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Authors
Cohen, Adam L
Calfee, David
Fridkin, Scott K
et al.

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

Adam L. Cohen, MD, MPH; David Calfee, MD, MS; Scott K. Fridkin, MD; Susan S. Huang, MD, MPH; John A. Jernigan, MD; Ebbing Lautenbach, MD, MPH, MSCE; Shannon Oriola, RN, CIC, COHN; Keith M. Ramsey, MD; Cassandra D. Salgado, MD, MS; Robert A. Weinstein, MD; for the Society for Healthcare Epidemiology of America and the Healthcare Infection Control Practices Advisory Committee

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 underestimates 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-

From the Divisions of Bacterial Diseases (A.L.C.) and Healthcare Quality Promotion (S.K.F.), Centers for Disease Control and Prevention, Atlanta, Georgia; the Department of Medicine, Mount Sinai School of Medicine, New York, New York (D.C.); the Division of Infectious Diseases, University of California Irvine Medical Center (S.S.H.), Orange, and Sharp Metropolitan Medical Campus (S.O.), San Diego, California; the Departments of Medicine and Epidemiology, University of Pennsylvania, Philadelphia, Pennsylvania (E.L.); the Departments of Safety and Infection Control, Pitt County Memorial Hospital, and the Department of Medicine, The Brody School of Medicine at East Carolina University, Greenville, North Carolina (K.M.R.); Medical University of South Carolina, Charleston, South Carolina (C.D.S.); Cook County Bureau of Health Services and Rush Medical College, Chicago, Illinois (R.A.W.).

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TABLE 1. Definitions Used for Epidemiologic Classification of Infections With Multidrug-Resistant Organisms (MDROs)

Classification	Definition
Temporal	
Hospital-onset	Specimen was collected from patient after defined time period of hospitalization to best reflect that the pathogens were acquired in the hospital. Recommended definition is based on specimens being collected >3 calendar days after patient was admitted to the hospital (first day is date of admission). This is known as the "3 midnight rule." For example, if a patient is admitted to the hospital at any time on a Monday, only MDROs that are isolated after midnight Wednesday night would be considered to represent hospital-onset infection (ie, specimen was collected on day 4 of hospitalization). All hospital-onset infections are considered healthcare-associated.
Community onset	Specimen was collected before defined time period of hospitalization to best reflect that the pathogens were acquired either in the community (including other institutions or homes) or during a previous hospitalization. Recommended definition is based on specimens being collected ⩽3 calendar days after the patient was admitted to the hospital. A subset of community-onset infections may be healthcare-associated.
Clinical	
Healthcare-associated	Categorization requires evaluation of the patient's clinical history, as well as the timing of specimen collection for clinical cultures. Patient has an identified association with recent healthcare delivery, such as current or recent hospitalization, use of an indwelling venous catheter, residence in a long-term care or rehabilitation hospital, recent surgery, and/or receipt of outpatient dialysis. These types of exposure to healthcare settings may vary as a result of study design and availability of data. Therefore, if data are available, community-onset infections (see above) could be categorized as healthcare-associated, to better understand the role played by healthcare facilities in the potential transmission of MDROs.
Nosocomial	Categorization requires evaluation of the patient's clinical history, as well as the timing of specimen collection for clinical cultures. The infection in a patient was likely to have been acquired during the hospital stay, without any evidence that infection was incubating or present on admission.
Community-associated	Categorization requires the evaluation of the patient's clinical history, as well as the timing of specimen collection for clinical cultures. Patient has no documented healthcare-associated risk factors (ie, community-onset infection [see above] and there is no identified association between patient and recent healthcare delivery).

terventions.[1] However, it is unclear which metrics for monitoring MDROs and the infections they cause are the best, because most metrics are not standardized.

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.*[1] 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.[2,5] Healthcare facilities

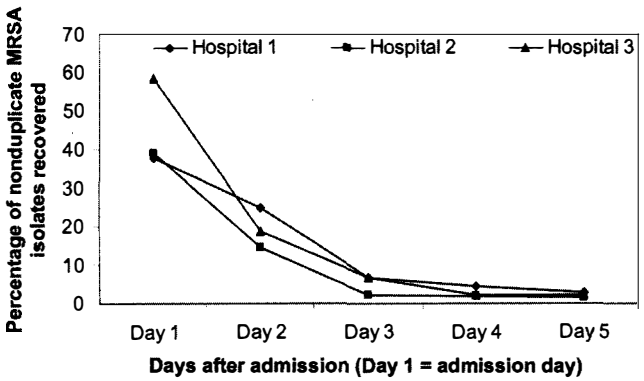

FIGURE. Percentage of strains of methicillin-resistant *Staphylococcus aureus* (MRSA) isolated from clinical cultures at 3 hospitals in the first 5 days of hospitalization, by day after admission. Hospital 1 reported 1,865 isolates, hospital 2 reported 1,319 isolates, and hospital 3 reported 1,004 isolates. 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).

should define MDR gram-negative bacilli on the basis of local scenarios, and the definition should be consistent over time to ensure valid longitudinal comparisons. For example, multidrug-resistant *Pseudomonas aeruginosa* may be considered to be isolates that are resistant to 3 or more classes of antimicrobials (eg, carbapenems, piperacillin, quinolones, and aminoglycosides), and extended-spectrum cephalosporin–resistant *Klebsiella pneumoniae* may be considered to be isolates that are resistant to either ceftriaxone or ceftazidime. This document does not address *Clostridium difficile,* which is considered by some to be an MDRO and has been addressed elsewhere.[6]

Infection and colonization. MDROs might be associated with either symptomatic illness (ie, clinical disease or infection) or asymptomatic carriage (ie, colonization). Differentiating colonization from infection can be difficult; clinical assessments for therapy and for surveillance of healthcare-associated infections often require the accumulation of additional 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. Because many considerations are involved in identifying clinical infections, selecting metrics that minimize the need for clinical interpretation can allow for more consistent and objective surveillance.[7,8] For example, the recovery of pathogenic organisms from certain clinical specimens is almost universally associated with clinical infection; these specimens include blood[9] and samples from other normally sterile body sites, such as cerebrospinal fluid, pleural fluid, synovial or joint fluid, bone, pericardial fluid, and peritoneal fluid.[10] In contrast, the isolation of MDROs from specimens of nonsterile body sites, which include sputum and wounds, does not necessarily 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 nosocomial 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 healthcare-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). Healthcare-associated disease encompasses hospital-onset infections and includes infections with disease onset in the community in persons with recent exposures to healthcare delivery.[11] For the routine categorization of MDRO infection, definitions for nosocomial MDRO infections would be useful for distinguishing MDRO infections associated with the current hospital stay from MDRO infections associated with exposures unrelated to the current hospital stay. However, the need to apply clinical considerations (such as the incubation period, the presence of infection at the time of admission by review of symptoms, or recent hospital discharges) to the classification of infection can be burdensome to apply facility wide.

One strategy for addressing this issue of classification of infection is to use proxy, laboratory-based MDRO metrics based on the timing of culture results relative to hospital admission. Specifically, we recommend that an MDRO be considered hospital-onset if the organism is isolated after the third calendar day of hospitalization, with the first day being the day of admission (the admission date is determined as the date a patient occupies a room for an overnight stay, not the date of an outpatient and/or emergency department visit; Table 1). This recommendation is made for the following reasons: (1) a calendar-day definition is easier to apply than the 48-hour rule; (2) it reduces variability in application of the definition by infection prevention and control staff; and (3) it ensures that patients have been hospitalized for at least a full 48 hours. Few MDRO infections have known incubation periods, but a recent evaluation of 3 hospitals in the Chicago area found that most MRSA isolates were cultured from samples obtained within the first 3 days after admission, which suggests that most community-associated MRSA infections will be identified by hospital day 4 (Figure). This definition is to be distinguished from the definition of the National Healthcare Safety Network and from other nosocomial infection definitions, which require chart review and bedside

TABLE 2. Definitions of Recommended Metrics for Multidrug-Resistant Organisms (MDROs) and the Infections They Cause

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		
Antibiogram	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[a]
Nosocomial, organism-specific infection incidence or incidence density rate	Clinical culture data only	No. of hospital-onset MDRO infections meeting standard infection criteria[c]
Organism-specific, device-associated incidence density rate[d]	Clinical culture data only	No. of device-associated MDRO infections[c]
Organism- and procedure-specific incidence density rate[e]	Clinical culture data only	No. of procedures associated with MDRO infection[c]
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[f] rate based on clinical culture data with or without AST	Clinical culture data with or without AST data	No. of first MDRO isolates (regardless of specimen source) per patient for each unit or HCF $\leq$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[g]
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[f]

NOTE. AST, active surveillance testing; HCF, healthcare facility.

[a] 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.

[b] 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.

[c] Definitions are from the Centers of Disease Control and Prevention's National Healthcare Safety Network.[10]

[d] For example, patients with ventilator-associated pneumonia due to multidrug-resistant gram-negative bacilli.

[e] For example, patients with methicillin-resistant *Staphyloccus aureus* surgical site infection.

[f] 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 HCF, as outlined in Table 1, to attribute colonization or infection to prior hospital exposure.

[g] 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 $\geq$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).

TABLE 2. *(Continued.)*

Denominator	Surveillance interval	Location of use
None	Continuous	Whole HCF
Total no. of isolates (both susceptible and resistant) per patient for each unit or HCF	At least annually	Whole HCF (consider use for specific units or populations)
100 patient admissions (incidence); 1,000 patient-days (incidence density)[b]	Monthly	Specific units (consider use for whole HCF)
100 patient admissions (incidence); 1,000 patient-days (incidence density)[b]	Monthly	Specific units (consider use for whole HCF)
1,000 device-days	Monthly	Specific units (consider use for whole HCF)
100 procedures	Monthly (or quarterly if needed)	Not applicable
100 patient admissions (prevalence); 1,000 patient-days (prevalence density)[b]	Monthly	Specific units (consider use for whole HCF)
100 patient admissions (prevalence); 1,000 patient-days (prevalence density)[b]	Monthly	Specific units (consider use for whole HCF)
100 patient admissions	Monthly	Specific units (consider use for whole HCF)
100 patient admissions	Point in time	Specific units (consider use for whole HCF)
100 patient admissions (incidence); 1,000 patient-days (incidence density)[b]	Monthly	Specific units (consider use for whole HCF)
100 patient admissions (incidence); 1,000 patient-days (incidence density)[b]	Monthly	Specific units (consider use for whole HCF)

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[12]; in one study, subsequent MRSA infections occurred in 29% of patients within 18 months of a previous colonization or infection.[13] Similarly, colonization with VRE and MDR gram-negative bacilli can also be prolonged, lasting for more than 1 year.[14-16]

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.

TABLE 3. Recommended Metrics for Specific Multidrug-Resistant Organisms (MDROs) and the Infections They Cause in a Healthcare Setting

Category and name of metric	Type of metric[a]	Comments
Tracking patients		
Line list	Basic	Initial part of any risk assessment; identifies patients with a prior history of colonization or infection. This might be the only metric necessary for rare MDROs (e.g., vancomycin-resistant *Staphylococcus aureus* and some MDR gram-negative bacilli).
Monitoring susceptibility patterns		
Antibiogram	Basic	Please refer to CLSI document [37].
Estimating infection burden		
Incidence rate of hospital-onset bacteremia	Basic	Basic for all MDROs. For MDR gram-negative bacilli, specifically, this metric could be especially useful for monitoring its emergence.
Nosocomial, organism-specific infection incidence or incidence density rate	Advanced	Useful for assessing the burden of a specific organism, regardless of extrinsic risk factors (e.g., catheter or ventilator use).
Organism-specific, device- or procedure-associated incidence or incidence density rate	Advanced	Useful for assessing the burden of specific device-associated infections or specific populations (e.g., orthopedic patients).
Estimating exposure burden		
Overall prevalence rate based on clinical culture data	Advanced	Reasonable initial risk assessment. This metric underestimates the hidden reservoir for MRSA [25], VRE [24], and MDR gram-negative bacilli. This metric could be especially useful for MRSA infection or colonization in an intensive care unit because it follows the same trends as overall prevalence based on clinical culture and AST data [25]. If coupled with point prevalence AST data, this metric allows an assessment of the degree to which clinical culture data alone underestimate the full reservoir. This metric will be especially useful for an HCF that wants to monitor patients that are affiliated with it; on the other hand, this metric will be more difficult to interpret for HCFs that share patient populations.
Overall prevalence rate based on clinical culture and AST data	Advanced	Very useful for robust assessment of intervention if conducting AST.[b]
Admission prevalence rate based on clinical culture data with or without AST	Advanced	Useful adjunct metric if there is concern about importation from the community or another HCF.
Point prevalence rate	Advanced	Useful adjunct metric for HCFs not conducting routine AST. Helps provide an estimate of the degree to which clinical culture data underestimate the full reservoir. Could help guide HCFs to decide when to initiate AST in select populations or units. Very useful part of a risk assessment to define high-risk areas or populations of an HCF.
Quantifying hospital-associated acquisition		
Incidence rate of hospital-onset MDRO colonization or infection based on clinical culture data	Basic for MRSA; advanced for VRE and MDR gram-negative bacilli	Useful for VRE and MDR gram-negative bacilli in certain circumstances only, such as during an outbreak or for monitoring emergence, because it substantially underestimates the hidden reservoir [24]. MRSA colonization or infection is also substantially underestimated, but estimates will likely correlate with rates in which AST data are added.
Incidence rate of hospital-onset MDRO colonization or infection based on clinical culture and AST data	Advanced	Provides a more accurate metric than incidence based on clinical culture data, if conducting routine AST.[c]

NOTE. AST, active surveillance testing; CLSI, Clinical and Laboratory Standards Institute; HCF, healthcare facility; MDR, multidrug-resistant; MRSA, methicillin-resistant *S. aureus*; VRE, vancomycin-resistant *Enterococcus*.

[a] All facilities should use the basic metrics in all circumstances. The context in which advanced metrics are recommended is noted in the comments. The use of the advanced metrics does not supplant the use of the basic ones.

[b] This metric could be used in place of overall prevalence rate based on clinical culture data.

[c] This metric could be used in place of incidence rate based on clinical culture data.

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

TABLE 4. Recommendations for Future Research on Multidrug-Resistant Organisms (MDROs) and the Infections They Cause

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 (eg, 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.[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.[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.[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).[24,25] 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.[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.[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 upfront need for financial resources and places an increased burden on the clinical laboratory; thus, appropriate planning is warranted, particularly in areas of low prevalence.[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.[25] According to one study, however, this is not the case for rates of acquisition of VRE in the ICU.[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.[1] The sensitivity of commonly employed AST techniques ranges from 50% to 90%, and sensitivity varies depending on the bacteria detected and the method used.[31-34] 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.[35,36]

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 growing problem and may require the additional collection of data to confirm a rise in incidence or incidence density.

The essential elements of the line list include patient identification, source of specimen and date of first positive result, 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).[37] 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[38] and MDR gram-negative bacilli.[39] 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.[37] 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.[40]

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.[9] 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[41,42] and VRE[43] 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.[44-46] 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 β-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 endemicity where heightened surveillance or AST would be helpful. Rhame and Sudderth[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).[55]

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.[25] The usefulness of this metric for MDR gram-negative bacilli might vary depending on the genus involved.[56] 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.[24] 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.[57] 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 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.[58] 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.[59,60]

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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Address reprint requests to Adam L. Cohen, MD, MPH, Division of Bacterial Diseases, Centers for Disease Control and Prevention, 1600 Clifton Road, MS C-23, Atlanta, GA 30333 (dvj1@cdc.gov).

REFERENCES

1. Siegel JD, Rhinehart E, Jackson M, Chiarello L; Healthcare Infection Control Practices Advisory Committee. Management of multidrug-resistant organisms in healthcare settings, 2006. Available at: http://www.cdc.gov/ncidod/dhqp/pdf/ar/mdroGuideline2006.pdf. 2006. Accessed June 24, 2008.
2. Paterson DL. The epidemiological profile of infections with multidrug-resistant *Pseudomonas aeruginosa* and *Acinetobacter* species. *Clin Infect Dis* 2006; 43 Suppl 2:S43–48.
3. Harris AD, McGregor JC, Furuno JP. What infection control interventions should be undertaken to control multidrug-resistant gram-negative bacteria? *Clin Infect Dis* 2006; 43 Suppl 2:S57–61.
4. Jones RN. Global epidemiology of antimicrobial resistance among community-acquired and nosocomial pathogens: a five-year summary from the SENTRY Antimicrobial Surveillance Program (1997–2001). *Semin Respir Crit Care Med* 2003; 24:121–134.
5. Falagas ME, Koletsi PK, Bliziotis IA. The diversity of definitions of multidrug-resistant (MDR) and pandrug-resistant (PDR) *Acinetobacter baumannii* and *Pseudomonas aeruginosa*. *J Med Microbiol* 2006; 55:1619–1629.
6. McDonald LC, Coignard B, Dubberke E, Song X, Horan T, Kutty PK. Recommendations for surveillance of *Clostridium difficile*–associated disease. *Infect Control Hosp Epidemiol* 2007; 28:140–145.
7. National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992 through June 2004, issued October 2004. *Am J Infect Control* 2004; 32:470–485.
8. Yokoe DS, Noskin GA, Cunnigham SM, et al. Enhanced identification of postoperative infections among inpatients. *Emerg Infect Dis* 2004; 10: 1924–1930.
9. Trick WE, Zagorski BM, Tokars JI, et al. Computer algorithms to detect bloodstream infections. *Emerg Infect Dis* 2004; 10:1612–1620.
10. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care–associated infection and criteria for specific types of infections in the acute care setting. *Am J Infect Control* 2008; 36:309–332.
11. Klevens RM, Morrison MA, Nadle J, et al. Invasive methicillin-resistant *Staphylococcus aureus* infections in the United States. *JAMA* 2007; 298: 1763–1771.
12. Sanford MD, Widmer AF, Bale MJ, Jones RN, Wenzel RP. Efficient detection and long-term persistence of the carriage of methicillin-resistant *Staphylococcus aureus*. *Clin Infect Dis* 1994; 19:1123–1128.
13. Huang SS, Platt R. Risk of methicillin-resistant *Staphylococcus aureus* infection after previous infection or colonization. *Clin Infect Dis* 2003; 36:281–285.
14. Pacio GA, Visintainer P, Maguire G, Wormser GP, Raffalli J, Montecalvo MA. Natural history of colonization with vancomycin-resistant enterococci, methicillin-resistant *Staphylococcus aureus*, and resistant gram-negative bacilli among long-term-care facility residents. *Infect Control Hosp Epidemiol* 2003; 24:246–250.
15. Byers KE, Anglim AM, Anneski CJ, Farr BM. Duration of colonization with vancomycin-resistant *Enterococcus*. *Infect Control Hosp Epidemiol* 2002; 23:207–211.
16. Baden LR, Thiemke W, Skolnik A, et al. Prolonged colonization with vancomycin-resistant *Enterococcus faecium* in long-term care patients and the significance of "clearance." *Clin Infect Dis* 2001; 33:1654–1660.
17. Hindler JF, Stelling J. Analysis and presentation of cumulative antibiograms: a new consensus guideline from the Clinical and Laboratory Standards Institute. *Clin Infect Dis* 2007; 44:867–873.
18. White RL, Friedrich LV, Burgess DS, Brown EW, Scott LE. Effect of removal of duplicate isolates on cumulative susceptibility reports. *Diagn Microbiol Infect Dis* 2001; 39:251–256.
19. Horvat RT, Klutman NE, Lacy MK, Grauer D, Wilson M. Effect of duplicate isolates of methicillin-susceptible and methicillin-resistant *Staphylococcus aureus* on antibiogram data. *J Clin Microbiol* 2003; 41: 4611–4616.
20. Lee SO, Cho YK, Kim SY, Lee ES, Park SY, Seo YH. Comparison of trends of resistance rates over 3 years calculated from results for all isolates and for the first isolate of a given species from a patient. *J Clin Microbiol* 2004; 42:4776–4779.
21. Lucet JC, Grenet K, Armand-Lefevre L, et al. High prevalence of carriage of methicillin-resistant *Staphylococcus aureus* at hospital admission in elderly patients: implications for infection control strategies. *Infect Control Hosp Epidemiol* 2005; 26:121–126.
22. Furuno JP, McGregor JC, Harris AD, et al. Identifying groups at high risk for carriage of antibiotic-resistant bacteria. *Arch Intern Med* 2006; 166:580–585.
23. Binkley S, Fishman NO, LaRosa LA, et al. Comparison of unit-specific and hospital-wide antibiograms: potential implications for selection of empirical antimicrobial therapy. *Infect Control Hosp Epidemiol* 2006; 27: 682–687.
24. Huang SS, Rifas-Shiman SL, Pottinger JM, et al. Improving the assessment of vancomycin-resistant enterococci by routine screening. *J Infect Dis* 2007; 195:339–346.
25. Huang SS, Rifas-Shiman SL, Warren DK, et al. Improving methicillin-resistant *Staphylococcus aureus* surveillance and reporting in intensive care units. *J Infect Dis* 2007; 195:330–338.
26. 2005 AHA Annual Survey. Health Forum, L.L.C. Available at: http://www.vtexplor.org/Downloads/. Accessed September 2, 2008.
27. Salgado CD, Farr BM. What proportion of hospital patients colonized with methicillin-resistant *Staphylococcus aureus* are identified by clinical microbiological cultures? *Infect Control Hosp Epidemiol* 2006; 27:116–121.

28. Lucet JC, Chevret S, Durand-Zaleski I, Chastang C, Regnier B. Prevalence and risk factors for carriage of methicillin-resistant *Staphylococcus aureus* at admission to the intensive care unit: results of a multicenter study. *Arch Intern Med* 2003; 163:181–188.
29. Eveillard M, Lancien E, Barnaud G, et al. Impact of screening for MRSA carriers at hospital admission on risk-adjusted indicators according to the imported MRSA colonization pressure. *J Hosp Infect* 2005; 59:254–258.
30. Diekema DJ, Edmond MB. Look before you leap: active surveillance for multidrug-resistant organisms. *Clin Infect Dis* 2007; 44:1101–1107.
31. Mertz D, Frei R, Jaussi B, et al. Throat swabs are necessary to reliably detect carriers of *Staphylococcus aureus. Clin Infect Dis* 2007; 45:475–477.
32. D'Agata EM, Gautam S, Green WK, Tang YW. High rate of false-negative results of the rectal swab culture method in detection of gastrointestinal colonization with vancomycin-resistant enterococci. *Clin Infect Dis* 2002; 34:167–172.
33. Lautenbach E, Harris AD, Perencevich EN, Nachamkin I, Tolomeo P, Metlay JP. Test characteristics of perirectal and rectal swab compared to stool sample for detection of fluoroquinolone-resistant *Escherichia coli* in the gastrointestinal tract. *Antimicrob Agents Chemother* 2005; 49:798–800.
34. Marchaim D, Navon-Venezia S, Schwartz D, et al. Surveillance cultures and duration of carriage of multidrug-resistant *Acinetobacter baumannii. J Clin Microbiol* 2007; 45:1551–1555.
35. Robicsek A, Beaumont JL, Paule SM, et al. Universal surveillance for methicillin-resistant *Staphylococcus aureus* in 3 affiliated hospitals. *Ann Intern Med* 2008; 148:409–418.
36. Harbarth S, Fankhauser C, Schrenzel J, et al. Universal screening for methicillin-resistant *Staphylococcus aureus* at hospital admission and nosocomial infection in surgical patients. *JAMA* 2008; 299:1149–1157.
37. Clinical and Laboratory Standards Institute (CLSI). Analysis and presentation of cumulative antimicrobial susceptibility test data: approved guideline. 2nd ed. Vol. 25. No. 28. Wayne, PA: CLSI, 2005:M39–A2.
38. Fridkin SK, Edwards JR, Tenover FC, Gaynes RP, McGowan JE Jr. Antimicrobial resistance prevalence rates in hospital antibiograms reflect prevalence rates among pathogens associated with hospital-acquired infections. *Clin Infect Dis* 2001; 33:324–330.
39. Bantar C, Alcazar G, Franco D, et al. Are laboratory-based antibiograms reliable to guide the selection of empirical antimicrobial treatment in patients with hospital-acquired infections? *J Antimicrob Chemother* 2007; 59:140–143.
40. Pakyz AL. The utility of hospital antibiograms as tools for guiding empiric therapy and tracking resistance. Insights from the Society of Infectious Diseases Pharmacists. *Pharmacotherapy* 2007; 27:1306–1312.
41. Huang SS, Yokoe DS, Hinrichsen VL, et al. Impact of routine intensive care unit surveillance cultures and resultant barrier precautions on hospital-wide methicillin-resistant *Staphylococcus aureus* bacteremia. *Clin Infect Dis* 2006; 43:971–978.
42. Shitrit P, Gottesman BS, Katzir M, Kilman A, Ben-Nissan Y, Chowers M. Active surveillance for methicillin-resistant *Staphylococcus aureus* (MRSA) decreases the incidence of MRSA bacteremia. *Infect Control Hosp Epidemiol* 2006; 27:1004–1008.
43. Price CS, Paule S, Noskin GA, Peterson LR. Active surveillance reduces the incidence of vancomycin-resistant enterococcal bacteremia. *Clin Infect Dis* 2003; 37:921–928.
44. Fowler VG Jr, Boucher HW, Corey GR, et al. Daptomycin versus standard therapy for bacteremia and endocarditis caused by *Staphylococcus aureus. N Engl J Med* 2006; 355:653–665.
45. Erbay A, Ergonul O, Stoddard GJ, Samore MH. Recurrent catheter-related bloodstream infections: risk factors and outcome. *Int J Infect Dis* 2006; 10:396–400.
46. Fowler VG Jr, Sakoulas G, McIntyre LM, et al. Persistent bacteremia due to methicillin-resistant *Staphylococcus aureus* infection is associated with agr dysfunction and low-level in vitro resistance to thrombin-induced platelet microbicidal protein. *J Infect Dis* 2004; 190:1140–1149.
47. Health Protection Agency. Surveillance of Healthcare Associated Infections Report 2007. Available at: http://www.hpa.org.uk/webw/HPAweb&HPAwebStandard/HPAweb_C/1196942166935?p=1158945066450. Accessed June 24, 2008.
48. Merrer J, Santoli F, Appere de Vecchi C, Tran B, De Jonghe B, Outin H. "Colonization pressure" and risk of acquisition of methicillin-resistant *Staphylococcus aureus* in a medical intensive care unit. *Infect Control Hosp Epidemiol* 2000; 21:718–723.
49. Bonten MJ, Slaughter S, Ambergen AW, et al. The role of "colonization pressure" in the spread of vancomycin-resistant enterococci: an important infection control variable. *Arch Intern Med* 1998; 158:1127–1132.
50. Weinstein RA, Kabins SA. Strategies for prevention and control of multiple drug-resistant nosocomial infection. *Am J Med* 1981; 70:449–454.
51. Ostrowsky BE, Trick WE, Sohn AH, et al. Control of vancomycin-resistant *Enterococcus* in health care facilities in a region. *N Engl J Med* 2001; 344:1427–1433.
52. Rhame FS, Sudderth WD. Incidence and prevalence as used in the analysis of the occurrence of nosocomial infections. *Am J Epidemiol* 1981; 113:1–11.
53. Berthelot P, Garnier M, Fascia P, et al. Conversion of prevalence survey data on nosocomial infections to incidence estimates: a simplified tool for surveillance? *Infect Control Hosp Epidemiol* 2007; 28:633–636.
54. Gastmeier P, Brauer H, Sohr D, et al. Converting incidence and prevalence data of nosocomial infections: results from eight hospitals. *Infect Control Hosp Epidemiol* 2001; 22:31–34.
55. Harris AD, Kotetishvili M, Shurland S, et al. How important is patient-to-patient transmission in extended-spectrum beta-lactamase *Escherichia coli* acquisition. *Am J Infect Control* 2007; 35:97–101.
56. Flynn DM, Weinstein RA, Nathan C, Gaston MA, Kabins SA. Patients' endogenous flora as the source of "nosocomial" *Enterobacter* in cardiac surgery. *J Infect Dis* 1987; 156:363–368.
57. Institute for Healthcare Improvement. Institute for Healthcare Improvement. How-to guide: reduce methicillin-resistant *Staphylococcus aureus* (MRSA) infection, 2006.Available at: http://www.ihi.org/IHI/Programs/Campaign/MRSAInfection.htm. Accessed June 24, 2008.
58. Curran ET, Benneyan JC, Hood J. Controlling methicillin-resistant *Staphylococcus aureus:* a feedback approach using annotated statistical process control charts. *Infect Control Hosp Epidemiol* 2002; 23:13–18.
59. Calfee D, Salgado CD. Detection and prevention of methicillin-resistant *Staphylococcus aureus* (MRSA) in acute care hospitals. *Infect Control Hosp Epidemiol* 2008, in press.
60. Association for Professionals in Infection Control and Epidemiology (APIC). Guide to the Elimination of Methicillin-Resistant *Staphylococcus aureus* (MRSA) Transmission in Hospital Settings. Washington, DC: APIC; March 2007.
61. Chaberny IF, Sohr D, Ruden H, Gastmeier P. Development of a surveillance system for methicillin-resistant *Staphylococcus aureus* in German hospitals. *Infect Control Hosp Epidemiol* 2007; 28:446–452.