Recommendations for Metrics for Multidrug-Resistant Organisms in Healthcare Settings: SHEA/HICPAC Position Paper

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EXECUTIVE SUMMARY

Monitoring multidrug-resistant organisms (MDROs) and the infections they cause in a healthcare setting is important to detect newly emerging antimicrobial resistance profiles, to identify vulnerable patient populations, and to assess the need for and effectiveness of interventions; however, it is unclear which metrics are the best, because most of the metrics are not standardized. This document describes useful and practical metrics and surveillance considerations for measuring MDROs and the infections they cause in the practice of infection prevention and control in healthcare settings. These metrics are designed to aid healthcare workers in documenting trends over time within their facility and should not be used for interfacility comparison.

The following MDROs are addressed: (1) methicillin-resistant Staphylococcus aureus; (2) vancomycin-resistant Enterococcus species; (3) multidrug-resistant gram-negative bacilli; and (4) vancomycin-resistant S. aureus. We convened a working group of experts that reviewed current practices, the peer-reviewed literature, and existing guidelines on surveillance strategies and key metrics.

We propose that healthcare facilities use the following 4 routine metrics to monitor MDROs and the infections they cause: (1) an MDRO-specific line list for tracking patients who have acquired an MDRO; (2) an antibiogram for monitoring susceptibility patterns of isolates recovered from patients; (3) the incidence of hospital-onset MDRO bacteremia, which is an objective, laboratory-based metric that is highly associated with invasive disease and does not require chart review to estimate infection burden; and (4) clinical culture results, to measure incidence of infection or colonization, to quantify the number of people whose MDRO acquisition is healthcare associated. In addition, healthcare facilities may want to calculate both the overall prevalence of carriage and the prevalence of carriage at admission, the latter of which can be useful in detecting importation of methicillin-resistant S. aureus into healthcare facilities, to estimate the exposure burden. Active surveillance testing can augment and increase the accuracy of some metrics. Healthcare facilities not performing active surveillance testing might wish to consider point-prevalence screening, to help assess how much the number of positive clinical culture results understimates the hidden reservoir of MDROs. It is important to understand the limitations of all proxy metrics. Because of the paucity of published research findings focused on this area of study, most recommendations were based on opinion and were heavily influenced by the perceived usefulness and simplicity of the metric for assessing MDROs in the hospital setting and for determining the impact of interventions.

INTRODUCTION

Multidrug-resistant organisms (MDROs) are microorganisms that are resistant to one or more therapeutic classes of antimicrobial agents.1 Healthcare facilities are monitoring MDROs in a variety of ways because of the increasing incidence of MDRO infections, the severity of infection caused by MDROs, changes in reporting requirements, and recommendations by the Healthcare Infection Control Practices Advisory Committee (HICPAC).2-4 Such monitoring is important for the detection of newly emerging resistance profiles, the identification of vulnerable patient populations, and the assessment of the need for and the effectiveness of in-
The purpose of this document is to define reasonable and practical metrics and surveillance considerations for MDROs that will help detect changes in occurrence of MDRO colonization or infection in response to interventions in healthcare settings. This document should be used as a guide for hospital epidemiologists and infection control professionals for choosing the metrics most appropriate and useful for their specific setting. These recommendations offer standardization and increase reliability in the utility of the metric for local prevention efforts; however, these metrics should not be used for interfacility comparison, because the best means of risk adjustment have not been identified. Therefore, these metrics should not be promoted for external reporting purposes until after appropriate validation studies have identified the best measures for such reporting. Process metrics, such as the percentage of healthcare facilities that adhere to active surveillance testing (AST) or that comply with hand hygiene and contact precautions, are used by many facilities but are not addressed in this document, which focuses on outcome metrics.

The Centers for Disease Control and Prevention (CDC) and the Society for Healthcare Epidemiology of America (SHEA) convened a working group of experts to review the existing published and unpublished literature and guidelines on MDRO metrics and surveillance strategies. The working group consisted of experts from the CDC, SHEA, HICPAC, and the Association for Professionals in Infection Control and Epidemiology.

**Issues to Consider When Using MDRO Surveillance Methods**

**Pathogens.** The MDROs of greatest concern to healthcare facilities include (1) methicillin-resistant *Staphylococcus aureus* (MRSA), (2) vancomycin-resistant enterococci (VRE), (3) multidrug-resistant (MDR) gram-negative bacilli (such as *Enterobacter*, *Klebsiella*, *Acinetobacter*, and *Pseudomonas* species and *Escherichia coli*), and (4) vancomycin-resistant *S. aureus.*

**The MDROs of greatest concern to healthcare facilities include (1) methicillin-resistant *Staphylococcus aureus* (MRSA), (2) vancomycin-resistant enterococci (VRE), (3) multidrug-resistant (MDR) gram-negative bacilli (such as *Enterobacter*, *Klebsiella*, *Acinetobacter*, and *Pseudomonas* species and *Escherichia coli*), and (4) vancomycin-resistant *S. aureus.* For some MDR gram-negative bacilli, such as carbapenem-resistant *Enterobacter* species and extended-spectrum β-lactamase—producing *Klebsiella* species, the specific drug resistance patterns cause concern because of the challenges they present in treatment and infection prevention. However, no standard definitions exist for multiple drug resistance for many gram-negative bacilli. Healthcare facilities...
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tion) or asymptomatic carriage (ie, colonization). Differen­
tial evidence other than a positive microbiological test  

case definition of ventilator-associated pneumonia. Be­

growth MDROs often reflect endotracheal colonization. 

should define MDR gram-negative bacilli on the basis of local  

clinical scenarios, and the definition should be consistent over time to ensure valid longitudinal comparisons. For example, mul
tidrug-resistant *Pseudomonas aeruginosa* may be considered to be isolates that are resistant to 3 or more classes of anti
microbials (eg, carbapenems, piperacillin, quinolones, and aminoglycosides), and extended-spectrum cephalosporin-resistant *Klebsiella pneumoniae* may be considered to be isolates that are resistant to either ceftaxone or cefazidime. This document does not address *Clostridium difficile*, which is considered by some to be an MDRO and has been addressed elsewhere. 

**Infection and colonization.** MDROs might be associated with either symptomatic illness (ie, clinical disease or infection) or asymptomatic carriage (ie, colonization). Differen
tiating colonization from infection can be difficult; clinical assessments for therapy and for surveillance of healthcare-associated infections often require the accumulation of addi
tional evidence other than a positive microbiological test result. For example, cultures of respiratory-tract specimens that grow MDROs often reflect endotracheal colonization. Without substantial supporting evidence, culture-positive specimens may neither represent clinical infection nor fulfill the case definition of ventilator-associated pneumonia. Be
cause many considerations are involved in identifying clinical infections, selecting metrics that minimize the need for clin
ical interpretation can allow for more consistent and objective surveillance. For example, the recovery of pathogenic or
organisms from certain clinical specimens is almost universally associated with clinical infection; these specimens include blood and samples from other normally sterile body sites, such as cerebrospinal fluid, pleural fluid, synovial or joint fluid, bone, pericardial fluid, and peritoneal fluid. In con
trast, the isolation of MDROs from specimens of nonsterile body sites, which include sputum and wounds, does not nec
essarily represent clinical disease.

**Hospital-onset and community-onset infections.** Infections identified in patients after 48–72 hours of hospitalization or 48–72 hours after hospital discharge are often defined as noso
comial in the absence of evidence of active or incubating infection on admission. Nosocomial infections are also often termed “hospital-onset” and are only a subset of all health
care-associated disease; “hospital-onset” is defined using only information related to the timing of specimen collection in relation to hospital admission. Hospital-onset categorization is easier to apply than categorization requiring clinical evaluation, but it is less specific for identifying true nosocomial infections, because the assessment of recent healthcare exposures or of whether an infection may have been incubating at the time of admission is lacking (Table 1).

![Figure](image)

**Figure.** Percentage of strains of methicillin-resistant *Staphylococcus aureus* (MRSA) isolated from clinical cultures at 3 hospitals in the first 5 days of hospitalization, by day after admission. Hospital 1 reported 1,865 isolates, hospital 2 reported 1,319 isolates, and hospital 3 reported 1,004 isolates. All isolates were nonduplicates (ie, the first isolate recovered from each patient during the reporting period). The percentages of isolates stabilized after day 3 for hospitals 1 and 3, and after day 2 for hospital 2. The percentages of isolates obtained after day 5 were 23% for hospital 1, 42% for hospital 2, and 12% for hospital 3 (data were supplied courtesy of Bala Hota, Cook County Bureau of Health Services, Chicago, IL).
or infection to prior hospital exposure. History of MORO colonization or infection, had no positive clinical or AST result during the first 3 days of hospitalization, or had not been tested during the first 3 days of hospitalization) who subsequently has either a positive AST result or clinical culture of a sample obtained ≥ 3 calendar days after admission.

- Healthcare acquisition of an MORO occurs in a patient without MORO colonization or infection on admission (because the patient either had no prior history of colonization or infection, had no positive clinical or AST result during the first 3 days of hospitalization, or had not been tested during the first 3 days of hospitalization) who subsequently has either a positive AST result or clinical culture of a sample obtained ≥ 3 calendar days after admission.

For example, patients with methicillin-resistant Staphylococcus aureus (MRSA) bacteremia, ventilator-associated pneumonia due to multidrug-resistant gram-negative bacilli, or MRSA surgical site infection.

Quantifying healthcare acquisition

- Incidence or incidence density rate of hospital-onset MDRO based on clinical culture data
- Incidence or incidence density rate of hospital-onset MDRO based on clinical culture and AST data

Estimating exposure burden

- Overall prevalence or prevalence density rate based on clinical culture data
- Overall prevalence or prevalence density rate based on clinical culture and AST data
- Admission prevalence rate based on clinical culture data with or without AST
- Point prevalence rate based on point prevalence surveys
- Quantifying healthcare acquisition

Definitions of Recommended Metrics for Multidrug-Resistant Organisms (MDROs) and the Infections They Cause

- Table 2

| Category, name of metric | Type of microbiologic data required | Numerator |
|--------------------------|-------------------------------------|-----------|
| Tracking patients Line list | Clinical culture data (and AST data if available) | Patients with newly recovered MDRO isolates (regardless of specimen source), by HCF |
| Monitoring susceptibility patterns Antibigram | Clinical culture data only | No. of first susceptible clinical isolates (regardless of specimen source) per patient for each unit or HCF |
| Estimating infection burden Incidence or incidence density rate of hospital-onset bacteremia | Blood culture data only | No. of MDRO isolates recovered from blood samples (separated by 14 days) for each unit or HCF ≥ 3 calendar days after admission to unit or HCF |
| Nosocomial, organism-specific infection incidence or incidence density rate | Clinical culture data only | No. of hospital-onset MDRO infections meeting standard infection criteria |
| Organism-specific, device-associated incidence density rate | Clinical culture data only | No. of device-associated MDRO infections |
| Organism- and procedure-specific incidence density rate | Clinical culture data only | No. of procedures associated with MDRO infection |
| Estimating exposure burden Overall prevalence or prevalence density rate based on clinical culture data | Clinical culture data only | No. of first MDRO isolates (regardless of specimen source) per patient for each unit or HCF, regardless of time patient spent in unit or HCF; and no. of patients with history of colonization or infection |
| Overall prevalence or prevalence density rate based on clinical culture and AST data | Clinical culture and AST data | No. of first MDRO isolates (regardless of specimen source) per patient for each unit or HCF, regardless of time patient spent in unit or HCF; and no. of patients with history of colonization or infection |
| Admission prevalence rate based on clinical culture data with or without AST | Clinical culture data with or without AST | No. of first MDRO isolates (regardless of specimen source) per patient for each unit or HCF ≥ 3 calendar days after admission to unit or HCF; and no. of patients with history of colonization or infection |
| Point prevalence rate based on point prevalence surveys | Clinical culture and AST data | No. of MDRO isolates (regardless of specimen source) per patient for each unit or HCF |
| Quantifying healthcare acquisition Incidence or incidence density rate of hospital-onset MDRO based on clinical culture data | Clinical culture data only | No. of first MDRO isolates from clinical specimens only (regardless of specimen source) per patient for each unit or HCF ≥ 3 calendar days after admission to unit or HCF, excluding patients with history of colonization or infection |
| Incidence or incidence density rate of hospital-onset MDRO based on clinical culture and AST data | Clinical culture and AST data | No. of first MDRO isolates (regardless of specimen source and including AST), per patient for each unit or HCF ≥ 3 calendar days after admission to unit or HCF, excluding patients with history of colonization or infection |

- AST, active surveillance testing; HCF, healthcare facility.
- A patient might be counted more than once during a surveillance period if the positive blood culture results are for specimens obtained at least 14 days apart; similarly, multiple isolates from the same patient should not be counted if they are obtained within 14 days of the first positive culture result, even if it spans 2 surveillance periods.
- Prevalence density and incidence density differ from prevalence rate and incidence rate in their denominators: for the prevalence or incidence density, the number of patient-days is used as the denominator; for the prevalence or incidence rate, the number of admissions to hospital is used as the denominator.
- Definitions are from the Centers of Disease Control and Prevention’s National Healthcare Safety Network.
- For example, patients with ventilator-associated pneumonia due to multidrug-resistant gram-negative bacilli.
- For example, patients with methicillin-resistant Staphylococcus aureus surgical site infection.
- A subset of admission-prevalent MDRO isolates may be attributable to patients who were previously hospitalized or who visited an outpatient clinic, but the degree of variability in accessing these data and the lack of a standard definition to apply limit our recommendation of the admission prevalence rate as defined here. HCFs may choose to further categorize isolates on the basis of patient exposure to the HCP, as outlined in Table 1, to attribute colonization or infection to prior hospital exposure.
- Healthcare acquisition of an MDRO occurs in a patient without MDRO colonization or infection on admission (because the patient either had no prior history of MDRO colonization or infection, had no positive clinical or AST result during the first 3 days of hospitalization, or had not been tested during the first 3 days of hospitalization) who subsequently has either a positive AST result or clinical culture of a sample obtained ≥ 3 calendar days after admission. Furthermore, using different types of AST techniques with varying sensitivities may affect the acquisition metrics (e.g., switching from polymerase chain reaction [PCR]-based AST to culture-based AST, or using PCR-based AST at admission and culture-based AST at discharge).
| Denominator | Surveillance interval | Location of use |
|-------------|-----------------------|-----------------|
| None | Continuous | Whole HCP |
| Total no. of isolates (both susceptible and resistant) per patient for each unit or HCF | At least annually | Whole HCP (consider use for specific units or populations) |
| 100 patient admissions (incidence); 1,000 patient-days (incidence density) | Monthly | Specific units (consider use for whole HCP) |
| 100 patient admissions (incidence); 1,000 patient-days (incidence density) | Monthly | Specific units (consider use for whole HCP) |
| 1,000 device-days | Monthly | Specific units (consider use for whole HCP) |
| 100 procedures | Monthly (or quarterly if needed) | Not applicable |
| 100 patient admissions (prevalence); 1,000 patient-days (prevalence density) | Monthly | Specific units (consider use for whole HCP) |
| 100 patient admissions (prevalence); 1,000 patient-days (prevalence density) | Monthly | Specific units (consider use for whole HCP) |
| 100 patient admissions | Monthly | Specific units (consider use for whole HCP) |
| 100 patient admissions | Point in time | Specific units (consider use for whole HCP) |
| 100 patient admissions (incidence); 1,000 patient-days (incidence density) | Monthly | Specific units (consider use for whole HCP) |
| 100 patient admissions (incidence); 1,000 patient-days (incidence density) | Monthly | Specific units (consider use for whole HCP) |

assessment to determine the presence of active or incubating infection. Without these clinical assessments, a temporal definition of hospital-onset colonization or infection will result in a conservative underestimate of MDRO colonization or infection attributable to the hospital stay, but it is likely a more specific measure (fewer false positive findings) for ascertainment of nosocomial MDRO colonization or infection.

Patients with a history of colonization or infection. Patients might be persistently colonized with an MDRO, and the duration of colonization depends on the MDRO. MRSA can be carried in the nares for more than 1 year; in one study, subsequent MRSA infections occurred in 29% of patients within 18 months of a previous colonization or infection. Similarly, colonization with VRE and MDR gram-negative bacilli can also be prolonged, lasting for more than 1 year.

To identify the prevalence or incidence of MDRO colonization or infection, knowing which patients have a history of colonization or infection ("historically positive") is important. A patient with a history of colonization or infection is one with a known positive clinical or surveillance test result (from the healthcare facility where the patient is being treated or from another healthcare facility where the patient could have received medical care) at the time he or she is being admitted to the new healthcare facility for treatment. We recommend that, once a patient has tested positive for MDRO colonization or infection at any healthcare facility, that patient should be considered to have this status indefinitely (ie, "once positive, always positive"). If the referring facilities lack the pertinent data, then we recommend that, at a minimum, the new facilities try to identify patients with a history of MDRO positivity by searching their own laboratory records for MDRO isolates from the year before admission.
Surveillance period. We recommend that MDRO data be reviewed regularly for trends and for assessment of response to specific interventions. In general, we recommend that assessment of clinical cultures be performed monthly, with an appropriate calculation of both numerators and denominators. These values can later be used to calculate annual pooled rates of monthly calculations. For small facilities with only infrequent cases of MDRO colonization or infection, all metrics might need to be calculated quarterly or annually, to make them more meaningful. In an outbreak situation, daily or weekly calculations could be warranted.

Duplicate MDRO isolates from the same patient. Duplicate isolates can be defined operationally as all MDRO isolates recovered from specimens collected after initial isolation of
| Topic | Comments |
|-------|----------|
| Definitions for nosocomial infection or colonization | Little consensus exists regarding the precise definition for nosocomial infection or colonization. Research is urgently needed that focuses on investigating the diversity of approaches and, more importantly, determining the effects of different definitions on the results of surveillance. This would include definitions for timing (e.g., 48 hours, 72 hours, 2 days, or 3 days), definitions for presence of healthcare-associated risk factors on admission or readmission of patient, and definitions for attributing infections to a particular HCF. Elucidation of this issue will also permit greater standardization of practice in all HCFs. |
| Metric for MDRO colonization or infection in other healthcare settings | Nearly all data on which this guideline is based were derived from adult acute care hospitals. However, more and more individuals are cared for in other healthcare settings (e.g., long-term care, rehabilitation, and long-term acute care facilities). Whether the recommended metrics would also be accurate and practical in these healthcare settings is unknown. Research focusing on developing and validating metrics of MDRO infection or colonization in other healthcare settings is thus urgently needed. |
| Elucidating the epidemiology of colonization with MDROs | Although some data have been published regarding the duration of colonization with MRSA, fewer data exist for other MDROs. A clearer characterization of the duration of colonization, and of the risk factors for prolonged colonization, is critical to determining better strategies for identifying and tracking patients colonized with such pathogens. This will also be relevant to determining better strategies for identifying patients with a prior history of MDRO colonization and for clarifying the “number at risk” during surveillance activities. Further evaluation of the correlation between colonization pressure and prevalence metrics could be useful. If HCFs have developed specific protocols for identifying patients no longer colonized or infected with a specific MDRO, the HCFs can use these protocols to consider these patients decolonized. Of note, there are currently no consensus guidelines for confirming decolonization of patients with MDROs. |
| Determining the impact of including or excluding “at risk” patients in the numerator or denominator of the metrics proposed | Although data have been published focusing on colonization or infection with VRE and with MRSA in tertiary care intensive care units, few data are available for other healthcare settings or other organisms. One simple method that could help remove data for the initial hospital days for which the patient is not at risk for nosocomial acquisition is to subtract the number of admissions from the total number of patient-days and multiply that number by 3. In addition, further assessment of the impact of removing prevalent cases from the denominator is needed. |
| Defining optimal anatomic sites to sample for surveillance | It is increasingly recognized that collecting culture samples from different anatomic sites might result in differing abilities to identify a colonized patient. Clearly, the optimal anatomic site or combination of anatomic sites to sample will differ for each organism. Identifying the most sensitive, but also the most practical, approach to optimizing the yield of surveillance cultures is necessary. |
| Risk adjustment | Valid risk adjustment of these metrics has not been established in the scientific literature, and correlating proxy metrics with gold standards could allow some of these metrics to be compared between HCFs. |
| Development and evaluation of new metrics | There are many new metrics that can be evaluated for their utility, such as the following metrics of incidence: (1) new cases of MRSA acquisition per 1,000 patient-days [61] and (2) new cases of MRSA acquisition per 1,000 laboratory specimens. |

**Note.** HCF, healthcare facility; MRSA, methicillin-resistant *S. aureus*; VRE, vancomycin-resistant *Enterococcus*. 
the MDRO from the same patient during the defined surveillance period, regardless of specimen source. For most metrics, only the first MDRO isolate recovered from a patient during a given surveillance period should be included, so that the rates of MDRO colonization or infection are not overestimated.\textsuperscript{17,20} Although recurrent positive blood culture results can occur for the same patient after treatment, discrete episodes of bacteremia should be considered separate events. Recommendations for handling this specific situation (ie, recurrent positive blood culture results) are discussed below, in the subsection "Estimating Infection Burden."

**Location and patient population.** Surveillance may be conducted throughout the healthcare facility or in specific areas, such as high-risk units (eg, intensive care units [ICU]), locations with a historically high prevalence of MDRO colonization or infection (eg, specialty care areas, such as hematology and oncology wards, inpatient dialysis units, burn units, and long-term care areas), and units where interventions are planned or occurring. In addition, facilities might want to monitor specific patient populations with characteristics that place them at increased risk for acquiring MDROs.\textsuperscript{1,21,22} Because this document is a guide for the use of metrics for evaluation of MDROs to inform local intervention efforts, we recommend, at a minimum, that the metrics be used in hospital units planning or conducting interventions. For location-specific metrics, MDRO colonization or infection should be attributed to the location of the patient at the time of specimen collection. Use of an additional hospital-wide metric can allow one to evaluate the impact of MDROs outside of the intervention area. Stratification of the findings of some metrics by location can demonstrate differences that are of clinical utility, such as with antibiograms, which demonstrate the higher prevalence of resistance to antimicrobials among MDRO isolates recovered from ICUs patients, compared with those recovered from all other hospital patients.\textsuperscript{23} Stratification of the findings of other proposed metrics has not been well studied to date.

**Prevalence and incidence metrics.** The prevalence rate of MDRO infection or colonization is the total number of patients with MDRO infection or colonization in a specific population during a specified period of time. An incidence rate of MDRO infection or colonization is the total number of patients with newly acquired MDRO infection or colonization in a specific population during a specified period. For most MDRO metrics, we recommend calculating a simple prevalence or incidence per 100 patients admitted to the hospital, because it is easily understood and provides the same relative quantification as the metrics that use population density (ie, a denominator of patient-days).\textsuperscript{1,21,22} If desired, calculating prevalence density or incidence density will better account for length of patient stay (ie, all days during which patients are at risk for MDRO infection or colonization). Prevalence density and incidence density differ from prevalence rate and incidence rate in their denominators: for the prevalence or incidence density, the number of patient-days is used as the denominator; for the prevalence or incidence rate, the number of admissions to the hospital is used as the denominator. A patient-day is the period between a census-taking hour or specific time of day and that same exact hour or time of day on the following calendar day (eg, midnight to midnight). We recommend that partial days be excluded from the total patient-day count unless the partial day is the day of admission.\textsuperscript{26}

For accuracy, the denominators for incidence metrics can be adjusted for the at-risk population; patients may not be considered “at risk” for MDRO colonization or infection if they have been in the hospital for 3 or fewer calendar days, or if they have had prior colonization or infection, depending on the metric. Nevertheless, for simplicity, we recommend proxy measures in which all admitted patients or all patient-days are included in the denominator rather than counting only those admitted patients or patient-days in which the patient is at risk for colonization or infection. The rationale for this recommendation is that, in general, identifying patients or patient-days at risk is time-consuming and not standard procedure; also, we do not know at this time whether using patients or patient-days at-risk will substantially affect the interpretation of data trends at most facilities. Furthermore, patient-days attributed to patients colonized or infected with an MDRO (ie, patient-days that would arguably be removed from the denominator) still represent time the patient is at risk for acquiring a second strain of the same MDRO. We recognize that including all patients in the denominator might artificially lower the incidence rate and that changes in length of stay over time may affect trends in a facility. This recommendation is best applied to hospitals with a low prevalence of MDRO colonization or infection. Hospitals with short lengths of stay could disproportionately underestimate the incidence of MDRO colonization or infection because fewer cases will be identified 3 days after admission.

**AST.** Given that colonization is by definition asymptomatic, AST, which includes use of active surveillance cultures and other laboratory techniques for identifying MDROs, significantly increases detection of colonized patients in a facility.\textsuperscript{17,18,27-29} VRE and MDR gram-negative bacilli are often present only in the gastrointestinal tract and might not be routinely detected by clinical cultures. In addition to detecting the hidden reservoir, AST also increases the detection of MDRO carriage, thus lessening the likelihood that carriers will be misclassified as having new nosocomial acquisition of an MDRO. Although AST enables metrics to be substantially more accurate by reducing misclassification, it creates an up-front need for financial resources and places an increased burden on the clinical laboratory; thus, appropriate planning is warranted, particularly in areas of low prevalence.\textsuperscript{30} Fortunately, estimates of the rate of recovery of MDROs from clinical cultures often parallel estimates derived from AST for acquisition of MRSA in the ICU.\textsuperscript{25} According to one study, however, this is not the case for rates of acquisition of VRE in the ICU.\textsuperscript{24} For VRE, and likely for MDR gram-negative bacilli, metrics based on AST provide better estimates of
MDRO prevalence and rates of healthcare-associated acquisition (hereafter healthcare acquisition), because asymptomatic colonization is very common.

Many aspects of an AST program will influence the reproducibility and validity of the results. These include the choice of anatomic sites for specimen collection, which MDRO is measured, the testing and reporting method, and compliance with AST among eligible patients. The sensitivity of commonly employed AST techniques ranges from 50% to 90%, and sensitivity varies depending on the bacteria detected and the method used. Healthcare facilities may or may not choose to conduct AST; 2 recent studies offer conflicting findings as to whether AST for MRSA, followed by measures to prevent transmission by identified carriers, can significantly reduce MRSA disease burden.

Description of MDRO Metrics

We have divided the recommended MDRO metrics into 5 categories based on the purpose of the metrics: (1) tracking patients, (2) monitoring susceptibility patterns, (3) estimating infection burden, (3) estimating exposure burden, and (5) quantifying healthcare acquisition. For each category, we will discuss the recommended metrics and surveillance methods. The metrics and their definitions are summarized in Table 2.

Tracking patients. The most basic, time-honored method for tracking MDROS is the line list, which is essentially an annotated case count. For each hospital unit or healthcare facility, the first MDRO isolate recovered from a patient, regardless of source of specimen, is added to a list. The line list is not a rate and has no denominator. It does not have a defined surveillance period because the list is continually updated. The line list is derived using data from clinical cultures and AST, if available.

The line list has several uses. It is simple and could be the only essential metric for rare MDROS, such as vancomycin-resistant S. aureus and some MDR gram-negative bacilli. For more common MDROS, such as MRSA, the line list provides identification of patients with a history of infection or colonization, for calculating prevalence or incidence rates. The line list can be used to trigger and follow outbreak investigations for new or rapidly emerging MDROS. An increase in the number of cases in a healthcare facility may signify a hospital location at time of specimen collection, date of admission, and date of last discharge from the healthcare facility. Operationally, the line list could be an electronic system that flags patients admitted to a facility for rapid identification and contact isolation if they have a history of MDRO colonization or infection. Classification of MDROs can be made as outlined in Table 1.

Monitoring susceptibility patterns. A commonly used metric for cumulative susceptibility to antimicrobial agents is the antibiogram (ie, the proportion of isolates of a specific pathogen susceptible to a specified agent). Historically, the main purpose of the antibiogram has been to provide guidance for antimicrobial prescribing practices; however, the antibiogram can also be used to monitor progress in assessing the proportion of MDROS resistant to certain antibiotics of interest. Although this proportion is identified on the basis of clinical culture results without confirmation of infection, it is still useful in assessing resistance among isolates that can lead to infection. Nevertheless, the antibiogram might underestimate the resistance of isolates that definitively cause infection for some pathogens, such as MRSA and MDR gram-negative bacilli. Although antibiograms are easily constructed using common laboratory systems, they have the following disadvantages: (1) a decrease in the number of patients infected with an MDRO (and not the proportion of isolates susceptible) is often the goal of intervention, and this goal may not be reflected in the proportion metric reported in the antibiogram; (2) many healthcare facilities only construct annual, facility-wide antibiograms, an approach that might not allow evaluation of a unit-specific intervention; (3) the percentage of isolates susceptible may change slowly in response to an intervention; and (4) the antibiogram might not translate well to rates of antibiotic resistant infection among patients with confirmed disease.

The Clinical and Laboratory Standards Institute (CLSI) guideline document provides recommendations for how to construct an antibiogram. We support the CLSI recommendations that antibiograms be created only for species with at least 30 isolates tested, and they should include only isolates from clinical cultures and not isolates from AST. In outbreak situations, facilities might choose to create antibiograms for fewer than 30 isolates, to assess whether they have similar profiles. Only the first isolate recovered from a patient during a surveillance period should be included. Isolates that produce test results indicating intermediate resistant should not be classified as susceptible. The CLSI recommends constructing antibiograms at least annually; in some circumstances, facilities might want to construct antibiograms monthly or quarterly, to monitor quickly changing susceptibility patterns. Concerns and further suggestions on the construction of antibiograms have been described elsewhere.

Estimating infection burden. When monitoring an MDRO, facilities should have some estimate of the overall burden of the MDRO at their institution. One metric minimally influenced by variation in practices of clinical testing is the incidence of hospital-onset MDRO bacteremia. Blood samples for culture are routinely drawn in response to fever. Positive blood culture results are simple to identify, are highly likely to represent infection, and are a well-validated metric. In addition, this metric has been shown to decrease in response to interventions to prevent MDRO infections in published studies from institutions with high rates of MRSA and VRE bacteremia.
We recommend that a proxy for MDRO bacteremia be defined as a blood culture positive for an MDRO, excluding those blood culture results obtained within 14 days after a previous episode of bacteremia due to the same MDRO. We recommend the 14-day interval to differentiate between persistent bacteremia and relapse or recurrent bacteremia. According to this surveillance definition (ie, proxy for MDRO bacteremia), a patient might have more than 1 episode of bacteremia in a surveillance period if the time from the last positive blood culture result to the next is at least 14 days. Two separate episodes of bacteremia should be counted, even if the 14-day interval spans 2 surveillance periods. We recommend using the 14-day interval to ensure that the second culture sample is obtained well after the median length of time needed to sterilize the bloodstream when treating bacteremia.\(^4\)\(^{-6}\) Although using this proxy measure for bloodstream infection may not always reflect true disease (occasionally an MRSA or VRE blood culture isolate may represent skin contamination), this metric has some demonstrated success related to prevention of MDRO infection and has had some success as part of a national system used by the Health Protection Agency in the United Kingdom.\(^47\)

Another metric that may be useful to healthcare facilities is the incidence of nosocomial, organism-specific infection, such as the incidence of MRSA infection. This metric would include a clinical evaluation of all specimens representing infection with an MDRO as defined by the CDC.\(^10\) Facilities might also want to monitor infections with specific organisms in specimens other than blood by calculating an organism-specific, device- or procedure-associated incidence density. For example, institutions might want to consider a specific metric of infection burden when monitoring an increase of Acinetobacter baumannii pneumonia in ventilated patients, extended-spectrum \(\beta\)-lactamase–producing \(K.\) pneumoniae infection in patients with indwelling urinary catheters, or MRSA surgical site infections in patients who recently underwent coronary artery bypass graft procedures.

**Estimating exposure burden.** The metrics for exposure burden track the amount of exposure that patients in a healthcare facility have to patients who are either colonized or infected with an MDRO and who could potentially transmit the MDRO to them. This colonization pressure is an independent risk factor for healthcare acquisition of MRSA\(^48\) and VRE,\(^49\) and has been calculated in several ways in research studies. We recommend a simple approach that should help healthcare facilities gauge whether exposure levels are high and should potentially explain any ongoing transmission of MDROs. For MRSA colonization or infection in healthcare facilities where AST is not routinely performed, we recommend calculating an overall prevalence based on clinical cultures, including those from specimens from patients with MDRO isolates identified and those from specimens from patients with a history of colonization. Clinical cultures include all cultures of samples gathered to evaluate possible infection and not gathered as part of AST; for example, this includes culture of catheter tips to evaluate for infection. This metric is helpful for MRSA, in particular, because prevalence based on clinical cultures alone has been shown to be correlated with prevalence based on AST and clinical cultures. Nevertheless, prevalence based on clinical cultures alone significantly underestimates the full reservoir and illuminates only the tip of the “resistance iceberg.”\(^50\) In healthcare facilities where AST is conducted, this metric should also include patients with positive AST results. This metric will be especially useful for institutions that care for patients who do not seek health care outside of the institution’s system; on the other hand, this metric will be more difficult to interpret for facilities that share patient populations.

Repeated point prevalence surveys can demonstrate decreased prevalence over time in response to active infection prevention and control interventions, as was shown in a large study of VRE by Ostrowsky et al.\(^51\) Such surveys can be an important adjunct to ongoing, monthly surveillance, because they can be used in addition to recommended metrics and can help the staff of a healthcare facility gauge the magnitude by which clinical cultures alone underestimate prevalence at a given institution. The results of point prevalence surveys could help identify areas with high MDRO endemity where heightened surveillance or AST would be helpful. Rhame and Suddeth\(^52\) proposed a mathematical model to estimate the incidence rate from prevalence surveys. Although evaluations of this formula have demonstrated that the prevalence of nosocomial infections is related to the incidence,\(^53\) this does not replace the direct metric of incidence, and measurement of point prevalence is not recommended as a routine practice.\(^54\)

Another useful exposure burden estimate is admission prevalence. This metric allows healthcare facilities to identify the magnitude of importation of an MDRO in the facility. It can also help identify whether importation is due to the readmission of recently discharged patients or to the transfer of patients from other healthcare facilities. A positive MDRO test result from the emergency department should be counted in an admission prevalence, if the specimen is obtained while the patient is awaiting admission.

**Quantifying healthcare acquisition.** Determining the rate of healthcare acquisition of MDROs is the outcome that allows the most direct assessment of the effectiveness of prevention programs. Healthcare acquisition is a term that includes not only environmental, patient-to-patient, and healthcare personnel–to–patient transmission but also de novo development of drug resistance, such as resistance due to antibiotic pressure. Virtually all new occurrences of MRSA or VRE colonization are the result of transmission, but antibiotic pressure might influence the likelihood of transmission and could be an important factor in the development of infections with MDR gram-negative bacilli (eg, \(Enterobacter\) species with inducible cephalosporin resistance).\(^35\)
The recommended metric for healthcare acquisition of most MDROs is the incidence rate based on clinical culture results. This metric applies to all hospitals but may underestimate or misclassify incident cases in the absence of AST. Nevertheless, in certain situations, such as MRSA colonization or infection in ICUs, the incidence rate based on clinical culture results could be a reasonable proxy. The usefulness of this metric for MDR gram-negative bacilli might vary depending on the genus involved. Patients with a history of MDRO colonization or infection must be excluded from the numerator because their inclusion will artificially inflate the incidence rate. Similarly, one could consider removing these patients from the denominator, especially for areas of high prevalence, to prevent the artificial deflation of the incidence rate. However, we do not recommend this practice, because it is labor intensive and may not affect the assessment of trends within facilities.

Use of AST will identify the transmission of MDROs better than use of clinical cultures alone, but even incidence rates based on both AST and clinical cultures are only an estimate of the rate of healthcare acquisition. AST will have its greatest impact in detecting the transmission of MDROs unlikely to be detected by clinical cultures alone, such as VRE. If an incidence rate based on both clinical cultures and AST is used to demonstrate the acquisition of MDROs in a healthcare facility, it would be useful to show that a particular patient had a baseline negative AST result and then became colonized or infected during his or her hospital stay. This type of assessment might be preferable for a research study or at an institution with sufficient staff to stratify by hospital area, where patients are or are not evaluated by AST. For the purpose of routine MDRO surveillance, we recommend defining a likely transmission event as an MDRO-positive clinical culture or AST result for any patient who previously had no MDRO colonization or infection on admission (because the patient either had no prior history of MDRO colonization or infection, had no positive clinical or AST result during the first 3 calendar days of hospitalization, or had not been tested during the first 3 days of hospitalization).

**Recommended metrics for specific MDROs.** Table 3 lists the recommended metrics for MRSA, VRE, and MDR gram-negative bacilli. For vancomycin-resistant *S. aureus*, use of a line list is sufficient, because this organism is extremely rare. Recommendations have been categorized as "basic" or "advanced." Those metrics labeled "basic" are routinely used as standard practice or are believed to be central to making a meaningful assessment of the impact of a prevention intervention. Those metrics labeled "advanced" are of great benefit in certain hospital settings, and the context in which these advanced metrics are recommended is noted in the comments in Table 3. All healthcare facilities should use the basic metrics in all circumstances; the use of the advanced metrics does not supplant the use of the basic ones. Several of the advanced metrics could be critically important to the assessment of MDROs, but they might not be applicable in all hospital settings. These categorizations are mostly expert opinions that are based on common practices or interpretations of the empirical evidence in the literature.

Other surveillance methods have been proposed to monitor quality of care. For example, determining the number of days between infections and using control charts could be useful in the context of quality improvement and could help to communicate nosocomial infection rates to hospital staff. These methods can be used in addition to our recommendations.

The surveillance of MDROs requires the ongoing support of microbiology laboratory technicians, infection prevention and control professionals, information technology specialists, and healthcare facility administrators. Conventional methods for microbiological culture can result in a delay of up to 5 days before results are available. Rapid detection methods, such as culture with media containing chromogenic enzyme substrates, and molecular detection methods, such as polymerase chain reaction assays, are being increasingly used, although they are more expensive and have not been shown to improve overall patient safety. Healthcare facilities could choose one method over the other depending on their assessment of the MDRO. A number of documents are available for guidance on performing a risk assessment for MRSA infection.

This document provides important insights into the need for future research. As noted previously, substantial deficiencies exist in the medical literature available. Additional considerations for future research include determining strategies for decolonization, improving interfacility communication on MDROs and the infections they cause, and assessing what constitutes a patient at high risk of acquiring various MDROs (Table 4).

**Limitations.** Healthcare facilities must be consistent with their use of surveillance methodology and metric definitions if comparison of data from different time periods in a hospital is desired. For example, once a healthcare facility introduces AST, comparison with the data from earlier time periods will require the appropriate handling of the AST results to make temporal comparisons valid. The majority of the recommended metrics are neither stratified by risk factors nor validated by an abundance of published studies. Therefore, these metrics are designed to be used by healthcare facilities to track changes over time and should not be used for interfacility comparison, for a number of reasons. First, it is difficult, if not impossible, to identify a gold standard for measuring MDRO infection and colonization in a healthcare setting, so metrics will differ because of variations in the processes used to collect data, in the patient population, and in specimen collection practices. Second, the metrics proposed in this document include both direct and proxy metrics, and the validity of proxy metrics has not been well established. Third, a valid risk adjustment of these metrics has not been
established in the scientific literature. Lastly, some of the metrics that we recommend were taken from studies of MDROs in healthcare facilities with high rates of MDRO-related disease, and therefore they might not be applicable to healthcare facilities with lower rates of MDRO-related disease.

Limited data exist for some of our recommendations, particularly for metrics of MDR gram-negative bacilli. There is a paucity of data on the burden of MDROs in the pediatric population and for nonhospitalized patients; thus, little guidance exists on the best metrics to use for these patient populations. Most of the metrics presented here were created on the basis of experience in other healthcare facilities and on the basis of studies undertaken in adult acute care hospitals.

**SUMMARY**

The assessment of MDRO infection and colonization should include the identification of known carriers, the detection of hospital-specific and healthcare-associated acquisition, an estimation of the burden of serious infection, an understanding of the reservoir affecting the transmission of MDROs, and an evaluation of the effect of intervention. Several strategies can be used to obtain data that aid in this assessment. We have defined and categorized the recommended metrics for each of these aspects of measuring MDRO infection and colonization, for use by healthcare facilities.

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