with changing antibiotic use patterns and selective pressures over time.

Second, sampling. Day and colleagues sampled diverse reservoirs to investigate the source of bacteremia-causing *E coli*; another strength of the study. Sampling is always challenging. Studies must balance logistical feasibility with selection bias avoidance. Large numbers of *E coli* were screened to identify the predominant ESBL-producing members within each source population. Still, this finding represents a tiny fraction of the total diversity of circulating *E coli*, and ignores *E coli* isolates that are highly genetically similar across sources but have lost (or never had) ESBL-encoding mobile genetic elements. Selection for resistant-only isolates would miss any such link. Finding any genomic match between human and non-human source isolates, even between a pair of singleton STs, could be important to public health, especially in the face of extensive *E coli* diversity and finite study sample sizes. A single introduction of a highly successful resistant clone might suffice to trigger the next (non-ST131) pandemic.

The repeated emergence in *E coli* and other uropathogens of novel resistance genes, encoding not just ESBLs but also colistin and carbapenem resistance, has been linked genetically to food animal sources.[7] Several new lineages are emerging, some of which (eg, ST1193) might ultimately supplant ST131.[8] To detect newly emerging, multidrug-resistant *E coli* lineages, stand-alone research studies might not be enough. Distributed surveillance systems that involve better integrated human and animal health systems and food inspection agencies, with sharing of carefully curated local and regional epidemiological and *E coli* genome sequencing data, will be required to counter the public health and medical threats posed by resistant and non-resistant, *E coli* causing bloodstream and other extraintestinal infections.

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I declare no competing interests.



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# Infectious disease consultation lowers candidaemia mortality

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In *The Lancet Infectious Diseases*, Carlos Mejia-Chew and colleagues report the results of a retrospective cohort study investigating the effect of infectious disease consultation on mortality and management of patients with candida bloodstream infections.[1] 42-day (22% *vs* 47%; p<0·0001) and 90-day mortality (29% *vs* 51%; p<0·0001) was significantly lower in the infectious disease consultation group versus the group without an infectious disease consultation. In the Cox proportional hazard model with inverse weighting by the propensity score, infectious disease consultation was associated with a hazard ratio of 0·81 (95% CI 0·73–0·91; p<0·0001) for mortality. Duration of antifungal therapy was longer and central line removal, echocardiography, and ophthalmological examination were more frequently done in the infectious disease consultation group. The large number of 1691 patients included and the statistical method used for survival analysis are major strengths of the study and an improvement compared with earlier studies.[2–4] Ishikane and colleagues[5] reported results from a similar setting but the number of patients included was much smaller (n=275). Similar results were obtained including a 46% reduction in 30-day mortality. Additionally, patients with an infectious disease

consultation were more likely to receive the appropriate definitive antifungal therapy.

Guidelines are provided by professional organisations with the aim of facilitating the management and treatment of candidaemia.[6] In clinical practice it might be challenging to comply with these guidelines due to a scarcity of familiarity but also because of complexity.[7] We think that the high proportion of patients (14%) with a candida bloodstream infection who did not receive any antifungal treatment and did not have an infectious disease consultation is a particularly alarming finding. 90-day mortality in these untreated patients was high (67%). The most common reason for withholding antifungal therapy was the fact that the positive blood culture was considered to be caused by a contaminant. In the study by Ishikane and colleagues,[5] 10% of patients with candidaemia in the non-infectious disease consultation group did not receive any antifungal agent, while in the study of Menichetti and colleagues,[8] this rate was 26%. The European Society of Clinical Microbiology and Infectious Diseases 2012 guidelines for the diagnosis and management of candida diseases are clear about the necessity to treat each and every patient in whom candida is cultured from a blood sample.[6]

How optimal care for patients with a candida bloodstream infection is organised might vary in different settings and is dependent on the availability and clinical training of staff including infectious disease physicians, medical microbiologists, and infectious disease pharmacists. In countries with a clinically orientated medical microbiology or laboratory medicine training (eg, Netherlands, Belgium), a telephone call to report the positive blood culture to the treating physician is often accompanied by clear advice to start antifungal treatment, order additional diagnostic procedures to detect organ involvement, and the removal of indwelling lines. In complex cases, infectious disease physician involvement plays an essential role as the global clinical, diagnostic, and therapeutic context is accounted for in their advice.

In several institutions, infectious disease consultation is part of an antifungal stewardship programme.[4,8] In the University of Mississippi Medical Center (Jackson, MS, USA) real-time electronic notifications of blood cultures positive for yeasts are sent to the antimicrobial stewardship pharmacist with a telephone call from the microbiology laboratory to a nurse or member of the primary team.[4] The pharmacist does a comprehensive review of the patient's chart and contacts the primary team, if needed, to provide recommendations regarding initiation of appropriate antifungal therapy, infectious disease consultation, and, when required, other candidaemia management interventions.[4] In Duke University Hospital (Durham, NC, USA), an automatic infectious disease consultation for patients who are hospitalised with fungaemia was implemented.[9]

In conclusion, as was shown previously for *Staphylococcus aureus* bloodstream infections,[10] this study showed that infectious disease consultation provides a significant survival benefit in patients with candidaemia. We believe every hospital should have an expert management strategy addressing all individual cases of candidaemia. The need for such expert management should be incorporated in all future candidaemia management guidelines.

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# Implications of non-prescription antibiotic sales in China

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The Article by Jie Chang and colleagues published in *The Lancet Infectious Diseases*[1] is very timely. It reflects a crucial need for concerted efforts to reduce irrational use of antibiotics to lower rising antimicrobial resistance.[2–4] Overuse has resulted in antibiotics becoming the most commonly used drugs globally.[3,5] Antimicrobial resistance increases morbidity, mortality, and costs because health systems run out of options to treat common infectious diseases.[1,2,6,7] Low-income and middle-income countries (LMICs), including China, are a particular concern given their increasing overuse of antibiotics[8] coupled with a greater effect of antimicrobial resistance than in high-income countries, because of living conditions, including poor sanitation, malnutrition, and high population density.[8]

A particular issue in LMICs is inappropriate non-prescription antibiotic sales for self-limiting diseases, such as diarrhoea and upper respiratory tract infections (URTIs) caused by viruses.[1,3–5,7,8] Concerns are exacerbated by often shorter courses than those recommended and inappropriate antibiotics being dispensed.[3] Overall, non-prescription sales of antibiotics in LMICs account for up to 93% of dispensed antibiotics, with up to 100% of pharmacists dispensing antibiotics without a prescription in some LMICs, despite legislation against such practice.[1,4,5,8,9] Ours and others' experience is that non-prescription antibiotic sales are driven by multiple reasons, including pressure from patients and financial reasons (ie, profit-motivated community pharmacists fearing the loss of clients seeking antibiotics to competitors, and high proportions of patients who cannot afford physician fees who opt to self-medicate and for out-of-pocket purchases). Ease of access to antibiotics and weak enforcement of regulations also enhance non-prescription sales. Cultural issues and poor levels of education[1,5,8] also affect patients' behaviour.

Consequently, community pharmacists are a crucial component to improve the management of patients with URTIs and paediatric diarrhoea, particularly because they are often the first health-care professional that patients consult.[1,10] However, there are concerns regarding their knowledge of antibiotics, antimicrobial stewardship, and antimicrobial resistance.[1,11–13] Initiatives are needed to address this problem.

The comprehensive approach by Chang and colleagues[1] using simulated clients provides further insight into non-prescription sales of antibiotics in China, where the authorities are seeking to change behaviour. The use of simulated clients helps to gain an accurate insight into not only pharmacists' but also other health professionals' behaviour towards antibiotics.[1,8,10] Although there are still concerns with the high proportion of non-prescription sales of antibiotics among community pharmacists across China (48·5% for paediatric diarrhoea and 70·1% for URTIs), and only a limited number asked the simulated clients about taking other medicines (6·6–9·7%) or their allergies and issued advice on medicine taking (16·1–29·2%), there were encouraging signs. Sales were significantly less common in urban areas, when a pharmacist was on duty, and when the pharmacy was part of a chain.[1] In addition, multiple initiatives in Shaanxi province, including stricter regulations for dispensing antibiotics, a qualified pharmacist's presence to dispense antibiotics, increased frequency of unannounced pharmacy inspections, punishments for antibiotics misuse, and improving pharmacists' education, resulted in decreasing antibiotic sales between 2011 and 2017.

From the findings of Chang et colleagues' study and our experience, we believe that several strategies can be implemented to reduce non-prescription antibiotic sales. These strategies include improving pharmacists' knowledge and practice of antimicrobial stewardship, starting in pharmacy school in addition to the use of the internet and educational workshops after qualification,[1] and making pharmacists more aware of the WHO AWaRe antibiotic list, particularly which antibiotics not to dispense, as well as developing and implementing national guidelines for pharmacists.[1,4,10,14] Other activities include reinforcing legislation where