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Cost-Effectiveness of Linezolid versus Vancomycin among Patients with Methicillin-Resistant *Staphylococcus aureus* Confirmed Nosocomial Pneumonia in China

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ABSTRACT

Objective: To estimate the cost-effectiveness of intravenous linezolid as a first-line agent against intravenous vancomycin in treating methicillin-resistant *Staphylococcus aureus*–confirmed nosocomial pneumonia in four Chinese cities. **Methods:** A decision-analytic model of 4-week time horizon was used to conduct cost-effectiveness analyses from the payer's perspective. Clinical outcomes and resource use data were derived from a head-to-head trial, supplemented with local cost estimates based on hospital data via an expert panel. A series of scenario analyses were conducted to evaluate the impact of uncertainty around model inputs. All results were reported in 2012 Chinese Renminbi. **Results:** The predicted probability of overall treatment success was 0.629 and 0.602 for linezolid and vancomycin, respectively. Total inpatient costs varied across the four cities, ranging from ¥58,835 to ¥86,894 for linezolid and ¥58,390 to ¥87,033 for vancomycin, respectively. Linezolid was demonstrated to be a dominant treatment strategy in Guangzhou. In Beijing, Nanjing, and Xi'an, incremental cost-effectiveness ratios in terms of additional successfully treated patient were ¥1,861, ¥163, and ¥16,509, respectively. Dominance by linezolid was observed in some scenario analyses with parameters such as treatment duration, inclusion of cost of managing adverse events, and drug acquisition costs being the main drivers of cost-effectiveness results. **Conclusions:** Despite linezolid's higher drug acquisition cost, its superior clinical efficacy renders it a likely cost-effective alternative for the treatment of methicillin-resistant *Staphylococcus aureus*–confirmed nosocomial pneumonia as compared with branded vancomycin from the payer perspectives of Beijing, Guangzhou, Nanjing, and Xi'an.

Keywords: cost-effectiveness, linezolid, methicillin-resistant *Staphylococcus aureus*, nosocomial pneumonia, vancomycin.

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Introduction

Nosocomial pneumonia (NP) caused by *Staphylococcus aureus* is the most commonly observed infection within the hospital setting in the United States, Europe, and Asia including China [1], with increasing evidence of resistance to methicillin [2,3]. In a review based on published clinical studies conducted in Europe, the prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) in clinical settings could be as high as approximately one-third of all clinical isolates of *S aureus* [4]. In another study with a special focus on ventilator-associated pneumonia, a rate of up to 80% was reported [5]. In China, a study concluded a mean MRSA prevalence of 50.4%, with the highest in Shanghai (80.3%), followed by Beijing (55.5%) and Shenyang (50.0%) [6]. MRSA infections are associated with considerable attributable mortality and morbidity resulting in high health care burden [7,8].

Vancomycin has always been a standard treatment for MRSA infection [9]. The presence of vancomycin-intermediate *S aureus*, however, has become increasingly more common [10,11]. Concerns over its nephrotoxicity, inadequate penetration into lungs, and the need for intravenous (IV) administration may limit its use.

Linezolid is an oxazolidinone antibiotic and has a unique mechanism of action that inhibits bacterial protein synthesis at

Conflict of interest: Y. Chen and P. Hajek are the employees of the Pfizer group of companies. C. Chen worked for Pfizer Investment Co. Ltd at the time of the study conduct and manuscript development. X. Wang, B. Wu, H. Kang and Q. Li have either served as a speaker, an advisory board member or a study investigator for Pfizer Investment Co. Ltd. S.C. Tan, D. A. Patel and X. Gao have worked as consultants in various projects for Pfizer group of companies.

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an early stage of the process. Because of its unique mechanism of action, cross-resistance with other antimicrobials does not develop easily [12]. In addition, the oral bioavailability of linezolid is almost 100% [13], thus allowing IV to oral therapy switch without changing the antibacterial agent or dosage regimen.

Compared with vancomycin, linezolid is relatively new and has been approved in China for the treatment of skin and soft tissue infections and hospital-acquired and community-acquired pneumonia. Superior efficacy of linezolid compared with vancomycin was demonstrated in a recently published head-to-head MRSA NP clinical study by Wunderink et al. [14].

Previous cost-effectiveness studies showed that linezolid was cost-effective compared with vancomycin in treating NP across different country settings, such as Brazil [15], Germany [16], Spain [17], and the United States [18,19]. To our knowledge and through a review of literature, there has not been any published cost-effectiveness study comparing linezolid against vancomycin in a Chinese setting. This study attempted to fill this gap by evaluating the cost-effectiveness of linezolid against vancomycin in treating MRSA confirmed NP from a payer's perspective across four geographically representative Chinese cities—Beijing, Nanjing, Guangzhou, and Xi'an—given that there exist wide variations in affordability as measured by gross domestic product per capita and in health care cost across different regions in China. Despite the fact that cost-effectiveness analysis is not currently formally required in the evaluation process for national reimbursement drug listing, a single cost-effectiveness threshold may not be applicable in the context of China.

Methods

Overall Model Description

A decision-analytic model was developed to estimate relevant costs and health outcomes of linezolid or vancomycin for hospitalized patients with MRSA-confirmed NP. Clinical and resource use parameters used in this study were identified from the Wunderink et al. [14] trial and its subsequent post hoc published analysis [20], while the local resource use and cost data were provided through review of local published literature and surveys with local clinicians who were experienced in managing MRSA confirmed NP. The incremental cost-effectiveness ratio (ICER) in terms of additional successfully treated patient was performed in the context of each city included in this study.

Cost-Effectiveness Model Structure

The model starts with a hypothetical patient for suspected or confirmed gram positive NP (Fig. 1). The empirical treatment with IV vancomycin or linezolid was considered for a period of 2 days before culture results were available. On MRSA confirmation with laboratory results, the patient was placed on first-line treatment with linezolid or vancomycin for up to a maximum of 14 days. Possible outcomes of first-line treatment were: 1) treatment success (resolution of symptoms or clinical improvement); 2) treatment failure due to lack of efficacy; 3) discontinuation due to adverse events (AEs); and 4) death. In case of treatment failure or discontinuation caused by AEs, the patient was switched to second-line treatment on day 7 of the first-line treatment. The same maximum therapy duration of 14 days was assumed for second-line treatment. The model also included an additional hospital stay of 1.7 and 2 days in the event of adverse event or treatment failure, respectively, based on the post hoc data analysis of Wunderink et al. trial [20] and inputs from local clinical experts. Because of lack of relevant published data, clinical inputs for second-line treatment were assumed to be the same as those of the first-line treatment, which were primarily obtained from the Wunderink et al. [14] trial. Consistent with previously published NP economic models [19,21], third-line treatment was not considered in this study because it was believed that most of the relevant costs and outcomes would be captured in the first and second lines of treatments. In accordance with the feedback from local clinical experts, patients who failed first-line linezolid were assumed to switch to second-line vancomycin and vice versa. Therefore, in the absence of post-hospitalization data, a time horizon of 4 weeks of an episode of NP caused by MRSA was adopted in line with the standard clinical practice mentioned above. In a separate study by De Cock et al. [16], the same clinical consideration was applied with similar hospital lengths of stay of 28.1 days being reported for both study and comparator groups treated with linezolid and vancomycin, respectively. In addition, a local retrospective database analysis reported an average length of hospital stay of 23.8 days among 610 patients treated for NP in 13 tier-3A hospitals in China [22]. Furthermore, it is unlikely that there will be significant differences in terms of cost and effectiveness between two study groups upon recovery and discharge from hospitals.

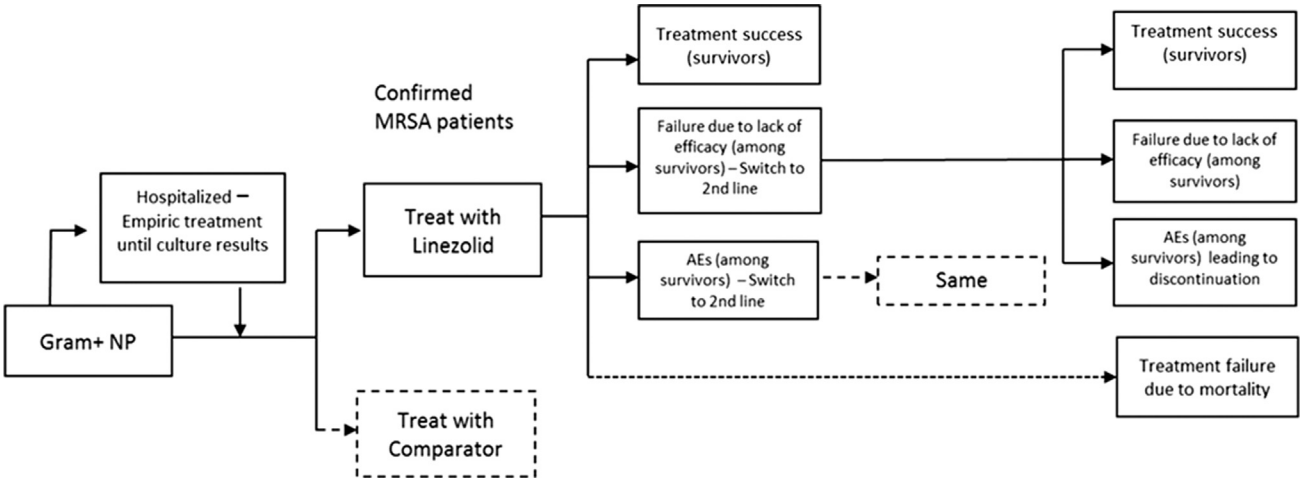

Fig. 1 – A decision-analytic model structure. AEs, adverse events; MRSA, methicillin resistance *staphylococcus aureus*; NP, nosocomial pneumonia.

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