



Antimicrobial susceptibility testing profiles of ESBL-producing *Enterobacterales* isolated from hospital and community adult patients in Blantyre, Malawi

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ABSTRACT

Objective: There is a paucity of data on antimicrobial resistance (AMR) in Malawi. Here we present a study of AMR of extended-spectrum β -lactamases-producing *Enterobacterales* (ESBL-E) isolated from hospital and community settings in Blantyre, Malawi.

Design and Methods: A cross-sectional study was conducted between March and November 2020, involving 403 adult participants aged ≥ 18 years. Screening for ESBL-E was performed using CHROMagar ESBL medium. Production of ESBLs was confirmed by a combination disk test method. Antimicrobial susceptibility was tested using the agar disk diffusion method in accordance with the Clinical Laboratory Standards Institute's 2019 guidelines. **Results:** The mean resistance rate of ESBL-E to antimicrobial agents tested was 49.2% (range from 1.4%–92%). The highest resistance rates were observed for trimethoprim-sulfamethoxazole (92%), amoxicillin and ceftriaxone (79%), doxycycline (75%) and gentamicin (72%). Carbapenems (meropenem and imipenem) were highly active against isolates. The overall rate of multi-drug resistant (MDR) ESBL-E was 47%. The highest MDR was found in *Yersinia enterocolitica* (51%) and the least in *Serratia* spp. (40%).

Conclusions: We found a high resistance rate of ESBL-E isolates to antimicrobial agents; the majority were MDR. Surveillance systems are recommended to monitor AMR in Malawi.

INTRODUCTION

Extended-spectrum β -lactamases (ESBLs) are, often plasmid-mediated, enzymes with hydrolytic power against penicillin, cephalosporins (except cephamycins) and one or more oxymino- β -lactams, such as cefotaxime, ceftazidime and aztreonam; ESBLs are inhibited by clavulanic acid (Bush and Jacoby, 2010; Rawat and Nair, 2010). ESBLs constitute the most important antimicrobial resistance (AMR) mechanism of *Enterobacterales*. ESBL-producing *Enterobacterales* (ESBL-E) have been recognized by the World Health Organization as a major public health threat (Tacconelli et al., 2018; WHO, 2017). Noting that all clinically significant *Enterobacterales* are ESBL-producing species, the most common isolates causing hospital and community infections are *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter* spp. and *Proteus* spp. (Bitew and Tsige, 2020;

Gangoue-Pieboji et al., 2006; Ghadiri et al., 2012; Moglad, 2020; Zavala-Cerna et al., 2020). Strains of ESBL-E are the most frequent cause of hospital-acquired infections in the urinary tract, bloodstream and surgical site (Gaynes and Edwards, 2005; Musicha et al., 2017; Tumbarello et al., 2011; Zavala-Cerna et al., 2020). Members of the order *Enterobacterales*, particularly *E. coli* carrying CTX-M enzymes, are an increasingly common cause of community-acquired infections caused by ESBL-producing bacteria (Søråas et al., 2013). These bacteria can develop antibiotic resistance either by *de novo* mutations or through mobile genetic elements carrying resistant genes (Roca et al., 2015). Moreover, irrational use of antimicrobial agents in humans, animals and crop production has been reported as the major factor accelerating the emergence and dissemination of AMR in bacteria (Katakweba et al., 2018; Marshall and Levy, 2011; Roca et al., 2015).

Previous studies have provided evidence of the global variation of ESBL-E prevalence with the highest rates observed in resource-

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Table 1
Social-demographic and Clinical Characteristics of the Study Participants

Characteristics	Median (IQR) or n (%)	p-value
Age (years), median(IQR)	32 (25-42)	0.1
Sex		0.7
Male	178 (44%)	
Female	225 (56%)	
Marital status		0.6
Married or cohabiting	254 (63%)	
Not married	149 (37%)	
Education		0.4
College or university	18 (4%)	
Secondary	151 (38%)	
Primary	175 (43%)	
No formal education	59 (15%)	
Occupation		0.4
Employed	101(25%)	
Self-employment/business	101(25%)	
Student	29(7%)	
Unemployed	172(43%)	
Type of specimen		0.006
Rectal swab	195 (48%)	
Urine	101 (25%)	
Wound swab	107 (27%)	
Type of participant		0.05
Hospital/inpatients	107(27%)	
Community/outpatients	296(73%)	
Admission days, Median(IQR)	12(6-15)	0.3
Surgery in the past 3 months		0.02
Yes	95(24%)	
No	308(76%)	
Prior antibiotic use in the past 3 months		0.1
Yes	150(37%)	
No	253(64%)	

constrained countries (Cantón et al., 2008; Coque et al., 2008; Jean and Hsueh, 2011; Reinert et al., 2007; Sader et al., 2004). However, reports on AMR profile of ESBL-producing pathogens are limited in Malawi, and Blantyre in particular. Because resistance patterns may vary significantly between hospital and community settings, understanding this variation is important for empirical selection of effective, ESBL-targeted antibiotic therapy to improve patient outcomes. Thus our study was conducted to determine AMR profile of ESBL-E isolates from hospital and community patients in Blantyre, Malawi.

Material and methods

Study setting and design

We conducted a cross-sectional study from March to November 2020 at Queen Elizabeth Central Hospital (QECH) (hospital setting) and 3 outpatient health centres (Limbe, Ndirande and Zingwangwa) selected to represent community settings in Blantyre, Malawi. QECH is the second largest government hospital in Malawi and the affiliate of the University of Malawi College of Medicine (Currently Kamuzu University of Health and Allied Sciences, KUHeS). The hospital has an approximately 1000-bed capacity and provides free health care to more than 10 000 adults and 30 000 children per year (Musicha et al., 2017). The 3 health centres of Limbe, Ndirande and Zingwangwa were selected from 8 main public health centres that provide outpatient services to the 800 264+ population living in urban and peri-urban areas of Blantyre, Malawi; selection was based on the population distribution and geographical location of the 3 health centres, which permitted a large patient catchment area.

Study subjects and sample collection

Participants were all adults (aged ≥ 18) attending QECH or any of the 3 selected health centres in Blantyre for health services. One type of sample was collected from each admitted (hospital patient) or community patient (outpatient). Infected wound swab was randomly collected from 107 patients with wound infections admitted to different surgical and

burn wards at QECH. At the 3 health centres, 101 mid-stream urine samples from patients with clinically suspected urinary tract infection and 195 rectal swabs were randomly collected. Outpatients were recruited into the study irrespective of the reason for seeking health care. For each participant, data on age, sex, education, occupation, prior antibiotic use, prior surgery and length of hospital stay (admitted) were collected using a structured questionnaire. The collection of clinical samples was done by either the study clinician or nurse in the health facilities in accordance with standard operating procedures.

Bacteria enumeration, identification and confirmation of ESBL production

Culture of ESBL-E was performed according to the manufacturer's instructions using a selective chromogenic medium (CHROMagar ESBL, Paris, France) and incubated in aerobic conditions at 37°C for 24–48 hours. Identification of ESBL-producing *Enterobacterales* was made on the basis of colony morphology and isolated species confirmed using standardised biochemical substrate strips according to the manufacturer's instructions (Microbact Gram negative identification system, Oxoid, UK). ESBL production by the isolates was confirmed by a combination disk test using MASTDISCS ID ESBL detection disks set D52C (Mast Group Ltd., Merseyside, UK) as reported previously (Carter et al., 2000). The combination disks used were cefotaxime (CTX-30 μ g) and ceftazidime (CAZ-30 μ g) with and without clavulanic acid (CA-10 μ g). Quality control was performed using *Klebsiella pneumoniae* ATCC 700603 (ESBL-producing) and *E. coli* ATCC 25922 (non-ESBL producing).

Antimicrobial susceptibility testing

The antimicrobial susceptibility testing (AST) on ESBL-E was performed using the agar disc diffusion method on a Mueller-Hinton agar. Eleven commonly prescribed antimicrobial agents of different classes, including penicillin, carbapenems, cephalosporins, aminoglycosides and quinolones, were used. Antimicrobial agent discs used and their concentrations, in accordance with the Clinical and Laboratory Standards Institute (CLSI) 2019 guidelines, were as follows: amoxicillin (10 μ g),

Table 2
Distribution of ESBL-E isolates (n=73) by Type of Clinical Specimen and Settings

ESBL-E	Settings		Clinical specimen			Total (%)
	Hospital	Community	Rectal swab	Urine	Wound swab	
<i>C. freundii</i>	1	0	0	0	1	1 (1)
<i>Enterobacter spp</i>	2	3	2	1	2	5 (7)
<i>Escherichia coli</i>	5	33	29	4	5	38 (52)
<i>Klebsiella spp</i>	9	4	4	0	9	13 (18)
<i>M. morgani</i>	1	0	0	0	1	1 (1)
<i>P. mirabilis</i>	2	0	0	0	2	2 (3)
<i>Providencia spp</i>	1	1	0	1	1	2 (3)
<i>Serratia spp</i>	3	2	0	2	3	5 (7)
<i>S. sonnei</i>	0	1	1	0	0	1 (1)
<i>Y. enterocolitica</i>	2	3	3	0	2	5 (7)
Total (%)	26(36)	47(64)	39(53)	8(11)	26(36)	73 (100)

cefepime (30 µg), ceftriaxone (30 µg), trimethoprim-sulfamethoxazole (2/25 µg), meropenem (10 µg), imipenem (10 µg), amikacin (30 µg), gentamicin (10 µg), nitrofurantoin (300 µg), doxycycline (30 µg) and ciprofloxacin (5 µg). Briefly, inoculum was suspended in 0.9% normal saline and the turbidity adjusted equivalent to 0.5 McFarland standard corresponding to approximately 1.5 × 10⁸ CFU/mL. Using a sterile pipette, 20 µl of bacteria suspension was dispensed onto a Mueller Hinton agar plate, spread evenly using a sterile plate spreader and allowed to dry. Antimicrobial agent disks were then placed on an agar plate using a disk dispenser. Plates were then inverted and incubated at 37°C overnight. The zones of bacterial growth inhibition around each antimicrobial drug were measured to the nearest millimetre using a ruler and the size of the zone of inhibition interpreted according to the criteria recommended by CLSI of 2019.

Data analysis

Data obtained were entered and cleaned in Microsoft Excel and exported to STATA version 12.0 (Stata Corp LP, College Station, USA) for statistical analysis. Descriptive summary statistics were determined as frequencies and proportions for categorical variables and median (interquartile range [IQR]) for continuous variables. To compare the differences between groups, Chi-square and Fisher’s exact test (where ap-

plicable) and Student’s *t*-test were used for analysis of dichotomous and continuous variables, respectively. A *P*-value of <0.05 was considered significant.

Results and discussion

Social-demographic and clinical characteristics

A total of 403 adult patients were recruited in the study. Sociodemographic and clinical characteristics of study participants are presented in Table 1. The median age of participants was 32 years (IQR 25–42; range 18–90 years), and the male to female ratio was 1:1.3. The majority were community participants (73%), 64% were married or cohabiting, 43% had primary education and 43% were unemployed. Most participants had no history of surgery (76%), and 64% had not used antibiotics in the past 3 months.

Distribution of ESBL-E isolated by clinical specimen and setting

From the 403 samples, 73 (18%, 95% CI=14%–22%) ESBL-E were isolated and tested for antimicrobial susceptibility. The distribution of ESBL-E isolates by clinical specimen and study setting is presented in Table 2. Of the 73 ESBL-E isolates, the majority were isolated from com-

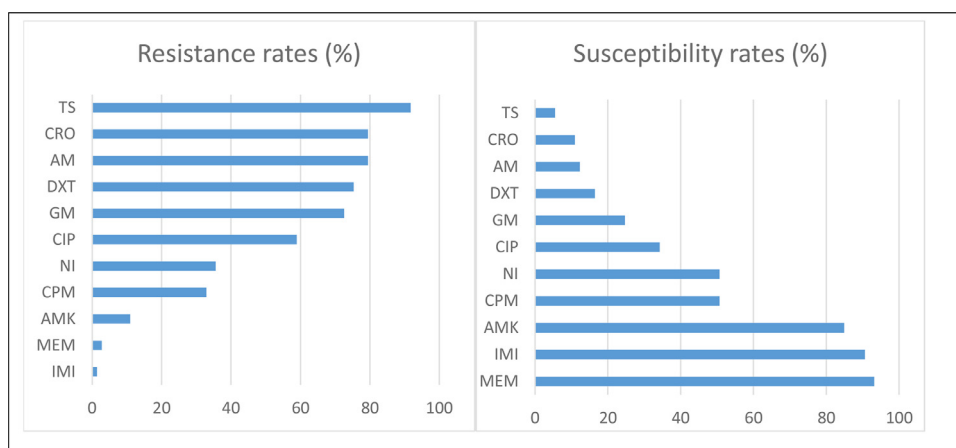


Figure 1. Antimicrobial resistance and susceptibility pattern of ESBL isolates

Key:

AM	Amoxicillin	AMK	Amikacin
CIP	Ciprofloxacin	CPM	Cefepime
CRO	Ceftriaxone	IMI	Imipenem
DXT	Doxycycline	MEM	Meropenem
GM	Gentamicin	NI	Nitrofurantoin
TS	Trimethoprim-Sulfamethoxazole		



Figure 2. MDR resistance patterns of most common isolated ESBL-E species to different antimicrobial agents (n[>]2)
Key:

AM	Amoxicillin	AMK	Amikacin
CIP	Ciprofloxacin	CPM	Cefepime
CRO	Ceftriaxone	IMI	Imipenem
DXT	Doxycycline	MEM	Meropenem
GM	Gentamicin	NI	Nitrofurantoin
TS	Trimethoprim-Sulfamethoxazole		

community patients and rectal swabs; 64% (n=47) and 53% (n=39), respectively. The difference between carriage of ESBL-E in community and hospital patients was statistically significant (P=0.05). Further, the type of clinical specimen and surgery performed in the past 3 months was significantly associated with the presence of ESBL P=0.006 and P=0.02, respectively (Table 1). *E. coli* was the most predominant ESBL-E isolated in community settings (70%, 33/47) and *Klebsiella* spp. was the most frequent isolated bacteria in hospital settings (35%, 9 of 26). *E. coli* accounted for 74% (29/39) and 50% (4/8) of isolates from rectal swab and urine, respectively, while 35% (9/26) of wound swab isolates were *Klebsiella* spp.

Antimicrobial susceptibility testing patterns of ESBL-E isolates

The average rate of resistance (mean ±SD) to antimicrobial agents tested was 49.2 (±33.7) (range 1.4%–92%), Figure 1. The highest resistance rate of all ESBL-E was found in trimethoprim-sulfamethoxazole

(92%) followed by amoxicillin and ceftriaxone (79%), doxycycline (75%) and gentamicin (72%). The high level of resistance against trimethoprim-sulfamethoxazole, ceftriaxone, amoxicillin, doxycycline and gentamicin observed in this study are comparable with findings of previous studies. In the past, high rates of resistance have been observed for amoxicillin (87%), piperacillin (74%) and trimethoprim-sulfamethoxazole (73%) (Gangoue-Pieboji et al., 2006). In addition, our results confirm the high resistance reported previously for cotrimoxazole, amoxicillin, gentamicin, chloramphenicol and ceftazidime in the same setting (Gray et al., 2006). In Africa, and Malawi in particular, trimethoprim-sulfamethoxazole, amoxicillin, ceftriaxone and doxycycline are extensively used. They are available at an affordable cost over the counter even though they are prescription-only medicines, possibly explaining their high resistance rates.

We found the highest antimicrobial susceptibility rate of ESBL-E isolates was to carbapenems; on average, meropenem was 93% active against isolates and imipenem was 91% active. The average rate of

antimicrobial susceptibility of all isolates to aminoglycosides was relatively high compared with cephalosporins and quinolones. All isolates were 85% susceptible to amikacin compared with 50% susceptibility to cefepime and 34% to ciprofloxacin (Figure 1). When comparing the susceptibility of different species to antimicrobials, we found that *E. coli*, *Klebsiella* spp., *Serratia* spp. and *Yersinia enterocolitica* were 100% susceptible to imipenem. For Meropenem, *E. coli* and *Serratia* spp. were 100% susceptible, *Klebsiella* spp. was 92% susceptible, and *Y. enterocolitica* was 80% susceptible (figure 2). Amikacin was 100% active against *Y. enterocolitica*, 84% active against *E. coli*, 80% active against *Enterobacter* spp. and *Serratia* spp., and 77% active against *Klebsiella* spp. (Figure 2). Our findings are consistent with a study that found a 40%–100% susceptibility rate of ESBL-E to carbapenems (Gangoue-Pieboji et al., 2006; Ghadiri et al., 2012). Because carbapenems are currently the last drugs of choice to treat infections caused by ESBL-producing pathogens and are not readily available in Malawi, the higher susceptibility of ESBL-E isolates to carbapenems found in this study was predictable. Nevertheless, further investigation is required to elucidate carbapenem resistance rates among ESBL-E isolates in the same setting to provide a clear overview.

Multi-drug resistance patterns of the most common isolated ESBL-E species to different antimicrobial agents

In our study, there was a high prevalence of multi-drug resistance (MDR) in ESBL-E. The highest MDR was found in *E. coli* and the least in *Serratia* spp. *E. coli* was 89% resistant to ceftriaxone, trimethoprim-sulfamethoxazole (87%), amoxicillin (81%), doxycycline (79%), gentamicin (76%) and ciprofloxacin (63%). All *Klebsiella* spp. were resistant to trimethoprim-sulfamethoxazole, 84% to amoxicillin and 75% to doxycycline. MDR profile of ESBL-E isolates is presented in Figure 2. The high prevalence of MDR in clinical isolates of *Enterobacteriales* has been reported previously (Malik and Elhag, 2019; Zavala-Cerna et al., 2020). One possible explanation for the high MDR rates found in the present study could be that all bacteria spp. subjected to AST were ESBL producers, which may confer resistance to a wide range of antimicrobial agents. The extensive use of amoxicillin, ampicillin and ceftriaxone in Malawi as the only cephalosporins available in the past could explain the development of resistance against these drugs (Gray et al., 2006).

Limitations

Our study could have overestimated the resistance rates of ESBL-E because it was conducted in a single Malawian city and the number of ESBL-E was not large enough to represent the epidemiology of ESBLs in the country as a whole. Nevertheless, the method used to phenotypically screen and confirm ESBL producers in this study could increase the accuracy and discriminatory power for detecting ESBL bacteria.

Conclusions

We found a high rate of resistance against antimicrobial agents tested. The majority of ESBL-Es were MDR. We recommend routine AST testing and screening for ESBLs to guide patient management and that a surveillance system is put in place to monitor AMR in Malawi.

Ethical considerations

The study was approved by the University of Malawi College of Medicine Research Ethics Committee (COMREC) with approval No. P.07/19/2720 of 22 November 2019. The Blantyre District health office provided permission to access hospitals for data collection. Written informed consent was obtained from patients before they were enrolled in the study. For patients without formal education, informed consent was obtained from legally authorised representatives.

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Conflict of interest

The authors declare that they have no competing interests

Author's contributions

OGO, RSM, SA and SFR conceived and designed the study. OGO, RSM and TSN collected the data. OGO analysed, interpreted the data and drafted the article. SA, SFR and TSN critically revised the article for important intellectual content. All authors approved the final version to be submitted for publication.

References

- Bitew A, Tsige E. High Prevalence of Multidrug-Resistant and Extended-Spectrum β -Lactamase-Producing Enterobacteriaceae: A Cross-Sectional Study at Arsho Advanced Medical Laboratory, Addis Ababa, Ethiopia. *J Trop Med* 2020;2020:1–7. doi:10.1155/2020/6167234.
- Bush K, Jacoby GA. Updated functional classification of β -lactamases. *Antimicrob Agents Chemother* 2010;54:969–76. doi:10.1128/AAC.01009-09.
- Cantón R, Novais A, Valverde A, Machado E, Peixe L, Baquero F, et al. Prevalence and spread of extended-spectrum β -lactamase-producing Enterobacteriaceae in Europe. *Clin Microbiol Infect* 2008;14:144–53. doi:10.1111/J.1469-0691.2007.01850.X.
- Carter MW, Oaktton KJ, Warner M, Livermore DM. Detection of extended-spectrum beta-lactamases in klebsiellae with the Oxoid combination disk method. *J Clin Microbiol* 2000;38:4228–32.
- Coque TM, Baquero F, Canton R. Increasing prevalence of ESBL-producing enterobacteriaceae in Europe. *Eurosurveillance* 2008;13:19044. doi:10.2807/ese.13.47.19044-en.
- Gangoue-Pieboji J, Koulla-Shiro S, Ngassam P, Adiojo D, Ndumbe P. Antimicrobial activity against gram negative bacilli from yaounde central hospital. *Cameroon Afr Heal Sci* 2006;6:232–5.
- Gaynes R, Edwards JR. Overview of nosocomial infections caused by gram-negative bacilli. *Clin Infect Dis* 2005;41:848–54. doi:10.1086/432803.
- Ghadiri H, Vaez H, Khosravi S, Soleymani E. The antibiotic resistance profiles of bacterial strains isolated from patients with hospital-acquired bloodstream and urinary tract infections. *Crit Care Res Pract* 2012;2012:1–6. doi:10.1155/2012/890797.
- Gray KJ, Wilson LK, Phiri A, Corkill JE, French N, Hart CA. Identification and characterization of ceftriaxone resistance and extended-spectrum β -lactamases in Malawian bacteraemic Enterobacteriaceae. *J Antimicrob Chemother* 2006;57:661–5. doi:10.1093/jac/dkl037.
- Jean SS, Hsueh PR. High burden of antimicrobial resistance in Asia. *Int J Antimicrob Agents* 2011;37:291–5. doi:10.1016/j.ijantimicag.2011.01.009.
- Katakweba AAS, Muhairwa AP, Lupindu AM, Damborg P, Rosenkrantz JT, Minga UM, et al. First Report on a Randomized Investigation of Antimicrobial Resistance in Fecal Indicator Bacteria from Livestock, Poultry, and Humans in Tanzania. *Microb Drug Resist* 2018;24:260–8. doi:10.1089/mdr.2016.0297.
- Malik IA, Elhag KM. Characterisation of extended-spectrum b-lactamases among multidrug resistant Enterobacteriaceae from Sudan. *J Pure Appl Microbiol* 2019;13:61–8. doi:10.22207/JPAM.13.1.06.
- Marshall BM, Levy SB. Food animals and antimicrobials: Impacts on human health. *Clin Microbiol Rev* 2011;24:718–33. doi:10.1128/CMR.00002-11.
- Moglad EH. Antibiotics profile, prevalence of extended-spectrum beta-lactamase (ESBL), and multidrug-resistant Enterobacteriaceae from different clinical samples in Khartoum State, Sudan. *Int J Microbiol* 2020;2020:1–6. doi:10.1155/2020/8898430.
- Musicha P, Cornick JE, Bar-zeev N, French N, Masesa C, Denis B, et al. Trends in antimicrobial resistance in bloodstream infection isolates at a large urban hospital in Malawi (1998–2016): a surveillance study. *Lancet Infect Dis* 2017;17:1042–52. doi:10.1016/S1473-3099(17)30394-8.
- Rawat D, Nair D. Extended-spectrum β -lactamases in gram negative bacteria. *J Glob Infect Dis* 2010;2:263. doi:10.4103/0974-777x.68531.
- Reinert RR, Low DE, Rossi F, Zhang X, Wattal C, Dowzicky MJ. Antimicrobial susceptibility among organisms from the Asia/Pacific Rim, Europe and Latin and North America collected as part of TEST and the in vitro activity of tigecycline. *J Antimicrob Chemother* 2007;60:1018–29. doi:10.1093/jac/dkm310.
- Roca I, Akova M, Baquero F, Carlet J, Cavalieri M, Coenen S, et al. The global threat of antimicrobial resistance: Science for intervention. *New Microbes New Infect* 2015;6:22–9. doi:10.1016/j.nmni.2015.02.007.
- Sader HS, Jones RN, Gales AC, Silva JB, Pignatari AC. SENTRY antimicrobial surveillance program report: Latin American and Brazilian results for 1997 through 2001. *Braz J Infect Dis* 2004;8:25–79. doi:10.1590/S1413-86702004000100004.
- Søråas A, Sundsfjord A, Sandven I, Brunborg C, Jenum PA. Risk Factors for Community-Acquired Urinary Tract Infections Caused by ESBL-Producing Enterobacteriaceae

- A Case-Control Study in a Low Prevalence Country. *PLoS One* 2013;8:69581. doi:[10.1371/journal.pone.0069581](https://doi.org/10.1371/journal.pone.0069581).
- Tacconelli E, Carrara E, Savoldi A, Harbarth S, Mendelson M, Monnet DL, et al. Discovery, research, and development of new antibiotics: the WHO priority list of antibiotic-resistant bacteria and tuberculosis. *Lancet Infect Dis* 2018;18:318–27. doi:[10.1016/S1473-3099\(17\)30753-3](https://doi.org/10.1016/S1473-3099(17)30753-3).
- Tumbarello M, Trecarichi EM, Bassetti M, De Rosa FG, Spanu T, Di Meco E, et al. Identifying patients harboring extended-spectrum- β -lactamase-producing Enterobacteriaceae on hospital admission: Derivation and validation of a scoring system. *Antimicrob Agents Chemother* 2011;55:3485–90. doi:[10.1128/AAC.00009-11](https://doi.org/10.1128/AAC.00009-11).
- WHO, 2017. <http://www.who.int/medicines/publications/global-priority-list-antibiotic-resistant-bacteria/en/> (accessed June 23, 2020).
- Zavala-Cerna MG, Segura-Cobos M, Gonzalez R, Zavala-Trujillo IG, Navarro-Perez SF, Rueda-Cruz JA, et al. The Clinical Significance of High Antimicrobial Resistance in Community-Acquired Urinary Tract Infections. *Can J Infect Dis Med Microbiol* 2020;2020:1–7. doi:[10.1155/2020/2967260](https://doi.org/10.1155/2020/2967260).