# Rethinking Contact Isolation for Multidrug-Resistant Organisms

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**Purpose and Overview:**

Although applied widely in the control of multidrug-resistant organisms, the current practice of contact precautions faces increased scrutiny. After defining key concepts in infection prevention and providing a historical perspective on the evolution of contact precautions, recent clinical trial evidence will be reviewed regarding the effectiveness of contact precautions, particularly for MRSA or in the ICU setting. Then, unintended consequences and alternatives to contact precautions will be discussed. Finally, a conceptual framework will be briefly outlined to provide clinicians a more rational and nuanced approach to the application of contact precautions in their particular healthcare setting.

**Educational Objectives:**

- Distinguish between horizontal and vertical interventions in infection prevention.
- Summarize recent clinical trial evidence regarding the effectiveness of contact precautions and active surveillance for multidrug-resistant organisms in the ICU.
- List 4 unintended, negative consequences of contact precautions on patients or the healthcare system.
- Describe factors that influence the likelihood of benefit from contact precautions in a specific healthcare setting.

## Introduction

In 1945, the year in which he shared the Nobel Prize for the discovery of penicillin, Sir Alexander Fleming presciently warned of the potential development of resistance from antibiotic misuse and the deadly consequences of such an event.

“The microbes are educated to resist penicillin and a host of penicillin-fast organisms is bred out … In such cases the thoughtless person playing with penicillin is morally responsible for the death of the man who finally succumbs to infection with the penicillin-resistant organism. I hope this evil can be averted” [1].

Fleming’s prophetic words unfortunately were realized shortly after the advent of penicillin. Now, the growing worldwide specter of multidrug-resistant organisms (MDRO) has reached a tipping point, gaining the international community’s attention and raising concerns about a “post-antibiotic era” [2]. In general, MDRO are defined as bacteria that are resistant to one or more classes of antimicrobial agents. In 2013, the Centers for Disease Control (CDC) released its first antibiotic threat report, detailing the problem of antimicrobial resistance in the US and estimating that over two million infections and 23,000 deaths per year are caused by antibiotic-resistant organisms [3]. The CDC recommends 4 core actions to address this threat: 1) preventing infections from occurring and resistant bacteria from spreading; 2) tracking resistant bacteria; 3) improving the use of antibiotics (through antimicrobial stewardship); and 4) promoting development of new antibiotics and diagnostic tests for resistant bacteria.

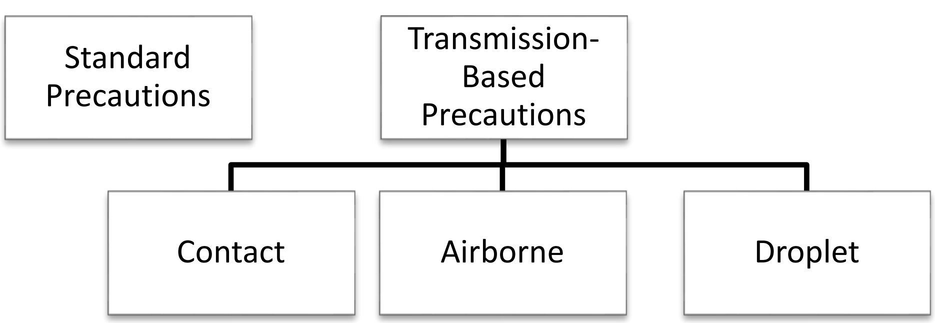
A key strategy for preventing the spread of MDROs is the use of Standard and Transmission-Based Precautions, a centerpiece of infection prevention (IP) in healthcare facilities. CDC and infectious diseases guidelines recommend the routine use of Contact Precautions (CP) for epidemiologically important MDROs, including methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), *Clostridium difficile*, and multidrug resistant Gram negative bacilli [4, 5]. However, some healthcare epidemiologists have questioned the widespread use of CP that results from active surveillance or screening, particularly for MRSA [6]. Spurred by several recent high-profile studies, the controversies surrounding CP have spilled into major medical journals, resulting in calls for a re-examination of isolation practices for endemic MRSA and VRE [7, 8]. Finally, the mainstream media have spotlighted the underappreciated negative effects of contact isolation on patient care and emotional well-being [9]. Herein, we will review key IP definitions and strategies to prevent MDRO transmission, summarize recent medical evidence regarding CP, particularly for MRSA and ICU patients, and highlight potential unintended negative effects in order to provide a more rational and nuanced approach for implementing CP in diverse healthcare settings.

## Infection Prevention Basics: Definitions and Historical Perspective

*Key Concepts and Definitions*

Strategies to prevent MDRO transmission fall into several broad categories: patient and provider hygiene, environmental cleaning, antibiotic stewardship, and isolation precautions. With regards to the latter, the CDC advocates a dual approach **(Figure 1)**. **Standard precautions** are IP practices that apply to all patients, regardless of suspected or confirmed infection status, based on the principle that all blood, body fluids, or secretions may contain transmissible pathogens [10]. These measures include hand hygiene, use of personal protective equipment (PPE) based on anticipated exposure, appropriate cleaning of soiled patient care equipment and environment, safe handling of needles and sharps, and respiratory hygiene/cough etiquette. Importantly, Standard Precautions are considered "the primary strategy for the prevention of healthcare-associated transmission of infectious agents among patients and healthcare personnel" [10]. Appropriate use of PPE in Standard Precautions requires an understanding of routes of transmission and critical thinking on the part of the healthcare personnel (HCP). **Transmission-Based Precautions** are additional control measures for patients known or suspected to be colonized or infected with epidemiologically important pathogens and include 3 categories: Contact, Airborne, and Droplet Precautions [10]. **Contact Precautions** prevent transmission of pathogens spread by direct or indirect contact with the patient or the patient's environment. In addition to preferring single patient rooms, CP involve the use of gown and gloves for all interactions with the patient or potentially contaminated environment. The principal rationale for CP is the important epidemiologic role that healthcare personnel contamination plays in the transmission of key MDROs between patients. **Airborne Precautions** prevent transmission of pathogens that remain infectious over long distances suspended in air such as tuberculosis. Patient placement in a negative pressure room is preferred, and an N95 respirator should be worn. **Droplet Precautions** prevent transmission of pathogens spread through droplets from close respiratory or mucous membrane contact. Patient placement in a private room is preferred, and a surgical mask is worn.

**Figure 1. CDC Dual Approach to Precautions: Standard and Transmission-Based Precautions**



Another key concept is **colonization pressure,** defined as the number of patient-days from colonized or infected patients divided by the total patient-days on a given unit. Colonization pressure consistently predicts risk of nosocomial MDRO transmission, and high levels of colonization pressure can become the dominant risk determinant for MDRO acquisition, indirectly suggesting that reducing colonization pressure is important [11]. In determining whom to isolate, clinical cultures only identify 15-20% of all patients colonized with an MDRO [12]. Therefore, **active surveillance cultures** (ASC) have been used to identify all patients colonized with a particular MDRO. For actionable results, a rapid turnaround (generally < 24 hours) is needed using validated tests from established body sites for screening. For example, MRSA surveillance uses either FDA-approved chromogenic agar medium or direct specimen polymerase chain reaction (PCR), most commonly from a nasal swab, while VRE screening is typically done by rectal swab PCR [13]. A strategy of systematic surveillance for a MDRO coupled with isolation of all colonized patients in a specific unit or hospital-wide is termed **active detection and isolation** (ADI). Finally, it is helpful to place these activities in the context of two approaches to infection prevention: horizontal and vertical interventions (**Table 1**). **Horizontal interventions** aim to reduce the infection risk from a broad range of pathogens with standardized approaches that are not pathogen specific [14, 15]. Examples of horizontal interventions include standard precautions, universal chlorhexidine (CHG) bathing to reduce the pathogen burden on patients' skin, or antimicrobial stewardship. **Vertical interventions** aim to reduce the infection risk from a specific pathogen, usually by ASC for asymptomatic carriers, contact precautions for colonized or infected patients, and targeted decolonization when an established method is available [14, 15]. The use of ADI for MRSA is a common example of a vertical intervention. While practically the two approaches often coexist, the relative effectiveness of and the priority given to the two approaches has been strongly debated in the literature [6, 14-16]. The rationale for horizontal interventions is that HCP do not know which MDRO will be entering their facility next.

**Table 1. Comparison of Horizontal and Vertical Approaches to Infection Prevention**

| Strategy | Horizontal | Vertical |
|---|---|---|
| **Goal** | **Reduce risk of broad range of pathogens**; Population-based | **Reduce infection or colonization with specific pathogen**; Pathogen-based |
| **Scope** | Universal | Selective or Universal |
| **Examples** | Hand Hygiene/Standard Precautions<br>CHG Bathing<br>Antimicrobial Stewardship | Active surveillance cultures<br>Active Detection and Isolation for MDRO<br>MRSA Nasal Decolonization |

*Historical Perspective of Isolation Precautions*

The initial US isolation guidelines in 1970 established a basic categorization for isolation precautions in an era marked by poor hand hygiene compliance and minimal science in infection prevention. After a brief update in 1975, a substantive expansion occurred in 1983 with the CDC Guideline for Isolation Precautions in Hospitals. Shortly after, two major events in the mid-1980s raised the level of awareness surrounding infection surveillance and control. First, the explosion of the HIV epidemic and concerns regarding healthcare worker exposure led to the introduction of universal precautions and body substance isolation, the precursors of standard precautions. Second, the dissemination of results from the CDC-sponsored Study on the Efficacy of Nosocomial Infection Control (SENIC Project), headed by Dr. Robert Haley, established the importance of a multifaceted infection surveillance and control program for reducing nosocomial infections and highlighted the unrealized potential of such interventions across the nation's hospitals [17]. The next decade of infection prevention research and experience culminated in the first Healthcare Infection Control Practices Advisory Committee (HICPAC) isolation guidelines published in 1996.

Dramatic rises in MRSA and VRE and a growing body of literature of successful reductions in transmission spurred the Society for Healthcare Epidemiology of America (SHEA) to draft 2003 guidelines strongly advocating for ASC in all hospitals as "essential to identify the reservoir for spread of MRSA and VRE infections and make control possible using the CDC's long-recommended contact precautions" [18]. One year later, a draft revision of the HICPAC isolation precautions guidelines was released, with the final version published in 2007 serving as the current CDC guidance to hospitals [5, 10]. The major divergence between the two guidelines was that, while recommending contact precautions for all patients known to be colonized or infected with MDROs, the HICPAC guidelines stopped short of recommending ASC as a core strategy for all hospitals [19]. Instead, a two-tiered approach was advocated with baseline control measures for all healthcare facilities and an intensified set of measures, which included ASC as an option, only if failure to control MDRO transmission with the first tier measures. The HICPAC guidelines importantly acknowledged the limitations of the available literature on MDRO control including: the preponderance of quasi-experimental or methodologically flawed studies, often in the setting of a local epidemic; the use of multiple interventions (average of 7-8) in a "bundle," limiting the ability to determine the effects of specific interventions; and the lack of data to inform practices in non-acute care settings or for less studied pathogens (i.e. multidrug resistant Gram negatives) [5]. A key emphasis, thus, was that "selection of interventions for controlling MDRO transmission should be based on assessments of the local problem, the prevalence of various MDRO and feasibility" [5].

Despite the tiered approach suggested by the CDC, widespread adoption of ASC, particularly for MRSA, gained momentum across the country. Public organizations such as the Reduce Infection Deaths and Institute for Healthcare Improvement (IHI) highlighted ASC for MRSA as a key performance measure for quality and patient safety [13]. In 2007, a national Veterans' Affairs (VA) healthcare initiative mandated ASC for MRSA as part of a broader strategy to transform its culture of infection prevention. Finally, several states passed legislation requiring MRSA screening for all admitted patients despite the objections of medical societies [20]. Yet, provider uncertainty regarding the utility of CP as currently practiced is prevalent. A recent survey of infectious diseases specialists about their hospitals' practices found that, despite high rates of contact precautions (91% for MRSA and/or VRE) and active surveillance in parts of the hospital (76% for MRSA; 32% for VRE), only 38% of respondents believed their current practices were effective at preventing MDRO transmission (24% unsure; 38% did not believe) [21]. This lack of clarity and confidence stems partially from the conflicting evidence for the current application of CP, which we will examine next.

**Contact Precautions: Examining the Evidence**

Although widely studied since their introduction, the evidence base regarding contact precautions has been plagued by confusion and controversy. As previously discussed, much of the ambiguity is related to flaws in study design such as lack of control groups, an inability to determine the relative contributions of bundled interventions, and a mixture of studies from epidemic and non-epidemic settings. Additionally, the greatest successes with aggressive ASC and contact precautions come from European countries with very low baseline prevalence of MDROs, making such interventions cost-effective but limiting generalizability to areas with higher endemic MDRO prevalence [22]. These limitations led the HICPAC committee to conclude that "it has not been possible to determine the effectiveness of individual interventions that would be appropriate for all healthcare facilities to implement in order to control their target MDROs" [5]. However, since the publication of these guidelines, several important studies have been published with strengths in terms of methodological rigor or power that shed light on a more rational, evidence-based approach. We will briefly review five recent studies, which focus on control of MRSA or nosocomial transmission in the ICU.

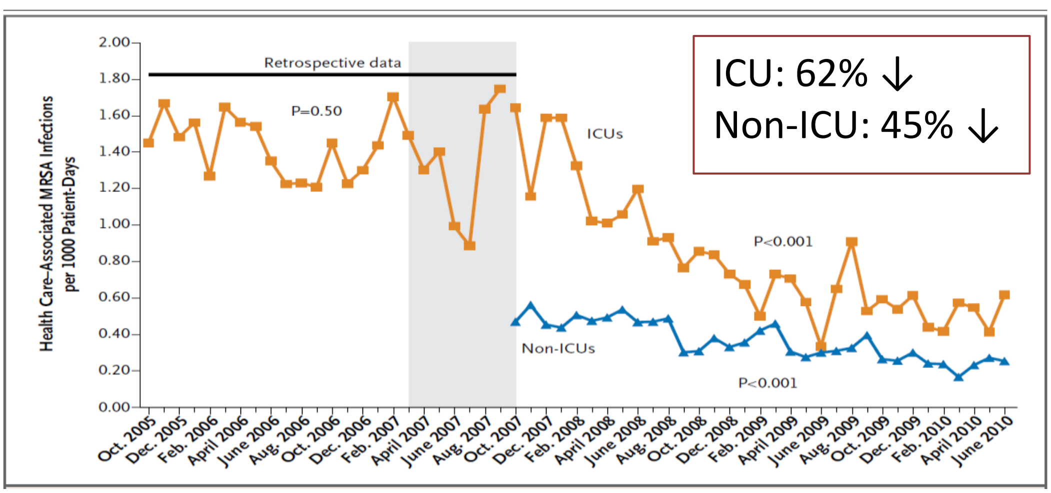
1. *STAR*ICU Trial* [23]

In the Strategies to Reduce Transmission of Antimicrobial Resistant Bacteria in Intensive Care Units (STAR*ICU) trial, Huskins et al. performed an unblinded, cluster-randomized trial in 18 ICUs with over 9000 patients comparing the effects of ADI for MRSA and VRE versus usual care (contact precautions only for positive clinical cultures) on the primary endpoint of incident colonization or infection with MRSA or VRE. Despite a substantial increase in the use of gloves and contact precautions in colonized or infected patients (92% of ICU days in intervention ICUs vs. 38% in control ICUs; p<0.001), there was no difference seen in incidence of colonization or infection with MRSA or VRE, adjusting for baseline incidence (40.4 per 1000 patient-days and 35.6 per 1000 patient-days in intervention and control arms, respectively; p=0.35). Valid criticisms of this study include suboptimal rates of compliance with hand hygiene and PPE, prolonged turnaround time for reporting of surveillance results (mean 5.2 days), and an intervention period of only 6 months. However, despite these limitations, the results of this highly anticipated NIH study gave pause to previously strong advocacy for universal ADI.

2. *Veterans' Administration MRSA Prevention Initiative* [24]

Published in the same issue with the STAR*ICU study, Jain et al. reported on the results of the implementation of an "MRSA bundle" in all acute care wards of the VA healthcare system using a before-and-after interrupted time series analysis. Components of the bundle included universal nasal surveillance for MRSA on admission, unit transfer, and discharge; CP for MRSA-colonized patients; emphasis on improving hand hygiene compliance; institutional culture change regarding infection prevention; and support for an MRSA prevention coordinator at each hospital. Over a 33-month period in 150 hospitals including over 8 million patient days, impressive declines were shown in MRSA transmission rates (ICU: 17% and non-ICU:21%; p<0.001 for trends) as well as decreased rates of health care-associated MRSA infections (ICU: 62% and non-ICU: 45%; p<0.001 for trends) (**Figure 2**). Interestingly, a small subset of hospitals also reported on other pathogens, showing a 73% reduction in non-ICU VRE infections and 61% reduction in non-ICU *C. difficile* infections. Healthcare-associated infection (HAI) rates within the VA have continued to decline, and similar strategies have been applied to other organisms, leading to well-deserved national praise of the VA's efforts [25].

**Figure 2. National Rates of MRSA Healthcare Associated Infections in VA Facilities** [24]



However, appropriate caution is warranted in extrapolating the VA data too broadly. First, the before-and-after design without a control group precludes establishment of causality. Second, the simultaneous “bundled” interventions limits assessment of relative effects of the individual components such as ADI for MRSA. Indeed, post-hoc mathematical modeling of the VA data by external groups suggests that the MRSA ADI contributed to only a small fraction of the reduction in infection rates (< 5%) [26]. The improvements in VRE and *C. difficile* rates also suggest that the horizontal interventions (better hand hygiene, culture change, more IP resources) played a larger role in the improvements seen [27]. Third, contribution from other concomitant infection-control initiatives such as central venous catheter and ventilator-associated pneumonia bundles cannot be excluded. Finally, a comparison study between two VA hospitals showed no difference in MRSA transmission rates between the full MRSA bundle and one that only used gloves and omitted gowns [28]. Therefore, while the VA healthcare system should be applauded for its sustained commitment to and success in reducing HAIs, the data’s limitations for assessing the individual components of the MRSA bundle must be acknowledged.

3. *REDUCE MRSA Trial* [29]

In 2013, the Randomized Evidence of Decolonization versus Universal Clearance to Eliminate MRSA (REDUCE MRSA) trial was published by Huang et al. comparing three MRSA control strategies in a pragmatic, cluster-randomized trial of 74 ICUs in 43 hospitals. The study had a 12 month baseline period, followed by an 18 month intervention period with over 74,000 patients randomized to one of 3 arms: MRSA ADI alone; MRSA ADI + targeted decolonization with intranasal mupirocin and daily CHG bathing for 5 days; or universal decolonization with intranasal mupirocin and daily CHG bathing without screening. Overall compliance rates with the protocol in the three arms were high. Universal decolonization was the most effective strategy, with a 37% reduction in the primary end point of MRSA clinical cultures and 44% reduction in bloodstream infection from any pathogen **(Table 2)**. The targeted decolonization arm was intermediate in its effects while the MRSA ADI alone arm did not significantly impact the primary or secondary endpoints from baseline. A non-significant trend toward reduction in MRSA bloodstream infections was also seen in the universal decolonization arm. Limitations of the study include an imbalance of bone marrow transplant units in the universal decolonization arm, which accounted for a higher baseline rate of bloodstream infection from coagulase negative staphylococci, and the absence of data on mupirocin or CHG resistance. The incremental benefit from the intranasal mupirocin is also unknown. However, this pragmatic “comparative-effectiveness” trial of MRSA control strategies supports horizontal strategies such as CHG bathing over the vertical strategy of MRSA ADI in the ICU setting [14, 30]. Several decision-analytic modeling studies have also identified universal decolonization as the most cost-effective MRSA prevention strategy for the ICU [31, 32].

**Table 2. REDUCE MRSA Trial: Primary and Secondary Outcomes (HR and 95% CI) [29]**

| | ADI Arm | Targeted Decolonization Arm | Universal Decolonization Arm | P |
|---|---|---|---|---|
| **MRSA clinical cultures** | 0.92 (0.77-1.10) | **0.75 (0.63-0.89)** | **0.63 (0.52-0.75)** | 0.01 |
| **MRSA Bloodstream Infection** | 1.23 (0.82-1.85) | 1.23 (0.80-1.90) | 0.71 (0.48-1.08) | 0.11 |
| **Any Bloodstream Infection** | 0.99 (0.84-1.16) | **0.78 (0.66-0.91)** | **0.56 (0.49-0.65)** | <0.001 |

4. *BUGG Trial* [33]

Employing a different approach, the Benefits of Universal Glove and Gown (BUGG) trial conducted by Harris et al. compared universal CP to standard use of CP with a 3-month baseline and 9-month intervention period in a cluster randomized trial of 20 medical and surgical ICUs enrolling over 26,000 patients. The primary outcome measure was acquisition of MRSA or VRE based on ICU admission and discharge surveillance. Comparing rates from the baseline and intervention period, there was no difference in the composite of MRSA or VRE acquisition between the two groups; however, a significant decrease in MRSA acquisition in the universal CP arm was seen (3 fewer MRSA acquisitions/1,000 patient days). Important secondary safety outcomes showed a decrease in health care worker visits but higher hand hygiene compliance on room exit in the universal CP group, with no statistical difference in frequency of adverse events by the IHI trigger tool. Device-related HAIs and mortality were not different between groups. The authors concluded that, despite the negative primary outcome, the decrease in MRSA acquisition merits follow-up studies, and the similar rates of adverse effects was reassuring from a patient safety perspective. The lingering question remains whether the statistical reduction in MRSA acquisition rate is clinically meaningful enough to justify the economic costs and burdens on patients and providers resulting from increased CP use.

5. *MOSAR WP3 Trial* [34]

Finally, Derde et al. combined a cluster randomized trial with an interrupted time series study to evaluate the incremental impact of a vertical strategy of ADI for MRSA in 13 European ICUs and over 8500 patients. The primary outcome was acquisition of MRSA, VRE or highly resistant Enterobacteriaceae determined by surveillance swabs. The baseline 6-month period without intervention demonstrated mean hand hygiene compliance of 52%. In phase 2 lasting for 6 months, the impact of a program to optimize hand hygiene and universal CHG bathing was analyzed with an interrupted time series, demonstrating an improvement in hand hygiene to a mean of 69% and 100% use of CHG. In phase 3 lasting for 12 months, the ICUs were randomized to either chromogenic agar or rapid PCR-based screening as a part of an ADI strategy, while hand hygiene and CHG bathing rates remained high (77% and 100%, respectively). The results showed a significant reduction in transmission of MDRO in phase 2, driven primarily by decrease in MRSA acquisition. However, there was no further reduction in MRSA acquisition with implementation of ADI, regardless of the type of screening. This uniquely-designed study confirms the importance of horizontal strategies such as improved hand hygiene and CHG in reducing MRSA transmission, but it brings into question the incremental benefit of an ADI strategy in the context of optimized hand and patient hygiene. Unfortunately, none of the interventions were effective at reducing acquisition of highly resistant Enterobacteriaceae, suggesting that these emerging pathogens may require a different approach for control, perhaps focusing on antimicrobial stewardship.

*Conclusions*

Several conclusions emerge from this review of recent studies despite the many remaining, open questions. First, the evidence supporting a vertical strategy of universal ADI, particularly for MRSA, is increasingly questioned. The lack of strong evidence for ADI is illustrated in **Table 3** and confirmed by a recent meta-analysis rating the strength of evidence for universal MRSA screening as low [35]. Importantly, no randomized, interventional study has compared the effect of adding contact precautions to the rigorous application of standard precautions on MRSA or VRE acquisition rates. Second, an emerging consensus is that horizontal strategies, such as efforts to improve hand hygiene or change culture, are more likely to be successful at achieving sustained reductions in HAIs although the long-term cost-effectiveness and unintended effects of interventions like universal gowns and gloves or CHG bathing require further study [14]. Third, the improved quality of research in terms of study design and rigor are encouraging and hopefully will provide a roadmap to answer open questions with regards to other pathogens (carbapenem-resistant Enterobacteriaceae [CRE]), other healthcare settings (nursing homes and LTACs), and other dimensions of infection prevention (guidance on safe discontinuation of CP and implementation science to improve adherence to Standard Precautions). It is important to recognize that a “one size fits all approach” does not apply and that whatever interventions are implemented require HCP training followed by audit and feedback to bedside providers in order to achieve success.

## Table 3: Evidence for Specific Interventions to Control MRSA Transmission[8]

| | Trial design | Setting | Screening and isolation | Gloves and gowns | Hand hygiene | Decolonisation | | Masks |
|---|---|---|---|---|---|---|---|---|
| | | | | | | Universal | Targeted | |
| Robicsek et al (2008)[13] | Observational study | Hospital-wide | Effective as part of a bundle* | .. | .. | .. | Effective as part of a bundle | Not included in bundle |
| Harbarth et al (2008)[17] | Prospective interventional cohort study | Surgical wards | Not effective* | .. | .. | .. | Not effective | .. |
| Jain et al (2011)[14] | Observational study | Hospital-wide | Effective as part of a bundle† | Effective as part of a bundle† | Effective as part of a bundle† | .. | .. | .. |
| Huskins et al (2011)[19] | RCT | ICUs | Not effective‡ | Not effective | .. | .. | .. | Not included in bundle |
| Huang et al (2013)[20] | RCT | ICUs and stem-cell transplantation units | Not effective | .. | .. | Effective | Effective§ | .. |
| Harris et al (2013)[21] | RCT | ICUs | .. | Effective¶ | .. | .. | .. | .. |
| Lee et al (2013)[10] | Prospective interventional cohort study | Surgical wards | Not effective alone‖ | .. | Not effective alone** | .. | .. | Not included in bundle |
| Climo et al (2013)[22] | RCT | ICUs | .. | .. | .. | Effective | .. | .. |
| Derde et al (2014)[23] | Hybrid prospective interventional cohort study and RCT†† | ICUs | Not effective | .. | Effective as part of a bundle | Effective as part of a bundle | .. | Not included in bundle |

..=intervention was not assessed. ICU=intensive-care unit. MRSA=meticillin-resistant *Staphylococcus aureus*. RCT=randomised controlled trial. *Interventions included also rapid PCR testing and decolonisation of MRSA carriers. †Hand hygiene was the single most important factor in an independent post-hoc analysis.[15] ‡Screening results did not return in reasonable time. §Targeted decolonisation was effective, but less effective than universal decolonisation. ¶No intervention effect on the primary outcome was noted (acquisition of both vancomycin-resistant *Enterococcus* and MRSA), whereas universal glove and gown use had a significant effect on the secondary outcome (MRSA acquisition alone). ‖On clean surgery wards, the strategy was effective. **Both strategies together were effective. ††The study was only randomised for the comparison of rapid screening versus conventional screening, but not for other interventions.

## Unintended Consequences of Contact Precautions

Despite uncertainty of its effectiveness from existing literature, widespread implementation of CP would be more easily justified if it posed no harm to patients. However, a growing body of evidence points to a number of adverse outcomes associated with CP. These unintended effects can be broadly grouped into negative effects on patients, negative effects on the healthcare system, and ethical considerations.

### *Negative Effects on Patients*

A 2009 systematic review identified 4 major domains of negative effects on patients related to CP: 1) Decreased contact with HCP; 2) Increased delays in care and non-infectious adverse events; 3) Increased symptoms of psychological distress; and 4) Decreased patient satisfaction [36]. Early observational studies in medical and surgical settings documented that patients in CP were visited only half as often by HCP with decreased duration of contact, despite similar severity of illness to non-CP counterparts [37, 38]. An observational study of morning rounds at 2 university medical centers found that attending physicians examined fewer CP patients compared to non-CP patients (35% vs. 73%, $p < .001$), but no difference for senior residents [39]. The previously discussed BUGG trial showed a significant 17% reduction in frequency of

HCP visits in patients in the CP arm, consistent with prior literature but of smaller magnitude [33].

Even more concerning, data suggests quality of care deficiencies as measured by process measures and non-infectious adverse events. Observational studies have shown delays in ED admissions, hospital unit transfers, and discharges comparing isolated to non-isolated patients [40, 41]. In a retrospective matched study of 1 Canadian general medicine cohort and 1 US congestive heart failure (CHF) cohort, Stelfox et al. documented clear differences in safety of care between patients isolated for MRSA and controls [42]. Isolated patients were significantly more likely to have incomplete or unrecorded vital signs, to have days without nursing or physician documentation, and among isolated CHF patients, significantly lower rates of inpatient cardiac testing, evidence-based medications on discharge, documented CHF education, and timely follow-up appointments. Most strikingly, isolated patients were 6 times more likely to experience preventable adverse events, primarily driven by supportive care failures such as falls and pressure ulcers. Other studies have confirmed higher rates of preventable adverse events in isolated patients although one recent cohort failed to show an improvement in these rates with removal of CP [43, 44]. Reassuringly, there was no increase in preventable adverse events in the universal CP arm of the BUGG trial although the detection tool used may not have adequately captured all adverse events [33].

An extensive body of literature describes the psychological impact of CP on patients though much of this work is hampered by the use of only qualitative methods and a lack of controls, which is critical given high depression rates in hospitalized patients [36]. A matched cohort study of 40 geriatric patients in a rehabilitation unit showed significantly higher rates of depression (77% vs. 33%, $p < .01$) and higher mean anxiety scores (15 vs. 8.6, $p <.01$) in those on CP vs. controls [45]. A general medicine matched cohort, comparing CP and non-CP patients, revealed similar depression and anxiety scores on admission, but higher depression and anxiety scores after one week in isolation [46].

The use of CP typically has negatively affected patient satisfaction as measured by formal complaints or post-discharge interviews [42, 47]. However, studies with validated patient satisfaction surveys have failed to demonstrate a significant effect on overall patient satisfaction while length of stay appears to be an important modifying factor [48].

*Negative Effects on Healthcare System*

Although the effects on patients remain of first importance, widespread implementation of CP also imposes significant burdens on the healthcare system. The most direct consequence is increased time required of HCP in delivering care, which although trivial for a single encounter can be substantial in aggregate. Other delays in patient care, transfers, and discharges discussed above can negatively affect hospital throughput and bed capacity. The use of active surveillance for MDROs represents an enormous cost and volume of testing for the laboratory, depending on the intensity of screening implemented [13]. Increased rates of preventable adverse events and sagging patient satisfaction scores may have implications for hospital reimbursement in the era of pay-for-performance models. Conversely, the threats of Medicare non-reimbursement and public reporting of HAIs may pressure hospitals to implement infection control practices of unproven effectiveness. CP may also lead to decreases in adherence to quality indicators such as pneumonia performance measures [49]. An increasing proportion of patients in CP also has been associated with decreased adherence to isolation practices by HCP, with a tipping point of 40% of patients isolated identified in a recent study [50]. Finally, the financial and human resources required of the hospital and IP program to implement a comprehensive program of CP and active surveillance, to provide ongoing education to other HCP, and to monitor for adherence to all elements of the program is substantial [13]. The choice to use an aggressive, vertical approach of ADI for a specific pathogen carries a real opportunity cost that must be considered, diverting money and resources from other important infection prevention efforts [51].

*Ethical Considerations*

A final concern involves the ethical questions raised by the use of CP [52]. Traditionally, infection control practice has emphasized the ethical principles of non-maleficence and justice with lesser focus on patient autonomy [53]. Two additional relevant ethical principles are the doctrine of double effect and the precautionary principle. The doctrine of double effect gives justification to “the possibility of harming certain individuals to bring about other goods,” if certain conditions are met [53]. In applying the doctrine of double effect to CP, the possibility of isolated patients receiving less HCP attention (a potential harm) might be justified for the sake of reducing nosocomial transmission to others (a potential benefit). The precautionary principle serves to “justify anticipatory preventive action despite incomplete scientific evidence” [53]. This principle might dictate that CP for certain MDROs with limited treatment options is appropriate as a “precaution” despite evidentiary uncertainty. However, several thorny ethical questions must be considered. First, there is the question of who should bear the costs associated with CP when the potential benefits derived are not for the isolated individual [51, 52]. Next, issues of fairness are raised when CP are only applied to patients identified by clinical cultures and not asymptomatically colonized patients or when CP and active surveillance are only applied in a narrow, vertical focus for a particular organism. Lastly, the doctrine of double effect must be balanced by the concept of the least restrictive alternative, which “attempts to ensure that the pursuit of the public good does not infringe more than absolutely necessary on the rights of individuals” [51]. If an alternative strategy is proven to have salutary effects on MDRO transmission but imposes less burden on patients than CP, this strategy would be preferred from an ethical perspective.

*Conclusions*

The negative consequences of CP for patients and the healthcare system are a reality that have been largely under-recognized but must be considered in both hospital infection control policy and patient care. Hospital policymakers must balance potential patient benefits and harms and choose the most effective strategy with the least likelihood to negatively impact patients or encroach on their autonomy. They must also consider the opportunity cost of resources utilized for CP compared to other priorities. Individual HCW should closely monitor for chances to discontinue CP when appropriate and guard against latent tendencies to deliver suboptimal care to isolated patients. Finally, healthcare systems should prospectively monitor for adverse effects of CP and investigate creative strategies to mitigate these negative effects [13, 36].

**Alternative Approaches to HAI Prevention**

Although an exhaustive survey of alternate or complementary approaches besides CP for HAI prevention is beyond the scope of this review, a few important interventions merit brief mention. First, universal CHG bathing of all patients in a high-risk setting is a horizontal strategy that has gained recent traction. The REDUCE MRSA and MOSAR WP3 trials discussed above used universal CHG bathing in conjunction with other strategies and found reductions in all-cause bloodstream infections, MRSA clinical culture rates and MDRO acquisition, respectively [29, 34]. In addition, Climo et al. conducted a multicenter, cluster-randomized crossover ICU study, which demonstrated a 23% reduction in MDRO acquisition and 28% reduction in hospital-acquired bloodstream infections associated with daily CHG bathing [54]. Conversely, a more recent single center cluster-randomized crossover ICU study found no impact of daily CHG bathing on a composite outcome of multiple HAIs, but compliance with bathing was not reported [55]. Although the choice of HAIs in the composite end point and lack of adherence data can be questioned, this study suggests that the impact of CHG bathing is greater in settings with higher MDRO prevalence, and the development of CHG resistance remains a concern.

Second, universal gloving, with or without gowning, has been evaluated as a strategy with mixed results regarding HAI prevention and MDRO acquisition rates [33, 56-59]. The effect of any PPE-based interventions on hand hygiene compliance is a key determinant of success, and associated costs still limit widespread application. Third, selective digestive decontamination (SDD), involving administration of both systemic and topical antibiotics in ventilated patients, has consistently been associated with reduced HAIs and even decreased overall ICU mortality by 16% in a recent meta-analysis, the only ventilator-associated pneumonia prevention measure to show a mortality benefit [60, 61]. Despite lingering concerns of drug resistance and the intuitive aversion to prophylactic antibiotics in this setting, adequately powered studies of SDD in the contemporary North American ICU settings with high endemic MDRO rates are now warranted [62].

Finally, an increasing number of academic medical centers have reported stability or reductions in HAI rates in the context of strong horizontal approaches to infection control with limited or no use of CP for MRSA or VRE. At Dartmouth-Hitchcock Medical Center, Kirkland et al. demonstrated sustained control of *S. aureus* infections and healthcare-associated bloodstream infections over a 5 year period, using contact precautions only for patients with open wounds, diarrhea, or secretions regardless of organism [63]. The University of Massachusetts Medical Center discontinued CP for MRSA and VRE hospital-wide in 2010 with no increase in acquisition rate for either pathogen over the next 12 months [44]. After aggressive interventions to improve hand hygiene, to institute hospital-wide CHG bathing, and to recommend a "bare below the elbow" policy for HCP, Virginia Commonwealth University Medical Center discontinued CP for MRSA and VRE with no increase in hospital device-associated infections at an estimated cost savings of $700,000 annually (personal communication, M. Edmond). These examples demonstrate that CP, at least for MRSA and VRE, may be safely scaled back or discontinued in certain contexts for hospitals with a strong horizontal infection control foundation.

**Conceptual Framework for Decisions Regarding Contact Precautions**

Taking into account all available evidence, a key message is that any decisions regarding CP or other IP strategies require a detailed understanding and assessment of the local context. Legislative mandates or other "one-size-fits-all" approaches dictating the implementation of specific bundled interventions such as ADI for MRSA across a broad range of diverse healthcare settings are not supported by the current evidence and should be reconsidered by physicians actively involved in policymaking, including healthcare epidemiologists overseeing state HAI reduction and public reporting programs. A more rational and nuanced approach involves analysis of the local factors which may influence the likelihood of benefit from CP such as listed in **Table 4** [51]. For example, a hospital system with low hand hygiene compliance and inadequate environmental cleaning in the midst of an epidemic of CRE infections is very likely to benefit from an aggressive, multifaceted intervention including CP and even active surveillance. Conversely, an institution with a strong infrastructure and culture of infection prevention and environmental cleaning in the setting of low rates of endemic MDROs and HAIs is unlikely to benefit from extensive use of CP or ASC, but may negatively impact quality or patient safety with such interventions. Moreover, hospital IP programs should maintain continued vigilance so as to detect changes in local factors which might dictate necessary evolution in infection control strategies or allocation of resources.

**Table 4. Local Factors Influencing Likelihood of Benefit from Contact Precautions [51]**

| Local factor | Lower likelihood of benefit | Higher likelihood of benefit |
|---|---|---|
| Hand-hygiene compliance by health care workers | High | Low |
| Epidemiology of health care–associated infections | Low endemic rates | Epidemic or uncontrolled rates |
| Organism of concern | All or easily treatable | Selected or difficult to treat |
| Prevalence of organism | Common | Rare |
| Clinical features of source patient | Asymptomatic | Open wound, diarrhea, or uncontained secretions |
| Clinical features of patients at risk of infection | Healthy | Vulnerable to infection because of age, immune status, or other risks |
| Physical environment | Clean, spacious, single rooms | Crowded, dirty wards |
| Available resources | Limited | Plentiful |

## Conclusions

Despite extensive study and widespread application of CP in the control of MDROs, their effectiveness as currently practiced remains hotly debated. CP will continue to play an important role in epidemics or situations where novel pathogens arise with high transmissibility or limited treatment options. However, universal screening and CP for MRSA and VRE should be re-examined. In particular, hospitals with a strong horizontal IP program may be able to safely scale back universal CP or ASC for certain endemic pathogens. As highlighted by the recent Ebola outbreak, the importance of HCP education and training in proper use of recommended PPE with audit and feedback is critical to their effectiveness, and further implementation research into strategies to improve adherence are needed. The unintended consequences of CP for patients and healthcare systems must be acknowledged and, where possible, mitigated while their deployment is conducted in an ethically appropriate manner. Improvements in study design and research quality hopefully will yield critical guidance for the many, unanswered questions in this field. In the interim, IP teams, hospital administrators, and clinicians must carefully weigh the risks and benefits of any intervention within their local context to limit MDRO transmission and HAIs while improving patient care quality and safety.

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