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PERSPECTIVES

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Know your Microbe Foes: The Role of Surveillance in Combatting Antimicrobial Resistance

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Antibiotic-resistant organisms (AROs) are difficult and costly to treat, associated with high mortality rates, and are on the rise. In the United States, there is limited tracking of AROs, which can contribute to transmission and inhibit infection prevention interventions. Surveillance is limited by a lack of standardized methods for colonization screening and limited communication regarding patient ARO-status between healthcare settings. Some regional surveillance and reporting efforts are in place for extensively-resistant AROs such as carbapenem-resistant Enterobacterales (CRE), but need to be further expanded nationwide and to include other AROs such as extended-spectrum β-lactamase (ESBL) producing organisms. Increased surveillance of ARO infections and colonization will inform future targeted intervention and infection prevention strategies.

INTRODUCTION

Infections due to antibiotic-resistant organisms (AROs) are costly, have fewer treatment options, and have high rates of morbidity and mortality. The Centers for Disease Control and Prevention (CDC) estimates more than 2.8 million infections with AROs occur in the United States each year with more than 35,000 deaths [1].

Carbapenem-resistant Enterobacterales (CRE) and extended-spectrum β-lactamase producing Enterobacterales (ESBL-E) are AROs which pose urgent and serious threats, according to the CDC's 2019 Antibiotic Resistance Threats Report [1]. CRE are resistant to at least one carbapenem antibiotic and may be resistant to additional classes of antibiotics, leaving few treatment options. ESBL-E harbor genes which encode extended-spectrum β-lactamases. For surveillance purposes, the CDC phenotypically defines ESBL-E as resistant to at least one extended-spectrum cephalosporin (ceftazidime, cefotaxime, or ceftriaxone) [2]. As with CRE, these bacteria can

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Abbreviations: ARLN, Antibiotic Resistance Laboratory Network; ARO, antibiotic-resistant organism; ASC, active surveillance cultures; CDC, Centers for Disease Control and Prevention; CRAB, carbapenem-resistant *Acinetobacter baumanii*; CRE, carbapenem-resistant Enterobacterales; EIP, Emerging Infections Program; ESBL, extended-spectrum β-lactamase; ESBL-E, extended-spectrum β-lactamase producing Enterobacterales; ESC, extended-spectrum cephalosporin; HAI, healthcare-associated infection; ICD-10, *International Classification of Diseases, Tenth Revision*; MRSA, methicillin-resistant *Staphylococcus aureus*; MuGSI, Multi-site Gram-negative Surveillance Initiative; NHSN, National Healthcare Safety Network; UTI, urinary tract infection; VRE, vancomycin-resistant Enterococci; XDRO, extensively drug resistant organism.

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be resistant to other antibiotic classes, which can limit treatment. Bacteria in the Enterobacterales order, examples of which include *Escherichia coli* and *Klebsiella pneumoniae*, can cause a variety of life-threatening infections such as urinary tract infections (UTIs), blood stream infections (BSIs), and pneumonia. In the US alone, CRE and ESBL-E infections resulted in an estimated 1,100 and 9,100 deaths, respectively, in 2017 [1]. People can also be asymptomatically colonized with CRE, ESBL-E, and other AROs.

Microorganisms, including AROs, can transfer from person-to-person as well as between people and the environment [3,4]; therefore, surveillance is critical to stop transmission and create appropriate interventions. Surveillance for many AROs is limited, which may lead to further dissemination within hospitals, between hospitals, and throughout the community. This perspective will focus on ARO colonization and infection surveillance, with a particular emphasis on CRE and ESBL-E, specifically ESBL-*E. coli*.

TOPICS

ARO Infection Surveillance and Reporting

Infections due to AROs are the result of a clinical syndrome due to the presence of an ARO. While CRE infections have remained relatively stable since 2013, ESBL-E infections have increased, both in the hospital setting and in the community [1]. More public health measures exist for CRE surveillance and reporting, yet there is a marked gap in response for ESBL-E. Standardized methods and support for detecting ESBL-E colonization, tracking ESBL-E infections, and preventing ESBL-E transmission are lacking. For instance, there are no current recommendations for standardized universal screening for ESBL-E in the acute care setting. This hinders the ability to track and prevent ESBL-E transmission. More effort is needed to better understand and prevent ARO infections in healthcare and community settings.

The number of infections in both hospital and outpatient settings due to AROs is difficult to assess due to a lack of mechanism for reporting and tracking. In order to bill for hospitalizations, healthcare systems use national medical coding systems, such as the *International Classification of Diseases, Tenth Revision* (ICD-10). Infections as a diagnosis are generally well-coded, and when a patient has an infection, a coder assigns an appropriate ICD-10 code, sometimes with additional codes or modifiers to report the organism and antimicrobial resistance. However, both organism and drug resistance coding are frequently limited or inaccurate due to poor coding practices [5]. In one study, only 65.4% of ARO *Enterobacteriaceae* had the properly coded organism, and 3.3% had an ARO code [5]. Therefore, the use of hospital administrative data alone cannot reliably assess the frequency of AROs in hospitals. While organism and susceptibility pattern data can be attained through hospital microbiology laboratories, these data are not readily reported outside of the local level, and thus are of limited utility for nationwide tracking.

Limited surveillance and communication of a patient's ARO status occurs across healthcare networks. Patients often visit multiple healthcare facilities; however, information regarding a patient's ARO status may not be communicated across healthcare facilities as this is generally not required or regulated. For instance, during a CRE outbreak event in Chicago, patients of a particular hospital later visited other hospitals, including several where CRE was then later reported [6]. The outbreak was trackable due to the presence of New Delhi metallo-β-lactamase (NDM), a rare carbapenemase in Chicago at the time of the study. The hospital which shared the most patients from the original outbreak location had the highest incidence of outbreak-associated CRE [6]. This highlights the need to set up more regional surveillance of AROs to prevent dissemination among healthcare networks. Illinois has mandated CRE reporting through its extensively drug resistant organism (XDRO) registry, thus improving CRE surveillance [7,8]. Additionally, the registry works to improve inter-facility communication as healthcare facilities can use the registry to determine if a patient has previously had CRE. Systems, such as the Illinois XDRO registry described above, which promote communication between healthcare facilities regarding ARO-status are not routine. Enhanced ARO communication would allow for potential interventions such as contact isolation, enhanced environmental hygiene, or additional personal protective equipment requirements to prevent ARO transmission to others.

On a broader level, there is a lack of national reporting and surveillance of AROs. Carbapenemase-producing CRE has been a nationally notifiable organism to the CDC's National Notifiable Diseases Surveillance System (NNDSS) since 2018 [9]. As a notifiable organism, states voluntarily provide case surveillance data [10]. The CDC's Antibiotic Resistance Laboratory Network (ARLN) tracks carbapenemases and performs CRE colonization screening, if requested, following reported CRE-infections [11], but does not conduct CRE surveillance [12]. Other AROs, such as ESBL-E, are not currently notifiable at the national level.

Due to the lack of ARO infection tracking, incidences of ARO infection can be difficult to determine. As of July 2019, the Multi-site Gram-negative Surveillance Initiative (MuGSI) [2], an activity of the Healthcare-associated Infection Community Interface component of the CDC's Emerging Infections Program (EIP), began conducting

ESBL-E population- and laboratory-based surveillance. In an EIP pilot study, which occurred over a 3-month period in 2017 in select counties in New Mexico, New York, and Tennessee, Duffy et al. reported an overall ESBL-E infection incidence of 199.7 per 100,000 population [13]. Forty-seven percent of the ESBL-E infection cases in the study were considered community-associated [13], pointing to a need to strengthen community and environmental surveillance strategies. Importantly, MuGSI ESBL-E infection surveillance occurs across geographic regions, but as of 2022, is still limited in scope, occurring in one county each in Colorado, Maryland, New Mexico, and New York, two counties in Georgia, and four counties in Tennessee [2]. MuGSI also tracks CRE and carbapenem-resistant *Acinetobacter baumanii*.

The CDC's National Healthcare Safety Network (NHSN) tracks the following healthcare-associated infections (HAIs) in inpatients: central line-associated blood stream infections, catheter-associated UTIs, surgical site infections, some ventilator-associated events, methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremia, and *Clostridioides difficile* events [14]. For 2020, the NHSN reported 24.7% of *E. coli* isolates were resistant to extended-spectrum cephalosporins (ESCs) with an estimated 24.4% of isolates resistant in pediatric populations and 24.7% resistant in adults [15,16]. The NHSN data does not include all types of HAIs, nor does it encompass community-level data. Further, the data reported to NHSN may vary depending on state reporting requirements [17]. However, what these proportions show is that some AROs, including ESC-resistant *E. coli* (ie, potential ESBL-*E. coli*), are readily found in healthcare settings. Therefore surveillance and interventions are needed to prevent the spread of AROs in hospitals and beyond.

The SENTRY Antimicrobial Surveillance Program was established in 1997 and tracks pathogens and antimicrobial resistance trends from healthcare-associated and community-onset infections at participating centers worldwide [18]. In 2016, the prevalence of β-lactamase resistance genes among *E. coli* isolates was 11.6% for *E. coli*-causing UTIs and 16.1% for *E. coli*-causing BSIs among hospitalized patients from 36 states [19]. Of note, the SENTRY program has publicly available data, which is stratified by US census regions [20]; however, it is unclear which states or cities have hospitals participating as the SENTRY program is a service offered through JMI laboratories.

ARO Colonization Surveillance

In contrast to ARO infection, ARO colonization is asymptomatic. Depending on the ARO, colonization can occur at various body sites (eg, skin, gut, nares), and often precedes infection [21-23]. In particular, the gut can serve as a reservoir for AROs [22]. Gut colonization with ESBL-*E. coli* has been linked to increased risk for ESBL- *E. coli* UTIs [24]. The CDC estimates that 47% of ESBL-E infections are community-associated, making the spread of ESBL-E challenging to detect and contain [1]. Colonization surveillance across regions and demographics could provide insight into both community and healthcare-associated spread of AROs.

Globally, ESBL-E intestinal colonization prevalence is increasing worldwide, although the prevalence varies by region [25,26], with Southeast Asia noting the highest intestinal carriage of ESBL-*E. coli* among healthy individuals (27% prevalence) [25]. Fecal colonization surveillance in the US is limited, particularly among healthy individuals. In a 2004 study, which took place in Minnesota and Wisconsin, authors reported 0% and 2% prevalence of cephalosporin-resistant *E. coli* in 100 healthy vegetarians and 567 hospitalized patients, respectively [27]. In a 2011 study, 2% of 101 US military personnel based in Texas were colonized with multi-drug resistant *E. coli*, compared to 11% of 100 Afghanistan-based US military personnel [28], suggesting environmental risk factors for ARO colonization. Further, in a small 2012 study comprised of 60 travelers attending a New York travel medicine clinic, 1.7% of participants were colonized with ESBL-*E. coli* prior to traveling, and 25% of participants were colonized post-travel [29]. Given the fast-paced changing landscape of antimicrobial resistance, with estimated ESBL-*E. coli* or ESBL-E prevalence increases of 1.5-5.4% per year among healthy individuals [25,26], more current studies are needed to determine present-day ESBL-*E. coli* carriage throughout the US.

Data on ESBL-E colonization in the pediatric setting are even more limited. In a large pediatric multi-state study involving California, Texas, and Tennessee from 2013-2015, authors reported a 3.5% prevalence of ESBL-*E. coli* among 519 children, ages 14 days to 14 years [30]. It is unclear whether children in the US have higher or lower ESBL-E colonization than healthy adults.

Comparatively more studies are available, some highlighted here, regarding ARO colonization in long-term care facilities, nursing homes, and long-term acute care hospitals. In a 2016-2017 SHIELD Orange County point prevalence study from 18 nursing homes in Southern California, ESBL-E carriage was 34% (range 0-66%) [31]. The study also reported colonization prevalence of other AROs, specifically CRE, vancomycin-resistant Enterococci (VRE) and MRSA [31]. Like the SHIELD study, other groups have also taken a more regional approach to examine ARO colonization across healthcare facilities. In the Washington D.C. area, CRE colonization prevalence was 7% among seven long-term care facilities, with 5% prevalence among the area's acute-care hospitals. ESBL-E prevalence was not assessed at any

of the sites [32]. Therefore, some regions are beginning to survey ARO colonization across healthcare settings, including nursing homes; however, surveillance timing and methods are not standardized. Non-standardized surveillance approaches may be limited to isolated, single time point research studies and/or restricted to tackling surveillance of only the most extensively-drug resistant organisms such as CRE.

Domestic pets and farm animals can also be colonized with AROs. Cattle, pigs, sheep, poultry, and dogs have all been colonized with ESBL-*E. coli* [33,34]. The significance of animal reservoirs and routes of transmission (people to animals or the environment and vice versa) are still being determined. Surveillance studies incorporating a One Health approach (people, animals, and the environment) can aid in this assessment. In a study on Reunion Island (La Réunion, Département et Région d'Outre-Mer, France), located in the Southwest Indian Ocean, Miltgen et al. found a marked difference in ESBL-*E. coli* sequence types and resistance genes from animal sources (ST57, ST156; $bla_{\text{CTX-M-1}}$) compared to human sources (ST131, ST38, and ST10; $bla_{\text{CTXM-15}}$, $bla_{\text{CTX-M-27}}$, and $bla_{\text{CTX-M-14}}$), suggesting that in this setting animal-to-human transmission is not driving ESBL-*E. coli* colonization or infections in people [34]. Of note, this study did not include isolates from domestic animals living in shared spaces with people, but instead focused on cattle, pigs, poultry, and small ruminants [34].

ESBL-E Colonization and Infection Risk Factors

Both global and US-based studies have revealed potential risk factors for ESBL-E colonization in people. Risk factors for ESBL-E colonization in healthy individuals globally include prior antibiotic use (past 4 or 12 months) and international travel [26]. In the SHIELD study, ESBL-E colonization was associated with GI devices, a history of ESBL-E, and history of VRE [31]. In a systematic review and meta-analysis of >29,000 patients, gastric acid suppression was associated with CRE, ESBL, and VRE colonization [35], although infection data from UTIs were also included in the analysis. Household contacts are also an important consideration as patients can remain colonized, and strains can be shared among household contacts. In a study involving patients with community-associated ESBL-E infections in Spain, 16.7% of patients' household members were also colonized [36].

Colonization is a risk factor for ESBL-E infection [23,37,38]. In one study, wherein patients were screened for ESBL-E on admission to the ICU, 25% of the ESBL-E-colonized patients had a positive ESBL-E clinical culture during their hospital stay compared to 0.6% of those not colonized with ESBL-E [38]. Other risk factors for ESBL-E infection include prior antibiotic use [39,40], UTI history [39], chronic indwelling vascular hardware [40], age ≥43 years [40], recent hospitalization [40,41], and residence in a long-term care facility [41].

While many healthcare and environmental risk factors are now known, key epidemiological data are missing. It is unclear whether certain regions of the US have more ESBL-E colonization and infection or if certain populations (eg, healthcare personnel, agricultural workers, those living in shared housing) have increased risk.

ESBL-E Strain Characteristics

Ideally, increased ARO surveillance and reporting would be coupled with genome data to allow rapid early detection of new or emerging antimicrobial resistance genes and strains. Strain data is important for outbreak tracing and for potential differences in clinical outcomes. Worldwide among ESBL-E, CTX-M-type β-lactamases predominate, particularly those encoded by $bla_{\text{CTX-M-15}}$ and $bla_{\text{CTX-M-14}}$, with $bla_{\text{CTM-M-27}}$ emerging [42,43]. These ESBL-genes are often plasmid associated, which is concerning, as plasmids and their associated antibiotic-resistance genes are transferable between strains or even across larger taxonomical families (eg, all *Enterobacteriaceae*). ST131 is the *E. coli* strain most associated with CTX-M carriage. Among a subset of *E. coli* isolates that were sequenced in the 2017 EIP surveillance study, most isolates harbored CTX-M-type β-lactamases (98%), and ST131 was the most common strain type (53.6%) [13]. Similarly, the SENTRY program determined ST131 accounted for 53.6% of *E. coli* BSI isolates and 58.2% of UTI isolates from hospitalized patients throughout the US, with nearly all ESBL-*E. coli* isolates carrying CTX-M-type β-lactamases (99.3%) [19]. However, given the lack of community ESBL- *E. coli* colonization data, it is unclear if ST131 is the predominant ESBL-*E. coli* colonizing strain in communities in the US and which colonizing strains and plasmids are more associated with infection or transmission. Knowing more about the strains of ESBL-*E. coli* colonizing the gut and their associations with infection may help develop strain-specific strategies for prevention. For other AROs, the microbiome and metabolome play a role in colonization resistance, but a recent report from the Netherlands suggests this may not be the case for ESBL-*E. coli* [44].

Future Research and Potential Interventions

The CDC has outlined multiple approaches for managing AROs, broadly grouped into categories of administrative support, judicious use of antimicrobials, surveillance, standard and contact precautions, environmental measures, education, and decolonization [45] Successful ARO control may require a multi-category approach, and efforts specifically targeting one ARO may also af-

fect others. In one study targeting CRE-colonization in long-term acute care hospitals, not only was carbapenemase-producing *Klebsiella pneumoniae* colonization and infection decreased during the multi-faceted intervention, but so was all-cause bacteremia [46].

For ESBL-E infections, surveillance programs such as the SENTRY program and MuGSI are making strides in assessing ESBL-E infection surveillance nationwide. Future research is needed to determine the most effective interventions that prevent ARO dissemination in hospitals and the community. Additionally, collaborative approaches should be standardized and communication regarding the ARO-status among transferred patients amongst facilities should be enhanced, allowing facilities the opportunity to take infection prevention precautions.

Colonization surveillance is key to identifying and containing ESBL-E spread in the US. Active surveillance cultures (ASC) can identify people who are asymptomatically colonized with AROs in order to implement preventative measures. This may be limited due to cost and personnel resources, and intervention and surveillance strategies may differ depending on whether the community is a high- or low-endemic setting. In hospital settings, ASC colonization screening could take place upon hospital admission followed by increased infection prevention measures (eg, isolation precautions, single-use equipment) to prevent transfer between patients and healthcare personnel. For those who are colonized and most at-risk, microbiota-based strategies may be considered such as fecal microbiota transplant or engineered probiotics to prevent or reverse colonization.

More complete epidemiological studies will foster targeted interventions. Given some of the known risk factors for ARO and ESBL-E colonization and spread, specific interventions and practices could be established for certain at risk groups such as international travelers, residents of long-term care facilities, or household contacts. Antibiotic use is a risk factor, therefore antimicrobial stewardship is necessary in inpatient and outpatient settings. Future research is needed to find factors which protect against ARO colonization among those who are not yet colonized, and how to prevent community spread and progression to infection in those who are. Strain-specific data may be able to provide some insight into the emergence of new strains or strains of highest concern, which will allow a faster public health response. Some AROs such as ESBL-E also have potential reservoirs in the environment and animals Therefore, a multisector approach, which incorporates surveillance of people, animals, and the environment would assist in targeting prevention of transmission of AROs from different sources. For ESBL-E, present studies suggest that interventions with people, not food or agriculture would be most effective [47].

CONCLUSIONS AND OUTLOOK

ESBL-E colonization and infection incidence are increasing [25,48]; however, gaps remain in ESBL-E infection surveillance, and ESBL-E colonization surveillance is less standardized. Limited surveillance and reporting coupled with lack of interventions in the United States and worldwide will only lead to further ESBL-E transmission. While this perspectives piece has primarily focused on ESBL-E, the need for surveillance and reporting of both infections and colonization could be broadly applied to other AROs. It is time to accelerate testing of ARO colonization and infection prevention strategies. As many people are asymptomatically colonized and colonization does not pose an immediate risk, the challenge will be to find a strategy that is cost-effective, scalable, and where the benefits outweigh potential risks. To combat antimicrobial resistance, we first need to better understand the scope of the problem, from colonization prevalence to strain data, to best target infection prevention strategies for those most at-risk.

REFERENCES

1. CDC. Antibiotic Resistance Threats in the United States, 2019. Atlanta (GA): U.S. Department of Health and Human Services, CDC; 2019.
2. CDC. Multi-site Gram-negative Surveillance Initiative Atlanta, GA: U.S. Centers for Disease Control and Prevention; 2022 [updated February 25, 2022, May 13, 2022]. Available from: https://www.cdc.gov/hai/eip/mugsi.html
3. Redmond SN, Pearlmutter BS, Ng-Wong YK, Alhmidi H, Cadnum JL, Silva SY, et al. Timing and route of contamination of hospitalized patient rooms with healthcare-associated pathogens. Infect Control Hosp Epidemiol. 2021;42(9):1076-81. Epub 20210112. https://doi.org/10.1017/ice.2020.1367.
4. Chemaly RF, Simmons S, Dale C Jr, Ghantoji SS, Rodriguez M, Gubb J, et al. The role of the healthcare environment in the spread of multidrug-resistant organisms: update on current best practices for containment. Ther Adv Infect Dis. 2014 Jun;2(3-4):79–90.
5. Burnham JP, Kwon JH, Babcock HM, Olsen MA, Kollef MH. ICD-9-CM Coding for Multidrug Resistant Infection Correlates Poorly With Microbiologically Confirmed Multidrug Resistant Infection. Infect Control Hosp Epidemiol. 2017;38(11):1381-3. Epub 20170905. https://doi.org/10.1017/ice.2017.192.
6. Ray MJ, Lin MY, Tang AS, Arwady MA, Lavin MA, Runningdeer E, et al. Regional Spread of an Outbreak of Carbapenem-Resistant Enterobacteriaceae Through an Ego Network of Healthcare Facilities. Clin Infect Dis. 2018 Jul;67(3):407–10.
7. Trick WE, Lin MY, Cheng-Leidig R, Driscoll M, Tang AS, Gao W, et al. Electronic Public Health Registry of Extensively Drug-Resistant Organisms, Illinois, USA. Emerg Infect Dis. 2015 Oct;21(10):1725–32.
8. MRAIA. XRDO Registry Chicago, IL: Extensively Drug

Resistant Organism Registry; 2022 [June 27, 2022]. Available from: https://www.xdro.org/
9. CDC. Carbapenemase Producing Carbapenem-Resistant Enterobacteriaceae (CP-CRE) 2018 Case Definition Atlanta, GA: U.S. Centers for Disease Control and Prevention; 2021 [updated April 16, 2021, June 27, 2022]. Available from: https://ndc.services.cdc.gov/case-definitions/carbapenemase-producing-carbapenem-resistant-enterobacteriaceae-2018/
10. CDC. What is Case Surveillance? Atlanta, GA: U.S. Centers for Disease Control and Prevention; 2021 [updated September 29, 2021, June 27, 2022]. Available from: https://www.cdc.gov/nndss/about/index.html
11. CDC. Request CDC's AR Lab Network Test to Prevent the Spread of Emerging Carbapenem Resistance. In: Network AL, Prevention. U.S. Centers for Disease Control and Prevention, Control, editors. Atlanta, GA: U.S. Centers for Disease Control and Prevention. p. 1.
12. CDC. Tracking CRE in the United States Atlanta, GA: U.S. Centers for Disease Control and Prevention; 2020 [updated January 2, 2020, June 27, 2022]. Available from: https://www.cdc.gov/hai/organisms/cre/trackingcre.html
13. Duffy N, Karlsson M, Reses HE, Campbell D, Daniels J, Stanton RA, et al. Epidemiology of extended-spectrum beta-lactamase-producing Enterobacterales in five US sites participating in the Emerging Infections Program. Infect Control Hosp Epidemiol. 2022:1-9. Epub. 2017;20220214: https://doi.org/10.1017/ice.2021.496.
14. CDC. 2020 National and State Healthcare-Associated Infections Progress Report: Executive Summary. Atalanta (GA): U.S. Centers for Disease Control and Prevention; 2021.
15. CDC. Cephalosporin-resistant *E. coli* Atlanta, GA: U.S. Centers for Disease Control and Prevention; 2022 [May 10, 2022]. Available from: https://cdc-earwig.datawheel.us/profile/antibiotic-resistance/cephalosporin-resistant-ecoli
16. CDC. Antibiotic Resistance & Patient Safety Portal: Antibiotic Resistance HAI Data: Phenotype Analytical Definitions. In: Prevention. U.S. Centers for Disease Control and Prevention, editor. Atlanta, GA: U.S. Centers for Disease Control and Prevention; 2021.
17. CDC. States with HAI Reporting Mandates Atlanta, GA: U.S. Centers for Disease Control and Prevention; 2021 [updated June 29, 2021 June 7, 2022]. Available from: https://www.cdc.gov/hai/state-based/required-to-report-hai-nhsn.html
18. Fuhrmeister AS, Jones RN. The Importance of Antimicrobial Resistance Monitoring Worldwide and the Origins of SENTRY Antimicrobial Surveillance Program. Open Forum Infect Dis. 2019;6(Suppl 1):S1-S4. Epub 20190315. https://doi.org/10.1093/ofid/ofy346.
19. Mendes RE, Jones RN, Woosley LN, Cattoir V, Castanheira M. Application of Next-Generation Sequencing for Characterization of Surveillance and Clinical Trial Isolates: Analysis of the Distribution of beta-lactamase Resistance Genes and Lineage Background in the United States. Open Forum Infect Dis. 2019;6(Suppl 1):S69-S78. Epub 20190315. https://doi.org/10.1093/ofid/ofz004.
20. Laboratories JM. Sentry MVP Microbiology Visualization Platform North Liberty. Iowa: JMI Laboratories; 2022. [June 2, 2022], Available from https://sentry-mvp.jmilabs.com/app/sentry-public
21. Davis KA, Stewart JJ, Crouch HK, Florez CE, Hospenthal DR. Methicillin-resistant *Staphylococcus aureus* (MRSA) nares colonization at hospital admission and its effect on subsequent MRSA infection. Clin Infect Dis. 2004;39(6):776-82. Epub 20040827. https://doi.org/10.1086/422997.
22. Anthony WE, Burnham CD, Dantas G, Kwon JH. The Gut Microbiome as a Reservoir for Antimicrobial Resistance. J Infect Dis. 2021 Jun;223(12 Suppl 2):S209–13.
23. Ford CD, Lopansri BK, Coombs J, Gouw L, Asch J, Hoda D. Extended spectrum cephalosporin resistant enterobacteriaceae carriage and infection in patients admitted with newly-diagnosed acute leukemia. Am J Infect Control. 2022 May;20220527:S0196-6553(22)00443-6. https://doi.org/10.1016/j.ajic.2022.05.019.
24. Ruppe E, Lixandru B, Cojocaru R, Buke C, Paramythiotou E, Angebault C, et al. Relative fecal abundance of extended-spectrum-beta-lactamase-producing *Escherichia coli* strains and their occurrence in urinary tract infections in women. Antimicrob Agents Chemother. 2013;57(9):4512-7. Epub 20130708. https://doi.org/10.1128/AAC.00238-13.
25. Bezabih YM, Sabiiti W, Alamneh E, Bezabih A, Peterson GM, Bezabhe WM, et al. The global prevalence and trend of human intestinal carriage of ESBL-producing *Escherichia coli* in the community. J Antimicrob Chemother. 2021 Jan;76(1):22–9.
26. Karanika S, Karantanos T, Arvanitis M, Grigoras C, Mylonakis E. Fecal Colonization With Extended-spectrum Beta-lactamase-Producing Enterobacteriaceae and Risk Factors Among Healthy Individuals: A Systematic Review and Metaanalysis. Clin Infect Dis. 2016;63(3):310-8. Epub 20160503. https://doi.org/10.1093/cid/ciw283.
27. Sannes MR, Belongia EA, Kieke B, Smith K, Kieke A, Vandermause M, et al. Predictors of antimicrobial-resistant *Escherichia coli* in the feces of vegetarians and newly hospitalized adults in Minnesota and Wisconsin. J Infect Dis. 2008 Feb;197(3):430–4.
28. Vento TJ, Cole DW, Mende K, Calvano TP, Rini EA, Tully CC, et al. Multidrug-resistant gram-negative bacteria colonization of healthy US military personnel in the US and Afghanistan. BMC Infect Dis. 2013;13:68. Epub 20130205. https://doi.org/10.1186/1471-2334-13-68.
29. Weisenberg SA, Mediavilla JR, Chen L, Alexander EL, Rhee KY, Kreiswirth BN, et al. Extended spectrum beta-lactamase-producing Enterobacteriaceae in international travelers and non-travelers in New York City. PLoS One. 2012;7(9):e45141. Epub 20120920. https://doi.org/10.1371/journal.pone.0045141.
30. Islam S, Selvarangan R, Kanwar N, McHenry R, Chappell JD, Halasa N, et al. Intestinal Carriage of Third-Generation Cephalosporin-Resistant and Extended-Spectrum β-Lactamase-Producing Enterobacteriaceae in Healthy US Children. J Pediatric Infect Dis Soc. 2018 Aug;7(3):234–40.
31. McKinnell JA, Singh RD, Miller LG, Kleinman K, Gussin G, He J, et al. The SHIELD Orange County Project: Multidrug-resistant Organism Prevalence in 21 Nursing Homes and Long-term Acute Care Facilities in Southern California. Clin Infect Dis. 2019 Oct;69(9):1566–73.

32. Reuben J, Donegan N, Wortmann G, DeBiasi R, Song X, Kumar P, et al. Healthcare Antibiotic Resistance Prevalence - DC (HARP-DC): A Regional Prevalence Assessment of Carbapenem-Resistant Enterobacteriaceae (CRE) in Healthcare Facilities in Washington, District of Columbia. Infect Control Hosp Epidemiol. 2017;38(8):921-9. Epub 20170615. https://doi.org/10.1017/ice.2017.110.
33. Haenni M, Boulouis HJ, Lagrée AC, Drapeau A, Va F, Billet M, et al. Enterobacterales high-risk clones and plasmids spreading blaESBL/AmpC and blaOXA-48 genes within and between hospitalized dogs and their environment. J Antimicrob Chemother. 2022 Sep;77(10):2754–62.
34. Miltgen G, Martak D, Valot B, Kamus L, Garrigos T, Verchere G, et al. One Health compartmental analysis of ESBL-producing *Escherichia coli* on Reunion Island reveals partitioning between humans and livestock. J Antimicrob Chemother. 2022 Apr;77(5):1254–62.
35. Willems RP, van Dijk K, Ket JC, Vandenbroucke-Grauls CM. Evaluation of the Association Between Gastric Acid Suppression and Risk of Intestinal Colonization With Multidrug-Resistant Microorganisms: A Systematic Review and Meta-analysis. JAMA Intern Med. 2020 Apr;180(4):561–71.
36. Valverde A, Grill F, Coque TM, Pintado V, Baquero F, Canton R, et al. High rate of intestinal colonization with extended-spectrum-beta-lactamase-producing organisms in household contacts of infected community patients. J Clin Microbiol. 2008;46(8):2796-9. Epub 20080618. https://doi.org/10.1128/JCM.01008-08.
37. Goodman KE, Lessler J, Cosgrove SE, Harris AD, Lautenbach E, Han JH, et al. A Clinical Decision Tree to Predict Whether a Bacteremic Patient Is Infected With an Extended-Spectrum beta-Lactamase-Producing Organism. Clin Infect Dis. 2016;63(7):896-903. Epub 20160628. https://doi.org/10.1093/cid/ciw425.
38. Harris AD, McGregor JC, Johnson JA, Strauss SM, Moore AC, Standiford HC, et al. Risk factors for colonization with extended-spectrum beta-lactamase-producing bacteria and intensive care unit admission. Emerg Infect Dis. 2007 Aug;13(8):1144–9.
39. Larramendy S, Deglaire V, Dusollier P, Fournier JP, Caillon J, Beaudeau F, et al. Risk Factors of Extended-Spectrum Beta-Lactamases-Producing *Escherichia coli* Community Acquired Urinary Tract Infections: A Systematic Review. Infect Drug Resist. 2020;13:3945-55. Epub 20201103. https://doi.org/10.2147/IDR.S269033.
40. Flokas ME, Detsis M, Alevizakos M, Mylonakis E. Prevalence of ESBL-producing Enterobacteriaceae in paediatric urinary tract infections: A systematic review and meta-analysis. J Infect. 2016;73(6):547-57. Epub 20160728. https://doi.org/10.1016/j.jinf.2016.07.014.
41. Ben-Ami R, Rodríguez-Baño J, Arslan H, Pitout JD, Quentin C, Calbo ES, et al. A multinational survey of risk factors for infection with extended-spectrum beta-lactamase-producing enterobacteriaceae in nonhospitalized patients. Clin Infect Dis. 2009 Sep;49(5):682–90.
42. Castanheira M, Simner PJ, Bradford PA. Extended-spectrum beta-lactamases: an update on their characteristics, epidemiology and detection. JAC Antimicrob Resist. 2021;3(3):dlab092. Epub 20210716. https://doi.org/10.1093/jacamr/dlab092.
43. Bevan ER, Jones AM, Hawkey PM. Global epidemiology of CTX-M β-lactamases: temporal and geographical shifts in genotype. J Antimicrob Chemother. 2017 Aug;72(8):2145–55.
44. Ducarmon QR, Zwittink RD, Willems RPJ, Verhoeven A, Nooij S, van der Klis FRM, et al. Gut colonisation by extended-spectrum β-lactamase-producing *Escherichia coli* and its association with the gut microbiome and metabolome in Dutch adults: a matched case-control study. Lancet Microbe. 2022;3(6):e443-e51. Epub 20220420. . https://doi.org/10.1016/S2666-5247(22)00037-4.
45. CDC. Multidrug-resistant organisms (MDRO) Management Atlanta, GA: U.S. Centers for Disease Control and Prevention; 2015 [updated November 5, 2015, May 10, 2022]. Available from: https://www.cdc.gov/infectioncontrol/guidelines/mdro/index.html#anchor_1554732748
46. Hayden MK, Lin MY, Lolans K, Weiner S, Blom D, Moore NM, et al. Prevention of colonization and infection by *Klebsiella pneumoniae* carbapenemase-producing enterobacteriaceae in long-term acute-care hospitals. Clin Infect Dis. 2015;60(8):1153-61. Epub 20141223. https://doi.org/10.1093/cid/ciu1173.
47. Day MJ, Hopkins KL, Wareham DW, Toleman MA, Elviss N, Randall L, et al. Extended-spectrum beta-lactamase-producing *Escherichia coli* in human-derived and food-chain-derived samples from England, Wales, and Scotland: an epidemiological surveillance and typing study. Lancet Infect Dis. 2019;19(12):1325-35. Epub 20191022. https://doi.org/10.1016/S1473-3099(19)30273-7.
48. Thaden JT, Fowler VG, Sexton DJ, Anderson DJ. Increasing Incidence of Extended-Spectrum beta-Lactamase-Producing *Escherichia coli* in Community Hospitals throughout the Southeastern United States. Infect Control Hosp Epidemiol. 2016;37(1):49-54. Epub 20151013. https://doi.org/10.1017/ice.2015.239.