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#### Related Topics:

Frequently asked questions about the prevention and response to novel & targeted multidrug-resistant organisms (MDROs). Several reports, summarized below, describe decreases in MDROs following implementation of prevention strategies in healthcare facilities across a region. These prevention interventions targeted different MDROs and were applied in regions with different health systems and epidemiology but had common elements that include enhanced surveillance, education, communication, and improving infection prevention and control practices. In 1997, following a rapid increase in vancomycin-resistant enterococci (VRE) in the Siouxland region of Iowa, Nebraska, and South Dakota, Siouxland health officials created a task force to prevent further spread. In collaboration with CDC, the task force assessed the regional prevalence of VRE and implemented a coordinated response with a bundle of interventions that included colonization screening, infection control assessments, use of isolation and Transmission-Based Precautions for VRE carriers, and education, across 32 healthcare facilities in the region. The overall VRE prevalence at participating facilities decreased from 2.2% in 1997 to 1.4% in 1998, and to 0.5% in 1999 ( $p = 0.001$ ). The results of the study show that comprehensive efforts to identify and isolate patients with VRE can reduce transmission.<sup>1</sup> In 2006, Israeli acute-care hospitals (ACHs) faced clonal outbreaks of *Klebsiella pneumoniae* carbapenemase-producing *Klebsiella pneumoniae* that were not controlled by individual hospital measures. The Israeli Ministry of Health launched a nationwide intervention to limit further spread of antimicrobial-resistant bacteria in hospitals through creation of a national task force on antimicrobial

resistance and infection control and targeted interventions for carbapenem-resistant Enterobacterales (CRE), which included centralized reporting, isolation and Contact Precautions for known carriers, geographic separation for hospitalized carriers of CRE, and ACH site visits to assess infection control policies and laboratory methods for CRE identification. The national monthly incidence of CRE decreased from 55.5 cases per 100,000 patient-days prior to the intervention to 11.7 cases per 100,000 patient-days ( $p < .001$ ) in just over a year but did not return to pre-intervention baseline<sup>2</sup>. In 2008, after identifying that approximately 40% of CRE carriers in ACHs were discharged to long-term care facilities (LTCFs), the intervention was expanded to LTCFs, where similar interventions to those used in ACHs and early detection of carriers by serial point prevalence surveys (PPS) were implemented. The intervention decreased the incidence of CRE acquisition by approximately 50% across all LTCF types combined ( $p < 0.001$ ).<sup>3</sup> In response to an outbreak of Verona integron-encoded metallo- $\beta$ -lactamase-producing carbapenem-resistant *Pseudomonas aeruginosa* (VIM-CRPA) across multiple healthcare facilities in West Texas in 2017-2018, CDC and state and local health department partners implemented a regional prevention plan to slow the spread of VIM-CRPA in the area.<sup>4</sup> The prevention plan included (1) a baseline assessment of facility infection prevention and control (IPC) practices and point prevalence surveys (PPS) (baseline PPS conducted at 2 ACHs in medical and burn intensive care units [ICUs], a long-term acute care hospital [LTACH], a ventilator-capable skilled nursing facility [vSNF], a skilled nursing facility that does not care for ventilated residents [SNF], and an inpatient rehabilitation facility [IRF]); (2) a regional meeting of healthcare facilities to provide information and education; (3) periodic PPS and targeted admission screening; (4) recurring onsite facility IPC assessments; (5) mandating use of an interfacility transfer form; and (6) a monthly educational webinar series on MDRO prevention topics. Of the 16 ACHs, long-term care facilities, and IRFs in West Texas that were targeted for prevention activities based on patient transfer networks, 10 attended the regional

meeting, 9 had an initial onsite IPC assessment, and 5 agreed to participate in the prevention plan of which all 5 had cared for VIM-CRPA patients. One additional long-term care facility agreed to participate after the regional meeting and baseline IPC assessments were completed. Objective improvements in hand hygiene and thoroughness of environmental cleaning were observed at each facility during follow up IPC assessments, and PPS were successful in identifying multiple colonized individuals. Following implementation of the prevention plan in 2018, healthcare-associated VIM-CRPA infections per hospital admission declined by 9.8% per month (95% CI -0.156 to -0.0399,  $P=0.001$ ) through November 2019. Lee et al. (2016) modeled the impact of implementing the 2012 CDC CRE toolkit interventions on the spread of CRE throughout Orange County, California healthcare facilities.<sup>5</sup> Using an agent-based simulation model, the researchers predicted the spread of CRE under three scenarios: no specific control measures, uncoordinated facility-level infection control measures, and a coordinated regional effort. Control measures evaluated included admission screening and Contact Precautions for CRE carriers. Coordinated regional efforts were consistently more effective than uncoordinated facility-level interventions, which were more effective than scenarios with no infection control intervention. Slayton et al. (2015) demonstrated that a coordinated response to reduce CRE transmission, in which CRE carrier status was shared with a centralized public health authority and communicated to facilities upon patient transfer, resulted in a 74% reduction in CRE acquisitions over 5 years compared to an independent approach using an agent-based model in 10 inter-connected healthcare facilities.<sup>6</sup> Other modeling studies have assessed the impact of interventions targeted to specific facility types. Lee et al. (2021) evaluated the impact of a prevention bundle targeted to ACHs and LTACHs on the prevalence of CRE in the Chicago area using an agent-based model.<sup>7</sup> The prevention bundle consisted of admission screening, isolation or cohorting, and Contact Precautions for CRE carriers, a hand hygiene campaign, and daily chlorhexidine bathing. Results from

this study demonstrated a 5% reduction in CRE prevalence at 3 years when intervening in ACH ICUs compared to no intervention; a 4.6%– 17.1% reduction when intervening in LTACHs; and a 21% reduction when intervening in ACH ICUs and LTACHs. Using a similar model and bundle of interventions, Lee et al. (2021) concluded that targeting vSNFs and LTACHs resulted in the largest reductions in CRE prevalence (21% reduction compared to no intervention).<sup>8</sup> CDC performed modeling studies to assess the relative impact of different bundles of prevention interventions, implemented in different facility types and at different time points in a regional outbreak, on regional carbapenem-resistant Enterobacterales (CRE) prevalence. We adapted a previously published compartmental, regional transmission model<sup>9</sup> to estimate the impact of interventions on total CRE prevalence across networks of connected healthcare facilities. Findings are described in a published abstract and online pre-print.<sup>10</sup> Briefly, we assessed the effect of combinations of interventions to detect colonization (point prevalence surveys [PPS] and admission screening) and prevent transmission (enhanced infection prevention and control [IPC] practices and interfacility communication) at different facility types (acute care hospitals [ACH], long-term acute care hospitals [LTACHs], ventilator-capable skilled nursing facilities [vSNFs], and skilled nursing facilities that do not care for ventilated residents [SNFs]) and at time points before and after the importation of CRE. By evaluating the relative impact of combinations of interventions at different points in the epidemic we developed evidence-based recommendations, with the strongest recommendations for those interventions associated with the greatest reductions in regional prevalence. We also assessed implementation tradeoffs in our model by estimating the testing efficiency (i.e., screening tests per positive) of identifying new positives with admission screening compared to PPS screening and quantifying the relative benefit of admission screening at many facilities vs PPS at fewer facilities. We found that bundles with PPS and enhanced infection prevention and control practices in LTACHs and vSNFs had a greater

effect on network prevalence than admission screening in ACHs, LTACHs, and vSNFs and interfacility communication. Improving detection, through PPS and enhanced IPC in vSNFs and LTACHs, reduced transmission at all facility types in the region. Implementing prevention interventions after CRE introduction decreased transmissions and regional prevalence relative to no intervention but was less impactful than if interventions were in place before introduction. These findings informed the prevention strategy's focus on improving detection and infection control in influential facilities (LTACHs and vSNFs) and initiating activities before an MDRO spread widely in a region. While CRE was used to model the impact of prevention interventions on transmission and regional prevalence due to the availability of robust data, these general findings likely also apply to other emerging MDROs primarily transmitted in healthcare settings, such as *Candida auris*, although there may be some pathogen-specific differences. Facilities with longer lengths of stay that care for high-acuity individuals often disproportionately influence regional MDRO prevalence relative to their facility populations. LTACHs and vSNFs are facilities that often have these traits; however, other facility types and units may share these characteristics. Health departments in jurisdictions without vSNFs or LTACHs should consider which facility types in their jurisdiction care for high-acuity patients with long average lengths of stay, or if there are other facilities that could be considered influential facilities in the region (e.g., based on frequent MDRO outbreaks). Examples of approaches to strengthen jurisdictional clinical laboratory surveillance include:

\*Note: The Council of State and Territorial Epidemiologists (CSTE) has recommended that all States and Territories enact policies to make carbapenemase-producing organisms (CPOs) reportable in their jurisdiction CSTE CPO Position Statement. The clinical laboratory evaluation ideally identifies topics or laboratories for targeted education or recommends strategic improvements. Examples of evaluation questions include: A PPS performed for multidrug-resistant organism (MDRO) prevention and in accordance with "Public Health

Strategies to Prevent the Spread of Novel and Targeted MDROs" is a public health intervention and is not generally considered to be human subjects research; therefore, IRB approval is not required under human research regulations. However, individual institutional policies may vary. Before testing, we recommend that verbal consent for screening be obtained from the patient/resident, unless facility policy requires written consent. This process should include explaining colonization screening to patients/residents (or their legal medical proxy) in a manner that they can understand, describe the process of collecting a swab, and convey possible risks, benefits, and actions that might result from their decision to either agree to or decline screening. Provide the patient/resident with enough time to ask questions and a written copy of the "Patient Screening FAQs" (Patient Screening FAQ and example verbal consent script: Public Health Departments | CRE | HAI | CDC; C. auris screening FAQ: Frequently asked Questions about Screening for Candida auris | Candida auris | Fungal Diseases | CDC). Admission screening is the use of colonization screening to identify an individual with a multidrug-resistant organism (MDRO) at the time of admission to a new healthcare facility or unit within the same facility to ensure timely infection prevention and control (IPC) action. Admission screening for carbapenemase-producing organisms (CPOs): CDC recommends that individuals with a history of an overnight stay in a healthcare facility or invasive procedure outside the United States in at least the past 6 months at minimum are screened for CPOs (rectal swab).<sup>111213</sup> Ideally, these patients should be placed in Contact Precautions (or Enhanced Barrier Precautions, for nursing home residents when Contact Precautions do not otherwise apply) while awaiting the results of screening tests, however this should not preclude screening. Identification of any CPO (including the presence of a carbapenemase-encoding gene, without an organism identified) during admission screening should result the patient being placed in Contact Precautions. Admission screening for Candida auris: CDC recommends that individuals with a history of an overnight stay in a healthcare facility or invasive

procedure outside the United States in the past 12 months are screened for *C. auris* (axilla/groin composite swab) (Screening for Candida auris Colonization | Candida auris | Fungal Diseases | CDC). Ideally, these patients should be placed in Contact Precautions (or Enhanced Barrier Precautions, for nursing home residents when Contact Precautions do not otherwise apply) while awaiting the results of screening tests, however this should not preclude screening. For patients with a history of an overnight stay in a healthcare facility or invasive procedures outside the United States in the last 6 months (for carbapenemase-producing organisms [CPO] admission screening) or the last 12 months (for *Candida auris* admission screening), CDC recommends using Contact Precautions (or Enhanced Barrier Precautions, for nursing home residents when Contact Precautions do not otherwise apply) and placing the patient/resident in a private room when available while awaiting admission screening results. When performing admission screening for other indications, Contact Precautions (or Enhanced Barrier Precautions, for nursing home residents when Contact Precautions do not otherwise apply) and a private room are not required while awaiting test results. However, in certain situations facilities may decide to implement these measures due to the high probability of a positive test result. For instance, an acute care hospital may use Contact Precautions and private room placement for patients transferred from a facility or unit with a known outbreak or high baseline multidrug-resistant organism (MDRO) prevalence while awaiting laboratory results. If preemptive Contact Precautions (or Enhanced Barrier Precautions) are not used, take steps to limit the risk of possible transmission to others, such as avoiding frequent room transfers and maintaining high levels of adherence to hand hygiene, environmental cleaning and disinfection, and Standard Precautions. Whenever individuals are roomed together, precautions should be taken to prevent transmission of infectious organisms between them, regardless of known MDRO colonization or infection status. These include: CLIA-validated screening tests for CPOs and *C. auris* are available through CDC's Antimicrobial Resistance Laboratory Network

(AR Lab Network) and include Screening for *C. auris* colonization should be conducted using a composite swab of the patient's bilateral axilla and groin. The preferred specimen source for CPO colonization screening is a rectal swab. When screening for carbapenemase-producing carbapenem-resistant *Acinetobacter baumannii* (CRAB) or carbapenem-resistant *Pseudomonas aeruginosa* (CRPA), health departments may wish to sample additional body sites to increase sensitivity; these sites can include respiratory specimens, wounds, and the skin (e.g. axilla/groin; for CRAB only). The epidemiology of known cases and the performance characteristics of the available tests should inform the selection of additional sites. For example, if several clinical cases were identified from respiratory cultures from patients on a ventilator unit, the addition of respiratory screening cultures could be considered. While the sensitivity of different specimen sources for CRAB colonization screening varies in the literature, one study demonstrated that culture-based screening of the skin using sponge swabs to sample large surface areas had the highest yield for *A. baumannii* (92%) compared to other anatomic sites alone; where testing skin using sponge swabs is available, this site may be used alone or in combination with rectal swabs.[i] When considering colonization screening for CPOs at non-rectal sites, consult with the laboratory that will conduct the screening to determine what specimen types are validated and the recommended approach based on the context for screening (e.g., acute outbreak vs prevention, setting in which screening will be performed). [i] Nutman A, Temkin E, Lellouche J, Ben David D, Schwartz D, Carmeli Y. Detecting carbapenem-resistant *Acinetobacter baumannii* (CRAB) carriage: Which body site should be cultured? *Infect Control Hosp Epidemiol*. 2020 Aug;41(8):965-967. The primary method of CPO colonization screening available through CDC's Antimicrobial Resistance Laboratory Network utilizes culture-independent diagnostic testing, which identifies targeted carbapenemase genes but does not identify the organism(s) harboring these genes. To identify associated organisms, laboratories must culture the carbapenemase gene-positive swab, a process



known as organism recovery. Organism recovery may be useful in a variety of different circumstances, including for surveillance and outbreak purposes to ascertain which organisms are associated with carbapenemase-production and, if further characterization is performed, to understand the molecular epidemiology of those organisms (e.g., MLST, carbapenemase gene variants, and relatedness). Decisions to perform organism recovery should be made through discussion with epidemiology and laboratory partners. When resources are limited, screening additional individuals for prevention and response activities should be prioritized over organism recovery. In general, CDC does not recommend screening individuals with a history of CPO colonization or infection to assess for decolonization to inform discontinuation of vertical infection control measures (e.g., Isolation and Contact Precautions in acute care settings and Enhanced Barrier Precautions in long term care settings). Among CPO carriers, colonization rates generally decrease over time following hospital discharge, but can be prolonged, especially among individuals with repeated hospitalizations.[i] In a meta-analysis evaluating the natural history of carbapenem-resistant Enterobacterales (CRE) colonization, the pooled colonization proportion of patients with CRE was 74% and 55% one- and six-months following initial identification, respectively.[ii] Among individuals in long-term care settings, duration of colonization may be even longer, with half of colonized long-term acute care hospital (LTACH) patients still colonized when readmitted after 9 months.[iii] Across multiple studies, predictors of prolonged CRE carriage have been found to include exposure to antimicrobials, presence of an invasive device, higher Charlson Comorbidity Index scores, number of hospital admissions, and admission from or discharge to a long-term care facility.<sup>14</sup>,[iv],[v] Presence of these predictors should be considered when deciding whether to rescreen an individual. The rare situations when assessing for CPO colonization clearance could be considered should be limited to those in which the patient has improved clinically and moved to progressively lower levels of care or has

resided in the community without hospitalization or long-term care for an extended period (>6 months) since a CPO was identified (e.g., a recovered trauma patient). In these situations, a decision to assess for decolonization should be made in consultation with public health. Generally, the minimum criteria for assessing for decolonization are: 6 months have elapsed since the individual's last positive culture, negative screening results from all relevant body sites (i.e., commonly colonized body sites and the original site of infection), collected when the patient has been off antibiotics at least 7-10 days, on at least two separate occasions a minimum of 7 days apart. [i] Zimmerman FS, Assous MV, Bdolah-Abram T, Lachish T, Yinnon AM, Wiener-Well Y. Duration of carriage of carbapenem-resistant Enterobacteriaceae following hospital discharge. *Am J Infect Control*. 2013;41(3):190-4. [ii] Bar-Yoseph H, Hussein K, Braun E, Paul M. Natural history and decolonization strategies for ESBL/carbapenem-resistant Enterobacteriaceae carriage: systematic review and meta-analysis. *J Antimicrob Chemother*. 2016;71(10):2729-39. doi: 10.1093/jac/dkw221 [iii] Haverkate MR, Weiner S, Lolans K, Moore NM, Weinstein RA, Bonten MJ, et al. Duration of Colonization With *Klebsiella pneumoniae* Carbapenemase-Producing Bacteria at Long-Term Acute Care Hospitals in Chicago, Illinois. *Open Forum Infect Dis*. 2016;3(4):ofw178. [iv] Feldman N, Adler A, Molshatzki N, Navon-Venezia S, Khabra E, Cohen D, Carmeli Y. Gastrointestinal colonization by KPC-producing *Klebsiella pneumoniae* following hospital discharge: duration of carriage and risk factors for persistent carriage. *Clin Microbiol Infect*. 2013;19(4):E190-6 [v] Schechner V, Kotlovsky T, Tarabeia J, Kazma M, Schwartz D, Navon-Venezia S, et al. Predictors of rectal carriage of carbapenem-resistant Enterobacteriaceae (CRE) among patients with known CRE carriage at their next hospital encounter. *Infect Control Hosp Epidemiol*. 2011;32(5):497-503

CDC does not recommend rescreening of *C. auris* carriers to assess for clearance. For *C. auris*, long-term follow-up of colonized patients in healthcare facilities, especially those patients who continue to require complex medical care, such as ventilator support,

suggests colonization persists for a prolonged period. Repeat colonization swabs have shown intermittent *C. auris* positivity; in a publication by Pacilli et al. (2020), among patients who had a positive *C. auris* screening result followed by one or more negative screening results, more than 50% had a subsequent positive screening result.[i] Colonization is prolonged; surveillance has identified patients who remained colonized for longer than 2 years.in [i] Pacilli M, Kerins JL, Clegg WJ, Walblay KA, Adil H, Kemble SK, et al. Regional Emergence of *Candida auris* in Chicago and Lessons Learned From Intensive Follow-up at 1 Ventilator-Capable Skilled Nursing Facility. Clin Infect Dis. 2020;71(11):e718-e725. A patient should generally not be re-screened if they have prior colonization or infection with the organism that is the focus of the response (e.g., a patient with a history of *C. auris* bloodstream infection should not be screened for *C. auris* as part of a point prevalence survey; a patient colonized with NDM [organism genus unknown] should not be rescreened during contact screening in response to detection of NDM-producing *Escherichia coli*). An individual with known colonization or infection with a CPO or *C. auris* may be rescreened as part of a public health response to identification of a targeted multidrug-resistant organism (MDRO) if the organism or mechanism that is the focus of the response differs from the organism and mechanism they are known to be colonized or infected with (e.g., a patient known to be colonized with a KPC-producing *Klebsiella pneumoniae* may be screened as part of a VIM-producing *Pseudomonas aeruginosa* outbreak). If an individual with a history of CPO or *C. auris* colonization or infection is re-screened as part of a public health prevention or response activity and is found to be negative for all organisms or mechanisms, this result should generally not be used to discontinue Transmission-Based Precautions or initiate assessment of decolonization, due to the potential for a false negative result (see FAQ 11 and 12 for more information). Chlorhexidine gluconate (CHG) is the most commonly used topical antiseptic in decolonization\* and source control\*\* regimens, and CHG bathing in combination with

use of anti-staphylococcal intranasal agents has been demonstrated to be effective at preventing methicillin-resistant *Staphylococcus aureus* (MRSA) infections and central line-associated bloodstream infections (CLABSIs) in large clinical trials.[i],[ii],[iii] Several studies have examined the impact of CHG bathing on skin concentrations of *C. auris*, carbapenemase-producing organisms (CPOs), and Gram-negative bacteria. In vitro, CHG has been shown to be effective against CPOs and *Candida auris*; however, the skin concentrations needed to effectively suppress CPOs and *C. auris* appear to be much higher than those required for *S. aureus*, 128 ug/mL and 625 ug/mL, respectively, compared to 18.75 ug/mL for MRSA, although it can be difficult to compare across studies.[iv],[v],[vi] Another study from Nadimpalli et al. (2019) found no association between CHG skin concentration and bacterial bioburden of MDROs.[vii] Skin concentrations needed for suppression of CPOs and *C. auris* may be difficult to achieve in clinical practice. In a study of routine CHG bathing among ventilator-capable skilled nursing facility residents to control *C. auris* transmission, only 7.3% of skin sites sampled had a concentration of 625 ug/mL or higher.<sup>25</sup> In a second study of routine CHG bathing to control CPOs among long-term acute care hospital (LTACH) patients, 74% of skin sites sampled achieved a concentration of 128 ug/mL immediately following a CHG bath; however, that number decreased to 40% immediately prior to their next CHG bath.<sup>23</sup> High skin concentrations of CHG were not associated with deleterious disruptions of commensal skin organisms. Several studies have assessed the impact of CHG bathing on colonization and infection by multidrug-resistant Gram-negative bacteria. In a single center interventional cohort study among patients admitted to an intensive care unit with endemic levels of multidrug-resistant Gram-negative bacteria in Spain, researchers added routine CHG bathing for all mechanically ventilated patients and patients colonized with MDROs. The intervention reduced the incidence of MDRO colonization by Gram-negative bacteria from 19.9% to 16.8% ( $p=0.02$ ), however there were no reductions in hospital-onset infections caused

by MDROs.[viii] In a multicenter stepped wedge interventional study by Hayden et al. (2015), researchers implemented a bundled intervention that included universal daily CHG bathing, admission screening, serial point prevalence surveys, Contact Precautions and geographic isolation, healthcare-worker education, and adherence monitoring to determine the effect on colonization by *Klebsiella pneumoniae* carbapenemase (KPC)-producing Enterobacterales in LTACHs.[ix] The primary outcome of KPC-producing Enterobacterales rectal colonization prevalence declined from 45.8%, during the preintervention period, to 34.3% postintervention ( $P < 0.001$ ); however, it is not possible to estimate the impact that CHG bathing alone had on this decline. In addition, preliminary results from two interventional studies of universal CHG bathing in combination with nasal iodophor (povidone-iodine) compared to routine care in multiple LTACHs and nursing homes without bundled interventions did not show significant reductions in carbapenem-resistant Enterobacterales (CRE) colonization prevalence, although the number of CRE carriers identified was too small to draw meaningful conclusions.[x],[xi] Furthermore, two recent meta-analyses assessing the impact of CHG bathing on Gram-negative bacteria did not identify any significant reductions in infections caused by these organisms.[xii],[xiii] Finally, while in vitro studies suggest that CHG bathing has the potential to reduce colonization burden by *C. auris* and CPOs, there are examples of continued *C. auris* and CPO outbreaks in ACH and vSNF settings despite enhanced infection prevention and control (IPC) practices that included the use of chlorhexidine bathing.<sup>19</sup>[xiv],[xv] Considering the evidence above, CHG bathing may be considered for the prevention and control of CPOs or *C. auris*; however, it is not routinely recommended solely for this purpose alone and should be implemented with other infection control interventions. Healthcare facilities that choose to incorporate CHG bathing for CPO or *C. auris* prevention should provide ongoing training and adherence monitoring to ensure appropriate application. Healthcare facilities that routinely conduct CHG bathing as part of prevention programs for other HAIs such as

MRSA and CLABSI should continue to do so; however, if severe outbreaks of CPOs or *C. auris* occur, facilities should review these practices as part of a comprehensive review of IPC practices to ensure suboptimal application is not contributing to transmission. When conducting colonization screening of skin sites, samples should be collected as long as possible after a patient's last CHG bath to avoid false negative screening results. \*\* Source control is the use of antimicrobials and/or antiseptics to reduce the burden of colonization in individuals without complete elimination the organism. [i] Climo MW, Yokoe DS, Warren DK, Perl TM, Bolon M, Herwaldt LA, et al. Effect of daily chlorhexidine bathing on hospital-acquired infection. *N Engl J Med*. 2013;368(6):533-42. [ii] Huang SS, Septimus E, Kleinman K, Moody J, Hickok J, Avery TR, et al. Targeted versus universal decolonization to prevent ICU infection. *N Engl J Med*. 2013;368(24):2255-65. [iii] Huang SS, Singh R, McKinnell JA, Park S, Gombosev A, Eells SJ, et al. Decolonization to Reduce Postdischarge Infection Risk among MRSA Carriers. *N Engl J Med*. 2019;380(7):638-650. [iv] Lin MY, Lolans K, Blom DW, Lyles RD, Weiner S, Poluru KB, et al; Centers for Disease Control and Prevention Epicenter Program. The effectiveness of routine daily chlorhexidine gluconate bathing in reducing *Klebsiella pneumoniae* carbapenemase-producing *Enterobacteriaceae* skin burden among long-term acute care hospital patients. *Infect Control Hosp Epidemiol*. 2014;35(4):440-2. [v] Popovich KJ, Lyles R, Hayes R, Hota B, Trick W, Weinstein RA, et al. Relationship between chlorhexidine gluconate skin concentration and microbial density on the skin of critically ill patients bathed daily with chlorhexidine gluconate. *Infect Control Hosp Epidemiol*. 2012;33(9):889-96. [vi] Proctor DM, Dangana T, Sexton DJ, Fukuda C, Yelin RD, Stanley M, et al. Integrated genomic, epidemiologic investigation of *Candida auris* skin colonization in a skilled nursing facility. *Nat Med*. 2021 ;27(8):1401-1409 [vii] Nadimpalli G, O'Hara LM, Leekha S, Calfee DP, Miller LG, Pineles L, et al. Association between chlorhexidine gluconate concentrations and resistant bacterial bioburden on skin. *Infect Control Hosp Epidemiol*.

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31478517. The impact of antimicrobial stewardship on the prevention of colonization or infection by multidrug-resistant Gram-negative bacteria has been assessed in multiple studies, primarily at acute care hospitals. Several demonstrated reductions in the incidence of colonization or infection following antimicrobial stewardship interventions; however, many of these were smaller quasi-experimental "before and after" studies and/or ecological analyses that included antimicrobial stewardship as part of larger prevention bundles.[i],[ii],[iii],[iv],[v],[vi] Specific antimicrobial stewardship interventions associated with reductions in multidrug-resistant Gram-negative bacteria include antibiotic preauthorization, prospective audits and feedback, clinical decision support, treatment recommendations, and education and training; the magnitude of reductions in colonization and infections reported was highly variable. In a 2017 systematic review and meta-analysis, Baur et al. evaluated the effect of antimicrobial stewardship on antimicrobial-resistant bacteria and *C. difficile*, finding that antimicrobial stewardship programs were associated with a 51% reduction ( $p < 0.0001$ ) in the incidence of multidrug-resistant Gram-negative bacteria infections and colonization.<sup>34</sup> Many studies included in this meta-analysis implemented stewardship activities as part of prevention bundles that included infection prevention and control interventions; studies which included stewardship as part of a larger infection control bundles had a greater impact on the incidence of antimicrobial-resistant bacteria and *C. difficile* than those with antimicrobial stewardship interventions alone (31% vs 19%). There is little to no evidence on the impact of stewardship interventions for the prevention of *Candida auris* infections or colonization, however one study found that exposure to carbapenems and systemic antifungals was associated with *C. auris* colonization.[vii] More research is needed to clarify the direct impact and the most effective antimicrobial stewardship interventions for carbapenemase-producing organism and *C. auris* prevention. Based on current evidence, antimicrobial stewardship remains a critical part of healthcare patient safety efforts. Antimicrobial stewardship



practices should be assessed during MDRO prevention or response-focused infection control assessment and response consultations at healthcare facilities. [i] Baur D, Gladstone BP, Burkert F, Carrara E, Foschi F, Döbele S, et al. Effect of antibiotic stewardship on the incidence of infection and colonisation with antibiotic-resistant bacteria and *Clostridium difficile* infection: a systematic review and meta-analysis. *The Lancet Infectious Diseases*. 2017;17(9):990-1001. [ii] Carrara E, Conti M, Meschiari M, Mussini C. The role of antimicrobial stewardship in preventing KPC-producing *Klebsiella pneumoniae*. *J Antimicrob Chemother*. 2021;76(Suppl 1):i12-i18. [iii] Cipko K, Cuenca J, Wales E, Harris J, Bond S, Newton P, Miyakis S. Implementation of an antimicrobial stewardship programme and reduction in carbapenemase-producing *Enterobacterales* in an Australian local health district. *JAC Antimicrob Resist*. 2020;2(3):dlaa041. [iv] Giacobbe DR, Del Bono V, Mikulska M, Gustinetti G, Marchese A, Mina F, et al. Impact of a mixed educational and semi-restrictive antimicrobial stewardship project in a large teaching hospital in Northern Italy. *Infection*. 2017;45(6):849-856. [v] Giacobbe DR, Salsano A, Del Puente F, Campanini F, Mariscalco G, Marchese A, et al. Reduced Incidence of Carbapenem-Resistant *Klebsiella pneumoniae* Infections in Cardiac Surgery Patients after Implementation of an Antimicrobial Stewardship Project. *Antibiotics (Basel)*. 2019 Aug 28;8(3):132. [vi] Rodríguez-Baño J, Pérez-Moreno MA, Peñalva G, Garnacho-Montero J, Pinto C, Salcedo I, et al. Outcomes of the PIRASOA programme, an antimicrobial stewardship programme implemented in hospitals of the Public Health System of Andalusia, Spain: an ecologic study of time-trend analysis. *Clin Microbiol Infect*. 2020;26(3):358-365. [vii] Rossow J, Ostrowsky B, Adams E, Greenko J, McDonald R, Vallabhaneni S. Factors Associated With *Candida auris* Colonization and Transmission in Skilled Nursing Facilities With Ventilator Units, New York, 2016-2018. *Clin Infect Dis*. 2021;72(11):e753-e760. Tier 1 organisms or mechanisms are those that have never (or very rarely) been identified in the United States and for which experience is extremely limited. For these organisms, environmental sampling can inform the extent of

environmental contamination and the role the environment plays in transmission. For this reason, the threshold to perform environmental sampling for Tier 1 responses is lower than for organisms and mechanisms in Tiers 2-4. The role of the environment in transmission of organisms in Tiers 2-4 is generally well-understood, and environmental sampling during public health responses to these MDROs is most often conducted when there is a suspected point source (e.g., a persistently contaminated device) or when transmission continues despite improvements in infection control practices and the underlying epidemiology suggests an environmental point source. When performed during public health responses to MDROs in Tiers 2-4, environmental sampling should be hypothesis driven. When considering whether to pursue environmental sampling, consult with a laboratory that has experience processing environmental samples. Environmental testing methods differ from standard clinical microbiology practices and require specialized expertise. Consult with the laboratory prior to sampling to plan an informative environmental sampling strategy. Design the sampling strategy to test specific hypotheses and/or to inform specific infection prevention and control recommendations. Upon completion of environmental sampling, consult with experts to interpret results. Negative results may reflect the limitations of the sampling or testing approach rather than the true absence of environmental contamination, and this should be communicated with the healthcare facility prior to sampling. HAIs are associated with medical devices, complications following surgery, transmission between patients and healthcare workers, antibiotic overuse, and more. Languages Language Assistance Languages Language Assistance

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