Unit)	BMJ Open	The Reason and The Date					
Vital Signs	Disorder Of Consciousness							
	Tmax (°C)							
	Tmin(°C)							
	HR (beats/min)							
	RR (breaths/min)							
	BP(/ mmHg)							
Symptoms 1. Exacerbation 2. Alleviation 3. No-change	Cough							
	Sputum							
	Chest Pain							
	Shortness Of Breath							
	Moist Rales							
	Dry Rales							
Blood Routine	WBC (*10⁹/L)							
	Neu (*10⁹/L)							
	Lym (*10⁹/L)							
	HGB (g/L)							
	HCT (%)							
	PLT (*10⁹/L)							
Biochemistry	ALB (g/L)							
	LDH (U/L)							
	AST (U/L)							
	ALT (U/L)							
	ALP (U/L)							
	TBIL (umol/L)							
	DBIL (umol/L)							
	CK (U/L)							
	CTNI (ng/ml)							
	BUN (mmol/L)							
	Cr (mmol/L)							
	Glucose (mmol/L)							

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7.Treatment During Hospitalization

Antibiotics Use <input type="radio"/> Y <input type="radio"/> N				
Drug Name (Generic Name And Trade Name)	Route Of Administration	Drug Regimen	Start Time	Terminal Ttime
eg: Ceftriaxone (罗氏芬)	<input checked="" type="radio"/> Intravenous <input type="radio"/> Oral	2.0g, Qd	2014-3-2	2014-4-5
	<input type="radio"/> Intravenous <input type="radio"/> Oral			
	<input type="radio"/> Intravenous <input type="radio"/> Oral			
	<input type="radio"/> Intravenous <input type="radio"/> Oral			
	<input type="radio"/> Intravenous <input type="radio"/> Oral			
	<input type="radio"/> Intravenous <input type="radio"/> Oral			
	<input type="radio"/> Intravenous <input type="radio"/> Oral			
Antiviral Drugs Use <input type="radio"/> Y <input type="radio"/> N				
Drug name (Generic Name And Trade Name)	Route Of Administration	Drug Regimen	Start Time	Terminal Time
	<input type="radio"/> Intravenous <input type="radio"/> Oral <input type="radio"/> Inhalation			
	<input type="radio"/> Intravenous <input type="radio"/> Oral <input type="radio"/> Inhalation			
	<input type="radio"/> Intravenous <input type="radio"/> Oral <input type="radio"/> Inhalation			
Glucocorticoids Use <input type="radio"/> Y <input type="radio"/> N				
Drug name (Generic Name And Trade Name)	Route Of Administration	Drug Regimen	Start Time	Terminal Time
	<input type="radio"/> Intravenous <input type="radio"/> Oral <input type="radio"/> Inhalation			
	<input type="radio"/> Intravenous <input type="radio"/> Oral <input type="radio"/> Inhalation			
Vasopressors Use <input type="radio"/> Y <input type="radio"/> N				
Drug Name	Route Of Administration	Drug Regimen	Start Time	Terminal Ttime
Immunoregulation Drugs (Including Intravenous Immunoglobulin , Thymosins) <input type="radio"/> Y <input type="radio"/> N				
Drug Name	Route of administration	Drug Regimen	Start time	Terminal time

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Alternative/ Supportive Treatment			
Item	Use	Start Time	Terminal Time
Continuous Venous-venous Hemofiltration	<input type="radio"/> Y <input type="radio"/> N		
Extracorporeal Membrane Oxygenation (ECMO)	<input type="radio"/> Y <input type="radio"/> N		
Non-invasive Ventilation	<input type="radio"/> Y <input type="radio"/> N		
Invasive Ventilation	<input type="radio"/> Y <input type="radio"/> N		

8. Measurement Of T Lymphocyte Subsets

Date of specimen collection: ___Y ___M ___D

T lymphocyte subsets	CD4		/ml
	CD8		/ml
	CD4%		
	CD8%		
	NK		/ml
	NKT		/ml
	CD4/CD8		

Note: Without Time Limitation

9. Microbiological Examination

(1). Microbiological Examination In 48hrs After Admission Y N

Microbiological Examination For Sputum Or eEndotracheal aAspiration	
Date Of Specimen Collection: ___Y___M___D	
Item	Results
Direct Microscopy	<input type="radio"/> Good Quality Sputum (> 25 leukocytes and < 10 epithelial cells per × 100 magnification field) <input type="radio"/> Not Good Quality Sputum <input type="radio"/> Unknown
	<input type="radio"/> G+ Cocci <input type="radio"/> G+ Bacillus <input type="radio"/> G- Cocci <input type="radio"/> G- Bacillus <input type="radio"/> Positive Acid-fast Stain <input type="radio"/> None

<p>Bacteria Culture</p>	<ul style="list-style-type: none"> ○Streptococcus pneumoniae ○Haemophilus influenzae ○Pseudomonas aeruginosa ○Enterobacter cloacae ○Acinetobacter spp ○Stenotrophomonas maltophilia ○Escherichia coli ○Enterococcus faecium ○None Or Normal oropharyngeal flora 	<ul style="list-style-type: none"> ○Moraxella catarrhalis ○staphylococcus aureus ○Klebsiella pneumoniae ○Proteus spp ○Serratia marcescens ○Enterobacter aerogenes ○Enterococcus faecalis ○Others: _____
	<p>Drug Resistant Bacteria</p> <ul style="list-style-type: none"> ○Methicillin Resistance Staphylococcus aureus (MRSA) ○Vancomycin-resistant Enterococcus <p>Bacteria producing ESBLs:</p> <ul style="list-style-type: none"> ○Escherichia coli ○Enterobacter cloacae <p>non - fermentative bacteria.:</p> <ul style="list-style-type: none"> ○Acinetobacter baumannii ○Others: _____ 	
	<p>If Streptococcus pneumoniae , MIC for penicillin____ug/ml;</p> <ul style="list-style-type: none"> ○Not detected 	
	<p>If MRSA, MIC for Vancomycin____ug/ml;</p> <ul style="list-style-type: none"> ○Not detected 	
<p>Direct Microscopy</p>	<ul style="list-style-type: none"> ○Fungal Spore ○Cryptococcus neoformans 	<ul style="list-style-type: none"> ○Fungal Hyphae ○None
<p>Fungi Culture</p>	<ul style="list-style-type: none"> ○Spergillus Fumigatus ○Aspergillus terreus ○Candida Spp ○Undetected 	<ul style="list-style-type: none"> ○Aspergillusflavus ○Mucor Mucedo ○Cryptococcus Neoformans ○Others: _____
<p>Nucleic Acid Test For Respiratory Virus</p>	<ul style="list-style-type: none"> ○Influenza A H1N1 ○Influenza A H2N3 ○Nontypeable Influenza A ○Adenovirus ○Parainfluenza virus2 ○Parainfluenza virus 4 ○Rhinovirus ○Coronavirus OC43HKU1 ○Coronavirus 229ENL63 ○Bocavirus ○EB virus 	<ul style="list-style-type: none"> ○Avian influenza H7N9 ○Influenza A H5N1 ○Influenza B ○Parainfluenza virus 1 ○Parainfluenza virus 3 ○Respiratory syncytial virus A ○Respiratory syncytial virus B ○Enterovirus ○Herpes simplex virus ○Cytomegalovirus ○MERS-CoV

Nucleic Acid Test For Atypical Etiology	<input type="radio"/> Mycoplasma pneumoniae <input type="radio"/> Legionella spp	<input type="radio"/> Chlamydia pneumoniae
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(2).Microbiological Examination For BALF? Y N

Microbiological examination for BALF (Within One Week After Admission)	
Date Of Specimen Collection: <u> </u> Y <u> </u> M <u> </u> D	
Item	Results
Direct Microscopy	<input type="radio"/> G+ Cocci <input type="radio"/> G+ Bacillus <input type="radio"/> G- Cocci <input type="radio"/> G- Bacillus <input type="radio"/> Positive Acid-fast Stain <input type="radio"/> None
Bacteria Culture	<input type="radio"/> Streptococcus pneumoniae <input type="radio"/> Moraxella catarrhalis <input type="radio"/> Haemophilus influenzae <input type="radio"/> staphylococcus aureus <input type="radio"/> Pseudomonas aeruginosa <input type="radio"/> Klebsiella pneumoniae <input type="radio"/> Enterobacter cloacae <input type="radio"/> Proteus spp <input type="radio"/> Acinetobacter spp <input type="radio"/> Serratia marcescens <input type="radio"/> Stenotrophomonas maltophilia <input type="radio"/> Enterobacter aerogenes <input type="radio"/> Escherichia coli <input type="radio"/> Enterococcus faecalis <input type="radio"/> Enterococcus faecium <input type="radio"/> Others: _____ <input type="radio"/> None Or Normal oropharyngeal flora
	Drug Resistant Bacteria
	<input type="radio"/> Methicillin Resistance Staphylococcus aureus (MRSA) <input type="radio"/> Vancomycin-resistant Enterococcus
	Bacteria producing ESBLs:
	<input type="radio"/> Escherichia coli <input type="radio"/> Klebsiella pneumoniae <input type="radio"/> Enterobacter cloacae <input type="radio"/> Serratia marcescens
	non - fermentative bacteria.:
	<input type="radio"/> Acinetobacter baumannii <input type="radio"/> Pseudomonas aeruginosa <input type="radio"/> Others: _____
	If Streptococcus pneumoniae , MIC for penicillin _____ ug/ml;
	<input type="radio"/> Not Detected
	If MRSA, MIC for Vancomycin _____ ug/ml;
	<input type="radio"/> Not Detected
Direct Microscopy	<input type="radio"/> Fungal Spore <input type="radio"/> Fungal Hyphae <input type="radio"/> Cryptococcus neoformans <input type="radio"/> None

	If <i>Streptococcus pneumoniae</i> , MIC for penicillin ___ug/ml; <input type="radio"/> Not Detected	
	If MRSA, MIC for Vancomycin ___ug/ml; <input type="radio"/> Not Detected	
Fungi Culture	<input type="radio"/> <i>Candidiasis albicans</i> <input type="radio"/> <i>Candida tropicalis</i> <input type="radio"/> <i>Candida parapsilosis</i> <input type="radio"/> <i>Aspergillus fumigatus</i> <input type="radio"/> <i>Aspergillus terreus</i> <input type="radio"/> Undetected	<input type="radio"/> <i>Candida krusei</i> <input type="radio"/> <i>Candida glabrata</i> <input type="radio"/> <i>Cryptococcus neoformans</i> <input type="radio"/> <i>Aspergillus flavus</i> <input type="radio"/> <i>Mucor Mucedo</i> <input type="radio"/> Others: ____

(4)、Pleural Effusion? Y N

Pleural Effusion Test? Y N

Microbiological Examination For Pleural Effusion (Without Time Limitation)	
Date of Specimen collection: <u> </u> Y <u> </u> M <u> </u> D	
Pleural Effusion Routine	
Total Cell Count: ___×10 ⁶ /L; Multinuclear Cell: ___×10 ⁶ /L; Mononuclear Cells: ___×10 ⁶ /L	
Pleural Effusion Biochemistry	
LDH: ___U/L; ADA: ___U/L; Pr: ___g/L Glu: ___mmol/L Cl: ___mmol/L	
Item	Results
Bacteria Culture	<input type="radio"/> <i>Staphylococcus aureus</i> <input type="radio"/> <i>Moraxella catarrhalis</i> <input type="radio"/> <i>Haemophilus influenzae</i> <input type="radio"/> <i>Pseudomonas aeruginosa</i> <input type="radio"/> <i>Klebsiella pneumoniae</i> <input type="radio"/> <i>Enterobacter cloacae</i> <input type="radio"/> <i>Proteus spp</i> <input type="radio"/> <i>Acinetobacter spp</i> <input type="radio"/> <i>Serratia marcescens</i> <input type="radio"/> <i>Stenotrophomonas maltophilia</i> <input type="radio"/> <i>Enterobacter aerogenes</i> <input type="radio"/> <i>Escherichia coli</i> <input type="radio"/> <i>Enterococcus faecalis</i> <input type="radio"/> <i>Enterococcus faecium</i> <input type="radio"/> Others: _____ <input type="radio"/> None or Normal Oropharyngeal Flora
	Drug Resistant Bacteria <input type="radio"/> Methicillin resistance staphylococcus aureus (MRSA) <input type="radio"/> Vancomycin-resistant Enterococcus Bacteria producing ESBLs: <input type="radio"/> <i>Escherichia coli</i> <input type="radio"/> <i>Klebsiella pneumoniae</i> <input type="radio"/> <i>Enterobacter cloacae</i> <input type="radio"/> <i>Serratia marcescens</i> non - fermentative bacteria.: <input type="radio"/> <i>Acinetobacter baumannii</i> <input type="radio"/> <i>Pseudomonas aeruginosa</i> <input type="radio"/> Others: ____
Fungi Culture	<input type="radio"/> <i>Candidiasis albicans</i> <input type="radio"/> <i>Candida krusei</i> <input type="radio"/> <i>Candida tropicalis</i> <input type="radio"/> <i>Candida glabrata</i>

<input type="radio"/> Candida parapsilosis <input type="radio"/> Aspergillus fumigatus <input type="radio"/> Aspergillus terreus <input type="radio"/> Undetected	<input type="radio"/> Cryptococcus neoformans <input type="radio"/> Aspergillus flavus <input type="radio"/> Mucor Mucedo <input type="radio"/> Others: _
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(5)、Antigen Test In 48hr After Admission? Y N

Urinary antigen (in 48hr after admission)			
Date of specimen collection: <u> </u> Y <u> </u> M <u> </u> D			
Urinary Antigen For <i>Legionella</i> <i>spp</i>	<input type="radio"/> Positive	<input type="radio"/> Negative	<input type="radio"/> Undetected
Urinary Antigen For <i>Streptococcus pneumoniae</i>	<input type="radio"/> Positive	<input type="radio"/> Negative	<input type="radio"/> Undetected
Throat Swab Aantigen Test (In 48hr After Admission)			
Date Of Specimen Collection: <u> </u> Y <u> </u> M <u> </u> D			
Respiratory Syncytial Virus Antigen Test	<input type="radio"/> Positive	<input type="radio"/> Negative	<input type="radio"/> Undetected
Influenza A Antigen Test	<input type="radio"/> Positive	<input type="radio"/> Negative	<input type="radio"/> Undetected
Influenza B Antigen Test	<input type="radio"/> Positive	<input type="radio"/> Negative	<input type="radio"/> Undetected

(6)、Antibody Test? a) Y N

b) If Y, Titer Of Antibody In Paired Serum? Y, Interval days

N

Antibody Test (Without Time Limitation)	
Date Of Specimen Collection: <u> </u> Y <u> </u> M <u> </u> D	
<input type="radio"/> IgM for <i>Mycoplasmal pneumonia</i>	<input type="radio"/> IgM for Influenza A
<input type="radio"/> IgG for <i>Mycoplasmal pneumonia</i>	<input type="radio"/> IgM for Parainfluenza
<input type="radio"/> IgM for <i>Chlamydia spp</i>	<input type="radio"/> IgM for Q fever
<input type="radio"/> IgG for <i>Chlamydia spp.</i>	<input type="radio"/> IgM for Adenovirus
<input type="radio"/> IgM for <i>Legionella spp</i>	<input type="radio"/> IgM for Respiratory syncytial virus
<input type="radio"/> IgG for <i>Legionella spp</i>	<input type="radio"/> IgM for Parainfluenza 1,2,3

10、 Outcomes

(1).Treatment Failure Within 14 Days

Treatment Failure Within 14 Days (Multiple choices)		
(The Value Of The 1 st Day On Admission As The Baseline Data)		
1.Needs Invasive Ventilation	○Y ○N	
2.Needs Non-invasive Ventilation	○Y ○N	
3.Needs Vasopressors	○Y ○N	
4.Death	○Y ○N	
The Reasons For Treatment Failure		
1.CAP Progression	Pneumonia Progression	○Y ○N
2.CAP Complications	Pyothorax	○Y ○N
	Endocarditis	○Y ○N
	Meningitis	○Y ○N
	Others: _____	
3.Severe Sepsis Due To CAP	ARDS	○Y ○N
	Sepsis	○Y ○N
	Hepatic Failure	○Y ○N
	Renal Ffailure	○Y ○N
	Clotting Disorders,	○Y ○N
	Encephalopathy	○Y ○N
Others: _____		
4.Complications Or Underlying Disease Deterioration	Pulmonary Embolism	○Y ○N
	Myocardial Infarction	○Y ○N
	Arrhythmia	○Y ○N
	Gastrointestinal Bleeding	○Y ○N
	Congestive Heart Failure	○Y ○N
	COPD	○Y ○N
	Diabetes Mellitus	○Y ○N
	Nephropathy	○Y ○N
Others: _____		
5.Complications Due To Treatment	Hemopneumothorax	○Y ○N
	Allergic To Antibiotics	○Y ○N
	HAP/VAP	○Y ○N
	Vascular Catheter Infection	○Y ○N
	C. Difficile Infection	○Y ○N
	Iatrogenic Urinary Tract Infection	○Y ○N
Others: _____		
6.Unknown	○Y ○N	

(2). Complications During Hospitalization

Complications During Hospitalization	
Complications (Multiple Choices)	○Y ○N
Respiratory Failure ○Y ○N	ARDS ○Y ○N
Heart Failure ○Y ○N	Acute Myocardial Infarction ○Y ○N
Acute Liver Failure ○Y ○N	AcuteRenal Failure ○Y ○N
Septic Shock ○Y ○N	Stroke ○Y ○N
DIC ○Y ○N	Antibiotic Associated Diarrhea ○Y ○N
Arrhythmia ○Y ○N	MODS ○Y ○N
Pulmonary Embolism ○Y ○N	Deep Venous Thrombosis ○Y ○N
Ventilator Associated Pneumonia ○Y ○N	Gastrointestinal Bleeding ○Y ○N
Invasive Aspergillosis ○Y ○N	Mediastinal Emphysema ○Y ○N
Pneumothorax ○Y ○N	Nosocomial Bloodstream Infection ○Y ○N
Others ○Y ○N	If Y: _____

(3) . Outcomes

Clinical Stability Before Discharge	○Y ○N If Y, the date of clinical stability ____ Y ____ M ____ D. Meet the following seven criteria: Temperature<37.8°C for more than 24hr; Heart rate ≤100 beats/min ; Respiratory rate ≤24 breaths/min ;Systolic blood pressure ≥90 mm Hg ; Arterial oxygen saturation ≥90% or pO2 ≥ 60 mm Hg on room air ; Ability to maintain oral intake; Normal mental status.
Admitted to RICU/ICU?	○Y ○N If Y, The Date Of Admitted To RICU/ICU: ____ Y ____ M ____ D The Date Of Transfer From RICU/ICU: ____ Y ____ M ____ D
Discharging	The Date Of Discharging ____ Y ____ M ____ D Outcome ○Improvement ○Against-advice discharge ○Death If death, The Death Date ____ Y ____ M ____ D
Direct Cause Of Death (only one choice)	○Severe Pneumonia ○Respiratory Failure ○Shock○Heart Failure ○Acute Myocardial Infarction

	○Acute renal Failure	○Hepatic failure
	○DIC	○Stroke
	○Gastrointestinal Bleeding	○Others: _____

10. Cost And Economy Data

Total Expenses _____ Yuan:

Drugs Cost: _____ Yuan , Antimicrobials Cost _____ Yuan

Laboratory Testing Expenses: _____ Yuan

Bed Charge: _____ Yuan

Health Care Worker Labor Cost: _____ Yuan

Appendix 4: Definition of underlying diseases

- 1) Long-term smoking was defined as: cigarette smokers of 10 cigarettes/d during at least the previous year;
- 2) Alcoholism was defined as: drinking more than 5 bottles of beer (500ml / bottle) or half a catty liquor once in 2 weeks; or drinking more than 2.5 bottles of beer (500ml / bottle) or 2 ounce of white spirit per day for more than five years;
- 3) Long-term oral corticosteroids was defined as: oral prednisone $\geq 10\text{mg} / \text{d}$ or equivalent doses of other corticosteroids for more than 3 weeks.¹
- 4) Long-term inhaled corticosteroids was defined as: inhaled corticosteroid for more than 30 days, the daily dose wasn't limited;
- 5) COPD was defined as: persistent airflow limitation, $\text{FEV}_1 / \text{FVC} < 70\%$ post bronchodilator;
- 6) Asthma was defined by the history of respiratory symptoms such as wheeze, cough that varied over time and intensity, together with variable respiratory airway limitation;
- 7) Hypertension was defined as systolic blood pressure $\geq 140\text{mmHg}$ and /or diastolic blood pressure $\geq 90\text{mmHg}$ in resting status;
- 8) Coronary heart disease included angina pectoris, myocardial infarction, ischemic cardiomyopathy;
- 9) Chronic congestive heart failure was defined as cardiomegaly and ejection fraction $\leq 40\%$;

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4 10) Cerebrovascular diseases included transient ischemic attack, cerebral hemorrhage,
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6 subarachnoid hemorrhage, cerebral infarction, etc;
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10 11) Diabetes mellitus: included diabetes mellitus type 1 and diabetes mellitus type 2,
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12 not included impaired glucose tolerance and impaired fasting glycaemia;
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15 12) Chronic liver disease included chronic viral hepatitis, chronic alcoholic liver
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17 disease, chronic fatty liver disease, etc;
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20 13) Chronic kidney disease included diabetic nephropathy, hypertensive renal damage,
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22 chronic glomerulonephritis, chronic pyelonephritis, lupus nephritis, IgA nephropathy,
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24 nephrotic syndrome, hereditary kidney disease, etc;
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27 14) Connective Tissue Diseases include SLE, Sjogren's syndrome, rheumatoid
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29 arthritis, polymyositis / dermatomyositis, systemic vasculitis, ankylosing spondylitis,
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31 inflammatory bowel disease, hyperthyroidism, etc;
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34 15) Organ transplantation or bone marrow transplantation included solid organ
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36 transplanting, such as liver transplantation, kidney transplantation, lung
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38 transplantation or pancreas transplantation, etc and bone marrow transplantation;
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41 16) Aspiration risk factors included choking, drowning, nasal, pseudobulbar palsy,
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43 dementia, coma, poisoning, Parkinson's disease.
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46 17) Immunosuppressive therapy: was defined as systematic glucocorticosteroid (such
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48 as prednisone ≥ 10 mg/d for more than 3 weeks in the last month); cyclosporine or
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50 azathioprine use within 3 months, and methotrexate use ≥ 12.5 mg/week within 3
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52 months; biological modifiers such as etanercept and infliximab within 3 weeks.
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4 18) Immunocompromised status included HIV(+), chemotherapy/radiotherapy within
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6 6 months, immunosuppressive therapy, organ/bone marrow transplantation,
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8 splenectomy, hematological neoplasms.²
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11 19) Risk factors for pseudomonal infection was defined as chronic airway disease
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13 (bronchiectasis or COPD) and HCAP risk factors according to IDSA/ATS criteria.³⁻⁷
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17 20) Overtreatment was defined as: i) use of antipseudomonal β -lactams or β -lactams+
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19 fluoquinolones in hospitalized (not in ICU) patients without risk factors for
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21 pseudomonal infection; i i) use of β -lactams(antipseudomonal or not)+ fluoquinolones
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23 in ICU patients aged < 65yr without risk factors for pseudomonas infection; iii) use of
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25 anti-MRSA drugs in hospitalized (not in ICU) patients.³
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Appendix 5 Empirical antimicrobial regimens according to Chinese CAP guideline

Populations	Common pathogens	Anti-infective agents for initial empirical therapy	Comment
Outpatient treatment (Oral administration is recommended)			
Young adults without underlying disease(s)	<i>S. pneumoniae</i> , <i>M. pneumoniae</i> , <i>H. influenzae</i> , <i>C. pneumoniae</i> , influenza virus, adenovirus, <i>M. catarrhalis</i>	(1) Aminopenicillins, penicillins-β-lactamase-inhibitor combinations; (2) I or II generation cephalosporins; (3) doxycycline or minocycline; (4) respiratory quinolones; (5) macrolides	(1) Differentiate among bacterial pneumonia, <i>Mycoplasma</i> , <i>Chlamydia</i> and viral pneumonia based on clinical characteristics; (2) Mild pneumonia caused by <i>Mycoplasma</i> , <i>Chlamydia</i> , and virus is usually self-limited
Patients with underlying disease(s) or elderly patients (age ≥ 65 years)	<i>S. pneumoniae</i> , <i>H. influenzae</i> , <i>Enterobacteriaceae</i> such as <i>K. pneumoniae</i> , <i>C. pneumoniae</i> , influenza virus, RSV, <i>M. catarrhalis</i>	(1) Penicillins-β-lactamase-inhibitor combinations; (2) II or III generation cephalosporins (oral); (3) respiratory quinolones; (4) penicillins-lactamase-inhibitor combinations, II generation cephalosporins, III generation cephalosporins combined with doxycycline or minocycline or macrolides	Monotherapy with doxycycline or minocycline or macrolides is not recommended in patients with risk factors of resistant <i>S. pneumoniae</i> (1), such as age ≥ 65 years, underlying diseases (chronic cardiac, pulmonary, or renal diseases, diabetes mellitus, and immunosuppression), alcoholism, and β-lactams treatment within 3 months.
Inpatient treatment, non-ICU (Intravenous or oral administration)			

Young adults without underlying disease(s)	<i>S. pneumoniae</i> , <i>H. influenzae</i> , <i>M. catarrhalis</i> , <i>S. aureus</i> , <i>M. pneumoniae</i> , <i>C. pneumoniae</i> , influenza virus, adenovirus, other respiratory tract viruses	(1) Penicillin G, aminopenicillins, penicillins-β-lactamase-inhibitor combinations; (2) II or III generation cephalosporins, cephamycins, oxacephems; (3) the above drugs combined with doxycycline, minocycline or macrolides; (4) respiratory quinolones; (5) macrolides	(1) Only 1.9% of the <i>S. pneumoniae</i> isolates from adult CAP are resistant to intravenous penicillins in China. The percentage of intermediate strains is only about 9%. Intravenous penicillins are still effective in hospitalized patients infected with penicillin-intermediate <i>S. pneumoniae</i> when increasing the dosage (23, 161); (2) When atypical pathogens are suspected, doxycycline or minocycline or respiratory quinolones are preferred. Macrolides can be used in regions with lower resistance rate to mycoplasma
Patients with underlying disease(s) or elderly patients (age ≥ 65 years)	<i>S. pneumoniae</i> , <i>H. influenzae</i> , <i>Enterobacteriaceae</i> such as <i>K. pneumoniae</i> , influenza virus, RSV, <i>M. catarrhalis</i> , anaerobic bacteria, <i>Legionella</i>	(1) Penicillins-β-lactamase-inhibitor combinations; (2) III generation cephalosporins or their enzyme-inhibitor combinations, carbapenems such as cephamycins, oxacephems, ertapenem; (3) monotherapy of the above drugs or in combination with macrolides; (4) respiratory quinolones	(1) <i>Enterobacteriaceae</i> infection must be considered in patients with underlying disease(s) and elderly patients. The patients must be further evaluated for the risk of infection with ESBLs-producing <i>Enterobacteriaceae</i> ; (2) Elderly patients should be monitored for the risk factors of aspiration
Requirement for ICU admission (Intravenous administration is recommended)			
Young adults without underlying disease(s)	<i>S. pneumoniae</i> , <i>S. aureus</i> , influenza virus, adenovirus, <i>Legionella</i>	(1) Penicillins-β-lactamase-inhibitor combinations, III generation cephalosporins, cephamycins, oxacephems, ertapenem combined with macrolides; (2) respiratory quinolones	(1) <i>S. pneumoniae</i> is the most common pathogen. The other pathogens such as <i>S. aureus</i> , <i>Legionella</i> , influenza virus should also be considered (1, 2, 162-166); (2) During influenza seasons, attention must be paid to influenza viral infections. Combination with neuraminidase inhibitors should be considered. Attention should be paid to secondary <i>S. aureus</i> infection (167). The agents active against MRSA can be used in combination if necessary

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Patients with underlying disease(s) or elderly patients (age ≥ 65 years)	<i>S. pneumoniae, Legionella, Enterobacteriaceae</i> such as <i>K. pneumoniae, S. aureus</i> , anaerobic bacteria, influenza virus, RSV	(1) Penicillins-β-lactamase-inhibitor combinations, III generation cephalosporins or in combination with beta-lactamase inhibitors, carbapenems such as ertapenem combined with macrolides; (2) penicillins-β-lactamase-inhibitor combinations, III generation cephalosporins or in combination with beta-lactamase inhibitors, carbapenems such as ertapenem combined with respiratory quinolones	(1) Evaluate the risk of infection with ESBLs-producing <i>Enterobacteriaceae</i> ; (2) Physicians should be aware of the risk factors for aspiration and antimicrobial coverage of relevant pathogens
CAP with risk factors for <i>P. aeruginosa</i> infection and requirement for inpatient treatment or ICU admission (Intravenous administration is recommended)			
Patients with structural lung disease	<i>P. aeruginosa, S. pneumoniae, Legionella, Enterobacteriaceae</i> such as <i>K. pneumoniae, S. aureus</i> , anaerobic bacteria, influenza virus, RSV virus	(1) β-lactams with antipseudomonal activity; (2) quinolones with antipseudomonal activity; (3) β-lactams with antipseudomonal activity combined with quinolones or aminoglycosides with antipseudomonal activity; (4) combination of β-lactams, aminoglycosides and quinolones with antipseudomonal activity	Risk factors include: (1) airway <i>P. aeruginosa</i> colonization; (2) repeated doses of antibacterial drugs or glucocorticoids due to chronic airway disease. Combination therapy is recommended for patients with severe CAP or proven antimicrobial resistance

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Appendix 6: Definition of microbiological criteria of CAP:

Definite, if one of the following criteria was met:

4. Positive urinary antigen for *Legionella pneumophila* (LP, Binax Now L pneumophila urinary antigen test; Trinity Biotech, Bray, Ireland);
5. Positive urinary antigen for *Streptococcus pneumoniae* (Binax Now S pneumoniae urinary antigen test; Emergo Europe, The Netherlands);
6. Positive bacterial culture from blood or plural fluid except for coagulase negative *Staphylococcus spp.*
7. Paired sera with a fourfold or more increase in the titers of antibodies to *Mycoplasma pneumoniae* (MP), *Chlamydia pneumoniae*, *L pneumophila* or respiratory viruses (Influenza A and B, Parainfluenza, Adenovirus, Respiratory syncytial virus). Or Serum IgM antibody (MIF) \geq 1:16 for *Chlamydia pneumoniae*.

Probable, if one of the following criteria was met:

- a. Detection of respiratory virus in sputum/bronchoalveolar lavage (BALF)/throat swabs by Realtime-PCR (Zhijiang, Shanghai, China) according to manufacturer's instructions, including respiratory syncytial virus (RSV) types A and B, influenza virus (IFV) types A and B, parainfluenza virus (PIV) types 1, 2, 3 and 4, rhinovirus (HRV), enterovirus (EV), coronavirus (hCoV) types 229E, NL63, OC43 and HKU1, parapneumovirus (hMPV), and adenovirus (AdV), bocavirus;
- b. Bacteria isolated from purulent sputum (defined as an adequate quality sputum sample with > 25 leukocytes and < 10 epithelial cells per $\times 100$ magnification field) with compatible findings of Gram staining;
- c. Detection of *Mycoplasma pneumoniae* (MP), *Chlamydia pneumoniae* or *L pneumophila* in sputum/BALF/throat swabs by Realtime-PCR (Zhijiang, Shanghai, China)
- d. Positive antigen for Influenza A/B (Alere™, Clearview Exact Influenza A& B)

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4 e. Serum IgM antibody positive for *Mycoplasma pneumoniae* (MP), or Serum IgG
5 antibody (MIF) \geq 1:512 for *Chlamydia pneumoniae*.
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For peer review only

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5 **Appendix 7: CAP patients with definite and probable microbiological diagnosis**
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Etiology	Without risk factors for pseudomonal infection (n=409)				With risk factors for pseudomonal infection (n=329)	Total (n=738)
	age<65yr and not in ICU (n=182)	age<65yr and in ICU (n=29)	age≥65yr and not in ICU (n=162)	age≥65yr and in ICU (n=36)		
Bacterial	142 (19.2%)	14 (1.9%)	137 (18.6%)	34 (4.6%)	316 (42.8%)	643 (87.1%)
<i>Pseudomonas aeruginosa</i>	27	0	31	6	133	197
<i>Klebsiella pneumoniae</i>	30	9	27	10	54	130
<i>E. coli</i>	15	1	17	2	31	66
<i>Acinetobacter</i>	13	3	20	3	23	62
<i>Staphylococcus aureus</i>	7	3	10	7	24	51
<i>Enterobacter cloacae</i>	9	1	8	3	17	38
<i>Streptococcus pneumoniae</i>	9	1	5	1	9	25
<i>Stenotrophomonas</i>	8	1	10	2	4	25
<i>Enterococcus faecalis</i>	5	0	3	0	9	17
<i>Enterococcus faecium</i>	3	0	1	0	5	9
others	20	3	18	7	35	83
Atypical etiology	5 (0.7%)	0 (0.0%)	2 (0.3%)	0 (0.0%)	0 (0.0%)	7 (0.9%)
<i>Mycoplasma pneumoniae</i>	6	0	1	0	0	7
<i>Legionella pneumoniae</i>	0	1	2	0	0	3
<i>Chlamydia pneumoniae</i>	0	1	0	0	0	1
Virus	30 (4.1%)	8 (1.1%)	15 (2.0%)	1 (0.1%)	9 (1.2%)	63 (8.5%)
Influenza A virus	25	8	14	1	6	54
Rhinovirus	3	2	2	0	1	8
Influenza B virus	0	0	4	1	3	8
Adenovirus	6	1	0	0	0	7
Respiratory syncytial virus	1	0	0	0	0	1
Human metapneumovirus	0	0	1	0	0	1
Cytomegalovirus	1	1	0	0	0	2
Bacterials+viruses	4 (0.5%)	5 (0.7%)	6 (0.8%)	1 (0.1%)	4 (0.5%)	20 (2.7%)
Viruses+atypical pathogens	2 (0.3%)	2 (0.3%)	1 (0.1%)	0 (0.0%)	0 (0.0%)	5 (0.7%)

For peer review only

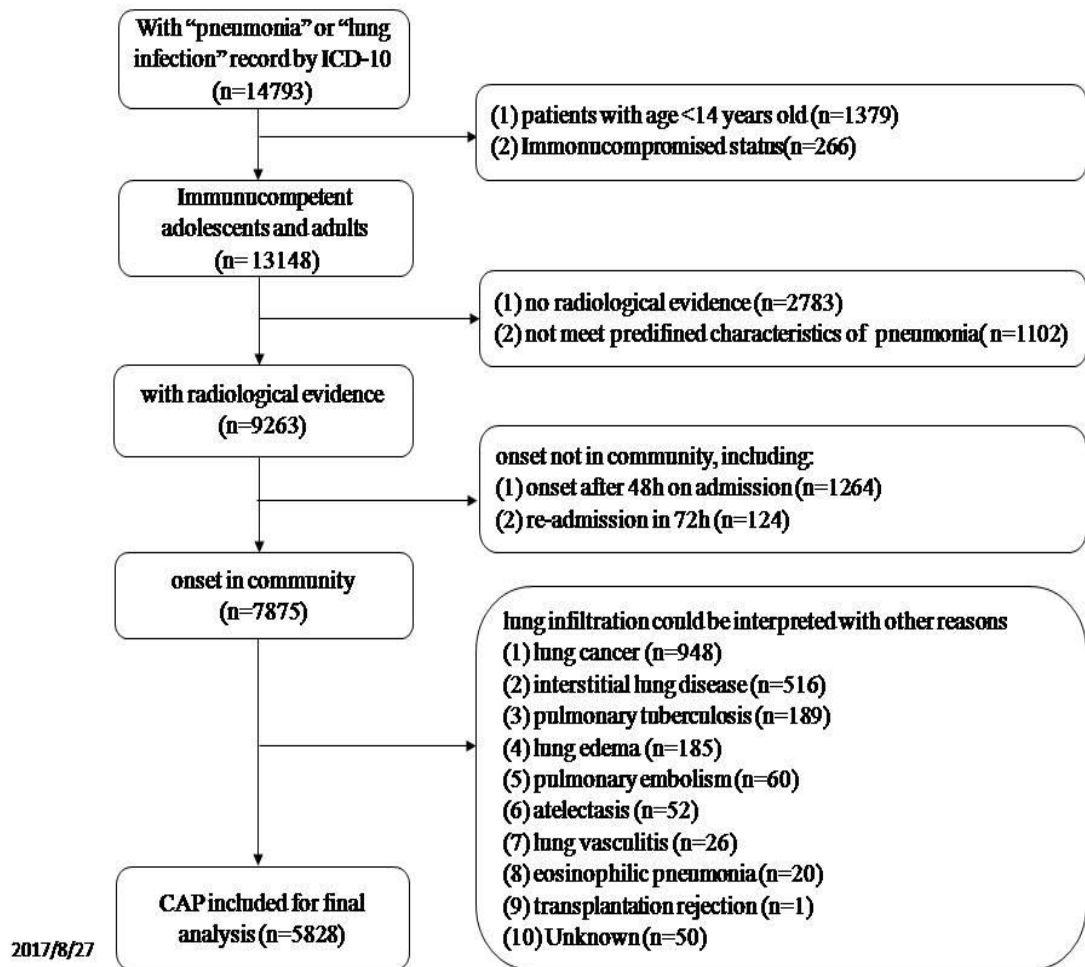
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Appendix 8: Sub-group analysis of 30-day mortality

Item	30-day mortality	P value
Severity of illness		
CURB-65		<0.001
0'	63 (2.7%)	
1'	93 (4.2%)	
2'	64 (7.2%)	
3'	15 (10.2%)	
4'	1 (5.0%)	
5'	1 (100.0%)	
PSI risk class		<0.001
I	26 (2.3%)	
II	27 (3.0%)	
III	24 (3.2%)	
IV	45 (7.0%)	
V	22 (12.2%)	
Age		>0.05
14~64 ys	108 (3.9%)	
65~74 ys	44 (4.1%)	
75~89 ys	81 (4.6%)	
≥90 ys	13 (7.0%)	
Gender		>0.05
Male	144 (4.6%)	
Female	102 (3.8%)	
Underlying Diseases		
None of any underlying disease	47 (2.9%)	
Chronic congestive heart failure	14 (6.9%)	<0.001

COPD	51 (6.4%)	<0.001
Malignant solid tumors	15 (5.9%)	<0.001
Chronic Renal diseases	11 (5.5%)	<0.001
Cerebrovascular Diseases	42 (4.7%)	<0.001
Connective Tissue Diseases	5 (4.5%)	0.003
Coronary Heart Diseases	50 (4.3%)	<0.001
Bronchiectasis	27 (4.3%)	<0.001
Hypertension	87 (4.2%)	<0.001
Asthma	14 (4.1%)	<0.001
Diabetes	36 (3.9%)	<0.001
Chronic Liver diseases	2 (2.2%)	>0.05
ICU admission		
Yes	56 (15.3%)	<0.001
No	190 (3.5%)	
Systemic glucocorticosteroids use in admission		
Yes	87 (5.6%)	<0.001
No	159 (3.7%)	

Appendix Figure 1 Patient screening algorithm for hospitalized CAP



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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (Page 1) (b) Provide in the abstract an informative and balanced summary of what was done and what was found (Page 3-4)
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported (Page 4-5)
Objectives	3	State specific objectives, including any prespecified hypotheses (Page 5)
Methods		
Study design	4	Present key elements of study design early in the paper (Page 6)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection (Page 6-9)
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants (Page 6-7) (b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable (Page 7-10)
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group (Page 6- 7)
Bias	9	Describe any efforts to address potential sources of bias (Page 7)
Study size	10	Explain how the study size was arrived at (Page 9)
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why (Page 9-10)
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (Page 9-10) (b) Describe any methods used to examine subgroups and interactions (Page 9-10) (c) Explain how missing data were addressed (Page 9) (d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy (Page 9-10) (e) Describe any sensitivity analyses (Page 9-10)

Continued on next page

Results

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (Page 10) (b) Give reasons for non-participation at each stage (Page 10, Appendix figure 1) (c) Consider use of a flow diagram (Appendix figure 1)
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (Page 10-11) (b) Indicate number of participants with missing data for each variable of interest (Table 1-5) (c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time <i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure <i>Cross-sectional study</i> —Report numbers of outcome events or summary measures (Page 10-15)
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (Page 10-15) (b) Report category boundaries when continuous variables were categorized (Page 11) (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses (Appendix 8)

Discussion

Key results	18	Summarise key results with reference to study objectives (Page 20-23)
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias (Page 23-24)
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence (Page 20- 23)
Generalisability	21	Discuss the generalisability (external validity) of the study results (Page 24)

Other information

Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based (Page 25)
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*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.