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## Hospital-acquired lower respiratory tract infections among high risk hospitalized patients in a tertiary care teaching hospital in China: An economic burden analysis

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### ABSTRACT

**Background:** Data on the economic burden of hospital-acquired lower respiratory tract infection (LRTI) among high risk hospitalized patients are lacking in China. This study aims to fill this knowledge gap.

**Methods:** We used a prospective matched cohort design, comparing patients with LRTIs and 1:1 matched patients without LRTIs. Study period was from January 2013 to December 2015 analyzing inpatients from high risk wards – intensive care unit (ICU), dialysis, hematology, etc. – in a tertiary hospital. Hospital information system and hospital infection surveillance system were applied to extract necessary information. The primary outcome was incidence of hospital-acquired LRTIs, and the secondary was economic burden outcomes, including incremental medical costs and prolonged length of stay (LOS). Wilcoxon's signed rank test was used to explore the differences in the economic burden.

**Results:** Among 5990 hospital visitors over the period of time, 895 (14.94%) had hospital-acquired LRTIs. We analyzed 340 patients with LRTIs and 340 respective controls without infections. The median hospital costs for patients with ICU-acquired LRTIs were significantly higher than those without LRTIs in other wards (\$12,301.17 vs. \$4674.64,  $P < 0.01$ ). The average attributable cost per patient was \$2853.93 (\$6916.48 vs. \$4062.55,  $P < 0.01$ ). Patients from hematology department had the longest LOS, at 15 days (25 days vs. 10 days,  $P < 0.01$ ). An LRTI led to an attributable increase in LOS by 8 days on average ( $P < 0.01$ ). Western medicine, treatment and laboratory test were the dominant contributors to the growth in overall medical costs in hospital-acquired LRTIs.

**Conclusions:** Hospital-acquired LRTI imposed considerable economic burden on patients hospitalized in high risk wards in China. This study provides the first data for economic evaluation of LRTI, highlighting the urgent need to establish targeted preventive strategies to minimize the occurrence of this complication to reduce economic burden.

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### Introduction

Hospital-acquired infection (HAI) is deemed as the most common adverse event in healthcare issues globally, seriously threatening the physical and mental health for hospitalized patients nationally and internationally. There exists great discrepancy in main HAI type between developed nations and developing countries. A most current investigation conducted by the U.S. Centers for Disease Control and Prevention (CDC) in 2017 has indicated

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that urinary tract is the most common site of HAI (20%) [1], contributing to more than 1 million HAI cases in the USA annually [2]. Unlike the United States [3], previous Chinese reports have stated that lower respiratory tract infection (LRTI) is the most frequently diagnosed HAI (49.43%) in China [4–6] with the highest incidence of LRTI events in the world [6], far outstripping that in American and European countries. Nevertheless, surveillance data and economic burden on LRTI from China are scant. This makes it necessary to perform LRTI surveillance and evaluate attributable economic burden in China so as to provide valuable results from the developing world.

Due to decreased immunity and large doses of antimicrobial applied during treatment, patients hospitalized in high risk wards in hospital settings (e.g. intensive care unit, hematology, dialysis, etc) are more susceptible to LRTIs than general population. These infections expose patients to potential risks and complications such as antibiotic resistance and flora imbalance. This would lead to poor clinical and economic outcomes in the long term, including increasing costs, longer hospital length of stay (LOS), and increased morbidity and mortality [7–9].

Studies about economic burden of hospital-acquired LRTI have been performed in the United States, England and Germany [10–12]. A U.S. study reported that LRTI extended hospital LOS by 11.03 days while increasing total hospital charges by \$28,160.95 per admission [10]. Another study in United Kingdom pointed out that positive precautions against LRTI episodes in advance contributed to 10% reduction in ex ante risk of contracting LRTI with an expected saving of \$984 [11]. Undoubtedly, hospital-acquired LRTIs impose a huge economic burden on healthcare systems at all levels-individual, national and global, in the form of inappropriate use in medical health resources, extended hospital stay and application of antimicrobial drugs for infection treatment.

LRTI preventive controls have become the vital national health priority among the foremost HAI issues facing potential victims in China. However, studies on the economic burden of LRTI among high risk hospitalized patients in China are currently lacking. Given the high prevalence and severity of LRTIs, this study aims to quantify the economic burden associated with LRTIs, and therefore promote medical facilities to prevent LRTIs and reduce medical expenses among patients hospitalized in high risk wards.

## Methods

### Study setting and participants

The study hospital is a tertiary care teaching hospital affiliated to Shandong University with 4500 beds and over 5000 full-time healthcare workers. The hospital is capable of accommodating approximately 136,000 inpatients and serving 3.17 million outpatients each year. This study was conducted in high risk wards on consecutive years from January 1st, 2013 to December 31st, 2015, including Intensive Care Unit (ICU), Department of Organ Transplantation (DOT), Department of Hemodialysis (DHs), Department of Hematology (DH), Department of Neurology (DN) and Department of Endocrinology (DE). The Institutional Review Board and the Ethics Committee of Shandong University approved this study.

All patients who were admitted into the high risk wards during the study period were eligible. Based on annual statistics reports from hospital infection surveillance system, medical wards with high LRTI incidence were regarded as high risk wards. The aforementioned six wards ranking high on the list of medical departments with high incidence of LRTI events were therefore included in this study. Adult patients aged 18 years or older with clear diagnosis as hospital-acquired LRTI and voluntary participation were enrolled. Patients admitted into the hospital less than

48 h were excluded. Those following high compliance with doctors' medical advice, particularly discharge orders, were preferred. It is because medical costs would be inaccurate if patients discharged on their own. Patients with serious cardiac or renal dysfunction and multiple infection sites and those with incomplete data were also excluded from this study.

### LRTI surveillance and exposure definition

Patients recruited in this study received similar physical examination and therapeutic regimen by surgeons or physicians in accordance with their conditions. An active prospective target infection surveillance was performed by trained infection control doctors through hospital infection surveillance system over the period, which can monitor and detect suspected LRTI events through emerged symptoms such as fever or high white blood cells count and so forth. Each LRTI case was confirmed by medical chart review provided by doctors and nurses who were in charge of the patients.

HAI is also called nosocomial infection (NI). NIs manifested after 48 h of hospital admission that were neither incubating nor acquired at admission. Criteria for nosocomial LRTI were recommended by the U.S. Centers for Disease Control and Prevention [13]. According to the CDC's definition, respiratory tract infections contain cases of "pneumonia" and "lower respiratory tract infection other than pneumonia" only. Cases and controls were defined mainly based on whether there was a final diagnosis of LRTI made by clinicians recorded in medical charts. The diagnosis was made, if clinical examination revealed the presence of a dull sound on percussion or crackling rales or chest radiographic evidence of new or progressive infiltration, consolidation, cavitation or pleural effusion after 48 h of initial hospitalization.

### Process of matching

Economic burden of LRTI was estimated by comparing all-cause cost outcomes between patients with and without LRTIs. A matched sample consisted of a patient with LRTI and 1:1 matched patient without infection. The matched adjusted analysis aimed to estimate incremental medical costs and hospital LOS among patients with versus without an LRTI event. Subjects were strictly matched on age, gender, residence (rural/urban area), Acute Physiology and Chronic Health Evaluation-II (APACHE-II) score, antimicrobial use, mechanical ventilation, surgical procedure, invasive operation and admission date, who otherwise had similar characteristics at baseline. Among which, APACHE-II scoring system as the most common, objective and accurate assessment tool, is routinely used in clinical practice to evaluate the severity of disease among hospitalized patients beyond disease categories. In previous work, a higher APACHE-II score correlated with a severe form of diseases and higher mortality rate [14]. Besides, the total length of hospital stay of control patients needed to be at least as long as that of case patients before onset of LRTI. We excluded infected subjects if a corresponding patient in control group cannot be well-matched.

### Data collection

Hospital infection surveillance system and hospital information system were applied to detect LRTI episodes and collect required data of patients. Information on patients' demographic characteristics, medical diagnosis, therapeutic regimen, hospital LOS, medical costs and nursing records was retrieved from hospital information system, while LRTI characteristics were obtained from hospital infection surveillance system using a predesigned form. Western medicine mainly included antibiotics, chemotherapeutic drugs and clinical nutrients in this study. Two well-trained investigators,

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