the choice of a high dose of ceftolozane–tazobactam in Kollef and colleagues' trial. However, the dose of meropenem used in the trial could have been suboptimal on the basis of studies[8,9] that assessed meropenem penetration into the epithelial lining fluid of patients with nosocomial pneumonia. For equivalent antibacterial activity to high-dose ceftolozane–tazobactam, higher doses of meropenem should have been given—ie, 2 g every 8 h, preferably via extended 3-h infusion.[9,10] The 2016 Infectious Diseases Society of America and American Thoracic Society guideline suggested the optimisation of pharmacokinetic and pharmacodynamic parameters before initiating treatment of nosocomial pneumonias,[10] but Kollef and colleagues' trial was designed before this guideline was published. Despite these pharmacokinetic–pharmacodynamic issues for meropenem, and even though in the microbiological intention-to-treat population the proportion of baseline *P aeruginosa* isolates that was resistant to study treatment was more than four times higher in the meropenem group (13%) than in the ceftolozane–tazobactam group (3%), neither 28-day all-cause mortality nor clinical response at test of cure (the primary and key secondary study outcomes) differed significantly between study arms in the subgroup of patients with ventilator-associated pneumonia, bacteraemia, or *P aeruginosa* infections.

Ceftolozane–tazobactam is a welcome addition to the antibiotic armamentarium for nosocomial pneumonia. Still, in view of the high dose used in this trial and the limited safety data available, close monitoring and surveillance of clinical practice and phase 4 safety registries will be necessary to better define the risk–benefit profile of this new antimicrobial.

*Andre C Kalil, Alexandre P Zavascki
Division of Infectious Diseases, Department of Internal Medicine, University of Nebraska Medical Center, Omaha, NE 68198, USA (ACK); Department of Internal Medicine, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil (APZ); Infectious Diseases Service, Hospital Moinhos de Vento, Porto Alegre, Brazil (APZ); and Infectious Diseases Service, Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil (APZ)
akalil@unmc.edu

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Non-typhoidal salmonella: invasive, lethal, and on the loose

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In *The Lancet Infectious Diseases*, the GBD 2017 Non-Typhoidal Salmonella Invasive Disease Collaborators[1] estimate the global burden of invasive non-typhoidal salmonella disease using Bayesian meta-regression tools. The results show a high but decreasing number of cases since 2005 with a continuously high case fatality rate, consistent with previous estimates. These findings show that serotypes of *Salmonella enterica* subspecies that cause invasive non-typhoidal salmonella disease are "low-incidence, high-consequence" pathogens.[2] The unique potentiation of mortality from invasive non-typhoidal salmonella disease through HIV infection, malnutrition, and malaria,[3] has further prompted investigation into the burden of this infectious disease in recent times to inform measures for mitigation.

The estimates are an important addition to the sparse literature on invasive non-typhoidal salmonella disease. The most recent estimate of disease burden involved information from only ten studies, of which 70% were from Africa.[4] Most of the 66 studies contributing to the GBD 2017 estimates still come from Africa, with a few from Asia and none from Latin America. The paucity of data, particularly from the Indian subcontinent, which shares many of the risk factors for invasive non-typhoidal salmonella disease with Africa (eg, urbanisation with large populations living in crowded and insanitary conditions with poor access to potable water), is one of several clear indications of the need for more epidemiological research on invasive non-typhoidal salmonella disease.

However, estimates of the burden of invasive non-typhoidal salmonella disease have as yet not been able to account for several other potentially important influences, such as exposure to neglected tropical diseases, as well as influenza and other viral diseases. Recent work has further shown the potential role of the microbiota in invasive salmonellosis.[5,6] Living in close proximity to a farm and other domestic animals, using animal faeces as manure in subsistence farming, watering of crops with water from drains and other contaminated water sources, along with unhygienic slaughtering of animals and meat processing are common practices in many developing countries. These factors might vary widely and be independent to access to safe drinking water. Global measures of these factors do not exist, but they might substantially affect the global burden of invasive non-typhoidal salmonella disease and therefore have implications for efforts to develop and deliver effective vaccines against the disease. These considerations make invasive non-typhoidal salmonella disease, which is caused by serovars for which both humans and animals are host species, an important infectious disease requiring a One Health approach for an effective reduction in burden, as is being pursued by WHO.[7]

Without adequate, geographically representative, epidemiological mapping of invasive non-typhoidal salmonella disease and investigation into the sources and transmission pathways of the disease, estimations of the global disease burden might continue to change with very wide margins. Making appropriate global health policy recommendations towards control of invasive non-typhoidal salmonella disease that are relevant to various regions and countries is challenging in the face of varying estimates. Around 6 years ago, less than 5% of clinically important infectious diseases were considered to have been mapped reliably.[8] Within Africa, for example, a recently published article on Kenya[9] was the first, and is likely to be the only study to date, to use subnational data on premature mortality across an entire country to systematically assess the spatial patterns of disease burden, taking into consideration the risk of infectious diseases and environmental and sociodemographic factors. This study showed significant spatial clusters of high numbers of years of life lost (YLLs) to premature mortality subnationally, with crowded households showing strongest associations with YLLs.[9] Such findings have important implications for targeting not only health but also other national policies. Now, more than ever, innovative applications of internet and mobile phone technology and infrastructure enable us to collect, share, and use new data to rapidly improve our knowledge of the burden of a wide range of infectious diseases in an increasingly accurate and efficient manner.

No vaccine against non-typhoidal salmonella disease is available for use in humans. However, by contrast with many other vaccine-preventable diseases, non-typhoidal salmonella disease has clearly defined major risk factors that are preventable through relatively simple solutions compared with vaccine development and deployment. Death from invasive non-typhoidal salmonella disease is usually due to delayed diagnosis and delayed treatment or treatment with inappropriate antibiotics. Particularly in developing countries, multidrug-resistant and even extensively drug-resistant salmonella serotypes[10] further compound the persistent high case fatality from invasive non-typhoidal salmonella disease. This threat raises the need for not only diagnostics to identify infection but also blood culture and sensitivity investigations to be available as part of routine clinical care and public health surveillance.

*John H Amuasi, *Jürgen May*
Bernhard Nocht Institute of Tropical Medicine, Hamburg, Germany (JM); and Kumasi Center for Collaborative Research in Tropical Medicine, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana (JHA)
may@bnitm.de

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Escherichia coli causing bloodstream and other extraintestinal infections: tracking the next pandemic

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In *The Lancet Infectious Diseases*, Michaela J Day and colleagues[1] present the results of a large genomic epidemiology study that asks whether a food source exists for extended-spectrum β-lactamase-producing *Escherichia coli* isolates (ESBL-*E coli*) that cause bloodstream infections in the UK. This question is controversial, with evidence both for and against the food-source hypothesis.[2,3] Disagreements tend to revolve around the discriminatory power of genotyping approaches used to characterise *E coli* and on the scope and appropriateness of *E coli* sampling from human and non-human sources in past molecular epidemiology studies. Implementation of highly discriminatory genome sequencing, as in the present study, will begin to provide high quality evidence to either refute or support the hypothesis.

The study compared the number and type of multilocus sequence types (STs) and β-lactamase genes in ESBL-*E coli* isolates collected in 2011–14 from human and non-human sources. Human sources of ESBL-producing *E coli* (n=718) included sewage samples, human faecal samples, and bloodstream infections. Non-human sources (n=218) included veterinary diagnostic specimens, dairy cattle faeces, and food products (beef, pork, chicken, berries, vegetables, and herbs). ST131 and ST10 isolates were identified in bloodstream and non-human samples, but were found to be genetically unrelated. ST69, ST117, and ST23 were also found in bloodstream and food samples, and ST602 in faeces and chicken meat, but genome similarity and evolutionary relationships across sources were not assessed. Three of the most common meat, slurry, and animal-source *E coli* STs in the study (ST10, ST117, and ST23) have been reported in other studies of human extraintestinal infections and were among the top 20 STs in a systematic review of human extraintestinal pathogenic *E coli* lineages.[4] CTX-M-1 β-lactamase was present in both human and non-human sources, including a single bloodstream ST117 isolate containing the CTX-M-1 enzyme. Because the STs that were common across sources were relatively rare, Day and colleagues conclude that the ESBL-*E coli* causing bacteremia do not arise from food animal sources. Two practical public health questions emerge from these results.

First, timing. The authors rightly focus on bacteremia, a severe infection with the biggest impact on medical services and costs. *E coli* ST131 has increased explosively over the past 20 years as a cause of all extraintestinal infections, including bacteremia,[5,6] yet its original source remains unknown. *E coli* strains that are currently causing bloodstream infections, especially *E coli* ST131, might be highly host-adapted and human host-restricted, and could be more closely linked to health-care system exposure than to environmental exposures. Contemporaneous sampling of food and environmental isolates is a strength of the paper, but might have missed the period in the past when a link with food sources was measureable. The difference in ST131 clades (B, C1, and C2) by source also suggests past divergence. Similarly, the predominant ESBL genes associated with human-adapted STs probably emerged in parallel with these *E coli* lineages,