

were diagnosed by intensivists. Interrater reliability between RAs for VAEs was high ( $\kappa$ , 0.71).<sup>1</sup> The clinical correlation between VAE surveillance and intensivists' clinical assessments was poor.

It is crucial to know that using  $\kappa$  value to assess agreement is a common mistake in reproducibility analysis. There are 2 important weaknesses of using a  $\kappa$  value to assess agreement of a qualitative variable: First, it depends upon the prevalence in each category, which means that it is possible to have a different  $\kappa$  value with the same percentage for both concordant and discordant cells! The  $\kappa$  value also depends upon the number of categories.<sup>2–5</sup> In such situations, a weighted  $\kappa$  is the preferable test because it gives an unbiased result. Moreover, for reliability analysis, an individual-based approach should be applied instead of a global average, which is usually applied for assessing the validity (accuracy) of a test.<sup>2–5</sup> Finally, reproducibility (ie, precision, reliability, repeatability, calibration) and validity (ie, accuracy, discrimination) are completely different methodological issues that should be assessed using appropriate tests.<sup>6–10</sup> It is crucial to know that to assess validity, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), the most appropriate tests are likelihood ratio positive and likelihood ratio negative as well as diagnostic accuracy and odds ratio.<sup>6–10</sup>

Kerlin et al concluded that prospective surveillance using VAE criteria is more reliable than traditional VAP surveillance and clinical VAP diagnosis; the correlation between VAEs and clinically recognized pulmonary deterioration is poor. Such a conclusion may be misleading due to the inappropriate use of a statistical test to assess reliability and validity.

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## Improved Outcomes When Antibiotic Prescribing Guidelines Are Followed by Healthcare Providers: A Colombian Example to Encourage Adherence in Hospital Settings

*To the Editor*—Over the past decade, the prevalence of antibiotic resistance has increased alarmingly worldwide, prompting the General Assembly of the United Nations to label this problem as the greatest threat to human health, sustainable development, and security. Latin American countries are largely affected by antibiotic resistance, which has not only persisted but spread, mainly due to mobile genetic elements carrying several resistance determinants.<sup>1</sup> Antimicrobial stewardship (AMS) and infection prevention are complementary, multidisciplinary approaches for curbing bacterial resistance.<sup>2</sup>

In Colombia, AMS programs have had a positive impact on optimizing antibiotic use, reducing resistance trends and even saving healthcare costs.<sup>2–4</sup> Locally developed antibiotic guidelines, based on epidemiological surveillance and clinical studies, assist healthcare providers in clinical decision making, thereby mitigating the overuse and misuse of antibiotics. To the best of our knowledge, no studies have addressed the degree to which healthcare providers in Colombia adhere to antibiotic guidelines when prescribing antibiotics to treat existing infectious disease.

TABLE 1. Clinical and Economic Outcomes in Patients with Complicated Urinary Tract Infection ( $n = 80$ )

Variable	Adherent Group, No. (%) ( $n = 54$ )	Nonadherent Group, No. (%) ( $n = 26$ )	Relative Risk	95% CI	P Value
Severe sepsis	4 (7)	8 (31)	0.24	0.08–0.72	.006
Other clinical complications <sup>a</sup>	6 (11)	9 (35)	0.32	0.12–0.80	.01
Change of antibiotic regimen after culture report	15 (28)	16 (62)	0.45	0.26–0.76	.003
Clinical improvement at the end of treatment	53 (98)	23 (89)	1.10	0.96–1.28	.06
Costs of laboratory tests and imaging, US\$ median (range)	174 (45–646)	278 (52–862)			<.05

NOTE. CI, confidence interval; RR, relative risk.

<sup>a</sup>Complications: bacteremia, septic shock, multiple organ dysfunction syndrome, renal failure.

As an initial step toward the assessment of adherence to antibiotic prescribing guidelines in a Colombian hospital, we present our preliminary findings from a prospective study conducted in a tertiary care hospital in Cali, Colombia. In this study, we aimed to determine the clinical and economic outcomes associated with adherence to antibiotic guidelines for treatment of complicated urinary tract infection (cUTI) in the emergency department (ED). These guidelines had been carefully implemented in the ED, and risk factors for multidrug-resistant bacteria and patient stratification by infection severity were also considered. Between January and August 2016, a total of 80 adult patients with cUTI were included in the study and were followed until the completion of their antibiotic regimens. Of those patients, 54 (68%) were empirically treated with an antibiotic regimen that adhered to the guidelines. Interestingly, no statistically significant differences in rates of adherence between specialists and general practitioners involved in the antibiotic prescription were detected ( $P = .42$ ). When adherent and nonadherent groups were compared (Table 1), clinical complications, change of antibiotic regimen after culture report, and higher costs of laboratory tests and imaging were factors associated with nonadherence to the antibiotic guidelines.

Overall, our findings demonstrate that both clinical and economic outcomes are significantly better for patients treated for cUTI in the ED according to antibiotic guideline recommendations. The adherence rate found in this study (68%) indicates a need for actions to increase compliance to antibiotic prescribing practices to an optimal level. Several barriers to physician adherence to clinical practice or AMS guidelines have been described in the literature, ranging from knowledge-related barriers (lack of familiarity or awareness) to attitude- and behavior-related barriers (lack of agreement, motivation, or outcome expectancy).<sup>5,6</sup> Such barriers should be addressed with tailored strategies. As a limitation, our study did not explore why healthcare providers did not follow antibiotic guidelines. Future studies aimed at elucidating barriers and strategies related to prescriber adherence to antibiotic guidelines in hospital settings in Colombia would serve as a cornerstone for driving AMS interventions.

Because there are no reports of adherence to therapeutic antibiotic guidelines published elsewhere in the country, our

findings represent an initial measure in Colombia; antibiotic prescribing practices should be monitored and improved. Many other healthcare institutions might also have room for improvement. Based on this framework, we posit that cultivating an understanding of healthcare providers' adherence to antibiotic prescribing guidelines is essential for identifying education and stewardship opportunities in hospital settings. Therefore, we encourage the development of new studies in the field of hospital epidemiology to investigate this health problem.

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## Deadly Sins of Antibiotic Abuse in China

*To the Editor*—China ranks first among the world's most frequent users of antibiotics.<sup>1</sup> In the hospital setting, ~70% of inpatients and ~20% of outpatients in China are prescribed antibiotics by doctors, which are both twice WHO's expectation for these rates.<sup>2</sup> In many developed countries and in the United States, these rates are ~30% of inpatients and ~15% of outpatients. The overuse of antibiotics not only may adversely affect their therapeutic efficacy but also may substantially increase the cost of health care and lead to lethal toxic or allergic reactions. Approximately 14,738,000 incidents of moderate-to-severe adverse effects related to antibiotic abuse are reported annually in China, and between 2001 and 2005, ~150,000 patients died annually of antibiotic abuse or overuse.<sup>3</sup> Moreover, off-label and blind use of antibiotics without pathogen culture and sensitivity test can lead to increased antimicrobial resistance.<sup>4</sup> Furthermore, the case-fatality rate of drug-resistant infections reached 11.7% in hospitalized patients in China in 2011.<sup>5</sup> Based on the data provided in the Mohnarin report,<sup>6</sup> between 2007 and 2008 the detection rates of methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-resistant *Staphylococcus epidermidis* (MRSE) were 73.6% and 79.5%, respectively, in 20 hospitals in China. These rates are by far the highest in history.

The irrational clinical practice of antibiotic use in China is mainly characterized by high frequency and intensity, long duration, high dose, abuse without definite indications, and the combination of multiple antibiotics without the support of evidence. The “7 deadly sins” behind antibiotic abuse in China include (1) blind dependence on antibiotics on the part of the patient, (2) lack of awareness of proper use of antibiotics on the part of the doctor, (3) compulsory acquisition of interest on the part of the hospital, (4) enormous loopholes in the drug sale and purchase market, (5) lack of strict management

systems, (6) ineffective administrative supervision,<sup>7–9</sup> and (7) longstanding hospital systems that compensate doctors according to their prescription practices. In addition, antibiotic abuse in animal husbandry is almost an open secret in China. Some scholars worry that the Chinese people will regret these lax antimicrobial policies and that China may even enter a “post-antibiotic era” in which antibiotics are not longer effective, which would undoubtedly constitute a humanitarian disaster.

Antibiotic abuse and other pressing public health challenges have attracted the attention of policy makers in the Chinese government. In May 8, 2012, the Chinese government officially issued an “unprecedentedly strict” (the network-based language prevailing in China) document concerning the management of clinical application of antibiotic agents. Mr. Xiaowei Ma, Deputy Minister of the Ministry of Health of China, said that the Ministry of Health would take further measures to curb antibiotic abuse (1) by including further intensifying the management of clinical application of antibiotic agents by setting up relevant policies, (2) by strictly implementing regulations about staged management of antibiotic agents and the prescription review system, (3) by progressively enhancing the construction of networks on clinical application of antibiotics and supervision of dynamic surveillance as well as early warning on antibiotic resistance, and (4) by immediately taking specific actions to rectify improper clinical application of antibiotic agents.<sup>10</sup>

Beyond China, antibiotic abuse has become a serious social issue threatening public health all over the world. We need to raise public awareness about the harmful nature of antibiotic abuse. Media should emphasize the importance of the rational use of antibiotics, and measures should be taken to improve public knowledge of both risks and benefits of antimicrobial therapy. In addition, education of doctors should be improved to ensure that they comply with such guidelines as well as the widely accepted recommendations for proper clinical diagnosis and treatment. Returning public hospitals to the track of public service, mobilizing the enthusiasm of medical workers, and preventing them from abusing antibiotics for personal gains are key to achieving the rational use of antibiotics.

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