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Adverse outcomes associated with contact precautions: A review of the literature

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Background: Contact Precautions (CP) are a standard method for preventing patient-to-patient transmission of multiple drug-resistant organisms (MDROs) in hospital settings. With the ongoing worldwide concern for MDROs including methicillin-resistant *Staphylococcus aureus* (MRSA) and broadened use of active surveillance programs, an increasing number of patients are being placed on CP. Whereas few would argue that CP are an important tool in infection control, many reports and small studies have observed worse noninfectious outcomes in patients on CP. However, no review of this literature exists.

Methods: We systematically reviewed the literature describing adverse outcomes associated with CP. We identified 15 studies published between 1989 and 2008 relating to adverse outcomes from CP. Nine were higher quality based on standardized collection of data and/or inclusion of control groups.

Results: Four main adverse outcomes related to CP were identified in this review. These included less patient-health care worker contact, changes in systems of care that produce delays and more noninfectious adverse events, increased symptoms of depression and anxiety, and decreased patient satisfaction with care.

Conclusion: Although CP are recommended by the Centers for Disease Control and Prevention as an intervention to control spread of MDROs, our review of the literature demonstrates that this approach has <u>unintended consequences</u> that are potentially deleterious to the patient. Measures to ameliorate these deleterious consequences of CP are urgently needed.

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Isolation has long been employed to control the spread of infectious diseases. During epidemics, it has been applied for short durations to many patients. Prior to the availability of effective therapy for mycobacterial disease, isolation was often used for years, as exemplified by tuberculosis sanitariums and leper colonies.

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With these forms of isolation, however, came social stigmatization and limited access to medical care.^{1,2} More recently, Blood and Body Fluid Precautions, introduced in the 1980s, in response to the HIV epidemic, were associated with social stigmatization of patients until they were replaced by Universal Precautions.³ Beginning in the 1960s, isolation was employed for longer duration within hospitals, first for protective isolation of severely immunocompromised patients⁴ and later to prevent cross-transmission from patients with multiple drug-resistant bacterial organisms (MDROs), principally methicillin-resistant *Staphylococcus aureus* (MRSA).⁵ Reports of psychologic stress and anxiety in patients in isolation appeared soon after the development of protective isolation.⁶

As Contact Precautions (CP) became more commonly used in an attempt to control the spread of various MDROs, including MRSA, awareness has grown regarding potential unintended consequences of CP. A 1997 *British Medical Journal* editorial raised the question "is it time to stop searching for MRSA?" in which the authors suggested that the use of CP may have a psychologically detrimental impact and cause patients to receive less medical attention, resulting in a delay of medical progress and discharge.⁷ These unsupported statements were soon followed by multiple studies on the subject that will be reviewed herein.

The large literature addressing the efficacy of CP to control MDROs has been reviewed elsewhere.⁸⁻¹² CP are the standard approach to managing hospitalized patients colonized or infected by MDROs.¹² Few discussions of hospital control of MRSA or other MDROs, however, are without mention of potential adverse outcomes related to CP.¹¹⁻¹⁴ A survey from one hospital found that the majority of physicians believed that CP were associated with worse outcomes.¹⁵ The Centers for Disease Control and Prevention (CDC) recommends that, while caring for patients on CP, hospitals should "counteract possible adverse effects on patient anxiety, depression, and other mood disturbances; perceptions of stigma; reduced contact with clinical staff; and increases in preventable adverse events."¹² Likewise, the Society for Healthcare Epidemiology of America and the Association of Professionals in Infection Control and Epidemiology, Inc, have recommended accurate determination of "the safety of isolation and optimizing practice to ensure the best outcome for patients."¹¹

Recent initiatives to control MRSA in the United States include mandatory active surveillance for highrisk patients at all hospitals in the state of Illinois and for all patients being admitted to hospitals within the federal Department of Veterans Affairs.^{16,17} Patients found to be colonized with MRSA will be placed into CP. Active surveillance is estimated to detect selected MDROS (MRSA and vancomycin-resistant *enterococcus*) in 3 to 6 times the number of patients identified by clinical cultures.¹⁸⁻²⁰ Now is therefore an opportune moment to consider the overall consequences of this routine infection control intervention. Although some studies have been synthesized by other sources,^{11,12,21} we know of no systematic review of the literature.

METHODS

We required studies to use the CDC definition of CP: the use of gowns and gloves for all staff who have contact with the patient or patient's environment, as well as housing patients in a single room or a room shared with other patients on CP.¹² The terms *barrier restriction, source isolation, CP,* and *contact isolation* were used synonymously. For all studies discussed in this review, patients were on CP because of MDROs.

In our literature review, a systematic search for studies or commentaries related to adverse outcomes and CP was completed via MEDLINE, PubMed, and Google Scholar search engines from 1970 to 2008. We also reviewed abstracts from the 2005-2007 annual scientific meetings of the Society for Healthcare Epidemiology of America. The search terms included adverse effects, outcomes, depression, anxiety, psychiatric, isolation, contact, source, barrier, precaution, and restriction. Articles that addressed adverse outcomes of patients on CP were reviewed, and those that were published in peer-reviewed journals with standardized collection of data or inclusion of control groups were described in greatest detail.

RESULTS

We found 15 articles evaluating adverse outcomes related to CP. One was rejected because of unclear indications for CP. Nine articles are described in greater detail because of standardized collection of data and inclusion of a control group.

Four main adverse outcomes related to CP were identified in this review. (1) CP are associated with less patient-health care worker (HCW) contact. (2) CP are associated with delays and more noninfectious adverse events. (3) CP are associated with increased symptoms of depression and anxiety. (4) CP are associated with decreased patient satisfaction with care.

CP are associated with less patient-HCW contact

Four studies examined HCW behavior toward patients on CP (see Table 1). Kirkland and Weinstein observed HCWs within a medical intensive care unit.²² Over 35 hours of observation, they documented hourly HCW room entry rate at 49% for patients on CP versus patients in regular intensive care unit rooms (P = .06), patient-HCW physical contact rate at 50% for patients on CP compared with non-CP patients (P = .03), and overall HCW duration in CP patient rooms at 62% of the time spent in non-CP rooms (P = .6). Using an embedded observer during morning rounds on a general medicine floor, Saint et al reported that attending physicians were half as likely to examine patients on CP (relative risk, 0.49, P < .001) (although senior residents were equally likely to examine patients on CP).²³ The most exhaustive study to examine the effects of CP on HCW behavior was performed by Evans et al among surgical intensive care unit and general surgery patients.²⁴ They observed that patient-HCW encounters were approximately half as frequent for patients on CP (5.3 vs 10.9 HCW hourly encounters, P < .001) and that in-room contact time with HCWs was 22% less in patients on CP (29 vs 37 minutes per hour, respectively, P = .008). Severity of illness as measured by Acute Physiology and Chronic Health Evaluation (APACHE) II score was similar between CP and non-CP groups.

One study reported no difference in HCW behavior between patients on CP and those not on CP.²⁵ Investigators randomized ventilator-dependent patients in the

	Setting	Design	Effect	Limitations	Implications
Kirkland and Weinstein, 1999 ²²	Medical ICU	Cohort: 35 hours observation (14 hours CP, 21 hrs non-CP), 219 room entries	2.1 vs 4.2 Hourly patient contacts by HCW for CP patients vs non-CP (P = .03).	Severity of illness not calculated.	HCWs less likely to visit ICU patients on CP.
			HCWs more likely to wash hands after seeing CP patients (83% vs 34%, respectively, P < .001).	No breakdown by HCW type.	
Saint et al, 2003 ²³	Morning rounds 2 university medical centers	Cohort: observed 139 patients (31 on CP)	Senior residents examined CP and non-CP equally (83% vs. 87%, respectively, $P = .58$). Attendings examined fewer patients on CP (35% vs. 73%, respectively; RR, 0.49, P < .001).	Physicians only. No severity of illness. Attendings may have returned to examine patients later.	Attending physicians less likely to examine patients on CP.
Evans et al, 2003 ²⁴	Surgical ICU and surgical inpatient units	Matched cohort: ~50 hours observations. 48 CP and non-CP observations. 485 room entries.	5.3 CP vs 10.9 non-CP overall ICU/Floor HCW encounters (P < .001). 22% less contact time with HCWs (29 CP vs 37 min non-CP per hour, $P = .008$).	Unclear total number of patients on CP. Interviews with few patients.	All HCWs spend less time with patients on CP, which is not explained by severity of illness.
		Patient interviews: 9 on CP, 17 non-CP	Care while on CP not perceived to be worse.		
Klein et al, 1989 ²⁵	Pediatric ICU	Safety monitoring of randomized controlled trial of CP.	Safety monitoring revealed no difference in number of contacts/ care at days 0, 1, 7 between 25 CP and 25 non-CP patients.	CP applied randomly without cultures. Pediatric. No criteria for patient selection (monitoring).	CP does not necessarily result in less HCW contact.

Table 1. Studies of health care worker behavior with patients on contact precautions

pediatric intensive care unit to CP or non-CP (without regard to carriage of MDROs) and evaluated adverse outcomes related to CP. As a safety monitoring practice, they selected 25 patients on CP and 25 not on CP (of 32 and 38 patients, respectively) and observed HCW contact for 1 hour each, finding no difference in rates of contact at days 0, 1, and 7. Although this safety monitoring study was embedded in a randomized controlled trial, details of patient selection for monitoring were not provided, and the strength of the conclusion is not that of a randomized controlled trial. It does, however, demonstrate that changes in provider setting may overcome the effects of CP.

CP are associated with delays and more noninfectious adverse events

In a report examining the financial impact of a program to remove patients from CP, pilot data revealed that patients on CP awaiting transfer to long-term care facilities experienced an average of 10.9 delaydays compared with 4.3 delay-days for similar patients not on CP.²⁶ The relative paucity of beds available for out-of-hospital care of patients on CP is presumably the reason for such a delay (Table 2).

Adverse events in patients on CP have been studied in a meticulously performed historical matched cohort reviewing charts for 150 patients on CP and 300 controls not on CP at 2 hospitals: one in Ontario, Canada, and the other in Massachusetts.²⁷ Two matched cohorts were formed: one composed of general medicine patients and the other of congestive heart failure patients. Controls occupied the same room before and after the case. The primary finding was a higher number of adverse events in patients on CP than those not on CP, both in absolute terms and adjusted for length of stay. A rate of **31** versus 15 adverse events/1000 days was observed in patients on CP versus those not on CP (P < .001). This difference reflected preventable adverse events (20 vs 3/1000 days, respectively, P < .001)

	Setting	Design	Effect	Limitations	Implications	
Goldszer et al, 2002 ²⁶	General hospital	Cohort	10.9 Delay-days for CP vs 4.3 delay-days non-CP prior to extended care facility. Admission delays from ER.	Methods not documented.	Raised issue of CP on patient flow.	
Stelfox et al, 2003 ²⁷	General medicine and cardiology inpatients: 2 centers	Historical matched cohort chart review: General medicine cohort 78 vs 156 controls.	Adverse events more frequent in patients on CP, 31/1000 days vs 15/ 1000 days, respectively ($P < .001$), which were preventable, 20 vs 3/ 1000 days, respectively ($P < .001$). Supportive care adverse events more common in CP (RR, 8.3; $P < .001$).	CP for <i>clinical</i> isolates. Limited adjustment for severity of illness or length of hospital stay.	Preventable adverse events appear to be more common in patients on CP.	
		CHF cohort 72 vs 144 controls.	Nonsignificant difference in mortality, 17% vs 10%, respectively (P = .16). Duration of hospitalization longer for patients on CP (31 vs 12 and 8 vs 6 days, respectively, $P < .001$). 8% of CP patients formal complaints vs 1% of non-CP $(P < .001)$.			

Table 2. Studies of systems of care and adverse events in patients on contact precautions

and not nonpreventable adverse events (11 vs 12/1000 days, respectively, P = .98). Preventable adverse events were all termed *Service Care Errors*, and included falls, pressure ulcers, and fluid/electrolyte disorders. General process of care measures, such as inappropriate documentation of vital signs (14% vs 9%, respectively, P < .001) and days without a physician note (26% vs 13%, respectively, P < .001) or nursing note (14% vs 10%, respectively, P < .001), were worse in CP patients. Congestive heart failure-specific process measures, including stress testing (14% vs 45%, P < .001) and evaluation of left ventricular function (57% vs 69%, P = .049), were worse in CP patients. Patient satisfaction was also modified and is discussed in the next section.

The main limitation of this study is concern about the appropriateness of the matched control group. APACHE II severity of illness scores and Charlson comorbidity index scores were similar between cases and controls. However, patients appear to have been isolated because of clinical isolates, which increases the chance that they had a hospital-acquired infection with MDROs, which is associated with increased morbidity.²⁸ The other limitation is that patients on CP had much longer stays than those not on CP (general cohort, 31 vs 12 days and congestive heart failure cohort, 8 vs 6 days, respectively, P < .001). Although some outcomes, such as rate of adverse events, were adjusted for length of stay, others, including all patient outcome and satisfaction measures, were absolute numbers and therefore are difficult to interpret. Whereas patient length of stay is a potential confounder for other results, it should also be seen as an outcome. CP cause delay in transfer to long-term care facilities.^{26,27} Those patients who are awaiting transfer to long-term care facilities are those who have the most need for supportive care and are at a higher risk of falls and bedsores. Therefore, the risk for increased length of stay associated with CP falls disproportionally on those with the most need for supportive care.

This study demonstrated an increase in preventable adverse events in patients on CP. The applicability of these results to patients on CP for positive active surveillance cultures instead of clinical cultures and the importance of confounding disease notwithstanding, this study established the importance of specific patient safety concerns when CP are applied.

CP are associated with increased symptoms of depression and anxiety

The literature related to psychological effects of isolation is extensive (Table 3). The bulk of this literature has been primarily descriptive of the psychological impact of protective isolation and serves as a background to explain sources of stress for patients on CP (See Gammon for a review⁶). Knowles provides a good summary of the qualitative literature relating to the psychology of patients on CP: most feel socially isolated and bored, many question the state of their health, but many also appreciate the privacy of a single room.²⁹ These papers rarely used validated measures of psychiatric disease and did not include a control group of patients not on isolation. Given that rates of depression at the time of hospital admission range from 18% to 40%,³⁰⁻³³ including a control group in studies of depression related to CP is vitally important.

In 1997, Kennedy and Hamilton studied a matched cohort of 32 spinal cord injury rehabilitation patients, half of whom were on CP.³⁴ Using the validated Beck Depression Inventory, they found a nonsignificant difference in depression scores (16.5 CP vs 12.3 not on CP). In a study in general inpatients, patients on CP were found to have higher levels of anxiety (12.8 vs 8.2, respectively, P < .001) and depression (12.5 vs 7.3, respectively, P < .001) by the validated Hospital Anxiety and Depression scale as well as lower self-esteem (14.4 vs 16.9, respectively, P < .005) and a perception of less control (11.4 vs 16.1, respectively, P < .001).³⁵ The investigators did not control for severity of illness in this study. Tarzi et al studied a group of elderly patients from a rehabilitation facility who had been hospitalized at least 4 weeks, using a matched cohort study design.³⁶ Participants in the 2 cohorts did not differ by age, sex, length of hospitalization, medical diagnosis, degree of disability, or cognitive function. Twenty-two patients on CP and 20 non-CP patients submitted to the Geriatric Depression Scale (GDS)-Short Form. Of those on CP, 77% had depression versus 33% of non-CP patients (P < .01). Anxiety scores were also higher in CP than non-CP patients (15 vs 8.6, respectively, P < .01). The observed size of effect is large and has particular importance to patients on CP in subacute and long-term care facilities.

Catalano et al performed a cohort study of 27 patients on CP compared with 24 patients not on CP.³⁷ An unreported number of the CP patients were evaluated within 48 hours of being placed on CP and *not* at time of admission. Of those on CP, 22% had a prior Axis I psychiatric diagnosis in comparison with 8% of the non-CP group (P = .17). The Hamilton Depression Rating Scale (HAM-D) and Hamilton Anxiety Rating Scale (HAM-A) were administered at admission, week 1, and week 2 for those still hospitalized. Depression scores were initially similar for CP patients and for non-CP patients (8.4 vs 8.5, respectively), but after 1 week those on CP had higher depression scores than those not on CP (10.7 vs 6.0, respectively, P <.001). After 2 weeks of inpatient stay, these differences persisted (11.5 vs 4.2, respectively, P < .001). Anxiety scores were also similar on admission between CP and non-CP patients (8.0 vs 8.4, respectively). After 2 weeks, those on CP had higher anxiety scores (11.1 vs 4.7, respectively, P < .001), and these differences continued at 2 weeks. The study was small, and those on CP had a higher baseline rate of Axis I psychiatric diagnoses. This study suggests that patients on CP have more depression and anxiety within 1 week of being placed on CP that persists for at least 2 weeks. The applicability of these findings to patients on CP because of positive active surveillance cultures rather than clinical cultures is not clear.

Depressive symptoms observed in these studies may, in part, contribute to other patient outcomes in patients on CP. Elderly patients with depression by a screening survey at hospital admission have a higher overall mortality.³⁸

CP are associated with decreased patient satisfaction with care

The effect of CP on patient satisfaction has been examined in a rehabilitation setting and among hospitalized inpatients (Table 3). Among those undergoing rehabilitation, anger has been commonly reported. In a geriatric population, both those on CP and not on CP had higher scores than previously reported on an anger scale, with a trend toward more anger in patients on CP (P = .06).³⁶ In a population of patients in rehabilitation after spinal cord injury, those patients on CP expressed more anger than those not on CP (12.4 vs 4.9, respectively, P = .037), 85% believed that CP had limited their rehabilitation, and 50% believed that it had affected their mood.³⁴

In an inpatient population, patients on CP were more likely to formally complain to the hospital (8%) vs 1%, respectively, P < .001) as well as have informal documentation of a complaint in the hospital chart (25% vs 3%, respectively, P < .001).²⁷ In a small survey of 9 patients on CP and 17 not on CP, patients on CP perceived less interaction with HCWs but reported a better quality of care.²⁴ There was also a trend toward CP patients being less comfortable interacting with nursing. In a survey directed exclusively at patient satisfaction, Gasink et al interviewed 43 patients on CP compared with 43 controls.³⁹ A trend toward being less likely to recommend the hospital to a friend was observed in patients on CP (81% vs 95%, respectively, P = .08), and patients on CP reported an inadequate explanation of medication side effects or other instructions from nursing staff (67% vs 93%, respectively, P = .007). However, they found no difference in any measure of patient satisfaction with their hospitalization when longer length of stay was accounted for

Table 3.	Studies	of	psycholog	gic and	ps	ychiatric	outcomes	of	patients	on	contact	precautions
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	Setting	Design	Effect	Limitations	Implications
Knowles, 1993 ²⁹	Inpatient unit	Series of interviews: 8 patients and their nurses.	Most patients expressed feeling neglected and isolated, some valued the privacy and solitude afforded by CP.	No selection criteria. No controls. No quantification of results.	Exploratory study showing many patients have negative feelings related to being on CP.
Kennedy and Hamilton, 1997 ³⁴	Spinal cord injury rehabilitation unit	Matched cohort: open-ended interview. 16 Cases/controls.	CP patients more angry about limitations in care. 12.4 vs 4.9, respectively, $P = 0.037$. Depression score in CP patients, 16.5 vs 12.3, NS). 85% of patients believed CP had limited rehabilitation.	Limited generalizability.	Patients on CP in rehabilitation unit angrier and trend toward more depression.
Gammon, 1998 ³⁵	Inpatients from 3 general hospitals	Matched cohort: 20 cases vs 20 controls	More anxiety (12.8 vs 8.2, P < .001)/depression (12.5 vs 7.3, $P < .001$), respectively. Lower self-esteem (14.4 vs 16.9, $P < .005$) and perception of less control (11.4 vs 16.1, P < .001), respectively.	Small study. Excluded patients with prior psychiatric diagnoses.	More anxiety and depression in patients on CP.
Davies and Rees, 2000 ⁴⁵ /Rees and Davies, 2000 ⁴⁶	Inpatient and rehabilitation units	Cohort: 21 consecutive patients on CP	 12/21 With mood disturbance: 7 patients depressed, 5 anxiety disorder. No controls. Anxiety correlated with being able to estimate duration of CP (P = .02). 	No controls. Duration of hospitalization unclear.	Depression and anxiety common in patients on CP. Contact with team and education important to satisfaction.
Tarzi et al, 2001 ³⁶	Rehabilitation unit	Matched cohort: 20 CP and 20 controls >65 yr of age	Depression, 77% of CP vs 33% non-CP patients (P < .01). Mean anxiety scores were higher in CP than non-CP patients (15 vs 8.6, P < .01), respectively.	Limited generalizability to general inpatients. High baseline rate of depression.	More depression with CP in rehabilitation units may be worse than general inpatients.
Catalano et al, 2003 ³⁷	Infectious disease/isolation units	Matched cohort: 27 CP, 24 non-CP	Depression scores higher after 1 week of CP (10.7 vs 6.0, respectively, P < .001). Anxiety scores higher after 1 week on CP (11.1 vs 4.7, respectively, P < .001).	CP patients more likely to have baseline Axis I diagnosis (22% vs 8%, respectively, P = .17).	Longitudinal study showing more anxiety and depression with CP.
Gasink et al, 2008 ³⁹	General hospital population	Case-control cross- sectional study: 43 CP vs 43 non-CP	Length of stay, 10 days CP vs 6 days non-CP ($P = .005$). Patients less likely to understand nursing explanations (67% vs 93% non-CP, P = .007). No difference in measures of satisfaction. 62% of patients believed CP provided benefit to them.	Majority of CP patients believed CP was of benefit to them.	Patient satisfaction with CP may not be significantly lower if they believe it is in their best interest.

with multivariable analysis.³⁹ This study emphasizes that length of stay is an important factor in interpreting patient satisfaction and that adequate patient education is an important part of applying CP because 62% of patients believed CP were in place for their benefit.

Approaches to minimize adverse outcomes associated with contact isolation

The CDC's 2007 guideline for isolation precautions recommends efforts to counteract possible adverse effects of CP.¹² However, no specific recommendations have been made by the CDC or other organizations. Most studies that demonstrated adverse outcomes associated with CP suggest reconsideration of CP as a means to prevent the spread of MDROs.^{22,24,27,34-36}

Interviews with 5 patients who reported negative experiences while on CP reported that education, improved communication with staff, and provisions to improve social contact while on CP would be beneficial.⁴⁰ An unpublished study reported in a review found that education prior to initiation of CP decreased anxiety and depression in patients on CP.⁴¹ Staff education has been advocated as a way to improve outcomes of patients on CP⁴²; however, this may have a limited effect because nurses have reported being aware of difficulties with CP but of having limited time to address them.²⁹

More frequent adverse events in patients on CP appear to be primarily service care errors. Increased staffing ratios of HCWs caring for patients on CP may potentially improve outcomes, but this has not been investigated. Higher nursing ratios in a general hospital population correlate with more rapid discharge, fewer nosocomial infections, and potentially a lower mortality.⁴⁵

Others have recommended educational interventions to encourage equally attentive care be provided to all patients, including decreasing the sense of social isolation by increased involvement of social work, physical therapy/occupational therapy, clinical psychology, and psychiatry services.²¹ Active monitoring for adverse outcomes related to CP have been suggested, including monitoring HCW-patient contacts, noninfectious adverse events, and patient satisfaction.²¹

CONCLUSION

CP are typically employed to isolate a patient who is colonized or infected with any of a number of MDROs. This intervention has been a mainstay of infection control programs for many decades. However, being placed on CP during an acute care hospitalization has been associated with less HCW contact, more service care errors, decreased satisfaction with care, and higher rate of depression and anxiety. There is no definitive study of adverse outcomes associated with CP, and no studies have examined patients placed on CP for colonization recognized because of active surveillance. Education of patients and hospital staff has been the most commonly suggested means to limit adverse outcomes.^{6,29,40,41}

In this review, we found that reports of adverse outcomes associated with CP are dispersed over many specialty journals and generally are methodologically weak. All studies are observational, and many contain methodologic problems such as lack of a control group or standardized inclusion criteria that limit their interpretation.⁴⁴ A publication bias toward studies showing worse outcomes with CP may also affect the available literature. Although all forms of isolation affect a patient's experience and potentially the quality of care they receive, this review was limited to CP because it is the most commonly used form of isolation in hospitals.

In the absence of a definitive study, we recommend efforts to improve patient education prior to initiation of CP along with education of staff regarding potential shortcomings of care received by patients on CP. For institutions that employ CP, we recommend monitoring to ensure that CP implementation is not detrimental to patient safety.²¹

The impact of adverse outcomes associated with CP may be large, given that both depression³⁹ and adverse events³⁰ have been documented to be approximately twice as common in patients on CP and that depression occurs in approximately <u>one third³⁰⁻³³</u> of medical inpatients and adverse events in up to 28% of inpatients.⁴⁷ In comparison, the <u>rate of hospital acquisition of MRSA</u> for general admissions is approximately <u>1 of 30</u>.¹⁸ and approximately <u>one quarter</u> of patients <u>acquiring MRSA</u> become <u>infected.¹⁸</u>

Further study of adverse outcomes in patients on CP is needed. Critical factors to address include evaluating psychiatric outcomes as well as adverse events in the same population, using carefully matched controls, using validated measures, and focusing on colonized patients to limit confounding by severity of illness. Adequate funding for appropriately designed multicenter studies is needed, given that findings from single centers will be limited by sample size and generalizability issues.

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