

Infection Control Strategies to Prevent Emergence and Transmission of Resistant Gram-Negative Bacteria



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KEYWORDS

- Multidrug-resistant gram-negative bacteria (MDR-GNB)
- Carbapenem-resistant *Enterobacterales* (CRE) • Infection prevention • Epidemiology

KEY POINTS

- MDR-GNB spread via transmission and de novo resistance, involving colonized patients, healthcare worker hands, shared equipment, environmental surfaces, and water sources.
- Hand hygiene, targeted contact precautions (CRE, CRAB, CRPA), and environmental cleaning are foundational, evidence-based components of effective MDR-GNB prevention bundles.
- Active surveillance is useful for CRE and CRAB in high-risk settings, but routine screening for ESBL or CRPA is not recommended outside outbreaks.
- *Whole-genome sequencing is transforming outbreak detection by better defining transmission pathways*, allowing more precise interventions.
- *Sustainable reduction of MDR-GNB infections requires coupling infection prevention strategies with a strong antimicrobial stewardship program* and collaboration with regional institutions, especially long-term care facilities.

MULTIDRUG-RESISTANT GRAM-NEGATIVE BACTERIA: INTRODUCTION

Multidrug-resistant gram-negative bacteria (MDR-GNB) are a diverse group of pathogens that have been identified as an urgent threat by the Centers for Disease Control

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Abbreviations	
AMS	antimicrobial stewardship
AnpC	Ambler-C <i>bla</i> _{AmpC}
CDC	Centers for Disease Control and Prevention
CP	contact precaution
CPE	carbapenemase-producing <i>Enterobacterales</i>
CRAB	carbapenem-resistant <i>Acinetobacter baumannii</i>
CRE	carbapenem-resistant <i>Enterobacterales</i>
CRPA	carbapenem-resistant <i>Pseudomonas aeruginosa</i>
ESBL	extended-spectrum β -lactamase
FMT	fecal microbiota transplantation
HAI	hospital-acquired infection
HCW	health care worker
HH	hand hygiene
ICU	intensive care unit
KPC	<i>Klebsiella pneumoniae</i> carbapenemase
LTCF	long-term care facility
MDR-GNB	multidrug-resistant gram-negative bacteria
MDRO	multidrug-resistant organism
NDM	New Delhi metallo-beta-lactamase
OXA-48	oxacillinase-48
SDD	selective digestive tract decontamination
SOD	selective oropharyngeal decontamination
WGS	whole-genome sequencing

and Prevention (CDC).¹ These bacteria readily acquire and disseminate resistance determinants and are associated with increased mortalities, prolonged length of hospital stays, and higher health care costs compared with drug-susceptible bacteria. This review summarizes evidence-based infection control measures aimed at halting the emergence and spread of the following 4 resistance phenotypes among MDR-GNBs (Table 1): (1) *Enterobacterales* resistant to extended-spectrum cephalosporins, including the Ambler-A extended-spectrum β -lactamases (ESBL) and the Ambler-C *bla*_{AmpC} (AmpC); (2) carbapenem-resistant (and/or carbapenemase-producing) *Enterobacterales* (CRE); (3) carbapenem-resistant *Pseudomonas aeruginosa* (CRPA); and (4) carbapenem-resistant *Acinetobacter baumannii* (CRAB).

Infection control measures in hospitals that address patient-to-patient transmission include (1) hand hygiene (HH), (2) contact isolation precautions, (3) patient cohorting, (4) environmental cleaning, (5) active surveillance programs to identify asymptomatic carriage, and (6) decolonization protocols. In contrast, tackling de novo emergence of resistance requires enforcing adherence to effective antimicrobial stewardship (AMS) policies.²

MULTIDRUG-RESISTANT GRAM-NEGATIVE BACTERIA: MECHANISMS OF RESISTANCE AND EPIDEMIOLOGY

MDR-GNB primarily acquire drug resistance through the following 2 mechanisms: (1) patient-to-patient transmission of MDR-GNB and/or their mobile genetic elements (eg, carbapenemases) (often through an intermediary, such as health care staff, the proximal environment, or shared equipment) or (2) de novo evolution of resistance, in which susceptible isolates, under antibiotic selective pressure, newly express an MDR phenotype, often mediated by the upregulation of chromosomal and/or transmissible gene expression (eg, AmpC, CMY-2) or alterations in outer membrane porin channels or efflux pumps owing to certain stressors.³

Table 1
Multidrug-resistant gram-negative bacteria nomenclature and abbreviations

	Abbreviation	Definition	Examples
Multidrug-resistant gram-negative bacteria	MDR-GNB	Gram-negative bacteria nonsusceptible to ≥ 3 classes of antimicrobials	
Extensively resistant gram-negative bacteria	XDR-GNB	Gram-negative bacteria nonsusceptible to ≥ 1 agent in all but ≤ 2 antimicrobial classes	
Carbapenem-resistant <i>Enterobacterales</i>	CRE	<i>Enterobacterales</i> phenotypically resistant to ≥ 1 carbapenem or detection of carbapenemase	<i>Klebsiella pneumoniae</i> , <i>E coli</i> , <i>Enterobacter cloacae</i> , <i>Serratia marcescens</i>
Carbapenemase-producing <i>Enterobacterales</i> (CPE)	CPE	<i>Enterobacterales</i> with detection of ≥ 1 carbapenemase	KPC, NDM, OXA-48, Verona integron-encoded metallo-beta-lactamase
Nonfermenting gram-negative bacteria	NF-GNB	Gram-negative bacteria incapable of fermenting glucose	<i>P aeruginosa</i> , <i>A baumannii</i> , <i>Stenotrophomonas maltophilia</i> , <i>Burkholderia cepacia</i> complex
Carbapenem-resistant <i>P aeruginosa</i>	CRPA	<i>P aeruginosa</i> phenotypically resistant to ≥ 1 carbapenem	
Carbapenem-resistant <i>A baumannii</i>	CRAB	<i>A baumannii</i> phenotypically resistant to ≥ 1 carbapenem	
Beta-lactamases			
Extended-spectrum beta-lactamases	ESBLs	Enzymes capable of hydrolyzing third- and fourth-generation cephalosporins in addition to penicillin agents	CTX-M, TEM, SHV
AmpC beta-lactamases	AmpC	Inducible enzymes (usually chromosomal) that when upregulated confer resistance to first- to third-generation cephalosporins & BL/BLIs	Frequently found in <i>E cloacae</i> , <i>Citrobacter freundii</i> , <i>S marcescens</i> , <i>P aeruginosa</i> , <i>A baumannii</i>

Abbreviations: BL/BLIs, beta lactam/beta lactamase inhibitors; CTX-M, cefotaximase-munich; SHV, sulfhydryl variable; TEM, temoneir.

ESBL-producing *Enterobacterales* have become widespread, for example, with 17.6% of *Escherichia coli* isolates from healthy individuals, and 21.1% of isolates from hospitalized patients, exhibiting ESBL production worldwide, although geographic differences exist.⁴ In North America, the prevalence of ESBL-producing *E coli* increased from 3.6% to 11.8% between 2007 to 2008 and 2021.⁵

CRE incidence has gradually increased globally, although in recent years, rates have remained stable in the United States. The epidemiology of carbapenemase-producing *Enterobacterales* (CPE) in the United States has also changed, with an increase in the relative proportions of New Delhi metallo-beta-lactamase (NDM) and oxacillinase-48 (OXA-48) and a decrease in *Klebsiella pneumoniae* carbapenemase (KPC).⁶ The New York City Department of Health reported from 2019 to 2024, annual NDM-positive CRE cases increased from 58 to 388, whereas KPC-positive CRE cases remained stable.⁷

P aeruginosa represents the most frequently isolated nonfermenting GNB causing hospital-acquired infections (HAIs) in the United States.⁸ In the United States, carbapenem resistance in *P aeruginosa* has traditionally been primarily attributed to alterations of the expression and/or function of chromosomal genes, such as the outer membrane porin OprD and multidrug efflux pumps and less frequently owing to carbapenemase production.⁹

CRAB is a significant health care-associated pathogen owing to its remarkable ability to survive for prolonged periods in the hospital environment—including ventilators and other intensive care unit (ICU) equipment. In the United States, carbapenem resistance among *A baumannii* isolates increased from 22.8% in 2018 to 33.3% in 2022 ($P = .0182$).¹⁰

RESERVOIRS OF MULTIDRUG-RESISTANT GRAM-NEGATIVE BACTERIA

Health Care Workers

Contaminated hands of health care workers (HCWs) likely serve as the most frequent vehicle of MDR-GNB transmission.^{11,12} Studies have shown a bacterial transfer rate from patients or their environment to the hands of HCWs as high as 33%.¹³ Factors that increase hand contamination risk include prolonged durations of care and contact with moist body sites or indwelling medical devices. A recent prospective study of 466 HCW observations identified *E coli* hand contamination in 6.2% of encounters and *Klebsiella* species hand contamination in 7.4% of encounters.¹⁴

Shared Medical Equipment

Shared equipment has been implicated in many instances of MDR-GNB transmission. Duodenoscopes have been identified as the source of many CRE outbreaks.¹⁵ Persistent contamination of complex elevator channels, despite appropriate high-level disinfection per instructions for use (IFUs), led to redesign of duodenoscopes, including the development of disposable endcaps to facilitate cleaning.¹⁶ Recent data suggest that endoscopes lacking elevator channels are also capable of CRE transmission, particularly in the setting of physical damage or mechanical defects that cause fluid intrusion.¹⁷ Contaminated bronchoscopes and other respiratory equipment are also a frequent source of potential MDR-GNB transmission, particularly because of CRPA.^{18,19}

Hospital Surfaces

Hospital rooms can serve as reservoirs of MDR-GNB contamination and potential transmission to HCWs and patients. Colonized or infected patients shed MDR-GNB

into the immediate surrounding environment, serving as a source of contact transmission, with HCWs often serving as the intermediate vector. Patients have a 5 times increased risk of HAI if the prior occupant was infected or colonized with the same organism.²⁰ CRE has been recovered from the surrounding of colonized patients, with highest rates of contamination found on the patient's pillow (68/204, 33%), infusion pump (19/120, 16%), and the bedside table (28/204, 14%).²¹

CRAB is particularly notorious for persistent environmental contamination. It has the ability to survive for long periods on inanimate surfaces, to resist desiccation and some disinfectants better than many other GNB, and effectively forms biofilms on medical equipment. CRAB has been recovered from nearly all high-touch surfaces in ICU rooms.^{22,23} Positive air samples for CRAB have also been found in a large proportion of colonized patients.²⁴

Water Reservoirs

Water sources have also been increasingly implicated in the transmission of MDR-GNB, with sinks being recognized as a frequent source of HAIs.²⁵ A recent systematic review of MDR-GNB outbreaks originating from water sources found CRPA most commonly implicated, followed by *Klebsiella pneumoniae* CRE, CRAB, and other MDR-GNB.²⁶ Drains, sink surfaces, faucets, and ice machines were implicated as environmental sources by molecular techniques in most outbreak reports.

Long-Term Care Facilities

Residents of long-term care facilities (LTCFs) have multiple risk factors for MDR-GNB acquisition, such as frailty, multimorbidity, indwelling devices, recent exposure to hospitals, increased colonization pressure, and frequent exposure to broad-spectrum antibiotics.^{27,28} Moreover, patients from LTCFs frequently cycle back and forth between different acute-care hospitals and LTCFs.²⁹

MULTIDRUG-RESISTANT GRAM-NEGATIVE BACTERIA PREVENTION STRATEGIES

Hand Hygiene

Optimizing HH compliance among staff is an essential intervention to control outbreaks of MDR-GNB (Table 2).^{30,31} A modeling analysis in the ICU setting demonstrated that HH is the most efficient measure in controlling ESBL acquisitions; improving HH compliance from 55% before patient contact and 60% after patient contact, to 80% before and after patient contact, would reduce the proportion of patients who acquire ESBLs within 90 days by 91%.³²

HH compliance among staff is a core performance measure of every infection control program, and it is important to recruit leaders to invest and allocate preventive resources to this task.

Contact Precautions

Contact precautions (CPs) include wearing a gown and gloves upon entry into the patient's environment and removing the gown and gloves before exiting the patient's immediate environment (Table 3). CPs are preferably used for patients in single rooms. Performing HH before donning gloves and after removal is a mandatory part of CPs. Most supportive studies for prevention of MDR-GNB transmission include the use of CPs in combination with other infection control measures.³³ Universal use of CPs in ICU patients does not appear to be more effective than targeted CPs for MDR-GNB carriers.³⁴ In addition to being an important component of bundled interventions to limit epidemic spread of MDR-GNB, CPs are simple and inexpensive.

Table 2 Evidence-based multidrug-resistant gram-negative bacteria infection prevention and control measures		
IPC Intervention	Definition	Comments
Hand hygiene	Washing or sanitizing hands before and after patient care	Highly effective but adherence is often suboptimal. Monitoring and feedback are essential to maintaining high HCW adherence
Contact precautions	Gown and glove use for all patient care	Data supporting use in endemic settings are strongest for CRE and <i>A baumannii</i> . Data do not support the use of CPs for ESBL prevention
Environmental cleaning	Surface disinfection of patient environment and equipment	Crucial to monitor compliance. Consider potential water sources (eg, sinks) in MDR-GNB outbreaks, particularly <i>P aeruginosa</i> and <i>A baumannii</i> . No-touch terminal room technology can reduce the risk of MDRO infection in subsequent room occupant
Medical device reprocessing	HLD/sterilization of invasive medical devices	Duodenoscopes associated with CRE transmission even when following the manufacturer's IFU. Bronchoscopes associated with CRPA transmission
Water management program	Comprehensive strategy to mitigate risk of waterborne pathogens	Proper room & sink design to minimize splash risk. Avoid fluid waste disposal in sinks & placement of patient equipment in splash zone
Antimicrobial stewardship	System to limit inappropriate use & optimize antimicrobial prescribing	Associated with 50% absolute risk reduction in MDR-GNB infection/colonization. Most effective when combined with infection control measures
Active surveillance	Screening cultures to detect asymptomatic MDR-GNB colonization	Effective in reducing CRE and CRAB transmission in epidemic and some endemic settings
Patient and HCP cohorting	Segregating MDR-GNB-infected or MDR-GNB-colonized patients in one geographic location with the use of dedicated HCP	Effective for epidemic CRE and CRAB control when bundled with other interventions. Low HCP morale has been reported
Patient decolonization	Topical CHG cutaneous decolonization or SDD/SOD	CHG data are more limited for MDR-GNB than methicillin-resistant <i>Staphylococcus aureus</i> /VRE. Utility of SDD/SOD depends on baseline antibiotic resistance prevalence and carries the risk of increased drug resistance. FMT for this purpose is still experimental

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Table 2
(continued)

IPC Intervention	Definition	Comments
Interfacility collaboration	Enhanced communications between facilities regarding patient MDR-GNB status & coordination with state health authorities	Improves early detection of silent MDR-GNB carriers. Strong data supporting a coordinated approach to epidemic CRE control. Crucial to incorporate acute-care hospitals and LTCFs

Abbreviations: CHG, chlorhexidine gluconate; HCP, healthcare provider; HLD, high-level disinfection; VRE, vancomycin-resistant enterococci.

Patients colonized or infected with CRE should always be subjected to CPs per CDC and international guidelines.^{35,36} Although data suggest CPE have much higher transmission potential than non-carbapenemase-producing CRE, current CDC guidelines do not differentiate between the 2 groups in terms of CP utilization.^{37,38}

Use of CPs is recommended for all patients infected or colonized with CRAB or CRPA by the World Health Organization,³⁹ as curbing the spread of carbapenem-resistant isolates is of paramount importance.⁴⁰ In a recent meta-analysis, the combination of standard and contact precautions, along with improving environmental cleaning, had effectively reduced infections with CRAB and CRPA (RR, 0.09 [0.01, 0.81]).⁴¹

Accumulated data suggest that CPs are ineffective in preventing ESBL transmission, likely related to the high incidence of undetected community-acquired colonization.⁹ During outbreaks or among high-risk populations (eg, neonates, severely immunosuppressed), CPs may still play a role in preventing ESBL acquisition.⁴²

Overuse of CPs has the potential to cause harm. Some observational studies have found that isolated patients receive less frequent personal contact from HCWs and higher rates of anxiety and medical errors, although this has not been confirmed in clinical trials.⁴³ Furthermore, as the burden of patients on CPs increases, HCW compliance with CPs and HH generally declines.⁴⁴

Surveillance

Every Infection Control Department, at every facility, should have a reliable electronic surveillance system to continuously monitor MDR-GNB incidence. The output of this constant surveillance activity should be frequently analyzed and should lead in “real-time” to rapid directed interventions to curb the acquisitions and spread of MDR-GNB.

Active Surveillance

The use of surveillance cultures to identify asymptomatically colonized patients has become an essential tool in MDR-GNB infection control programs. Active surveillance, paired with preemptive contact isolation, reduces colonization pressure and risk of patient-to-patient transmission and could decrease delays in initiation of appropriate antimicrobial therapy.^{36,45} The reliance on clinical cultures alone has been found to significantly underestimate MDR-GNB prevalence, and the use of active surveillance cultures has more accurately estimated the colonization pressure, in several health systems and units.⁴⁶

In many regions, the endemic prevalence of ESBL colonization in the community is so high that active surveillance is considered of questionable benefit.⁴⁷ Active surveillance should be limited only to situations in which its benefit outweighs the burden, such as in outbreak settings.⁴⁸

Table 3
Recommended multidrug-resistant gram-negative bacteria prevention strategies

Prevention Strategy	Organism	Recommendation	Key Details
Active surveillance	ESBL	Not routinely recommended	High community prevalence limits utility
	CRE	Recommended for selected high-risk populations	Base screening on local/regional epidemiology; use molecular assays to detect carbapenemase production
	CRAB	Recommended in endemic ICUs	Screen on admission and periodically thereafter; preferred sites include respiratory samples (ventilated patients only) and wide-area skin samples using designated wipes (using enriched broth and selective media)
	CRPA	Not routinely recommended	Consider only in outbreak settings
Containment—hand hygiene	All MDR-GNB	Strongly recommended	Core prevention measure; audit performance and provide unit-level feedback with oversight by hospital quality leadership
Containment—contact precautions	ESBL	Not routinely recommended	Limited effectiveness due to high baseline colonization
	CRE	Recommended	Applies to both carbapenemase-producing and non-carbapenemase-producing isolates
	CRAB	Recommended	Apply to all carriers
	CRPA	Recommended	Apply to all carriers
Containment—cohorting & dedicated staff	ESBL	Not routinely recommended	—
	CRE	Conditionally recommended	For carbapenemase-producing CRE during epidemics or in hyperendemic regions; not recommended for non-carbapenemase-producing CRE
	CRAB	Recommended in high-risk settings	During outbreaks or high endemicity in ICUs or LTACs
	CRPA	Not routinely recommended	Consider during outbreaks

Environmental cleaning & shared equipment	All MDR-GNB	Strongly recommended	Implement unit-specific protocols; ensure strict terminal cleaning after MDR-GNB carrier discharge Monitor cleaning quality (preferably quantitative) and disseminate results for quality improvement Audit compliance with HLD/sterilization of high-risk shared devices (eg, duodenoscopes, bronchoscopes) Designate trained teams and dedicated time for cleaning shared medical equipment
Antimicrobial stewardship	All MDR-GNB	Strongly recommended	Establish institutional AMS program with regular monitoring and feedback Track carbapenem use as a core stewardship metric to limit MDR-GNB acquisition
Decolonization	All MDR-GNB	Selective use only	SDD and SOD are not recommended for routine prevention in ICU patients Daily chlorhexidine bathing is recommended for ICU patients and should be considered for functionally dependent patients or those with central lines

Screening for CRE among high-risk populations is a practice recommended (in certain scenarios) by national and international guidelines.³⁵ Local screening policies should be based on regional epidemiology and risk factor stratification. Populations that may be targeted include functionally dependent patients, patients admitted from long-term acute care (LTAC) hospitals, other LTCFs or hospitals with known endemicity, and patients with prior travel to foreign countries with high CRE prevalence. The CDC recommends screening in health facilities and close contacts of known CRE carriers.⁴⁹ Additional periodic screening policies (eg, weekly) for hospitalized patients in certain high-risk units (eg, ICUs, hemato-oncologic units) may be considered during periods of epidemic spread.^{47,50}

Molecular methods for CRE surveillance may be superior to conventional cultures, owing to faster time to result and superior sensitivity, and are discussed elsewhere.⁵¹ For more details, kindly see the Daniel A. Ortiz and colleagues' article, "[Safer, Better, Faster, Stronger: Clinical Microbiology and Infection Prevention, A Great Duo in Action](#)," in the issue "Principles of Infection Prevention and Control in Health Care Settings, Part 1: Facility Management and Planning."

Active surveillance to prevent the spread of CRAB in hospitals may be beneficial in endemic regions or in epidemics. In the past, screening for *A baumannii* had the following 2 major limitations: (1) the best anatomic site for colonization detection, and (2) low sensitivity of the diagnostic methods.⁴⁵ However, use of axillary/groin sponges combined with enrichment broths and selective chromogenic media has increased the sensitivity of identifying asymptomatic CRAB carriers to more than 90%.^{52,53} Several quasi-experimental studies support active surveillance to reduce the incidence of CRAB in endemic or epidemic settings.^{54,55} In a Monte Carlo simulation analysis, even with a sensitivity of only 55%, active screening reduced *A baumannii* transmissions, infections, and deaths by 48%. As screening sensitivity approached 90% (achievable with usage of skin sponges, enrichment broths, and selective media), the reduction in transmissions, infections, and deaths had reached 78%.⁴⁵

There is no supportive evidence of establishing an active surveillance program to prevent the spread of CRPA in hospitals, and this practice is not recommended outside of specified epidemic settings. Sputum cultures, specifically among ventilated patients, coupled with rectal cultures, are the best sites to screen for CRPA carriage among ICU patients.⁵⁶

Cohorting Patients and Dedicated Staff

Physically cohorting patients infected or colonized with MDR-GNB and using dedicated staff to treat only these patients may reduce the colonization pressure and risk of transmission (see [Table 3](#)). The resource expenditure required to implement these measures are substantial, and supportive evidence for these practices for MDR-GNB prevention exists primarily in the control of CRE outbreaks and to a lesser extent CRAB, largely as part of multifaceted bundles.⁵⁷ A quasi-experimental study demonstrated that cohorting CRAB patients in internal medicine departments, combined with intensified hospital-wide cleaning, significantly reduced institutional CRAB bloodstream infection (BSI) incidence.⁵⁸ Modeling has shown that cohorting was the second most effective intervention in reducing ESBL acquisition in the endemic ICU setting, following HH.³² In Israel, the establishment of dedicated CRE cohort units with dedicated nursing staff nationwide curbed the emergence and spread of new CRE acquisitions nationwide.⁵⁹ United cohort units of different MDR-GNB should be strictly avoided, as mobile genetic elements are easily transferrable in these settings and can cross the interspecies barrier.⁶⁰

Leveraging Health Care Workers to Uncover Transmission Dynamics

Whole-genome sequencing (WGS) has revolutionized the understanding of multidrug-resistant organism (MDRO) transmission dynamics in health care settings.^{38,61} Using prospective WGS surveillance of all hospital-acquired clinical isolates identifies substantially more transmission events than conventional surveillance methods.⁶² WGS tools are effective in epidemic settings of MDR-GNBs, including outbreaks of ESBL GNB, CRE, CRAB, and CRPA.^{63–66} Recent studies show that use of prospective real-time WGS on all bacterial isolates has the potential for substantial cost-savings through abrogated outbreaks and reductions in costly HAIs.⁶⁷

Environmental Cleaning

Preventive bundles applied to successfully contain MDR-GNB outbreaks included environmental cleaning, sanitation, and disinfection.⁶⁸ The CDC recommends that hospitals optimize baseline institutional policies relating to environmental cleaning, including daily cleaning of occupied rooms and terminal cleaning after discharge.⁶⁹

A clustered randomized crossover trial demonstrated that placing single-use disinfecting wipes at each bedside significantly increased the cleaning frequency of high touch surfaces (OR = 3.73; $P < .0001$), which led to reductions in the environmental contamination of MDR-GNB (OR = 0.7; $P = .06$), reduced the incidence of MDR-GNB acquisitions by naïve patients (HR = 0.4; $P = .04$), and decreased overall in-hospital mortality (IRR = 0.8; $P = .03$).⁷⁰

Automated “no-touch” technologies, such as UVC-emitting and H₂O₂-based devices are increasingly used to augment terminal room disinfection; data supporting efficacy for prevention of HAIs are stronger for *Clostridium difficile* and vancomycin-resistant *Enterococci* rather than MDR-GNB.⁷¹

Monitoring of Cleaning

Monitoring of compliance with environmental cleaning via audits or other measures and distribution of regular cleaning audit reports are now fundamental requirements in hospitals and is reviewed in detail in the Philip C. Carling and Linda Homan’s article, “[Optimizing Patient-Zone Environmental Hygiene: The Way Forward](#),” in the issue “Principles of Infection Prevention and Control in Health Care Settings, Part 1: Facility Management and Planning.”⁶⁹ Using ATP bioluminometers has been associated with reduced acquisition of MDR-GNB.⁷²

Cleaning and Disinfection of Shared Medical Equipment

Shared equipment should be minimized in hospitals among patients with epidemiologically significant pathogens, such as MDR-GNB. Private phones, pens, vital signs monitors, computer keyboards, and mice are all established vectors for MDR-GNB transmission. Providing hospital staff with dedicated time for cleaning of shared medical equipment significantly reduced the incidence of HAIs in a large randomized Australian study.⁷³

Appropriate reprocessing of endoscopes and bronchoscopes is crucial to prevent transmission of MDR-GNB and is covered in detail in the Emily Sickbert-Bennett and colleagues’ article, “[Sterilization and High-Level Disinfection in 2026: New and Emerging Topics](#),” in the issue “Principles of Infection Prevention and Control in Health Care Settings, Part 1: Facility Management and Planning.”⁷⁴

Water Management Plan

Development of a water management plan is essential to mitigating risk of MDR-GNB transmission from water-borne environmental sources to patients. Proper sink and

room design plays an important role; splash risk can be minimized by using sinks with faucets that are offset from drains and ensuring adequate depth and slope of sink basins. Patient waste fluids should not be disposed of in sink drains, and medical equipment should not be stored underneath the sink or within the splash zone.⁷⁵

In settings where a reservoir of MDR-GNB is suspected or confirmed in sink drains, the optimal disinfection strategy is unclear and is discussed in detail elsewhere.⁷⁶

Transition to water-free care has shown success in eradicating some ICU outbreaks of MDR-GNB.⁷⁶ This typically involves removal of sinks from patient-care areas.

Antimicrobial Stewardship

AMS is a core measure in the prevention of MDR-GNB and is a core recommendation of the World Health Organization Antimicrobial Resistance strategy (see [Table 3](#)) and is discussed in detail in the Marten R. Hawkins and colleagues' article, "[Antimicrobial Stewardship for the Infection Control Professional: Mutual Collaboration for Mutual Benefit](#)," in the issue "Principles of Infection Prevention and Control in Health Care Settings, Part 1: Facility Management and Planning."

When properly implemented, AMS can result in large reductions in the overall use of some antimicrobials and reductions in MDR-GNB colonization or infection, both by decreasing the risk of de novo resistance evolution and by reducing the likelihood of exogenous acquisition. A meta-analysis of 32 studies of the effect of AMS on MDR-GNB acquisitions found an overall risk reduction of 51% (incidence ratio, 0.49; 95% CI, 0.35–0.68).⁷⁷ The maximal efficacy of AMS is achieved, while combined and coordinated in a bundle that addresses additional infection control measures (ie, HH, enhanced environmental cleaning).^{78,79}

The Role of Decolonization

Therapeutic options to eradicate MDR-GNB intestinal carriage using antimicrobials are limited (see [Table 3](#)).⁸⁰ Selective digestive tract decontamination (SDD) and selective oropharyngeal decontamination (SOD) (usually using oral colistin, aminoglycosides, and amphotericin) have been used in attempts to reduce pneumonia in ICUs, but experience in eliminating MDR-GNB colonization and infection is limited.

A small randomized, double-blind, placebo-controlled trial of SDD using oral gentamicin and oral colistin for CRE eradication found a significant reduction in positive CRE rectal cultures after the SDD regimen, compared with the placebo arm (OR = 0.13; $P < .01$).⁸¹ A larger 8000 patient randomized trial in European ICUs with high prevalence of antimicrobial resistance did not find that SOD or SDD (colistin, tobramycin, and nystatin) reduced risk of MDR-GNB bloodstream infections compared with daily chlorhexidine gluconate (CHG) bathing.⁸²

Use of daily bathing with chlorhexidine gluconate 2% wipes or 4% solution for cutaneous decolonization has been shown to reduce HAIs in ICU patients.⁸³ Data are mixed regarding the ability of daily CHG bathing to decrease MDR-GNB acquisitions, but the practice has become widespread among hospitalized patients owing to the limited associated risk and proven efficacy in all-cause HAI reduction.^{84,85}

Observation trials of fecal microbiota transplantation (FMT) performed for *C difficile* infection have shown promise in reducing MDR-GNB colonization.⁸⁶ Efficacy and safety data from larger cohorts will inform whether use of FMT or other live biotherapeutic products should be recommended for reducing colonization with MDR-GNB.⁸⁷

Collaboration with Long-Term Care Facilities

Because of the interconnectedness of hospitals and LTCFs, infection control interventions should ideally be implemented in parallel in both settings to maximize

effectiveness of prevention interventions across the continuum of care. In the Israeli nationwide CRE epidemic in 2006 to 2007, a decrease in new acquisitions was only evident after broadening the national prevention plan to include LTCFs.⁵⁹ Restrictions put in place to halt patient-to-patient transmission in LTCFs should ideally be tailored to a facility, based on its structure, its residents' characteristics, the local colonization pressure, and the overall level of care provided in the facility. Sharing of resources, standardizing education and training, and improving interfacility communication regarding MDRO colonization status can allow for a more integrated infection prevention approach across different health care settings.⁸⁸

SUMMARY

Antimicrobial resistance is a global iatrogenic complication of modern medical care. MDR-GNB are increasing in prevalence, with North America experiencing increasing incidence of community-onset ESBL-producing *Enterobacteriales* infections and an increasing proportion of metallo-beta-lactamase-producing CRE. CRAB and CRPA pose additional significant threats in hospitals, particularly ICUs. Methods to minimize risk of MDR-GNB in acute care hospitals are described in [Table 3](#).

CLINICS CARE POINTS

- Pearls: Hand hygiene remains the highest-yield intervention for preventing MDR-gram-negative bacteria (MDR-GNB) transmission; even modest improvements in adherence can substantially reduce acquisition rates.
- Environmental contamination is a major driver of transmission; prior room occupancy by an MDR-GNB-colonized patient significantly increases subsequent infection risk.
- Water reservoirs (eg, sinks, drains) are increasingly recognized sources of MDR-GNB outbreaks and should be incorporated into routine outbreak investigations.
- Contact precautions should be targeted, with strongest evidence supporting their use for carbapenem-resistant *Enterobacteriales* (CRE), *Acinetobacter baumannii* (CRAB), and *Pseudomonas aeruginosa* (CRPA).
- Active surveillance is most effective when applied selectively, particularly for CRE and CRAB in high-risk or endemic settings.
- Antimicrobial stewardship is central to prevention, with reductions in inappropriate antibiotic use associated with substantial decreases in MDR-GNB acquisition.
- Cohorting of patients and staff can reduce transmission during outbreaks, particularly for CRE and CRAB, when implemented as part of a bundled strategy.
- Whole-genome sequencing enhances outbreak detection and control by more precisely defining transmission pathways.
- Pitfalls: Routine use of contact precautions for ESBL-producing organisms is not supported in endemic settings and may lead to unintended harms without reducing transmission.
- Reliance on clinical cultures alone underestimates colonization burden, delaying recognition of transmission and outbreak dynamics.
- Failure to evaluate environmental and water sources may result in missed outbreak reservoirs, particularly for CRPA and CRAB.
- Assuming uniform transmission risk across MDR-GNB is misleading; carbapenemase-producing organisms often have higher transmissibility.
- Incomplete implementation of infection prevention bundles limits effectiveness; success depends on consistent, high-fidelity execution of all components.

- Cohorting dissimilar multidrug-resistant organisms may facilitate horizontal gene transfer and emergence of novel resistance patterns.
- Surveillance systems that do not trigger timely intervention have limited clinical value, emphasizing the importance of real-time data application.

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