and University College London, which received a proportion of funding from the National Institute for Health Research University College London Hospitals Biomedical Research Centre and Clinical Research Facility. ECW, VL, and BW are supported by the Biomedical Research Centre funding scheme. This study was supported jointly by the Biomedical Research Centre and core funding from the Francis Crick Institute, which receives its funding from Cancer Research UK, the UK Medical Research Council, and the Wellcome Trust. DLVB and RB are additionally supported by the Genotype-to-Phenotype (G2P) National Virology Consortium via UK Research and Innovation and the UK Medical Research Council. The funders of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding authors had full access to all the data and the final responsibility to submit for publication.

*Edward J Carr†, Mary Y Wu†, Joshua Gahir, Ruth Harvey, Hermaleigh Townsley, Chris Bailey, Ashley S Fowler, Giulia Dowgier, Agnieszka Hobbs, Lou Herman, Martina Ragno, Murad Miah, Phillip Bawumia, Callie Smith, Mauro Miranda, Harriet V Mears, Lorin Adams, Emine Haptipoglu, Nicola O'Reilly, Scott Warchal, Chelsea Sawyer, Karen Ambrose, Gavin Kelly, Rupert Beale, Padmasayee Papineni, Tumena Corrah, Richard Gilson, Steve Gamblin, George Kassiotis, Vincenzo Libri, Bryan Williams, Charles Swanton†, Sonia Gandhi, David LV Bauer†, *Emma C Wall†, on behalf of the Crick COVID Serology Consortium*
emma.wall@crick.ac.uk

†Contributed equally

COVID Surveillance Unit (MYW, GD, AH, LH, MR) and Worldwide Influenza Centre (RH, LA), The Francis Crick Institute (EJC, MYW, JG, HT, CB, ASF, MMua, PB, CSm, MMir, HVM, EH, NO'R, SW, CSa, KA, GK, RB, SG, GK, CSw, SG, DLVB, ECW), London, UK; University College London, London, UK (EJC, RB, VL, BW, CSw, SG, ECW); National Institute for Health Research University College London Hospitals Biomedical Research Centre and Clinical Research Facility, London, UK (JG, HT, CB, EH, VL, BW, ECW); London Northwest University Healthcare NHS Trust, London, UK (PP, TC); Central and North West London NHS Foundation Trust, London, UK (RG); Department of Infectious Disease, St Mary's Hospital, Imperial College London, London, UK (GK)

Published **Online** May 23, 2023 https://doi.org/10.1016/S1473-3099(23)00291-8

See **Online** for appendix

1 Tan CY, Chiew CJ, Pang D, et al. Protective immunity of SARS-CoV-2 infection and vaccines against medically attended symptomatic omicron BA.4, BA.5, and XBB reinfections in Singapore: a national cohort study. *Lancet Infect Dis* 2023; published online March 13. https://doi.org/10.1016/S1473-3099(23)00060-9.

2 Goh AXC, Chae S-R, Chiew CJ, et al. Characteristics of the omicron XBB subvariant wave in Singapore. *Lancet* 2023; **401:** 1261–62.

3 Boyton RJ, Altmann DM. Imprinted hybrid immunity against XBB reinfection. *Lancet Infect Dis* 2023; published online March 13. https//doi/org/10.1016/S1473-3099(23)00138-X.

4 Gov.UK. JCVI advises an autumn COVID-19 vaccine booster. 2023. https://www.gov.uk/government/news/jcvi-advises-an-autumn-covid-19-vaccine-booster (accessed April 25, 2023).

5 Wu M, Wall EC, Carr EJ, et al. Three-dose vaccination elicits neutralising antibodies against omicron. *Lancet* 2022; **399:** 715–17.

6 Yue C, Song W, Wang L, et al. ACE2 binding and antibody evasion in enhanced transmissibility of XBB.1.5. *Lancet Infect Dis* 2023; **23:** 278–80.

7 Hoffmann M, Arora P, Nehlmeier I, et al. Profound neutralization evasion and augmented host cell entry are hallmarks of the fast-spreading SARS-CoV-2 lineage XBB.1.5. *Cell Mol Immunol* 2023; **20:** 419–22.

8 Pinto D, Park Y-J, Beltramello M, et al. Cross-neutralization of SARS-CoV-2 by a human monoclonal SARS-CoV antibody. *Nature* 2020; **583:** 290–95.

9 Knezevic I, Mattiuzzo G, Page M, et al. WHO International Standard for evaluation of the antibody response to COVID-19 vaccines: call for urgent action by the scientific community. *Lancet Microbe* 2022; **3:** e235–40.

10 Cromer D, Steain M, Reynaldi A, et al. Neutralising antibody titres as predictors of protection against SARS-CoV-2 variants and the impact of boosting: a meta-analysis. *Lancet Microbe* 2022; **3:** e52–61.

Highly multidrug-resistant Gram-negative bacterial infections in war victims in Ukraine, 2022

From 2014 to 2020, higher rates of antimicrobial resistance were reported in military hospitals than in civilian hospitals in Ukraine, indicating the challenges associated with reducing the spread of antibiotic-resistant bacteria during conflict.[1] Identical clones of carbapenem-resistant isolates of the *Acinetobacter baumannii* complex has been described by a 2016 study in Ukrainian war victims treated in Germany, suggesting a possible spread in Ukrainian hospitals.[2]

To monitor the prevalence of antimicrobial-resistant infections in Ukraine, we conducted sentinel testing of hospitalised war victims with hospital-associated infections between February and September, 2022. The patients included in this study were those who required emergency surgery and intensive care due to severe burns, shrapnel wounds, and fractures. Swabs were taken from the skin and soft tissue of patients when signs of infection were observed in wounds or burn surfaces. Catheter tips from central venous catheters showing signs of infection were sent to the microbiology department for culture. Additionally, tracheobronchial aspirates were collected from patients with signs of ventilator-associated pneumonia who had received respiratory support for more than 72 h.

Because of resource limitations in Ukraine, the isolates were analysed at Lund University's clinical microbiology laboratory, followed by antibiotic susceptibility testing at the European Committee on Antimicrobial Susceptibility Testing (EUCAST) development laboratory. Disc diffusion testing was performed in accordance with EUCAST guidelines,[3] and for isolates that were either meropenem-resistant, or susceptible with increased exposure, broth microdilution was carried out according to the International Organization for Standardization method.[4] Ethical approval was obtained from the Committee on Bioethics, National Pirogov Memorial Medical University, Vinnytsya, Ukraine (protocol number 11; 10.11.2022).

Phenotypical characterisation was performed on 156 isolates retrieved from 141 patients, which included 133 adults with war injuries and eight newborn babies with ventilator-associated pneumonia (appendix p 1). Two separate strains were isolated from nine patients, and three were isolated from three patients. Among the 154 isolates tested, 89 (58%) were resistant to meropenem (appendix p 2), including 34 (76%) of 45 *Klebsiella*

	Ceftazidime–avibactam	Ceftolozane–tazobactam	Cefiderocol	Imipenem–relebactam	Meropenem–vaborbactam	Colistin
Enterobacterales (n=45)	80%	100%	78%	89%	84%	22%
Klebsiella pneumoniae (n=37)	86%	100%	81%	95%	92%	24%
Providencia stuartii (n=1)	100%	100%	0	100%	0	100%
Enterobacter spp (n=7)	57%	100%	71%	57%	57%	0
Pseudomonas aeruginosa (n=16)	81%	81%	38%	69%	69%	0
Acinetobacter baumannii complex (n=46)	NA	NA	24%†	NA	NA	0

Data shown as proportion (%) of resistant isolates.* Enterobacterales screened as positive for carbapenemases with the meropenem disk diffusion test (cutoff <28 mm) and *P aeruginosa*, and *A baumannii* complex interpreted as susceptibile or resistant for meropenem were included in the extended antimicrobial susceptibility testing. Broth micro-dilution was used for all agents except for cefiderocol, because EUCAST considers disk diffusion to be more reliable than minimum inhibitory concentration determination. EUCAST=European Committee on Antimicrobial Susceptibility Testing. *According to EUCAST clinical breakpoint tables.[3] †No clinical breakpoint, interpreted using cut-off corresponding to pharmacokinetic-pharmacodynamic breakpoint.

Table: **Extended antimicrobial susceptibility testing**

pneumoniae isolates, 38 (73%) of 52 *A baumannii* complex, 13 (57%) of 23 *Pseudomonas aeruginosa* isolates, and 4 (18%) of 22 *Enterobacter* spp isolates.

Extended antimicrobial susceptibility testing revealed that 52 (49%) of 107 strains were cefiderocol-resistant, including 35 (78%) of 45 Enterobacterales isolates, 6 (38%) of 16 *P aeruginosa* strains, and 11 (24%) of 46 *A baumannii* complex. Notably, 10 (9%) of 107 isolates were resistant to colistin, with *K pneumoniae* (n=9) and *Providencia stuartii* (n=1) being the affected species. Among 61 Enterobacterales and *P aeruginosa* isolates tested, 49 (80%) were resistant to ceftazidime–avibactam, 58 (95%) were resistant to ceftolozane–tazobactam, 51 (84%) were resistant to imipenem–relebactam, and 49 (80%) were resistant to meropenem–vaborbactam (table). Of note, nine (6%) of 156 isolates, all *K pneumoniae*, were resistant to all antimicrobials tested. Screening for carbapenemase genes revealed a dominance of $bla_{\text{NDM-group}}$ and $bla_{\text{OXA-48-like}}$, and no $bla_{\text{MCR1/2}}$ were detected.

The report highlights the extensive antibiotic resistance observed in Gram-negative bacteria isolated from injured hospitalised war victims with nosocomial infections in Ukraine. The study found that 89 (58%) of 154 isolates were resistant to meropenem. Although most strains (including 90% of those resistant to meropenem) were sensitive to colistin, nine (6%) of 156 isolates were resistant to all antibiotics tested, including newer β-lactam β-lactamase inhibitor combinations.

Infectious complications following trauma and surgery are prevalent, and despite access to broad-spectrum antibiotics such as colistin, cefiderocol, and various enzyme inhibitors, hospital-associated infections can still be challenging to treat. Ukraine's health-care system is under immense pressure due to limited resources, which makes infection prevention and control measures difficult to maintain, possibly leading to the spread of resistant organisms. Resource support from neighbouring European countries, including access to antimicrobial agents and provision of care for war victims, could help alleviate some of these challenges.

KR, ON, and EM conceived the study. Project administration was provided by KR. The study design was finalised by KR, GK, and EM. Prior collection and preparation of clinical isolates was done by ON, DD, FN, and VB. Further laboratory work was performed by EM, LW, and TK. Data curation, analysis, and visualisation were performed by EM, VA, KR, and OL. The manuscript was initially drafted by OL and KR, and critically revised by GK, EM, VA, TK, ON, LW, and DD. All authors approved the final version of the manuscript. KR reports support by the Knut and Alice Wallenberg Foundation (KR; grant number 2018.0318) and OL and KR from the governmental funding of research within the clinical sciences. KR reports support from the Anna and Edwin Berger Foundation, Swedish Heart Lung Foundation, the Skåne County Council's Research and Development Foundation, and Swedish Research Council (grant number 2019–01053). We thank Amra Basic and Lucia Ortega Roco of the EUCAST Development Laboratory; Fredrike Bechmann; and Ann-Cathrine Petersson of the Department of Clinical Microbiology, Infection Control and Prevention, Lund. All other authors declare no competing interests.

*Oskar Ljungquist, Oleksandr Nazarchuk, Gunnar Kahlmeter, Vigith Andrews, Thalea Koithan, Lisa Wasserstrom, Dmytro Dmytriiev, Nadiia Fomina, Vira Bebyk, Erika Matuschek, *Kristian Riesbeck*

kristian.riesbeck@med.lu.se

Division of Infection Medicine, Department of Clinical Sciences, Lund University, Lund, Sweden (OL); National Pirogov Memorial Medical University, Vinnytsia, Ukraine (ON, DD, NF, VB); EUCAST Development Laboratory, Växjö, Sweden (GK, EM); Clinical Microbiology, Laboratory Medicine, Lund, Sweden (VA, LW, KR); Clinical Microbiology, Department of Translational Medicine, Faculty of Medicine, Lund University, SE-20502 Malmö, Sweden (TK, LW, KR); Intensive Care Unit, Clinical Center for Thermal Injury and Plastic Surgery, Municipal Non-Profit Enterprise Vinnytsia Regional Clinical Hospital Vinnytsia Regional Council (ON, DD)

1 Kondratiuk V, Jones BT, Kovalchuk V, et al. Phenotypic and genotypic characterization of antibiotic resistance in military hospital-associated bacteria from war injuries in the Eastern Ukraine conflict between 2014 and 2020. *J Hosp Infect* 2021; **112:** 69–76.

2 Granzer H, Hagen RM, Warnke P, et al. Molecular epidemiology of carbapenem-resistant Acinetobacter baumannii complex isolates from patients that were injured during the eastern Ukrainian conflict. *Eur J Microbiol Immunol (Bp)* 2016; **6:** 109–17.

3 EUCAST. Antimicrobial susceptibility testing EUCAST disk diffusion method version 10. 2022. https://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Disk_test_documents/2022_manuals/Manual_v_10.0_EUCAST_Disk_Test_2022.pdf (accessed March 1, 2023)

4 ISO. Susceptibility testing of infectious agents and evaluation of performance of antimicrobial susceptibility test devices. 2019. https://www.iso.org/standard/70464.html (accessed Feb 1, 2023)
5 EUCAST. Breakpoint tables for interpretation of MICs and zone diameters version 13. 2023. https://www.eucast.org/clinical_breakpoints/ (accessed March 1, 2023)

Published Online May 16, 2023 https://doi.org/10.1016/S1473-3099(23)00311-0

Tracheobronchial tuberculosis and its sequelae in children and adolescents

The systematic review conducted by Igbokwe and colleagues[1] indicated that a considerable proportion of children and adolescents (aged <18 years) have extensive sequelae after tuberculosis, such as radiological residua after pulmonary tuberculosis, deformities after musculoskeletal and cutaneous tuberculosis, and somatic and psychosocial impairment after tuberculous meningitis. However, this systematic review seems to not fully appreciate the sequelae of tracheobronchial tuberculosis and its long-term effects on children and adolescents.

Tracheobronchial tuberculosis, defined as tuberculous infection of the mucous membranes of the trachea or bronchus, can be diagnosed by tracheoscopy. In adults (aged ≥18 years), 10–50% of patients with pulmonary tuberculosis were found to have concurrent tracheobronchial tuberculosis by diagnostic bronchoscopy.[2,3] More than 68% of patients with tracheobronchial tuberculosis might develop some degree of tracheobronchial stenosis, even after adequate chemotherapy.[2,3] Refractory tracheobronchial stenosis might eventually lead to persistent respiratory symptoms, respiratory failure, and death.[2,3] In children, an observational study revealed that 40–50% of children with pulmonary tuberculosis might also have concurrent tracheobronchial tuberculosis, as detected by tracheoscopy screening.[4] Unlike adults, however, the most common type of tracheobronchial tuberculosis in children is lymph node fistula, which accounts for 96·4% of tracheobronchial tuberculosis cases in this age group.[5] Furthermore, some children might also develop cicatricial stenosis of the trachea or bronchus. As the most serious sequela of tracheobronchial tuberculosis, cicatricial stenosis of the trachea or bronchus might not only lead to obstructive pneumonia and respiratory failure, but even lead to death in severe cases.[3-5]

Currently, diagnosis of tracheobronchial tuberculosis and its sequelae mainly relies on tracheoscopy. Due to the poor compliance of children with this invasive test and potential infectivity of pulmonary tuberculosis, the current rate of use of tracheoscopy in screening for tracheobronchial tuberculosis is extremely low, which also leads to missed diagnoses and misdiagnoses. Moreover, current epidemiological data on the incidence of tracheobronchial tuberculosis and its sequelae in children are scarce. Therefore, future research should include investigations and other related clinical studies of tracheobronchial tuberculosis and its sequelae in children and adolescents. This research would lead to a more comprehensive understanding of the incidence and harm of tracheobronchial tuberculosis and its sequelae in children and adolescents and further increase the understanding and attention of paediatricians to the disease and its sequelae. Non-invasive diagnostic methods should urgently be developed to improve the compliance of paediatric patients and reduce the occupational exposure of medical personnel during the diagnostic process.

We declare no competing interests. J-QH and S-LG contibuted equally.

*Ming-Jin Yang, Jian-Qing He, *Shu-Liang Guo*
guosl999@sina.com

Department of Respiratory and Critical Care Medicine, The First Affiliated Hospital of Chongqing Medical University, Chongqing 400016, China (M-JY, S-LG); Department of Respiratory and Critical Care Medicine, West China Hospital, Sichuan University, Chengdu, China (J-QH)

1 Igbokwe V, Ruby LC, Sultanli A, Bélard S. Post-tuberculosis sequelae in children and adolescents: a systematic review. *Lancet Infect Dis* 2023; **23:** e138–50.
2 Jung SS, Park HS, Kim JO, Kim SY. Incidence and clinical predictors of endobronchial tuberculosis in patients with pulmonary tuberculosis. *Respirology* 2015; **20:** 488–95.
3 Kashyap S, Solanki A. Challenges in endobronchial tuberculosis: from diagnosis to management. *Pulm Med* 2014; **2014:** 594806.
4 Goussard P, Gie R. The role of bronchoscopy in the diagnosis and management of pediatric pulmonary tuberculosis. *Expert Rev Respir Med* 2014; **8:** 101–09.
5 Liu F, Rao XC, Ma YY, et al. [Classification of tracheobronchial tuberculosis in 252 children]. *Zhonghua Jie He He Hu Xi Za Zhi* 2022; **45:** 282–88.

Published Online May 17, 2023 https://doi.org/10.1016/S1473-3099(23)00342-0

Engaging pharmacists and medicine vendors in antimicrobial stewardship in LMICs

The inappropriate dispensing of antimicrobials without a physician's prescription (ie, over the counter) is a widespread problem in low-income and middle-income countries (LMICs), particularly in Asia and Africa.[1] In a recent mixed-method systematic review published in *The Lancet Infectious Diseases*, Jinxi Li and colleagues[2] synthesised data from 52 countries and estimated a pooled prevalence of over-the-counter antibiotic dispensing of 63·4% (95% CI 59·6–67·1), with a significantly higher prevalence in LMICs than in high-income countries. Most of the identified reports were from sub-Saharan Africa (n=58), south Asia (n=51), or east Asia and Pacific (n=46), with a prevalence of 70·7% (95% CI 63·0–77·9), 49·7% (41·5–57·9), and 73·3% (66·7–79·4), respectively.[2] Because over-the-counter dispensing substantially contributes to the misuse and overuse of antimicrobials, this