

testing at regional hospitals to analyse samples from multiple facilities, and a hub-and-spoke model whereby high-volume sites conduct POC testing and serve as hubs for samples collected from other sites in their areas. Our results suggest that the strategy of POC testing at every antenatal care facility was the most expensive because of large capital costs and might be unaffordable for low-income countries.<sup>4</sup> Although syndromic management was the least expensive strategy, it resulted in fewer infections cured and considerable overtreatment. Among testing strategies, we found that the hub-and-spoke approach would offer the optimal cost per infection averted.

Modelling analyses that incorporate system dynamics—ie, patient volume, disease burden, infrastructure, and budget effects—could inform plans to scale-up testing to improve STI management globally. Our analysis suggests strategies for reducing costs and maximising impact by strategically situating POC testing. There are additional opportunities for cost reductions, such as integrating testing into antenatal care services, maximising multiplex capacity, and using existing but underused resources, such as the GeneXpert *Mycobacterium tuberculosis* testing network, which could reduce capital costs and have important clinical and public health benefits.

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## Bloodstream infections caused by Enterobacteriaceae in China

Andrew Stewardson and colleagues<sup>1</sup> Article provides a comprehensive understanding of the emerging threat of carbapenem-resistant Enterobacteriaceae (CRE) in low-income and middle-income countries (LMICs). Furthermore, it offers a reference for the burden of carbapenem resistance in China, which has announced a national action plan to combat antimicrobial resistance.<sup>2</sup> Therefore, future studies should focus on the prevalence and molecular characteristics of bloodstream infection-causing isolates from China.

The Blood Bacterial Resistant Investigation Collaborative Systems (BRICS) is a prospective, multicentre, observational study for tracking antimicrobial resistance among bloodstream infection-causing isolates in China (appendix pp 1–6). Here, we present data from 26 sentinel

hospitals of the BRICS project collected between January, 2014, and December, 2015. A set of 2569 non-duplicate Enterobacteriaceae isolates were included. *Escherichia coli* (n=1617) was the predominant species, followed by *Klebsiella pneumoniae* (n=570). 922 (57%) of 1617 *E coli* isolates and 171 (30%) of 570 *K pneumoniae* isolates produced extended-spectrum  $\beta$ -lactamases.

Notably, 83 meropenem non-susceptible isolates and 107 imipenem non-susceptible isolates were identified (the minimum inhibitory concentration cutoff for non-susceptible was  $\geq 2$  mg/L; appendix p 7), including 42 confirmed carbapenemase-producing Enterobacteriaceae (CPE) isolates, which were collected from 14 hospitals in 12 cities (appendix pp 8–11). The mean age of the 42 patients admitted to hospital was 61.1 years (SD 23.6), with a range of 1 year to 90 years, and 28 (62%) were male. 21 (50%) patients were admitted to the intensive care unit (including emergency and neonatal intensive care units). 15 (36%) patients died during the study, which is in line with previous studies on mortality attributable to CRE in LMICs.<sup>3,4</sup>

Among CPE isolates, 27 were *K pneumoniae* and five were *E coli* (appendix pp 8, 9). Although all isolates were resistant to a broad array of antimicrobials, most were susceptible to tigecycline, polymyxin B, and trimethoprim or sulfamethoxazole. Sanger sequencing showed that *bla*<sub>KPC-2</sub> was the most prevalent variant, in 31 (74%) of 42 isolates. Notably, multilocus sequence typing analysis showed that *K pneumoniae* sequence type (ST) 11 was the most common (22 [52%] of 42), followed by *E coli* ST167 (four [10%]) and *K pneumoniae* ST23 (two [5%]). ST11 KPC-2-producing *K pneumoniae* isolates were detected in ten hospitals and ST167 NDM-5-producing *E coli* isolates in



See Online for appendix

five. These data suggest clonal spread of these two clones, which needs to be closely monitored in the future.

Our data demonstrate the high prevalence of extended-spectrum  $\beta$ -lactamase-producing isolates and wide dissemination of CPE among bloodstream infection isolates in China. Since China has developed the national antimicrobial resistance surveillance network<sup>5</sup> and has committed to combatting antimicrobial resistance, we must also ensure that the financial support from the government continues to grow by emphasising the importance of CRE to public health.

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## The need for adequate research data on carbapenem use and resistance in Bangladesh

We read with interest the Article by Andrew Stewardson and colleagues,<sup>1</sup> which showed that carbapenem-resistant Enterobacteriaceae (CRE) bloodstream infections cause extended durations of hospital stay and increased mortality in patients in low-income and middle-income countries, including Bangladesh.

Enterobacteriaceae is a broad family of Gram-negative bacteria, with *Escherichia coli*, *Klebsiella* spp, and *Enterobacter* spp as the most common pathogens that cause both community-associated and health care-associated infections. Antibiotic resistance is considered one of the most pressing issues in the global health-care sector and CRE is a rising global problem.<sup>1</sup> As van Duin and Doi<sup>2</sup> discussed in their review, carbapenem resistance mediated by *Klebsiella pneumoniae* carbapenemase (KPC)-producing *K pneumoniae* and the New Delhi metallo- $\beta$ -lactamase is prevalent in south Asian countries, including Bangladesh.

The PANORAMA study considered data from tertiary-level hospitals in two low-income countries in south Asia (Bangladesh and Nepal), and effectively documented the increased mortality risk and prolonged hospital stay associated with CRE infections. However, this study only briefly mentioned the major social and health-care problems responsible for the alarmingly high CRE prevalence in Bangladesh, which include inadequate infection control initiatives, inadequate antimicrobial stewardship activities in the health-care sector, a culture of self-medication, and overuse of antibiotics in food production.<sup>1</sup> Ahmed and colleagues<sup>3</sup> highlighted current antibiotic resistance scenarios in Bangladesh; importantly, this

study found that inadequate surveillance data on antimicrobial resistance from 58 of the 64 districts of Bangladesh cannot accurately represent the country's current situation with regard to antimicrobial resistance. Studies have shown that in Bangladesh, 83% of prescriptions made in the community setting have no clinical justification for prescribing an antibiotic,<sup>4</sup> and in many cases physicians irrationally prescribe antibiotics to their patients without following any recommended guideline.<sup>4</sup> Unfortunately, studies have rarely focused on the use of carbapenems and their resistance mechanisms in Bangladesh.<sup>1,3,4</sup>

Research activities are required to justify the use of carbapenems and outcomes associated with CRE infections in Bangladesh. There is a huge unmet need for these aforementioned data as stakeholders are unable to take necessary actions without dependable research or surveillance data. Concerted efforts must therefore be made towards research to yield a data archive of actual carbapenem use and CRE prevalence in Bangladesh, and to establish a national antimicrobial resistance surveillance network.

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