healthcare-associated as well as community pathogens(90). Infections with these strains have most commonly presented as skin disease in community settings. However, intrinsic virulence characteristics of the organisms can result in clinical manifestations similar to or potentially more severe than traditional healthcare-associated MRSA infections among hospitalized patients. The prevalence of MRSA colonization and infection in the surrounding community may therefore affect the selection of strategies for MRSA control in healthcare settings.

IV. MDRO Prevention and Control

Prevention of Infections. Preventing infections will reduce the burden of MDROs in healthcare settings. Prevention of antimicrobial resistance depends on appropriate clinical practices that should be incorporated into all routine patient care. These include optimal management of vascular and urinary catheters, prevention of lower respiratory tract infection in intubated patients, accurate diagnosis of infectious etiologies, and judicious antimicrobial selection and utilization. Guidance for these preventive practices include the Campaign to Reduce Antimicrobial Resistance in Healthcare Settings (www.cdc.gov/drugresistance/healthcare/default.htm), a multifaceted, evidence-based approach with four parallel strategies: infection prevention; accurate and prompt diagnosis and treatment; prudent use of antimicrobials; and prevention of transmission. Campaign materials are available for acute care hospitals, surgical settings, dialysis units, LTCFs and pediatric acute care units.

To reduce rates of central-venous-line associated bloodstream infections(CVL-BSIs) and ventilator-associated pneumonia (VAP), a group of bundled evidence-based clinical practices have been implemented in many U.S. healthcare facilities(118, 141-144). One report demonstrated a sustained effect on the reduction in CVL-BSI rates with this approach(145). Although the specific effect on MDRO infection and colonization rates have not been reported, it is logical that decreasing these and other healthcare-associated infections will in turn reduce antimicrobial use and decrease opportunities for emergence and transmission of MDROs.

Prevention and Control of MDRO transmission

Overview of the MDRO control literature. Successful control of MDROs has been documented in the United States and abroad using a variety of combined interventions. These include improvements in hand hygiene, use of Contact Precautions until patients are culture-negative for a target MDRO, active surveillance cultures (ASC), education, enhanced environmental cleaning, and improvements in communication about patients with MDROs within and between healthcare facilities.

Representative studies include:

- Reduced rates of MRSA transmission in The Netherlands, Belgium, Denmark, and other Scandinavian countries after the implementation of aggressive and sustained infection control interventions (i.e., ASC; preemptive use of Contact Precautions upon admission until proven culture negative; and, in some instances, closure of units to new admissions). MRSA generally accounts for a very small proportion of *S. aureus* clinical isolates in these countries(146-150).
- Reduced rates of VRE transmission in healthcare facilities in the three-state Siouxland region (Iowa, Nebraska, and South Dakota) following formation of a coalition and development of an effective region-wide infection control intervention that included ASC and isolation of infected patients. The overall prevalence rate of VRE in the 30 participating facilities decreased from 2.2% in 1997 to 0.5% in 1999(151).
- Eradication of endemic MRSA infections from two NICUs. The first NICU included implementation of ASC, Contact Precautions, use of triple dye on the umbilical cord, and systems changes to improve surveillance and adherence to recommended practices and to reduce overcrowding(152). The second NICU used ASC and Contact Precautions; surgical masks were included in the barriers used for Contact Precautions(153).
- Control of an outbreak and eventual eradication of VRE from a burn unit over a 13-month period with implementation of aggressive culturing, environmental cleaning, and barrier isolation(154).
- Control of an outbreak of VRE in a NICU over a 3-year period with implementation of ASC, other infection control measures such as use of a waterless hand disinfectant, and mandatory in-service education(155).

- Eradication of MDR-strains of *A. baumannii* from a burn unit over a 16-month period with implementation of strategies to improve adherence to hand hygiene, isolation, environmental cleaning, and temporary unit closure(38).
- In addition, more than 100 reports published during 1982-2005 support the efficacy of combinations of various control interventions to reduce the burden of MRSA, VRE, and MDR-GNBs (Tables 1 and 2). Case-rate reduction or pathogen eradication was reported in a majority of studies.
- VRE was eradicated in seven special-care units(154, 156-160), two hospitals(161, 162), and one LTCF(163).
- MRSA was eradicated from nine special-care units(89, 152, 153, 164-169), two hospitals(170), one LTCF(167), and one Finnish district(171). Furthermore, four MRSA reports described continuing success in sustaining low endemic MDRO rates for over 5 years(68, 166, 172, 173).
- An MDR-GNB was eradicated from 13 special-care units(8, 9, 38, 174-180) and two hospitals (11, 181).

These success stories testify to the importance of having dedicated and knowledgeable teams of healthcare professionals who are willing to persist for years, if necessary, to control MDROs. Eradication and control of MDROs, such as those reported, frequently required periodic reassessment and the addition of new and more stringent interventions over time (tiered strategy). For example, interventions were added in a stepwise fashion during a 3-year effort that eventually eradicated MRSA from an NICU(152). A series of interventions was adopted throughout the course of a year to eradicate VRE from a burn unit(154). Similarly, eradication of carbapenem-resistant strains of *A. baumannii* from a hospital required multiple and progressively more intense interventions over several years(11).

Nearly all studies reporting successful MDRO control employed a median of 7 to 8 different interventions concurrently or sequentially (Table 1). These figures may underestimate the actual number of control measures used, because authors of these reports may have considered their earliest efforts routine (e.g., added emphasis on handwashing), and did not include them as interventions, and some ”single measures” are, in fact, a complex

combination of several interventions. The use of multiple concurrent control measures in these reports underscores the need for a comprehensive approach for controlling MDROs.

Several factors affect the ability to generalize the results of the various studies reviewed, including differences in definition, study design, endpoints and variables measured, and period of follow-up. Two-thirds of the reports cited in Tables 1 and 2 involved perceived outbreaks, and one-third described efforts to reduce endemic transmission. Few reports described preemptive efforts or prospective studies to control MDROs before they had reached high levels within a unit or facility.

With these and other factors, it has not been possible to determine the effectiveness of individual interventions, or a specific combination of interventions, that would be appropriate for all healthcare facilities to implement in order to control their target MDROs. Randomized controlled trials are necessary to acquire this level of evidence. An NIH-sponsored, randomized controlled trial on the prevention of MRSA and VRE transmission in adult ICUs is ongoing and may provide further insight into optimal control measures (http://clinicaltrials.gov/ct/show/NCT00100386?order=1). This trial compares the use of education (to improve adherence to hand hygiene) and Standard Precautions to the use of ASC and Contact Precautions.

Control Interventions. The various types of interventions used to control or eradicate MDROs may be grouped into seven categories. These include administrative support, judicious use of antimicrobials, surveillance (routine and enhanced), Standard and Contact Precautions, environmental measures, education and decolonization. These interventions provide the basis for the recommendations for control of MDROs in healthcare settings that follow this review and as summarized in Table 3. In the studies reviewed, these interventions were applied in various combinations and degrees of intensity, with differences in outcome.

1. ***Administrative support.*** In several reports, administrative support and involvement were important for the successful control of the target MDRO(3, 152, 182-185), and authorities in infection control have strongly recommended such support(2, 106, 107,

186). There are several examples of MDRO control interventions that require administrative commitment of fiscal and human resources. One is the use of ASC(8, 38, 68, 107, 114, 151, 152, 167, 168, 183, 184, 187-192). Other interventions that require administrative support include: 1) implementing system changes to ensure prompt and effective communications e.g., computer alerts to identify patients previously known to be colonized/infected with MDROs(184, 189, 193, 194); 2), providing the necessary number and appropriate placement of hand washing sinks and alcohol-containing hand rub dispensers in the facility(106, 195); 3) maintaining staffing levels appropriate to the intensity of care required(152, 196-202); and 4) enforcing adherence to recommended infection control practices (e.g., hand hygiene, Standard and Contact Precautions) for MDRO control. Other measures that have been associated with a positive impact on prevention efforts, that require administrative support, are direct observation with feedback to HCP on adherence to recommended precautions and keeping HCP informed about changes in transmission rates(3, 152, 182, 203-205). A “How-to guide” for implementing change in ICUs, including analysis of structure, process, and outcomes when designing interventions, can assist in identification of needed administrative interventions(195). Lastly, participation in existing, or the creation of new, city-wide, state-wide, regional or national coalitions, to combat emerging or growing MDRO problems is an effective strategy that requires administrative support(146, 151, 167, 188, 206, 207).

2. ***Education.*** Facility-wide, unit-targeted, and informal, educational interventions were included in several successful studies(3, 189, 193, 208-211). The focus of the interventions was to encourage a behavior change through improved understanding of the problem MDRO that the facility was trying to control. Whether the desired change involved hand hygiene, antimicrobial prescribing patterns, or other outcomes, enhancing understanding and creating a culture that supported and promoted the desired behavior, were viewed as essential to the success of the intervention. Educational campaigns to enhance adherence to hand hygiene practices in conjunction with other control measures have been associated temporally with decreases in MDRO transmission in various healthcare settings(3, 106, 163).

3. ***Judicious use of antimicrobial agents.*** While a comprehensive review of antimicrobial stewardship is beyond the scope of this guideline, recommendations for control of MDROs must include attention to judicious antimicrobial use. A temporal association between formulary changes and decreased occurrence of a target MDRO was found in several studies, especially in those that focused on MDR-GNBs(98, 177, 209, 212-218). Occurrence of C. difficile-associated disease has also been associated with changes in antimicrobial use(219). Although some MRSA and VRE control efforts have attempted to limit antimicrobial use, the relative importance of this measure for controlling these MDROs remains unclear(193, 220). Limiting antimicrobial use alone may fail to control resistance due to a combination of factors; including 1) the relative effect of antimicrobials on providing initial selective pressure, compared to perpetuating resistance once it has emerged; 2) inadequate limits on usage; or 3) insufficient time to observe the impact of this intervention. With the intent of addressing #2 and #3 above in the study design, one study demonstrated a decrease in the prevalence of VRE associated with a formulary switch from ticarcillin-clavulanate to piperacillin-tazobactam(221).

   The CDC Campaign to Prevent Antimicrobial Resistance that was launched in 2002 provides evidence-based principles for judicious use of antimicrobials and tools for implementation(222) www.cdc.gov/drugresistance/healthcare. This effort targets all healthcare settings and focuses on effective antimicrobial treatment of infections, use of narrow spectrum agents, treatment of infections and not contaminants, avoiding excessive duration of therapy, and restricting use of broad-spectrum or more potent antimicrobials to treatment of serious infections when the pathogen is not known or when other effective agents are unavailable. Achieving these objectives would likely diminish the selective pressure that favors proliferation of MDROs. Strategies for influencing antimicrobial prescribing patterns within healthcare facilities include education; formulary restriction; prior-approval programs, including pre-approved indications; automatic stop orders; academic interventions to counteract pharmaceutical influences on prescribing patterns; antimicrobial cycling(223-226);

computer-assisted management programs(227-229); and active efforts to remove redundant antimicrobial combinations(230). A systematic review of controlled studies identified several successful practices. These include social marketing (i.e. consumer education), practice guidelines, authorization systems, formulary restriction, mandatory consultation, and peer review and feedback. It further suggested that online systems that provide clinical information, structured order entry, and decision support are promising strategies(231). These changes are best accomplished through an organizational, multidisciplinary, antimicrobial management program(232).

4. ***MDRO surveillance.*** Surveillance is a critically important component of any MDRO control program, allowing detection of newly emerging pathogens, monitoring epidemiologic trends, and measuring the effectiveness of interventions. Multiple MDRO surveillance strategies have been employed, ranging from surveillance of clinical microbiology laboratory results obtained as part of routine clinical care, to use of ASC to detect asymptomatic colonization.

Surveillance for MDROs isolated from routine clinical cultures.

Antibiograms. The simplest form of MDRO surveillance is monitoring of clinical microbiology isolates resulting from tests ordered as part of routine clinical care. This method is particularly useful to detect emergence of new MDROs not previously detected, either within an individual healthcare facility or community-wide. In addition, this information can be used to prepare facility- or unit-specific summary antimicrobial susceptibility reports that describe pathogen-specific prevalence of resistance among clinical isolates. Such reports may be useful to monitor for changes in known resistance patterns that might signal emergence or transmission of MDROs, and also to provide clinicians with information to guide antimicrobial prescribing practices(233-235).

MDRO Incidence Based on Clinical Culture Results. Some investigators have used clinical microbiology results to calculate measures of incidence of MDRO isolates in specific populations or patient care locations (e.g. new MDRO

isolates/1,000 patient days, new MDRO isolates per month)(205, 236, 237). Such measures may be useful for monitoring MDRO trends and assessing the impact of prevention programs, although they have limitations. Because they are based solely on positive culture results without accompanying clinical information, they do not distinguish colonization from infection, and may not fully demonstrate the burden of MDRO-associated disease. Furthermore, these measures do not precisely measure acquisition of MDRO colonization in a given populaton or location. Isolating an MDRO from a clinical culture obtained from a patient several days after admission to a given unit or facility does not establish that the patient acquired colonization in that unit. On the other hand, patients who acquire MDRO colonization may remain undetected by clinical cultures(107). Despite these limitations, incidence measures based on clinical culture results may be highly correlated with actual MDRO transmission rates derived from information using ASC, as demonstrated in a recent multicenter study(237). These results suggest that incidence measures based on clinical cultures alone might be useful surrogates for monitoring changes in MDRO transmission rates.

MDRO Infection Rates. Clinical cultures can also be used to identify targeted MDRO infections in certain patient populations or units(238, 239). This strategy requires investigation of clinical circumstances surrounding a positive culture to distinguish colonization from infection, but it can be particularly helpful in defining the clinical impact of MDROs within a facility.

Molecular typing of MDRO isolates. Many investigators have used molecular typing of selected isolates to confirm clonal transmission to enhance understanding of MDRO transmission and the effect of interventions within their facility(38, 68, 89, 92, 138, 152, 190, 193, 236, 240).

Surveillance for MDROs by Detecting Asymptomatic Colonization

Another form of MDRO surveillance is the use of active surveillance cultures (ASC) to identify patients who are colonized with a targeted MDRO(38, 107, 241). This

approach is based upon the observation that, for some MDROs, detection of colonization may be delayed or missed completely if culture results obtained in the course of routine clinical care are the primary means of identifying colonized patients(8, 38, 107, 114, 151, 153, 167, 168, 183, 184, 187, 189, 191-193, 242-244). Several authors report having used ASC when new pathogens emerge in order to define the epidemiology of the particular agent(22, 23, 107, 190). In addition, the authors of several reports have concluded that ASC, in combination with use of Contact Precautions for colonized patients, contributed directly to the decline or eradication of the target MDRO(38, 68, 107, 151, 153, 184, 217, 242). However, not all studies have reached the same conclusion. Poor control of MRSA despite use of ASC has been described(245). A recent study failed to identify cross-transmission of MRSA or MSSA in a MICU during a 10 week period when ASC were obtained, despite the fact that culture results were not reported to the staff(246). The investigators suggest that the degree of cohorting and adherence to Standard Precautions might have been the important determinants of transmission prevention, rather than the use of ASC and Contact Precautions for MRSA-colonized patients. The authors of a systematic review of the literature on the use of isolation measures to control healthcare-associated MRSA concluded that there is evidence that concerted efforts that include ASC and isolation can reduce MRSA even in endemic settings. However, the authors also noted that methodological weaknesses and inadequate reporting in published research make it difficult to rule out plausible alternative explanations for reductions in MRSA acquisition associated with these interventions, and therefore concluded that the precise contribution of active surveillance and isolation alone is difficult to assess(247).

Mathematical modeling studies have been used to estimate the impact of ASC use in control of MDROs. One such study evaluating interventions to decrease VRE transmission indicated that use of ASC (versus no cultures) could potentially decrease transmission 39% and that with pre-emptive isolation plus ASC, transmission could be decreased 65%(248). Another mathematical model examining the use of ASC and isolation for control of MRSA predicted that isolating colonized or

infected patients on the basis of clinical culture results is unlikely to be successful at controlling MRSA, whereas use of active surveillance and isolation can lead to successful control, even in settings where MRSA is highly endemic.(249) There is less literature on the use of ASC in controlling MDR-GNBs. Active surveillance cultures have been used as part of efforts to successful control of MDR-GNBs in outbreak settings. The experience with ASC as part of successful control efforts in endemic settings is mixed. One study reported successful reduction of extended-spectrum beta-lactamase –producing Enterobacteriaceae over a six year period using a multifaceted control program that included use of ASC(245). Other reports suggest that use of ASC is not necessary to control endemic MDR-GNBs.(250, 251).

More research is needed to determine the circumstances under which ASC are most beneficial(252), but their use should be considered in some settings, especially if other control measures have been ineffective. When use of ASC is incorporated into MDRO prevention programs, the following should be considered:

- The decision to use ASC as part of an infection prevention and control program requires additional support for successful implementation, including: 1) personnel to obtain the appropriate cultures, 2) microbiology laboratory personnel to process the cultures, 3) mechanism for communicating results to caregivers, 4) concurrent decisions about use of additional isolation measures triggered by a positive culture (e.g. Contact Precautions) and 5) mechanism for assuring adherence to the additional isolation measures.
- The populations targeted for ASC are not well defined and vary among published reports. Some investigators have chosen to target specific patient populations considered at high risk for MDRO colonization based on factors such as location (e.g. ICU with high MDRO rates), antibiotic exposure history, presence of underlying diseases, prolonged duration of stay, exposure to other MDRO-colonized patients, patients transferred from other facilities known to have a high prevalence of MDRO carriage, or having a history of recent hospital or nursing home stays(107, 151, 253). A more commonly employed strategy involves obtaining surveillance cultures from all patients admitted to units experiencing

high rates of colonization/infection with the MDROs of interest, unless they are already known to be MDRO carriers(153, 184, 242, 254). In an effort to better define target populations for active surveillance, investigators have attempted to create prediction rules to identify subpopulations of patients at high risk for colonization on hospital admission(255, 256). Decisions about which populations should be targeted for active surveillance should be made in the context of local determinations of the incidence and prevalence of MDRO colonization within the intervention facility as well as other facilities with whom patients are frequently exchanged(257).

- Optimal timing and interval of ASC are not well defined. In many reports, cultures were obtained at the time of admission to the hospital or intervention unit or at the time of transfer to or from designated units (e.g., ICU)(107). In addition, some hospitals have chosen to obtain cultures on a periodic basis [e.g., weekly(8, 153, 159) to detect silent transmission. Others have based follow-up cultures on the presence of certain risk factors for MDRO colonization, such as antibiotic exposure, exposure to other MDRO colonized patients, or prolonged duration of stay in a high risk unit(253).
- Methods for obtaining ASC must be carefully considered, and may vary depending upon the MDRO of interest.
    - MRSA: Studies suggest that cultures of the nares identify most patients with MRSA and perirectal and wound cultures can identify additional carriers(152, 258-261).
    - VRE: Stool, rectal, or perirectal swabs are generally considered a sensitive method for detection of VRE. While one study suggested that rectal swabs may identify only 60% of individuals harboring VRE, and may be affected by VRE stool density(262), this observation has not been reported elsewhere in the literature.
    - MDR-GNBs: Several methods for detection of MDR-GNBs have been employed, including use of peri-rectal or rectal swabs alone or in combination with oro-pharyngeal, endotracheal, inguinal, or wound cultures. The absence of standardized screening media for many gram-

negative bacilli can make the process of isolating a specific MDR-GNB a relatively labor-intensive process(38, 190, 241, 250).

  - Rapid detection methods: Using conventional culture methods for active surveillance can result in a delay of 2-3 days before results are available. If the infection control precautions (e.g., Contact Precautions) are withheld until the results are available, the desired infection control measures could be delayed. If empiric precautions are used pending negative surveillance culture results, precautions may be unnecessarily implemented for many, if not most, patients. For this reason, investigators have sought methods for decreasing the time necessary to obtain a result from ASC. Commercially available media containing chromogenic enzyme substrates (CHROMagar MRSA(263, 264) has been shown to have high sensitivity and specificity for identification of MRSA and facilitate detection of MRSA colonies in screening cultures as early as 16 hours after inoculation. In addition, real-time PCR-based tests for rapid detection of MRSA directly from culture swabs (< 1-2 hours) are now commercially available(265-267), as well as PCR-based tests for detection of vanA and van B genes from rectal swabs(268). The impact of rapid testing on the effectiveness of active surveillance as a prevention strategy, however, has not been fully determined. Rapid identification of MRSA in one study was associated with a significant reduction in MRSA infections acquired in the medical ICU, but not the surgical ICU(265). A mathematical model characterizing MRSA transmission dynamics predicted that, in comparison to conventional culture methods, the use of rapid detection tests may decrease isolation needs in settings of low-endemicity and result in more rapid reduction in prevalence in highly-endemic settings(249).

- Some MDRO control reports described surveillance cultures of healthcare personnel during outbreaks, but colonized or infected healthcare personnel are rarely the source of ongoing transmission, and this strategy should be reserved for settings in which specific healthcare personnel have been epidemiologically implicated in the transmission of MDROs(38, 92, 152-154, 188).

5. ***Infection Control Precautions.*** Since 1996 CDC has recommended the use of Standard and Contact Precautions for MDROs "judged by an infection control program…to be of special clinical and epidemiologic significance." This recommendation was based on general consensus and was not necessarily evidence-based. No studies have directly compared the efficacy of Standard Precautions alone versus Standard Precautions and Contact Precautions, with or without ASC, for control of MDROs. Some reports mention the use of one or both sets of precautions as part of successful MDRO control efforts; however, the precautions were not the primary focus of the study intervention(164, 190, 205, 269-271). The NIH-sponsored study mentioned earlier (Section: *Overview of the MDRO control literature*) may provide some answers, http://clinicaltrials.gov/ct/show/NCT00100386?order=1).

Standard Precautions have an essential role in preventing MDRO transmission, even in facilities that use Contact Precautions for patients with an identified MDRO. Colonization with MDROs is frequently undetected; even surveillance cultures may fail to identify colonized persons due to lack of sensitivity, laboratory deficiencies, or intermittent colonization due to antimicrobial therapy(262). Therefore, Standard Precautions must be used in order to prevent transmission from potentially colonized patients. Hand hygiene is an important component of Standard Precautions. The authors of the *Guideline for Hand Hygiene in Healthcare Settings(106)* cited nine studies that demonstrated a temporal relationship between improved adherence to recommended hand hygiene practices and control of MDROs. It is noteworthy that in one report the frequency of hand hygiene did not improve with use of Contact Precautions but did improve when gloves were used (per Standard Precautions) for contact with MDRO patients(272).

MDRO control efforts frequently involved changes in isolation practices, especially during outbreaks. In the majority of reports, Contact Precautions were implemented for all patients found to be colonized or infected with the target MDRO (See Table 2).

Some facilities also preemptively used Contact Precautions, in conjunction with ASC, for all new admissions or for all patients admitted to a specific unit, until a negative screening culture for the target MDRO was reported(30, 184, 273).

Contact Precautions are intended to prevent transmission of infectious agents, including epidemiologically important microorganisms, which are transmitted by direct or indirect contact with the patient or the patient's environment. A single-patient room is preferred for patients who require Contact Precautions. When a single-patient room is not available, consultation with infection control is necessary to assess the various risks associated with other patient placement options (e.g., cohorting, keeping the patient with an existing roommate). HCP caring for patients on Contact Precautions should wear a gown and gloves for all interactions that may involve contact with the patient or potentially contaminated areas in the patient's environment. Donning gown and gloves upon room entry and discarding before exiting the patient room is done to contain pathogens, especially those that have been implicated in transmission through environmental contamination (e.g., VRE, *C. difficile,* noroviruses and other intestinal tract agents; RSV)(109, 111, 274-277).

Cohorting and other MDRO control strategies. In several reports, cohorting of patients(152, 153, 167, 183, 184, 188, 189, 217, 242), cohorting of staff(184, 217, 242, 278), use of designated beds or units(183, 184), and even unit closure(38, 146, 159, 161, 279, 280) were necessary to control transmission. Some authors indicated that implementation of the latter two strategies were the turning points in their control efforts; however, these measures usually followed many other actions to prevent transmission. In one, two-center study, moving MRSA-positive patients into single rooms or cohorting these patients in designated bays failed to reduce transmission in ICUs. However, in this study adherence to recommendations for hand hygiene between patient contacts was only 21%(281). Other published studies, including one commissioned by the American Institute of Architects and the Facility Guidelines Institute (www.aia.org/aah_gd_hospcons), have documented a beneficial relationship between private rooms and reduction in risk of acquiring MDROs(282). Additional

studies are needed to define the specific contribution of using single-patient rooms and/or cohorting on preventing transmission of MDROs.

Duration of Contact Precautions. The necessary duration of Contact Precautions for patients treated for infection with an MDRO, but who may continue to be colonized with the organism at one or more body sites, remains an unresolved issue. Patients may remain colonized with MDROs for prolonged periods; shedding of these organisms may be intermittent, and surveillance cultures may fail to detect their presence(84, 250, 283). The 1995 HICPAC guideline for preventing the transmission of VRE suggested three negative stool/perianal cultures obtained at weekly intervals as a criterion for discontinuation of Contact Precautions(274). One study found these criteria generally reliable(284). However, this and other studies have noted a recurrence of VRE positive cultures in persons who subsequently receive antimicrobial therapy and persistent or intermittent carriage of VRE for more than 1 year has been reported(284-286). Similarly, colonization with MRSA can be prolonged(287, 288). Studies demonstrating initial clearance of MRSA following decolonization therapy have reported a high frequency of subsequent carriage(289, 290). There is a paucity of information in the literature on when to discontinue Contact Precautions for patients colonized with a MDR-GNB, possibly because infection and colonization with these MDROs are often associated with outbreaks. Despite the uncertainty about when to discontinue Contact Precautions, the studies offer some guidance. In the context of an outbreak, prudence would dictate that Contact Precautions be used indefinitely for all previously infected and known colonized patients. Likewise, if ASC are used to detect and isolate patients colonized with MRSA or VRE, and there is no decolonization of these patients, it is logical to assume that Contact Precautions would be used for the duration of stay in the setting where they were first implemented. In general, it seems reasonable to discontinue Contact Precautions when three or more surveillance cultures for the target MDRO are repeatedly negative over the course of a week or two in a patient who has not received antimicrobial therapy for several weeks, especially in the absence of a

draining wound, profuse respiratory secretions, or evidence implicating the specific patient in ongoing transmission of the MDRO within the facility.

Barriers used for contact with patients infected or colonized with MDROs. Three studies evaluated the use of gloves with or without gowns for all patient contacts to prevent VRE acquisition in ICU settings(30, 105, 273). Two of the studies showed that use of both gloves and gowns reduced VRE transmission(30, 105) while the third showed no difference in transmission based on the barriers used(273). One study in a LTCF compared the use of gloves only, with gloves plus contact isolation, for patients with four MDROs, including VRE and MRSA, and found no difference(86). However, patients on contact isolation were more likely to acquire MDR-*K. pneumoniae* strains that were prevalent in the facility; reasons for this were not specifically known. In addition to differences in outcome, differing methodologies make comparisons difficult. Specifically, HCP adherence to the recommended protocol, the influence of added precautions on the number of HCP-patient interactions, and colonization pressure were not consistently assessed.

Impact of Contact Precautions on patient care and well-being. There are limited data regarding the impact of Contact Precautions on patients. Two studies found that HCP, including attending physicians, were half as likely to enter the rooms of(291), or examine(292), patients on Contact Precautions. Other investigators have reported similar observations on surgical wards(293). Two studies reported that patients in private rooms and on barrier precautions for an MDRO had increased anxiety and depression scores(294, 295). Another study found that patients placed on Contact Precautions for MRSA had significantly more preventable adverse events, expressed greater dissatisfaction with their treatment, and had less documented care than control patients who were not in isolation(296). Therefore, when patients are placed on Contact Precautions, efforts must be made by the healthcare team to counteract these potential adverse effects.

6. ***Environmental measures.*** The potential role of environmental reservoirs, such as surfaces and medical equipment, in the transmission of VRE and other MDROs has been the subject of several reports(109-111, 297, 298). While environmental cultures are not routinely recommended(299), environmental cultures were used in several studies to document contamination, and led to interventions that included the use of dedicated noncritical medical equipment(217, 300), assignment of dedicated cleaning personnel to the affected patient care unit(154), and increased cleaning and disinfection of frequently-touched surfaces (e.g., bedrails, charts, bedside commodes, doorknobs). A common reason given for finding environmental contamination with an MDRO was the lack of adherence to facility procedures for cleaning and disinfection. In an educational and observational intervention, which targeted a defined group of housekeeping personnel, there was a persistent decrease in the acquisition of VRE in a medical ICU(301). Therefore, monitoring for adherence to recommended environmental cleaning practices is an important determinant for success in controlling transmission of MDROs and other pathogens in the environment(274, 302).

   In the MDRO reports reviewed, enhanced environmental cleaning was frequently undertaken when there was evidence of environmental contamination and ongoing transmission. Rarely, control of the target MDRO required vacating a patient care unit for complete environmental cleaning and assessment(175, 279).

7. ***Decolonization.*** Decolonization entails treatment of persons colonized with a specific MDRO, usually MRSA, to eradicate carriage of that organism. Although some investigators have attempted to decolonize patients harboring VRE(220), few have achieved success. However, decolonization of persons carrying MRSA in their nares has proved possible with several regimens that include topical mupirocin alone or in combination with orally administered antibiotics (e.g., rifampin in combination with trimethoprim- sulfamethoxazole or ciprofloxacin) plus the use of an antimicrobial soap for bathing(303). In one report, a 3-day regimen of baths with povidone-iodine and nasal therapy with mupirocin resulted in eradication of nasal MRSA

colonization(304). These and other methods of MRSA decolonization have been thoroughly reviewed.(303, 305-307).

Decolonization regimens are not sufficiently effective to warrant routine use. Therefore, most healthcare facilities have limited the use of decolonization to MRSA outbreaks, or other high prevalence situations, especially those affecting special-care units. Several factors limit the utility of this control measure on a widespread basis: 1) identification of candidates for decolonization requires surveillance cultures; 2) candidates receiving decolonization treatment must receive follow-up cultures to ensure eradication; and 3) recolonization with the same strain, initial colonization with a mupirocin-resistant strain, and emergence of resistance to mupirocin during treatment can occur(289, 303, 308-310). HCP implicated in transmission of MRSA are candidates for decolonization and should be treated and culture negative before returning to direct patient care. In contrast, HCP who are colonized with MRSA, but are asymptomatic, and have not been linked epidemiologically to transmission, do not require decolonization.

IV. Discussion

This review demonstrates the depth of published science on the prevention and control of MDROs. Using a combination of interventions, MDROs in endemic, outbreak, and non-endemic settings have been brought under control. However, despite the volume of literature, an appropriate set of evidence-based control measures that can be universally applied in all healthcare settings has not been definitively established. This is due in part to differences in study methodology and outcome measures, including an absence of randomized, controlled trials comparing one MDRO control measure or strategy with another. Additionally, the data are largely descriptive and quasi-experimental in design(311). Few reports described preemptive efforts or prospective studies to control MDROs before they had reached high levels within a unit or facility. Furthermore, small hospitals and LTCFs are infrequently represented in the literature.
A number of questions remain and are discussed below.