CURRICULUM VITAE

LINDSAY CROFT, MS

CONTACT

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EDUCATION

2011-2015 (expected) **Ph.D. in Epidemiology**, Department of Epidemiology and Public Health, University of Maryland, Baltimore; Baltimore, Maryland

- Dissertation Mentor: Daniel Morgan, MD, MS
- Dissertation Title: "The Effect of Contact Precautions on Frequency of Hospital Adverse Events"

2009-2011 **Master of Science in Epidemiology**, Department of Epidemiology, College of Public Health, University of Iowa; Iowa City, Iowa

- Research Mentor: Loreen Herwaldt, MD
- Research Title: "Risk Factors for Surgical Site Infections After Pediatric Spine Operations"
- 4.0 cumulative GPA

2005-2009 **Bachelor of Science in Microbiology**, Washington State University; Pullman, Washington

- Research Mentor: Michael Konkel, PhD
- Honors Thesis: "Virulence of *Campylobacter jejuni* Isolates Amongst Different Eukaryotic Cell Lines"
- Graduated *magna cum laude*

RESEARCH EXPERIENCE

2012-Current

Graduate Research Assistant, Division of Genomic, Epidemiology, and Clinical Outcomes (GECO), Department of Epidemiology and Public Health (DEPH), University of Maryland, Baltimore (UMB)
Principal Investigator: Daniel Morgan, MD, MS

Title of Project: Patient Safety and Adverse Events
Project Responsibilities:

- Adverse event database setup, data entry, supervised double data entry, data cleaning for 20-site cluster randomized trial safety data
- Multivariable analysis methods including logistic, Poisson, and mixed effects Poisson regression for adverse event data from a cluster randomized trial and data from both electronic and paper-based chart reviews for adverse events

Apr-Sept. 2012

Graduate Research Assistant, Center for Vaccine Development, UMB, Baltimore, Maryland
Principal Investigator: Milagritos Tapia, MD

Project Responsibilities:

- Weekly maintenance of database for influenza vaccine clinical trial in Bamako, Mali
  - Communicated with primarily French-speaking study staff about participants needing follow-up and information on study outcomes
- Data cleaning for cohort study on rheumatic heart disease in Bamako, Mali, required frequent contact with study staff for corrections using paper-based records located in Mali

Sept. 2011-
Mar. 2012

Graduate Research Assistant, GECO, DEPH, UMB

Mentor: Daniel Morgan, MD, MS

- Literature searches on: healthcare worker hand hygiene surveys; validation process and analysis methods for the Center for Medicare Services instrument (Hospital Consumer Assessment of Healthcare Providers and Systems)
- Bivariate and multivariable logistic regression analysis
- Validation checks for electronic badges used in hand hygiene study conducted at the University of Maryland Medical Center (UMMC)

Mentor: Mary-Claire Roghmann, MD, MS

- Descriptive statistics and graphs for fiscal year trends in Quantiferon-Tuberculosis Gold test use in Baltimore Veterans Administration hospital
- Literature searches: traditional and molecular epidemiology of community *S. aureus* nasal colonization
- Analysis of environmental factors influencing *S. aureus* spa type and spa clonal complex concordance in Amish study population

Mentor: Kerri Thom, MD, MS

- Database validation for study examining risk factors for acquisition of *Acinetobacter* in UMMC medical and surgical intensive care units

Mentor: Anthony Harris, MD, MPH

- Database validation

June 2010-
May 2011

Graduate Research Assistant, University of Iowa Hospitals and Clinics, Iowa City, Iowa

Mentor: Loreen Herwaldt, MD

- Literature review, aided study design and modification of chart abstraction forms, consulted with orthopedic surgeon and infectious disease pediatrician requesting the study
- Data collection for 66-patient case control study
- Conducted statistical analysis; presented results at departmental poster session; communicated results to surgeon
- Study results presented by Dr. Herwaldt October 2011 at IDWeek, Boston, Massachusetts

2007-2008

Undergraduate Lab Assistant, School of Molecular Biosciences, Washington State University, Pullman, Washington

Mentor: Michael Konkel, PhD

- General buffer, media, antibiotic stock preparation along with other general lab duties
- Binding and internalization assays to measure virulence of *Campylobacter jejuni* clinical isolates
- Cell culture maintenance for various mammalian cell types including: INT407, Vero, MDCK, Caco-2, department swine epithelial cell line

PEER REVIEWED PUBLICATIONS

Croft LD, Harris AD, Pineles L, Langenberg P, Shardell M, Fink JC, Simoni-Wastila L, Morgan, DJ; Benefits of Universal Glove and Gown (BUGG) primary investigators. The effect of universal glove and gown use on adverse events in intensive care unit (ICU) patients. *Clin Infect Dis*. 2015 [epub ahead of print]. doi: 10.1093/cid/civ315.

Morgan DJ, Braun B, Milstone AM, Anderson D, Lautenbach E, Safdar N, Drees M, Meddings J, Linkin DR, **Croft LD**, Pineles L, Diekema DJ, Harris AD. (2015). Lessons learned from hospital Ebola preparation. *Infect Control Hosp Epidemiol*. doi:10.1017/ ice.2015.61.

Croft LD, Pottinger JM, Chiang HY, Ziebold CS, Weinstein SL, Herwaldt LA. Risk factors for surgical site infections after pediatric spine operations. *Spine*. 2015 Jan; 40(2): E112-9. doi: 10.1097/BRS.0000000000000693.

Arnold R, Rock C, **Croft L**, Gilliam BL, Morgan DJ. Reply to "therapeutic outcomes of pyogenic vertebral osteomyelitis requiring spinal instrumentation". *Antimicrob Agents Chemother*. 2014 Nov; 58(11): 7022. doi: 10.1128/AAC.04063-14.

Croft L, Sorkin J, Gallicchio L. Marital status and optimism score among breast cancer survivors. *Support Care Cancer*. 2014 Nov; 22(11): 3027-34. doi: 10.1007/s00520-014-2308-y.

Arnold R, Rock C, **Croft L**, Gilliam BL, Morgan DJ. Factors associated with treatment failure in vertebral osteomyelitis requiring spinal instrumentation. *Antimicrob Agents Chemother*. 2014; 58(2): 880-4. doi: 10.1128/AAC.01452-13.

Roghmann MC, Longinaker N, **Croft L**, Johnson JK, Lydecker AD, Stine OC. Molecular epidemiology of *Staphylococcus aureus* colonization in the Old Order of Amish of Lancaster county, Pennsylvania, USA. *Epidemiol Infect*. 2014 Aug; 142(8): 1722-6. doi: 10.1017/S0950268813002872.

Mehrotra P, **Croft L**, Day HR, Perencevich EN, Pineles L, Harris AD, Weingart SN, Morgan DJ. Effects of contact precautions on patient perception of care and satisfaction: a prospective cohort study. *Infect Control Hosp Epidemiol*. 2013 Oct; 34(10): 1087-93. doi: 10.1086/673143.

ABSTRACTS

Liquori M, **Croft L**, Mehrotra P, Day HR, Lamos E, Arnold R, Perencevich EN, Harris AD, Morgan DJ. (2015). Effect of Contact Precautions on adverse events by patient report and chart review. Oral presentation. Society for Healthcare Epidemiology of America, Orlando, FL, May 2015.

Croft LD, Harris AD, Pineles L, Langenberg P, Shardell M, Simoni-Wastila L, Morgan DJ, Benefits of Universal Glove and Gown (BUGG) Primary Investigators. (2014). The effect of universal glove and gown use on adverse events in the Benefits of Universal Glove and Gown (BUGG) cluster randomized trial. Oral presentation (presenting author). IDWeek 2014, Philadelphia, PA, October 2014.

Croft L, Mehrotra P, Day HR, Lamos B, Arnold R, Perencevich EN, Harris AD, Morgan DJ. (2013). Effect of Contact Precautions on frequency of hospital adverse events. Poster presentation (presenting author). Public Health Research Day at Maryland, College Park, MD, April 2014.

Croft L, Mehrotra P, Day HR, Lamos B, Arnold R, Perencevich EN, Harris AD, Morgan DJ. (2013). Effect of Contact Precautions on frequency of hospital adverse events. Poster presentation (presenting author). IDWeek 2013, San Francisco, CA, October 2013.

Mehrotra, **Croft L**, Day H, Perencevich E, Pineles L, Harris A, Weingart S, Morgan D. (2012). A qualitative and quantitative measurement of the effects of Contact Precautions on hospital patient satisfaction. Poster presentation. IDWeek 2012, San Diego, CA, October 2012.

Croft L, Pottinger JM, Chiang HY, Ziebold CS, Weinstein SL, Herwaldt LA. Risk factors for surgical site infections (SSIs) after pediatric spine operations (PSO). Oral Presentation. IDWeek 2011, Boston, MA, October 2011.

TEACHING EXPERIENCE

Fall 2014-
Spring 2015

Interdisciplinary Patient Safety and Quality Improvement at the Point of Care; Alison Duffy, PharmD, BCOP; Emily Heil, PharmD, BCPS; Meg Johantgen, PhD, RN; Daniel Morgan, MD, MS; Kerri Thom, MD, MS; UMB

- Content development: root cause analysis; mock event review
- Coordinator for seven 3-week training cycles for medical, pharmacy, and nursing students on rotation in UMMC intensive care units

Fall 2014

Principles of Epidemiology Teaching Assistant
Mona Baumgarten, PhD; Nancy Ellish, DrPH, MSPH; DEPH, UMB

Fall 2013 **Regression Analysis Teaching Assistant**
Hegang Chen, PhD; DEPH, UMB
- Guest lectured on global and partial F-tests; graded homework and data analysis project; answered student questions

Fall 2013 **Infectious Disease Epidemiology Teaching Assistant**
Samer El-Kamary, MBChB, MS, MPH; DEPH, UMB
- Managed class website and materials; wrote and graded midterm and final exams; held office hours
- helped students prepare weekly summary presentations
- graded and provided written feedback on final papers

Fall 2012 **Principles of Biostatistics Teaching Assistant**
Clayton Brown, PhD; DEPH, UMB

Summer 2012 **Principles of Epidemiology Teaching Assistant**;
Nancy Ellish, DrPH, MSPH; DEPH, UMB
- Attended twice weekly workshops; held office hours; conducted midterm review session

COMPUTER EXPERIENCE

Windows 7, Windows Vista, Windows XP, Windows 97 operating systems
2003/2007/2010 Microsoft Office Suite (Word, PowerPoint, Excel, Access)
SAS versions 9.1, 9.2, 9.3
MYSTAT 12
R 3.1.0 (coursework)

AWARDS AND HONORS

2015	Inducted into Phi Kappa Phi
2013	Awarded $1000 Trainee Travel Grant from Infectious Diseases Society of America (IDWeek 2013, San Francisco, CA)
2013	Selected to participate in Society for Healthcare Epidemiology of America "Posters in the Park" at IDWeek 2013
2011	Elected to Delta Omega Public Health Society
2009-2011	University of Iowa Department of Epidemiology Scholarship
2009	Inducted into Phi Beta Kappa Honor Society
2005-2009	Distinguished Regents full scholarship from Washington State University
2005-2009	Honors College member

INSTITUTIONAL LEADERSHIP AND SERVICE

Oct. 2012-Current

Graduate Student Association Representative for Department of Epidemiology and Public Health (DEPH), University of Maryland, Baltimore

Committees:

- Finance Committee (2013-current)
  - Review and grading of student applications for GSA Travel Grants
- Sokolove Outstanding Mentor Award Selection Committee (2013)

Other Responsibilities and Tasks:

- Set-up and hosting of registration table and assorted tasks for 2013 New Student Orientation Week
- Morning set-up and hosting of registration table, set-up of poster boards, assorted tasks for 2013-2015 University of Maryland, Baltimore Graduate Research Conference
- Greeting, providing programs, and guiding seating for graduates' guests; 2014 University of Maryland, Baltimore hooding ceremony

2013-2015

Student Recruitment Host, DEPH, University of Maryland, Baltimore

- Hosted department applicants to general and molecular epidemiology tracks
- Provided campus tours, escorted applicants to interviews with faculty, attended meals and social events to answer applicant questions, escorted applicants to and from hotel

2013 & 2014

"Big Sister" Student Mentor, DEPH, University of Maryland, Baltimore

- Attendance at orientation week events; email and in-person availability to answer questions and help 1st year PhD student acclimate to the university

ABSTRACT

Title of Dissertation: The Effect of Contact Precautions on the Frequency of Hospital Adverse Events

Lindsay Croft, Doctor of Philosophy, 2015

Dissertation Directed by: Daniel J. Morgan, MD, MS; Associate Professor, Department of Epidemiology and Public Health

Background: Contact Precautions are an infection control approach where patients with antibiotic resistant bacteria are isolated and disposable gloves and gowns are donned prior to room entry. Some studies suggest Contact Precautions may increase the occurrence of hospital adverse events. However, few studies have examined the effect of Contact Precautions on adverse events using a standard definition and accounting for the effect of severity of illness. We assessed whether Contact Precautions exposure was associated with patient adverse events in both ICU and non-ICU settings.

Methods: The relationship between universal use of Contact Precautions (universal glove and gown use for all patient contact, regardless of colonization) and adverse events in the intensive care unit (ICU) was studied using medical record review of 1800 randomly sampled patients equally distributed over a 20 ICU cluster randomized trial. To reduce the influence of severity of illness, eligible patients could not be colonized or infected with antibiotic resistant bacteria. Within a non-ICU setting, a prospective cohort of 296 patients at the University of Maryland Medical Center (UMMC) matched on initial 3 day length of stay and admission location was used to study the association between usual use of Contact Precautions and adverse events.

Results: The study of 1800 randomly selected patients from a cluster randomized trial of universal glove and gown use found that the rates of adverse events among patients in

universal glove and gown ICUs were not statistically different (IRR, 0.91; 95% CI, 0.59-1.42; p=0.68). The UMMC prospective cohort observed significantly fewer noninfectious adverse events among patients exposed to traditional Contact Precautions compared to unexposed patients (IRR, 0.70; 95% CI, 0.51-0.95; p=0.02).

Conclusions: In ICUs where healthcare workers donned gloves and gowns for all patient contact, patients were no more likely to experience adverse events than in control ICUs. In non-ICU settings Contact Precautions were associated with fewer noninfectious adverse events. Concerns about adverse events resulting from either universal glove and gown use or traditional use of Contact Precautions were not supported.

The Effect of Contact Precautions on the Frequency of Hospital Adverse Events

By
Lindsay D. Croft

Dissertation submitted to the Faculty of the Graduate School
of the University of Maryland, Baltimore in partial fulfillment
of the requirements for the degree of
Doctor of Philosophy
2015

DEDICATION

This dissertation is dedicated to my family for their unending love and support throughout my schooling:

Donna Croft
Alan Croft
Randy Croft
Tricia Croft

ACKNOWLEDGEMENTS

First and foremost I would like to thank my dissertation chair, Dr. Daniel Morgan, for all of his guidance and advice in navigating both the dissertation process and research in hospital epidemiology. I very much value the mentoring and encouragement he continuously provided. Dr. Morgan challenged and stretched me in a way that I benefited and grew as a researcher but his support and encouragement always made the challenges seem like things that could be overcome.

I'm also grateful for the advice on epidemiologic methods and mentoring from another committee member, Dr. Anthony Harris, as well as the opportunities both he and Dr. Morgan have provided me. Dr. Harris has an enthusiasm for learning and constantly challenging himself and he is committed to not only increasing the skills and knowledge of students but in spreading that enthusiasm for learning to the students he teaches and mentors.

I would also like to thank the three other members of my committee for their advice and feedback: Dr. Patricia Langenberg, Dr. Jeffrey Fink, and Dr. Linda Simoni-Wastila. Their clinical, statistical, and general feedback was very much appreciated. The insights and perspectives they provided challenged me to think more deeply about and better understand the studies comprising the dissertation work.

As the BUGG study coordinator, Lisa Pineles was invaluable in ensuring data completeness and explaining the data structure and organization for the first aim of my dissertation.

Without the efforts of Dr. Michael Liquori and Dr. James Ladd, my second aim would not have been possible. I appreciate their reviewing what must have felt like a

never-ending list of medical records. Their cheerful willingness to explain important clinical aspects to me as a non-physician during data collection and analysis was indispensable.

I would also like to thank the Epidemiology and Public Health faculty outside of my committee who spent time and effort teaching me as well as helping me grow as a scientist. The support of friends and classmates in the department was also crucial.

Finally, I'd like to thank my family for their years of love, support, and much needed humor.

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List of Abbreviations

ADE: adverse drug event

AHRQ: Agency for Healthcare Research and Quality (AHRQ)

APACHE II: Acute Physiology and Chronic Health Evaluation, version 2

BUGG: Benefits of Universal Glove and Gown

CCU: coronary care unit

CDC: Centers for Disease Control and Prevention

CDR: Central Data Repository

CI: confidence interval

CMI: case mix index

CMS: Centers for Medicare and Medicaid

DRGs: Diagnosis Related Groups

EDCs: expanded diagnosis clusters

HAIs: hospital-acquired infections

HCW: healthcare worker

HMPS: Harvard Medical Practice Study

ICC: intraclass correlation coefficient

ICD-9: International Classification of Diseases, 9^{th} Revision

ICUs: intensive care units

IHI: Institute for Healthcare Improvement

IRB: Institutional Review Board

IRR: incidence rate ratio

IOM: Institute of Medicine

List of Abbreviations (continued)

λ: rate

MERP: Medication Error Reporting and Prevention

MICU: medical intensive care unit

MICU-SICUs: combined medical-surgical intensive care unit

MRSA: methicillin-resistant Staphylococcus aureus

OR: odds ratio

SD: standard deviation

SICU: surgical intensive care unit

R_tR: rate ratio

UGG: universal glove and gown use

UMMC: University of Maryland Medical Center

US: United States

VAP: ventilator-associated pneumonia

VRE: vancomycin-resistant enterococci

I. BACKGROUND AND OBJECTIVES

A. Specific Aim 1

Determine if adverse events (also known as adverse safety events) are more common in patients in intensive care units (ICUs) randomized to universal glove and gown compared to control patients. Additionally, determine which subtypes of adverse events are more common.

1. Specific Aim 1.1

Determine if overall frequency of adverse events is associated with universal glove and gown use.

Hypothesis 1.1: Patients in ICUs randomized to use universal glove and gown have a higher rate of adverse events than patients in the control group ICUs.

2. Specific Aim 1.2

Determine if frequency of preventable adverse events is associated with universal glove and gown use.

Hypothesis 1.2: Preventable adverse events are more common for patients in ICUs randomized to universal glove and gown compared to control patients.

3. **Specific Aim 1.3**

   Determine if frequency of infectious adverse events (acquisition of healthcare-associated infections) is associated with universal glove and gown use.

   Hypothesis 1.3: Infectious adverse events are less common for patients in ICUs randomized to universal glove and gown compared to control patients.

4. **Specific Aim 1.4**

   Determine if frequency of severe adverse events is associated with universal glove and gown use.

   Hypothesis 1.4: Severe adverse events are more common for patients in ICUs randomized to universal glove and gown compared to control patients.

5. **Specific Aim 1.5**

   Describe which types of adverse events are most common in universal glove and gown use compared to control patients (cardiovascular, respiratory, renal or endocrine, hematologic, gastrointestinal, neurologic, hospital-acquired infection, and surgical events).

   Hypothesis 1.5: Certain types of adverse events (cardiovascular, respiratory, renal or endocrine, hematologic, gastrointestinal, neurologic, and surgical events) are more common in universal glove and gown use compared to controls. Adverse events that are hospital-acquired infections are less common in universal glove and gown use compared to controls.

B. Specific Aim 2

Determine if adverse events in general ward patients on Contact Precautions are more common than in patients not on Contact Precautions. Additionally, determine which subtypes of adverse events are more common.

1. Specific Aim 2.1

Determine if overall frequency of adverse events in general ward patients is associated with Contact Precautions use.

Hypothesis 2.1: General ward patients on Contact Precautions have more adverse events compared to ward patients who are not on Contact Precautions.

2. Specific Aim 2.2

Determine if frequency of preventable adverse events in general ward patients is associated with the use of Contact Precautions.

Hypothesis 2.2: Preventable adverse events are more common for patients on Contact Precautions compared to patients not on Contact Precautions.

3. Specific Aim 2.3

Determine if frequency of infectious adverse events (acquisition of healthcare-associated infections) is associated with use of Contact Precautions.

Hypothesis 2.3: Infectious adverse events are more common for patients on Contact Precautions compared to patients not on Contact Precautions.

4. **Specific Aim 2.4**

   Determine if frequency of severe adverse events is associated with the use of Contact Precautions.

   Hypothesis 2.4: Severe adverse events are more common for patients on Contact Precautions compared to patients not on Contact Precautions.

5. **Specific Aim 2.5**

   Describe which types of adverse events are most common among general ward patients (cardiovascular, respiratory, renal or endocrine, hematologic, gastrointestinal, neurologic, hospital-acquired infection, and surgical events).

   Hypothesis 2.5: Certain types of adverse events (cardiovascular, respiratory, renal or endocrine, hematologic, gastrointestinal, neurologic, hospital-acquired infection, and surgical events) are more common in patients on Contact Precautions compared to patients not on Contact Precautions.

C. Background and Rationale

1. Adverse Event Definitions

Many definitions for adverse events and subtypes of adverse events exist in the literature. However, the following definitions will be used in discussion of the studies (Glossary). An adverse event (or the alternative phrase adverse safety event) is an unintended physical injury resulting from or contributed to by medical or surgical care and not due to a patient's underlying condition.[1] These events are all-encompassing types of harm (i.e. they do not exclude special subtypes of events such as adverse drug events). Preventable adverse events are adverse events that are considered as probably or

definitely preventable by current practice standards, technology, and knowledge. Severe adverse events are adverse events which result in death, life-threatening, or serious harm to the patient. An example of a serious adverse event is one that results in organ dysfunction and life-threatening adverse events are those in which death is possible within a few hours without treatment.

Another subtype of adverse event is the infectious adverse event (or hospital-acquired infection), which is an infection that occurs in the hospital setting but was not present or incubating on admission. Adverse drug events are also a special type of adverse event and result from medical intervention with a drug. These events may include giving an incorrect medication, the correct medication at too high or low of a dose, and medication-induced "side effects" (e.g. a patient with a bleeding event following treatment with warfarin). Preventable adverse drug events are a subtype of adverse drug event that are considered probably or definitely preventable by current practice. Certain subtypes of adverse event are not mutually exclusive from other subtypes. For example, an infectious adverse event may be preventable, severe, both preventable and severe, or neither.

2. Overview of Burden and Cost of Adverse Events

In the healthcare setting, the term "adverse events" or, alternatively, "adverse safety events" refers to unintended physical injury resulting from or contributed to by medical care and not a patient's underlying disease.[1-4] The landmark study which investigated the frequency of hospital adverse events was the Harvard Medical Practice Study (HMPS).[5] Using a conservative estimate, this study estimated that among

hospitalized patients in New York, 3.7% would experience an adverse event each year. Of these, 13.6% experiencing an adverse event died and a further 2.6% would receive permanently disabling injuries. These findings were used by the Institute of Medicine (IOM) to estimate that approximately 98,000 Americans die each year from medical errors, leading the IOM report to extrapolate that this would rank as the eighth leading cause of death in the United States, killing more people than breast cancer, car crashes, or AIDS.[6] While the figures have been controversial so far as under- or overestimating the exact frequency of adverse events,[7-9] the report drew attention to adverse events in medical care and stimulated further research.

A Canadian study of hospital adverse events identified an incidence of 2.6 events per 100 patient days.[10] Among these, 9.1% of harms resulted in death or permanent disability and one-third were preventable. A systematic review examining studies of hospital adverse event incidence among hospitals in the United States, United Kingdom, Canada, Australia, and New Zealand found a median incidence of 9.2% in patients, although in the two US studies with reported details, there was a lower incidence (between 3-4%).[11] Of all studies included in the systematic review, approximately 7% of the adverse events resulted in death (another 7% received a permanent disability) and the majority of adverse events were operation- (39.6%) or drug-related (15.1%). Among the adverse events, 41% occurred in the operating room and only 3.1% occurred in the intensive care unit, in contrast to other studies.

The incidence of adverse events increases with age with geriatric patients experiencing adverse events from 5.3% to 60% of patients.[12] This range occurs based on whether extremely conservative definitions of "adverse" event are used and increases

when traditional medication-related adverse events such as falls or delirium are included.[12] A study of hospitalized Medicare patients found that 13.5% experienced an adverse event ranging in severity from prolonged hospital stay to death and another 13.5% experienced a temporary adverse event.[13] The study also estimated that 15,000 Medicare patients per month will experience an adverse event that contributes to their death. These estimates suggest adverse events are more common among older hospitalized patients.

The authors of a recent paper estimating the social costs of medical adverse events estimated there are 2.4 million injuries resulting from hospital care and somewhere between 39,000 and more than 108,000 preventable hospital deaths each year in the United States.[14] The study's estimates are based on a wide range of estimates in the literature. The cost of preventable inpatient injuries in 2006-adjusted dollars has been estimated at $6.7 billion and the total social cost of hospital adverse events resulting in injury or death between $348 and $913 billion. Similarly, estimates suggest Medicare spends approximately $4.4 billion each year on costs related to caring for the consequences of adverse events.[13] **There is clearly a high cost from adverse events directly to patients and economically to society.**

3. Risk Factors for Adverse Events

Increasing age has been associated with the occurrence of hospital adverse events. This has been seen with bivariate relationships, as in the Harvard Medical Practice Survey, where the mean number of adverse events were 1.5 times more common among middle age patients (45-64 years) compared to young adults (16-44 years).[5] The mean

number of adverse events doubled among patients 65 years and older compared to young adults. This relationship has been observed in subsequent studies, for both hospital and primary care settings, where elderly patients have more than five times as many adverse events as younger patients.[12,15-17] Age has been associated with subtypes of hospital adverse events, the adverse drug event (ADE) and preventable ADEs.[18,19] Aside from increased risk of adverse events, once an ADE occurs, increased age is also associated with risk of mortality and prolonged length of stay.[20]

In contrast to age, sex does not appear to be a risk factor for adverse events in most studies.[21,22] However, women may have 1.8 times higher odds of an adverse drug event than men.[19] The number, type, and severity of patient comorbidities also influence the risk of adverse events. A Danish study of changes in adverse event rate over time reported that certain ICD-9 diagnosis groups have almost 1.5 to 2.5 times increased odds of experiencing an adverse event compared to the baseline of patients with circulatory system diagnoses.[21] Examples of these diagnosis groups include neoplasm, respiratory, digestive, and genitourinary systems, and injury or poisoning. Among English primary care patients, having the most comorbidities significantly increases the risk of adverse events 8.5 times.[15] The extent of comorbidity was measured by categorizing the number of Expanded Diagnosis Clusters (EDCs) represented by a patient's conditions into "low," "moderate," and "high" although the study authors did not specify the number of EDCs used to define each category. The odds of an adverse drug reaction increase approximately 30% for each new comorbid condition and the odds of a preventable adverse drug event increase between 70 and 90 percent for each additional patient comorbid condition.[19] However, each of these studies with comorbidities and adverse

events are likely confounded by indication, making the true magnitude of risk due to comorbidities difficult to estimate.

With respect to severity of illness, in bivariable analysis, patients who experience an adverse event have a 3.6 point higher mean Acute Physiology and Chronic Health Evaluation (APACHE) II score than patients with no adverse event.[16] The APACHE II is an ICU measure of patient severity of illness upon hospital admission with a score calculated from several lab and vital sign measures. In addition, patients in the same study were significantly more likely to die and to be ventilated. However, the meaning of this association remains unclear. It is unknown the extent to which adverse events cause patients to become more ill as opposed to sicker patients having a higher risk of adverse events. Similarly, in a study of medical ICU patients, a measure of acute illness, the Acute Physiology Score, was significantly higher among patients with complications (by mean 5.8 units) than among patients that did not experience a complication.[17]

Among patients in two French medical ICUs, admission with organ failure of at least 2 systems had almost five times higher odds of non-ADE adverse events than patients admitted without such severe illness.[4] Also, in a three tertiary-care hospital study, case mix index (average hospital patient acuity) was significantly higher among patients who experienced an adverse event compared to patients who did not (1.78 versus 1.18; $p<0.0001$).[22] However, the authors reported this only in bivariable analysis and it is unclear how much the difference in case mix index is reflective of resources used to treat patients once the adverse event occurs, rather than a difference in patient severity of illness on admission.[22]

In addition to being an indication of patients who are more ill, length of stay is often adjusted for as an independent risk factor for adverse events. The odds for both adverse drug reactions and for preventable adverse drug events increase by more than 10% with each additional hospital day.[19] In another study, in bivariable analysis, patients experiencing an adverse event had, on average, a five day longer length of stay than patients that did not experience an adverse event.[16] However, it is unclear to what extent length of stay is a marker of sicker patients, a risk factor for adverse events, and the consequence of an adverse event occurring. In addition, length of stay can be a marker of practice setting (i.e. academic versus community hospital) and type of admission severity (ICU versus non-ICU).

In one of the few multivariable analyses of adverse events, Landrigan and colleagues adjusted for age, sex, race, insurance group, admission to surgical unit, obstetrical or gynecological service, and high risk of harm (based on ICD-9 code groupings within the study period).[23] However, estimates of the magnitude and direction of effect for each of these variables were not reported. Thus, it remains unclear the extent to which each of those factors is related to adverse event rate.

4. Standardized Trigger Tool Method to Detect Adverse Events

The Institute for Healthcare Improvement (IHI) Global Trigger Tool is designed as a method for adverse event detection through a structured patient chart review.[1] The trigger tool is designed for reviewing patient charts in a 20-minute timeframe and has a recommended order for chart review, beginning with discharge codes and summary, administered medications, and laboratory results, followed by other sections (operative

records, nursing and progress notes, etc.) if there is time remaining.[1] The tool consists of several "triggers" that cover aspects of cares (e.g. patient falls or pressure ulcers), medications, surgery, or ICU factors that are often associated with adverse event occurrence (Appendix A). The triggers included on the tool were identified using a combination of subject matter experts, literature reviews, and triggers identified from prior versions of trigger tools designed for specific types of adverse events.[1,24,25] These triggers were field-tested in hospitals and triggers with issues such as low positive predictive value were removed. The triggers themselves do not necessarily represent adverse events but serve as a signal that an adverse event may have occurred. When triggers are identified, chart reviewers then examine that part of the patient record more closely for evidence of a related adverse event.

The established method for use of the IHI Global Trigger Tool is the use of two reviewers that independently review the same patient records and provide the discharge summary for a third reviewer. The third reviewer is a physician who reviews the medical record discharge summary and makes a final determination regarding adverse event occurrence. This third reviewer is also responsible for deciding whether an adverse event occurred in the case of disagreement between initial reviewers.

5. Trigger Tool-Derived Estimates of Adverse Event Frequency

Estimates of adverse event frequency are generally higher when the IHI Global Trigger tool is used to identify adverse events compared to traditional chart review. The previous discussion of adverse event frequency used estimates primarily derived from chart reviews[5,11] although Forster and colleagues used a combination of direct

observation, chart review, and voluntary reporting[10] and the study of Medicare patients[13] used Present on Admission indicators, a modified Global Trigger Tool, 30-day readmission, and physician review to identify adverse events.

Among general hospitalized patients, estimates for the frequency of adverse events range between 18.1 and 50.8 adverse events per 100 admissions when the Global Trigger Tool is used.[22,23,26] Similarly, estimates of adverse event rates among general ward patients are between 68.1 and 91.0 events per 1000 patient-days[22,26] and the estimated rate rises to 113.0 adverse events per 1000 patient-days for ICU patients when measured using the IHI Global Trigger Tool.[27] Approximately 27% to 39.8% of patient charts reviewed in these studies contain at least one adverse event.[22,26,28,29] These trigger tool-derived estimates are higher than previously discussed estimates derived from other approaches. However, the definitions used to identify an adverse event are the same, or more stringent, than non-trigger tool methodologies, so are unlikely to be conflated estimates.

When methods of detecting ADEs are compared, 65% of ADEs are detected when chart reviews are performed, as compared to 45% with computer monitoring and 4% from stimulated voluntary report.[30] The number of adverse events identified by a method was compared to the total number of adverse events detected by any of the three methods. In only 12.3% of cases are ADEs detected from chart review also detected by computer monitoring. This suggests that the IHI Global Trigger Tool, a form of patient chart review, may detect more adverse events than other methods.

In a study comparing the performance of provider-reported events, patient safety indicators from the Agency for Healthcare Research and Quality (AHRQ), and the IHI

Global Trigger Tool at detecting adverse events, 95.6% of the events were detected using the Global Trigger Tool.[31] In contrast, only three of the 68 adverse events were identified by one of the other two methods but not the Global Trigger Tool. Sharek and colleagues report that the sensitivity and specificity of the IHI Global Trigger Tool are 49% and 94% for reviewers internal to an institution and 34% and 93% among external reviewers.[32] However, this report used "experienced reviewers" with the IHI Global Trigger Tool as the gold standard rather than a different detection method to calculate sensitivity and specificity.

Classen et al. conducted a larger, better-designed study for comparing adverse event detection with the IHI Global Trigger Tool to the AHRQ patient safety indicators and hospital incident reporting.[22] Using the "pooled" approach where an adverse event detected by any of the three methods was used as the comparison method, the IHI Global Trigger Tool was found to have sensitivity and specificity of 94.9% and 100%, respectively. In contrast, the next best method—AHRQ patient safety indicators—had a sensitivity of 5.8% and specificity of 98.5% while the hospital incident reporting system had a sensitivity and specificity of 0% and 100%.

The IHI Global Trigger Tool does not detect every adverse event that occurs among hospitalized patients. However, the trigger tool performs relatively well compared to older chart review practices and detects far more adverse events than other methodologies. The trigger tool also provides more standardized training and less subjective approach for determining adverse event occurrence compared to traditional chart review. **Currently, the IHI Global Trigger Tool is the strongest option for data**

on frequency of adverse events; the tool detects more adverse events than other methods and is less subjective than traditional chart review.

6. Frequency of Adverse Events: ICU versus General Ward Patients

As with adverse event studies among non-ICU hospital patients, comparing results between studies in ICU populations is made difficult by the wide variation in study outcomes, ranging from "complications" which include but are not limited to adverse events, to adverse events only, or both potential adverse events and events which actually occurred. However, the limited numbers of studies investigating adverse event frequency among ICU patients suggests that not only is adverse event frequency higher in ICU patients but that the types of adverse events may differ. In addition, ICU patients with complications are 2.5 times more likely to die than their ICU counterparts without complications and have 21% excess mortality.[17] This excess mortality related to complications among ICU patients is at least double the mortality discussed previously among non-ICU patients or mixed study populations.[10,11]

Over a ten-month study period, 14% of medical intensive care unit patients had at least one complication[17] which is a higher frequency than reported among studies of general ward patients. Another estimate, which excluded adverse drug events from the outcome, estimated that 41% of ICU patients experienced an adverse event and almost 80% of the major adverse event types were severe hypotension, respiratory distress, pneumothorax, or cardiac arrest.[4]

Among patients in either a medical intensive care unit (MICU) or coronary care unit (CCU), adverse events occurred in 20.2% of patients (45% of which were

preventable).[33] Of these adverse events, 19% were respiratory adverse events, 15% infectious, 12% cardiovascular, and 9% skin or soft tissue-related. Rothschild et al. argue that the higher rates of adverse events among ICU patients may be due to a variety of factors uniquely found in the ICU.[33] Among such factors, Rothschild and colleagues discuss the pace, physician training, case complexity, and high-risk decisions often made in situations with limited information.

The type of unit a patient is admitted to influences adverse event occurrence; patients admitted to a surgical unit have 2.6 times greater odds of experiencing an adverse event and more than three times the odds of experiencing a preventable adverse event compared to patients admitted to non-surgical units.[21] Adverse drug event rates also appear to be far higher in medical ICUs (19.4 ADEs per 1000 patient-days) compared to medical general care units (10.6 ADEs per 1000 patient-days; $p<0.05$) and non-significantly higher among surgical ICU patients than surgical general care units (10.5 ADEs per 1000 patient-days versus 8.9, respectively).[10] When adjusted for the number of drugs ordered in a day for each unit, medical ICUs still have a higher rate of ADEs (15.3 ADEs per 1000 patient-days) than either type of general care unit (approximately 13 per 1000 patient-days for both). Interestingly, when adjusted for the number of drugs ordered in a day for each unit, the rate for surgical ICUs (SICUs) decreases to below 9 ADEs per 1000 patient-days, very different from the rates observed in both types of general care units. Similarly, the rate of preventable ADEs and potential ADEs combined is almost two times higher among MICUs and SICUs, compared to medical and surgical general care units until adjusted for the number of drugs used since admission.[34] Once adjusted for medication use, the unit types no longer significantly differ. However, severity of the

preventable ADEs and potential ADEs is statistically greater among ICUs than general care units.

So far, Forster and colleagues are the only investigators to compare adverse event rates between ICU and general medicine units, as opposed to ADEs alone.[10] The authors compared adverse event rates in a cardiac surgical ICU, non-cardiac ICU, a general medicine unit, and an obstetrics unit and found a statistically significant difference in rate between the units. Both the cardiac and non-cardiac ICUs experienced rates of approximately 5.0 adverse events per 100 patient days while the general internal medicine and obstetrics rates (1.8 and 1.5 events per 100 patient-days) were lower. The types and frequencies of adverse events observed also differed by unit type. In the cardiac ICU, surgical complications (47%), hospital-acquired infections (19%), and procedural complications (11%) occurred most often while hospital-acquired infections (25%), procedural complications (24%), and therapeutic errors (19%) were the adverse events observed most often among non-cardiac ICU patients. In the general care unit, ADEs (30%), therapeutic errors (24%), and procedural complications (12%) occurred most frequently. Further, death or permanent disability as a result of an adverse event was more common in either ICU (between 3-5%) than among general medicine patients (0.4%).[10]

In light of the different rates of adverse events, as well as types of events experienced by patients in ICUs compared to general ward settings, it is inappropriate to assume that risk factors identified among the non-ICU hospital patient population are generalizable to the very different ICU patient population. **Studies investigating the**

association between Contact Precautions and adverse events should consider these populations separately.

7. Contact Precautions and Adverse Events

Contact Precautions are a transmission-based infection control method recommended by the Centers for Disease Control and Prevention.[35] The approach requires patients known to be colonized or infected with antibiotic resistant organisms to be placed in a single room or cohorted with other patients that have the same organism. Additionally, prior to room entry, healthcare workers must don gowns and gloves and remove them before room exit. These precautions are primarily intended to prevent transmission of resistant organisms to other patients via the hands and clothing of healthcare workers, rather than to protect the patient on Contact Precautions themselves. Contact Precautions may also be referred to as source isolation, barrier precautions, barrier nursing, or contact isolation. Contact Precautions may be used in additional situations but these uses were not the exposure focus for our studies.

In a review, Gammon emphasized the potential unintended psychological consequences of Contact Precautions in the late 1990s, highlighting that a mere five studies had investigated the psychological effects and most were descriptive in nature.[36] Among the potential effects a patient might experience, Gammon mentioned loss of control, distress, depression, anxiety, decreased social interaction, stigmatization, and behavioral changes in response to these effects. Since then, studies such as a cross-sectional study in a rehabilitation unit have suggested significantly higher depression and anxiety but not anger exist among patients on Contact Precautions compared to non-

Contact Precautions patients.[37] A matched cohort compared patients on Contact Precautions to non-Contact Precautions and reported significantly higher anxiety and depression scores among patients on Contact Precautions.[38] However both studies included small numbers of patients and did not attempt to adjust for confounding variables. A more recent matched cohort reported increased odds of depression among patients on Contact Precautions but found no association with anxiety and measured prevalent rather than incident depression.[39] A larger recent study has reported that while patients on Contact Precautions are admitted with higher mean depression and anxiety scores, patients did not develop more depression, anxiety, or negative moods such as anger, sadness, worry, or confusion after exposure to Contact Precautions compared to unexposed patients.[40]

One narrative-based, qualitative study of 26 healthcare workers reported that nurses felt that connections with patients and physical contact with them decreased when patients were on Contact Precautions.[41] In addition, nurses reported waiting to see a patient on Contact Precautions last and concern for patient injury due to delays in having to don gowns and gloves first.

More recently, attention has broadened in scope to include potential physical harms as unintended consequences of Contact Precautions use. However, a limited number of studies have investigated the possible association between Contact Precautions and physical adverse events to date. A key study by Stelfox et al. included both general admission patients and patients with an admitting diagnosis of congestive heart failure.[42] This study captured attention both for being one of the first studies to quantitatively assess the question of Contact Precautions and adverse events and for the extremely large

effect sizes it reported. The study found that patients on Contact Precautions had a 2.2-fold higher rate of adverse events compared to patients not on Contact Precautions and a striking, almost 7 times higher rate of preventable adverse events among patients on Contact Precautions. These results provided evidence that physical harms may be another unintended consequence of Contact Precautions use and that many of them were preventable. However, the study had several limitations. Among the limitations was an atypical definition of "adverse event" and a large fraction of the observed adverse events were actually due to events such as pressure ulcers or electrolyte imbalances. The mechanism by which Contact Precautions would result in electrolyte imbalances is unclear. Pressure ulcers may be more common because of less nursing contact and less attention to pressure ulcer prevention. Furthermore, the study had limited characterization of consequences for patients experiencing adverse events and confounding by indication for Contact Precautions. This is an issue since patients colonized or infected with antibiotic resistant organisms are more likely to experience adverse events associated with chronic illness and are also assigned to Contact Precautions. The failure to address this confounding by indication in the Stelfox study is a major concern.

In a more recent ICU-based study within a larger cluster randomized trial on patient safety, unadjusted rate ratios indicated that hypoglycemia, hyperglycemia, thromboembolic events, hemorrhage, and drug resistant ventilator-associated pneumonia (VAP) were adverse events occurring at a higher rate among patients on Contact Precautions.[43] Hazard ratios adjusted for age, transfer, patient type, chronic disease, immune suppression, patient acuity, diabetes symptoms on admission, and ICU staffing at admission indicated 1.5-fold increased rates of hypoglycemia and hyperglycemia

among patients on Contact Precautions. The analysis accounted for the idea that patients discharged alive have more time at risk of additional adverse events than patients who die while admitted. This would not completely address the confounding by indication issue discussed for the Stelfox et al. paper but improves the quality of inferences that may be drawn. However, the study was based on a select number of adverse events, which may not accurately represent the associations for all adverse events and used a non-standard definition of "adverse event." Additionally, the data were collected from a larger study designed to improve patient safety and thus has limited generalizability to all hospital adverse events.

Karki et al. employed a case-crossover design comparing patients on Contact Precautions for vancomycin-resistant enterococci (VRE) to themselves in an earlier period of the same hospitalization where they were not exposed to Contact Precautions.[44] While the study found the overall rate of adverse events was not significantly different for periods exposed to Contact Precautions versus not exposed (rate ratio = 1.04, p=0.70), it did find that falls and self-injury (rate ratio = 3.24) and medication administration errors (rate ratio = 1.55) were more common during Contact Precautions exposure periods. This partially conflicts with the results of Stelfox et al.[42] but there were many statistical tests employed (unadjusted for multiple tests) which were often based on small numbers.

Other studies have not found any significant association between Contact Precautions and adverse events. A matched case-control (matched on admission diagnosis of either heart failure or chronic obstructive pulmonary disease) compared methicillin-resistant Staphylococcus aureus (MRSA) carriers to non-carriers on adverse

event frequency.[45] The authors found no difference in the median number of complications and there was no statistically significant difference in unadjusted rate of complications per 1000 patient days, although the rate was actually lower among patients on Contact Precautions (52.2 complications per 1000 patient days vs. 64.8; p = 0.40). The safety analysis for a cluster randomized trial on universal glove and gowning (Benefits of Universal Glove and Gown, BUGG) also found no difference in mean rate of overall adverse events when the mean rate of adverse events per 1000 patient days at-risk for 10 intervention ICUs were compared to 10 control ICUs.[46] The study also found no statistical difference in adverse event rate when preventability and severity of events were considered, despite using an accepted definition for adverse events. However, these results were for a safety analysis of the trial and thus did not consider several factors: First, the study tested a group effect of universal glove and gown and adverse events rather than conducting an individual level analysis (which would also permit control of patient level factors such as acuity and age). Additionally, the safety analysis considered all adverse events together, without removing hospital-acquired infections (HAIs). This matters as, if universal glove and gowning is effective at preventing transmission of resistant organisms, the adverse event rate for HAIs would be expected to decrease among patients in intervention ICUs. However, if universal glove and gown use also increased the non-infectious adverse event rate compared to control ICUs, the opposing trends could mask any effect on adverse events and result in the observed findings.

Finally, a quasi-experimental study examining the effect of discontinuing Contact Precautions for MRSA and VRE reported higher rates of falls and pressure ulcers among patients colonized with MRSA or VRE.[47] As the rates of adverse events and the rates of

MRSA or VRE colonized patients did not change between the periods before and after the discontinuation of Contact Precautions, the authors argued that something other than Contact Precautions is responsible for adverse events among patients indicated for Contact Precautions.

There are limited numbers of studies and they have conflicting results,[42-46] partly due to methodological issues[42,44] and atypical definitions of adverse event.[42-45] The studies in this dissertation examined the association between Contact Precautions and adverse event rates and address a meaningful lack of consensus in the current patient safety literature. Furthermore, only one study has examined non-ICU patients without intermixing ICU patients.[45] **Given established knowledge that adverse event rates, types, and confounding variables may differ between ICU and non-ICU settings,[4,10,11,17,21,33] it was important to address these questions in both populations.**

8. Contact Precautions and Healthcare Workers: Suspected Mechanism for Increased Adverse Events

In one of the first studies to examine the effects of Contact Precautions on healthcare worker behavior, Kirkland and Weinstein reported that MICU healthcare workers entered the rooms of patients on Contact Precautions half as often (3.9 versus 7.9 times per hour) and also touched these patients only half as often (2.1 versus 4.2 times per hour) as patients not on Contact Precautions.[48] The average length of each interaction was non-significantly increased among Contact Precautions patients (4.5 minutes) compared to non-isolated patients (2.8 minutes). This increased contact time in spite of

fewer healthcare visits has been described as "bunching"[49] where the decreased frequency of visits leads to more tasks to complete per visit, increasing contact time.

Similarly, Saint and colleagues found that patients on Contact Precautions were half as likely to be examined by attending physicians as non-Contact Precautions patients (35% of the time versus 73%, respectively).[50] Among surgical unit patients (ICU and non-ICU), patients on Contact Precautions received 5.3 visits per hour from healthcare workers compared to 10.9 visits per hour for non-Contact Precautions patients.[51] Healthcare workers also spent less time with these patients each hour, even though patients on Contact Precautions had significantly greater severity of illness. A patient chart review for a matched case-control study where patients were matched on heart failure or chronic obstructive pulmonary disease led to similar conclusions.[45] Patients on Contact Precautions received 850 visits per 1000 patient-days from healthcare workers while non-isolated patients received over 980 visits per 1000 patient-days.

In a four-site cohort study, Morgan et al. also reported that patients on Contact Precautions received 36.4% fewer healthcare worker visits and almost 18% less contact time with healthcare workers each hour.[49] Finally, the cluster randomized trial of universal glove and gown use, BUGG, observed a significant decrease of one room entry by healthcare workers each hour among ICUs randomized to universal gown and glove use, compared to control ICUs.[46]

It has been suggested that this decreased frequency of healthcare worker contact is the mechanism through which Contact Precautions usage may lead to an increased rate of adverse events.[48,49,51] Stelfox et al. observed a significant reduction in quality of care and process measures among patients on Contact Precautions within the same study that

established a 2.4 times increase in adverse event rate compared to non-isolated patients.[42] While not irrefutable evidence of causality, the authors argued that the study strongly associated measures of healthcare worker behaviors and higher adverse event rate among patients on Contact Precautions and discussed the findings in mechanistic terms.

9. Rationale

Adverse events occur frequently among hospitalized patients in the United States and can have severe ramifications for patients, up to and including permanent disability and death.[5,6,10-12] Even temporary harms may prolong hospitalization and thus increase patient risk for additional adverse events.[19] In addition to physical and emotional costs to patients, adverse events have high economic costs each year.[13,14] Healthcare workers are known to visit patients on Contact Precautions less frequently than patients not on Contact Precautions,[45,46,48-51] which may be the route through which adverse events could occur more frequently among patients on Contact Precautions. To date, limited numbers of studies have investigated the potential association between Contact Precautions and adverse events.[42-46] Notably, the cohort study by Stelfox and colleagues found a doubling in rate of adverse events and a 7-fold increase in rate of preventable adverse events among patients on Contact Precautions compared to non-Contact Precautions patients.[42] However, the few other studies examining the issue have either found no association[45,46] or an increased rate of adverse events among different categories of adverse event from Stelfox et al.[43,44] The body of current literature on Contact Precautions and adverse events is inconclusive and some of the studies have uncontrolled confounding by indication[42]

while others use non-standard definitions of adverse event[42-45] which makes interpretation and comparison of results difficult.

The aims of the current study addressed an important, unresolved question regarding Contact Precautions and adverse events. Additionally, the first aim provided improvements in methodology such as randomization and exclusion of known colonized or infected patients. These measures helped reduce concerns of uncontrolled confounding that affected some of the previous studies. Also, both aims used a standard definition for adverse event which aids in interpretation of results and comparison with current and future adverse event literature. Both aims represent the largest studies to date of the research question. Furthermore, data collection on adverse event occurrence used the IHI Global Trigger Tool in both aims. The IHI Global Trigger Tool was a strong choice for adverse event detection as it detects more adverse events than other methods,[22,30-32] is less subjective than traditional chart review or voluntary reporting mechanisms, and uses a commonly accepted definition of adverse event. Finally, the ICU and general ward are very different environments with different rates of adverse event, types of potential adverse event, and different confounding variables. In light of these differences, it would have been inappropriate to assume that associations between Contact Precautions and adverse event rate in the ICU were generalizable to general ward patients and vice versa. Yet, little attention had previously been given to the relationship between Contact Precautions and adverse events within non-ICU settings specifically. The current two study aims separately examined the association between Contact Precautions and adverse events among these two unique patient settings.

II. STUDY METHODS

A. Aim 1

1. Study Overview

Aim 1 was a secondary analysis of a cluster-randomized trial that involved twenty study ICUs across the United States (Benefits of Universal Glove and Gown, BUGG). The study included 90 randomly selected patients from each ICU (1800 patients total) that were reviewed during the study for the occurrence of adverse events. These patients were sampled from study ICUs among patients not colonized with antibiotic resistant bacteria. This selection criterion was included in order to minimize confounding by indication. More severely ill patients (such as those colonized with antibiotic resistant bacteria) are more likely to experience adverse events[52,53] and patients with antibiotic resistant bacteria are exposed to glove and gown use, which can result in a non-causal association between glove and gown use and adverse events. Excluding colonized or infected patients from the study helped address this concern of confounding by indication. The analysis was conducted at the patient level although the analysis accounted for clustering by study site.

2. Outcomes

The main outcome for both Aim 1 and Aim 2 was the rate of patient adverse events, where adverse events were defined according to the IHI trigger tool definition: "unintended physical injury resulting from or contributed to by medical care"[1] and the injury was not a result of the patient's underlying condition. Adverse events were identified using the IHI Global Trigger Tool (detailed below) which involved a structured

review of patient charts followed by a physician review of the initial chart review. For Aim 1, the rate of adverse events was expressed as the number of adverse events experienced in the ICU divided by total person-time at-risk (ICU length of stay in days). As patients were at-risk of an adverse event during all time spent in an ICU, if a patient was readmitted to an ICU during the same hospital stay as the index ICU admission, the ICU length of stay during the readmission was included in the total denominator time at-risk.

IHI Global Trigger Tool

In the first aim, the IHI Global Trigger Tool was modified so that at each study site, a trained reviewer conducted the initial review and submitted the de-identified discharge summaries to the BUGG study coordinator at the University of Maryland. After records were received, two physician reviewers independently reviewed the discharge summaries to determine agreement with the findings of the initial reviewer. Discharge summaries were augmented with relevant medication or laboratory values when the initial reviewer identified an adverse event outside of the discharge summary. The physician reviewers were blinded to identity of the site (and thus universal gown and glove use). The two physician reviewers then met to discuss and came to consensus on any disagreements for adverse event occurrence. This modification was made to follow IRB requirements that no identifiable patient information was received by the University of Maryland.

In addition to the occurrence of an adverse event, the Global Trigger Tool categorizes severity of each adverse event using categories previously established by the

National Coordinating Council for Medication Error Reporting and Prevention (MERP).[1,54] The five categories of the MERP index relating to harm and used by the trigger tool range from "temporary harm to the patient and required intervention" (Category E on the MERP index) to "patient death" (Category I). Both study aims separated the measures of severity and consequence to the patient as has been done previously.[18,33,55,56] Severity was measured by a five-point Likert scale (minimal, clinically significant, serious, life threatening, death). Examples of the meanings of these categories are detailed in Appendix A. The measure of consequence to the patient was also a five-point Likert scale and included: limited, prolonged, temporary disability, permanent disability, death. Limited consequence is an indication that additional hospitalization time was less than one day, in contrast to "prolonged" which represented more than one day prolonged hospitalization or persistence of symptoms. The three additional adverse event classification schemes are displayed in the table below.

Table 1. Adverse Event Classification Schemes

1. Severity
Minimal
Clinically significant
Serious
Life-threatening
Death
2. Consequence for Patient
Limited
Prolonged
Temporary
Permanent
Death
3. Preventability
Definitely preventable
Probably preventable
Probably not preventable
Definitely not preventable

The study also added a four-point Likert scale to the data collection tool, as has been used previously to assess preventability.[18,23,33] This scale ranking is shown in the above table and included the categories definitely, probably, probably not, and definitely not preventable.

Secondary Outcomes

As stated previously, the main outcome for both dissertation aims was the rate of adverse events (an unintended physical injury resulting from or contributed to by medical care but not a result of underlying illness). The occurrence of adverse events was identified through patient chart review using the IHI Global Trigger Tool.

Secondary outcomes included: severe adverse events, preventable adverse events, infectious adverse events, and noninfectious adverse events. Severity was dichotomized to severe (serious, life threatening, death) and non-severe (significant, minimal). Preventability was dichotomized to include the "probably" and "definitely" preventable categories with non-preventable adverse events similarly collapsed to a single category of "non-preventable" for analysis. Infectious adverse events were defined as any adverse events categorized "hospital-acquired infection" during chart review (e.g. catheter-related bloodstream infection, ventilator-associated pneumonia, etc.). A full list of infections considered "hospital-acquired" is available in Appendix B. Noninfectious adverse events included all other categories of adverse events, excluding the hospital-acquired infections from analysis. Noninfectious adverse events were examined separately from infectious events as use of Contact Precautions is intended to decrease transmission of bacteria to other patients and may have had a separate impact on noninfectious adverse events

compared to infectious. As with the primary outcome, the secondary outcomes were expressed as adverse event rates (the number of the specific type of adverse events experienced in the ICU divided by total person-time at-risk, ICU length of stay in days).

The final secondary outcome was the system affected when an adverse event occurred. The systems of interest were: cardiovascular, respiratory, renal or endocrine, hematologic, gastrointestinal, neurologic, hospital-acquired infection, and surgical. Specific descriptions for which types of harms were categorized within a particular system are included in Appendix B. These categories of systems are the standard way of presenting general adverse event data[23] and provide clinicians with information on what types of effects exposures may have and which ones may be most amenable to intervention and prevention efforts.

3. Predictor

The predictor was whether the patient was in an ICU randomized to universal glove and gown or not. This was a binary exposure variable.

4. Covariates

The data for Aim 1 were from a randomized trial so confounding variables should have been distributed fairly evenly. However, exploratory analysis of potential confounding variables examined: type of ICU (medical or surgical), hospital type (academic versus non-academic), geographic location, size of ICU (number of beds), and intervention period average ICU length of stay (in days) as a surrogate for severity of illness. As an additional measure of severity of illness, the hospital case mix index was

obtained for each of the 20 sites. The Centers for Medicare and Medicaid (CMS) case mix index is a measure for average patient acuity of a hospital.[57,58] The case mix index uses the Medicare Severity Diagnosis Related Groups (DRGs) to categorize patients by principal and secondary diagnosis, age, procedures, comorbidities, complications, discharge status, and gender. Each of these DRGs has been assigned a standard weight by CMS for hospital use across the country. The case mix index represents the average patient acuity for a hospital by using the sum of the DRGs (for the past year) and dividing by the number of patients (discharged within the past year). All of the aforementioned factors were considered as potential confounders for each of the sub-aims of Aim 1.

5. Effect Modification

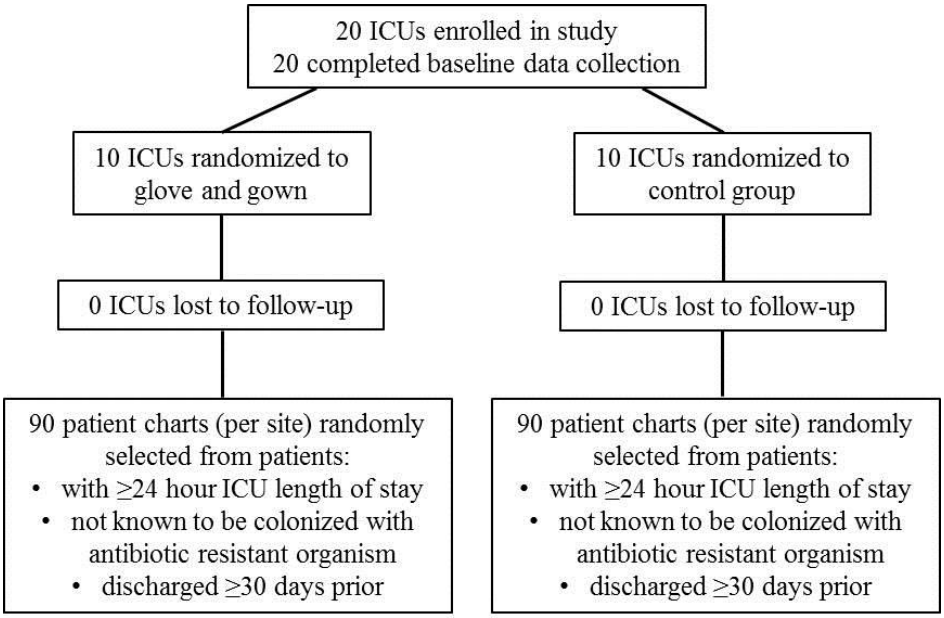
Four biologically plausible factors were considered a priori as potential effect modifiers for Aim 1 by adding an interaction term to the final model. Type of ICU, case mix index, academic hospital setting, and ICU bed size were the four factors considered. In the absence of any identified effect modification, the interaction terms were removed from the regression model.

6. Study Sample

The dataset for Aim 1 used adverse event data collected from the BUGG study. There were 20 ICUs (MICU, SICU, or combined MICU-SICU) in the BUGG study from across the United States. The study period was 10 months long (January 2012 to October 2012). ICU sites were excluded from the study if the hospital was performing active surveillance for methicillin-resistant Staphylococcus aureus (MRSA) or vancomycin-

resistant enterococci (VRE). The ICUs were pair-matched on 3-month baseline MRSA or VRE composite acquisition rates and then randomized to the intervention or control group within the pair-match for the 10 month study period. The intervention group healthcare workers wore gloves and gowns prior to any room entry (regardless of patient colonization with antibiotic resistant organisms). The control group observed current standard of care, donning gloves and gowns prior to room entry only for patients known to be colonized or infected with antibiotic resistant organisms. For seven months, 10 to 14 patient charts were randomly selected each month, per site, for review for adverse events using the Global Trigger Tool (a total of 90 charts per site, 1800 charts overall). For a patient to be eligible for review, the patient had to have stayed at least 24 hours in the study ICU and have been discharged more than 30 days prior to the time of chart review. Additional inclusion criteria were that patients were those known not to be colonized with antibiotic resistant bacteria. Figure 1 below illustrates patient selection for Aim 1.

Figure 1. Patient Chart Selection for Aim 1.



7. Statistical Analysis

For all sub-aims, univariate and bivariate analysis was conducted to examine the distributions of the study variables. Means and standard deviations, medians and interquartile ranges, histograms, etc. were used to examine the distributions of continuous variables. Categorical variables were examined using counts and percentages. Bivariate analysis was used to examine whether variables were potential confounders by checking for association of the variable with both Contact Precautions and occurrence of adverse event.

Aim 1a

The data for Aim 1 were from a cluster randomized trial which was clustered by ICU. The unit of analysis was individual patients. All exploratory and multivariable data analysis was conducted without consideration of the pair-match. Breaking the pair-

matching for analysis was appropriate as the pair-matched variables were unrelated to the research question and breaking the pair-match provided greater power. In the BUGG study, sites were pair-matched on 3-month baseline MRSA and VRE transmission. As the overall adverse event rate that was examined in Aim 1a was separate from the infectious adverse event rate analysis, the noninfectious adverse events were unlikely to be associated with baseline transmission rate. The pair-matching was done with respect to exposure status (treatment group assignment) and not based on outcome (noninfectious adverse events). As a result, conducting the analysis without accounting statistically for the pair-matching did not result in bias.

Bivariate analysis examined study variable distributions and number of missing values by treatment group (intervention versus control ICUs). The multivariable analysis reflected clustering by using a generalized linear mixed effects model with ICU as the clustering variable. The unit of analysis was individual patients. The outcome of adverse event rate was expressed as count of patient adverse events divided by ICU length of stay (LOS). As a result, a Poisson regression model was used in the mixed effects approach to model the log rate among individuals in the ICUs with universal glove and gown. The model offset was the ICU-specific length of stay. Individual patients within each cluster (site) were unordered so compound symmetry was the within-cluster variance-covariance matrix structure used. While standard bivariate analysis to examine confounding was conducted, these approaches did not account for the ICU level clustering. Bivariate analysis was considered based on magnitude of effect rather than statistical significance or confidence interval widths since they were incorrect due to clustering. Thus, confounding was also assessed by including covariates in a model with universal glove

and gown. The covariate was included into the model if the magnitude of the log rate ratio estimate for universal glove and gown changed meaningfully. Regardless of statistical significance or magnitude of change in the log rate ratio, patient acuity (CMS case mix index) and study site was included in the regression model.

Aims 1b, 1c and 1d

This study was powered for the primary aim (Aim 1a); Aims 1b, 1c, and 1d were exploratory analyses. The bivariate and multivariable analysis for preventable adverse events was conducted in the same manner as described for Aim 1a. The outcome modeled was rate of preventable adverse events (ratings of probably and definitely preventable) among patients in intervention ICUs compared to control ICUs. To examine Aim 1c, infectious adverse event outcomes were analyzed the same way as all other aims. The outcome modeled was the rate of all HAI adverse events among patients in universal gown and glove ICUs compared to patients in ICUs randomized to standard precautions. Similarly, the rate of noninfectious adverse events was modeled (all observed adverse events except HAIs). The rate of severe adverse events (serious, life-threatening, and death) was also modeled.

Aim 1e

The secondary outcomes outlined previously in the "Outcomes" section of the methods were bivariate, descriptive analysis only. The count and percent of adverse events in each of the eight pre-specified systems[23] were reported by treatment group (universal glove and gown or control ICU). Statistical testing of the difference in

proportion used either a chi-square or Fisher's exact test, as required by expected cell counts. The subtypes of adverse events within each system were presented as number and percent only, with no statistical testing performed.

8. Power and Sample Size

The power for the sample size of chart reviews collected in the BUGG data was calculated for a rate ratio with clustering by ICU. Individual patient level was the unit of analysis. Rates and size of effect were based on previous research noted below (adverse event rate among universal glove and gown patients: 17 per 1000 patient days; adverse event rate among Standard Precautions patients: 7 per 1000 patient days).[42] Within the BUGG study, the average ICU length of stay among intervention ICUs was 4.52 days (900 patients * 4.52 days = 4068 patient days at risk). The total time at risk among Standard Precautions patients was 3951 patient days (900 patients * 4.39 day average ICU length of stay among control ICUs). We calculated power under two assumptions of within-cluster correlation assuming both a within-cluster correlation of 0.01 (the most conservative estimate for ICC from Platt, et al.)[59,59] and an ICC of 0.001. With 90 observations per ICU, our calculated design effects were 1.89, assuming an ICC of 0.01, and 1.089 for an ICC of 0.001.

Table 2: Power Calculations for Rate of Adverse Events among Patients in ICUs Randomized to Universal Glove and Gown Use Compared to Rate of Adverse Events among Patients in ICUs Randomized to Usual Care

Rate Ratio ($\lambda_{\text{universal glove and gown}} / \lambda_{\text{standard precautions}}$)	Power (ICC = 0.01)	Power (ICC = 0.001)
2.0	0.58	0.82
2.1	0.63	0.87
2.2	0.71	0.91
2.3	0.76	0.94
2.4*	0.82	0.97

*Rate ratio observed among non-congestive heart failure patients in study by Stelfox, et al.[42]

Thus, using the intraclass correlation used by Platt et al.[59] and assuming a two-sided test with alpha of 0.05, the study was able to detect a 2.0 times higher rate of adverse events among patients in ICUs randomized to universal glove and gown than patients on Standard Precautions with 82% power (Table 2). Under a much more conservative estimate of the intraclass correlation (ICC = 0.01), the power to detect a rate ratio of 2.0 was lower. However, even under this most conservative intraclass correlation estimate by Platt and colleagues, the study still had 82% power to detect a rate ratio of 2.4. This was still a reasonable expected effect size as it is the effect size reported previously by Stelfox and colleagues among the non-congestive heart failure patients of their cohort.[42] A two times increase in the rate of adverse events among patients on universal glove and gown compared to Standard Precautions represents a clinically relevant increase that should prompt investigation into methods of reducing the occurrence of adverse events in patients on universal glove and gown. Limited power to detect smaller differences was a limitation of using previously collected data. However, this was the largest study to date and randomization of glove and gown use is a particular strength compared to past studies.

B. Aim 2

1. Study Overview

The second aim used a preexisting University of Maryland Medical Center (UMMC) cohort to conduct a prospective cohort study. The UMMC cohort was prospectively enrolled between 1/1/2010 and 11/17/2010 to investigate the association between Contact Precautions and depression and anxiety. All patients were recruited from general and surgical admission services (non-ICU patients). The cohort consisted of 148 patients on Contact Precautions individually matched to 148 non-Contact Precautions patients by floor location and an initial three-day length of stay. Patient charts were reviewed to identify adverse events that occurred during the patient's stay.

2. Outcomes

For the second aim, the standard method for the IHI Global Trigger Tool was used. For specifics of the IHI Global Trigger Tool measurement method, please see description of Aim 1 methods (Chapter II.A.2.IHI Global Trigger Tool). The PhD student and two physician reviewers received trigger tool training and were the three unblinded primary reviewers for the 296 cohort members. Each physician reviewer reviewed 148 of the cohort members (each half of the cohort contained both patients exposed and unexposed to Contact Precautions). Initial reviewers had access to the patient charts of cohort members and reviewed all relevant sections of the record, not just the discharge summaries. The dissertation chair, Dr. Daniel Morgan, was the final physician reviewer and made the final determination for any disagreements on events between primary reviewers. As in Aim 1, the final reviewer was provided with the patient discharge

summary and relevant information on medication or laboratory values when an adverse event was identified outside of the discharge summary.

Secondary Outcomes

As stated previously, the main outcome for both aims was the rate of adverse events (an unintended physical injury resulting from or contributed to by medical care but not a result of underlying illness). For Aim 2, the rate of adverse events was expressed as the total number of adverse events experienced during hospitalization (regardless of floor location) divided by total person-time at-risk (hospital length of stay in days). The occurrence of adverse events was identified through patient chart review using the IHI Global Trigger Tool.

Secondary outcomes included: severe adverse events, preventable adverse events, infectious adverse events, and noninfectious adverse events. Severity was dichotomized to severe (serious, life threatening, death) and non-severe (significant, minimal). Preventability was dichotomized to include the "probably" and "definitely" preventable categories. Infectious adverse events were considered as any adverse events categorized "hospital-acquired infection" during chart review (e.g. catheter-related bloodstream infection, ventilator-associated pneumonia, etc.). A full list of infections considered "hospital-acquired" is available in Appendix B. Noninfectious adverse events included all other categories of adverse events, excluding hospital-acquired infections from analysis. Noninfectious adverse events were examined separately from infectious events as use of Contact Precautions is intended to decrease transmission of bacteria to other patients and may have had a separate impact on noninfectious adverse events compared to infectious.

As with the primary outcome, the secondary outcomes were expressed as adverse event rates (the number of the specific type of adverse events experienced during hospital stay divided by total person-time at-risk, hospital length of stay in days).

The final secondary outcome was the system affected when an adverse event occurred. The systems of interest were: cardiovascular, respiratory, renal or endocrine, hematologic, gastrointestinal, neurologic, hospital-acquired infection, and surgical. Specific descriptions for which types of harms were categorized within a particular system are included in Appendix B. These categories of systems are the standard way of presenting general adverse event data[23] and provide clinicians with information on what types of effects exposures may have and which ones may be most amenable to intervention and prevention efforts.

3. Predictor

The predictor was whether the individual patient was on Contact Precautions or not, as obtained from a daily admissions list from the UMMC Central Data Repository (CDR). At UMMC, Contact Precautions involve donning of disposable gown and glove prior to entry and removal prior to exiting the room. Once a patient was enrolled in the matched cohort at three days after admission, the exposure status of patients did not change (non-Contact Precautions patients did not become Contact Precautions-exposed). The predictor was a binary exposure (Contact Precautions: yes or no). Patients on Contact Precautions were matched to patients not on Contact Precautions on enrollment location and initial three-day length of stay.

4. Covariates

For Aim 2, age (in years), gender, minority status, socioeconomic status, marital status, and education were assessed as potential confounding variables. In addition, patient Charlson comorbidity score was examined as a potential confounding variable as patients on Contact Precautions tend to have more illnesses and those with more comorbidities may also be at higher risk of adverse event(s). Additional confounding variables may have existed but were not collected from study participants. Each of the listed variables were analyzed as potential confounding variables for all of the sub-aims of Aim 2.

5. Effect Modification

No variables were considered a priori as effect modifiers for the second aim.

6. Study Sample

This second aim used a preexisting University of Maryland Medical Center (UMMC) cohort to conduct a prospective cohort study. The UMMC cohort was prospectively enrolled between 1/1/2010 and 11/17/2010 to investigate the association between Contact Precautions and depression and anxiety. All patients were recruited from general and surgical admission services (non-ICU patients). The admission services of the matched cohort participants are listed in Appendix C. The cohort consists of 148 patients on Contact Precautions individually matched to 148 non-Contact Precautions patients by floor location and an initial three-day length of stay. However, individual

patient length of stay was permitted to differ following the initial three-day length of stay eligibility criterion.

All exposure information and confounding variables were collected as part of the original prospective cohort study. However, information on the primary and secondary outcomes were collected as described above in the "Outcome" and "IHI Global Trigger Tool" sections.

7. Statistical Analysis

For all sub-aims, univariate and bivariate analysis were conducted to examine the distributions of the study variables. Means and standard deviations, medians and interquartile ranges, histograms, etc. were used to examine the distributions of continuous variables. Categorical variables were examined using counts and percentages. Bivariate analysis was used to examine whether variables were potential confounders by checking for association of the variable with both Contact Precautions and occurrence of adverse event.

Aim 2a

The outcome variable from Aim 2 was also a rate and was expressed as the count of patient adverse events divided by patient length of stay. As with Aim 1, the measure of association was a rate ratio comparing the adverse event rate in patients exposed to Contact Precautions versus the adverse event rate among patients not on Contact Precautions. As the outcome was a rate but the data were not clustered, a Poisson regression modeling approach was used. Exploratory data analysis was conducted as

described above. Decisions about covariates to include were made by including covariates identified in exploratory analysis one at a time in a model with Contact Precautions. The covariate was included in the regression model if a meaningful change in magnitude of the log rate ratio for Contact Precautions was observed. As no examined covariates produced meaningful changes in the coefficient estimate, we included biologically plausible variables such as age and Charlson comorbidity score regardless.

To address the matched nature of the cohort, the regression model included the matching variable of floor that a patient was recruited from as a covariate. The matched patients had the same initial length of stay (a cohort eligibility criterion) but length of stay subsequent to cohort entry could differ between the matched patients. As the UMMC cohort was individually matched on enrollment location, the multivariable model was adjusted for the enrollment location, regardless of statistical significance. This was the primary modeling approach since admission service is not a "close" matching variable like genetic variables would be.[60] The model offset was patient-specific time at risk (hospital length of stay in days) and standard errors were corrected using the scaled deviance approach.

Aims 2b-2e

The analysis used multivariable Poisson regression instead of clustered analysis. The bivariate and multivariable analysis for preventable adverse events was conducted in the same manner as described for Aim 2a. The outcome modeled was rate of preventable adverse events (ratings of probably and definitely preventable) among patients on Contact Precautions compared to patients not on Contact Precautions. To examine Aim

2c, infectious adverse event outcomes were analyzed the same way as all other aims. The outcome modeled was the rate of all HAI adverse events among patients on Contact Precautions compared to patients not on Contact Precautions. The rate of noninfectious adverse events was modeled similarly (all observed adverse events except HAIs). The rate of severe adverse events (serious, life-threatening, death) was also modeled but was adjusted only for matching due to small numbers of events.

Aim 2e used only descriptive analysis by Contact Precautions exposure status for the secondary outcomes outlined in the "Outcomes" section of Chapter II.B.2.Secondary Outcomes. Statistical testing of the difference in proportion used either a chi-square or Fisher's exact test, as required by expected cell counts. The subtypes of adverse events within each system were presented as number and percent only, with no statistical testing performed.

8. Power and Sample Size

The power for the sample size in the UMMC cohort was calculated for a rate ratio without clustering. Prior research on rates of adverse events among general medical inpatients[23] has reported 25 adverse events per 100 admissions. Applying this to the average length of stay among patients on standard precautions in the UMMC cohort (4.7 days), the rate of adverse events among patients on standard precautions would be 53.2 adverse events per 1000 patient days. With 148 patients and an average hospital length of stay among patients of 5.5 days, there were 814 patient days at risk among patients on Contact Precautions. Similarly, there were 695.6 total patient days at risk of adverse events among patients on standard precautions within the UMMC cohort.

For a two-sided test and alpha of 0.05, the study had 84% power to detect an 80% increase in adverse event rate (Table 3). For a smaller magnitude effect size, the study still had 75% power to detect a 70% higher rate of adverse events among patients on Contact Precautions ($R_tR = 1.7$). These were reasonable magnitudes of effect in light of the previous higher estimate ($R_tR = 2.2$) of Stelfox et al.[42] Also, an 80% increase in the rate of adverse events among patients on Contact Precautions represented a clinically relevant increase. As in Aim 1, the limited power to detect smaller effect sizes than this was a limitation of using previously collected data. However, this was still the largest study to date and represented an improvement over previous studies in the ability to control for confounding factors.

Table 3: Power Calculations for Rate of Adverse Events among Patients on Contact Precautions Compared to Rate of Adverse Events among Patients Unexposed to Contact Precautions

Rate Ratio ($\lambda_{contact\ precautions} / \lambda_{standard\ precautions}$)	Power
1.7	0.75
1.8	0.84
2.0	0.94
2.4*	0.996
2.5	0.998

*Rate ratio observed in study by Stelfox, et al. among non-congestive heart failure cohort members.[42]

III. THE EFFECT OF UNIVERSAL GLOVE AND GOWN USE ON ADVERSE EVENTS IN INTENSIVE CARE UNIT (ICU) PATIENTS[1]

Abstract

BACKGROUND No randomized trials have examined the effect of Contact Precautions or universal glove and gown use on adverse events. We assessed if gloves and gowns for all patient contact in the intensive care unit (ICU) changes adverse event rates.

METHODS From January 2012 to October 2012, intervention ICUs of the 20-site Benefits of Universal Gloving and Gowning cluster randomized trial required healthcare workers use gloves and gowns for all patient contact. We randomly sampled 1800 medical records of adult patients not colonized with antibiotic-resistant bacteria and reviewed for adverse events using the Institute for Healthcare Improvement Global Trigger Tool.

RESULTS 447 patients (24.8%) had ≥1 ICU adverse event. Adverse events were not associated with universal glove and gown use (incidence rate ratio (IRR) 0.81; 95% CI, 0.48-1.36). This did not change with adjustment for ICU type, severity of illness, academic hospital status, and ICU size, adverse event rates, IRR 0.91 (95% confidence interval [CI], 0.59-1.42; p=0.68). Rates of infectious adverse events also did not differ after adjusting for the same factors, IRR 0.75 (95% CI, 0.47-1.21; p=0.24).

[1]Lindsay Croft, Anthony D. Harris, Lisa Pineles, Patricia Langenberg, Michelle Shardell, Jeffrey C. Fink, Linda Simoni-Wastila, Daniel J. Morgan; Benefits of Universal Glove and Gown (BUGG) Investigators. *Clinical Infectious Diseases*, 2015 [epub ahead of print]:doi: 10.1093/cid/civ315

CONCLUSIONS In ICUs where healthcare workers donned gloves and gowns for all patient contact, patients were no more likely to experience adverse events than in control ICUs. Concerns of adverse events resulting from universal glove and gown use were not supported. Similar considerations may be appropriate regarding use of Contact Precautions.

Background

Healthcare-associated infections (HAIs) are an important cause of morbidity and mortality in hospitalized patients[61] but comprise only one type of adverse safety event experienced by hospitalized patients. Adverse events are unintended injuries resulting from or contributed to by medical or surgical care that are not due to an underlying condition.[1] Within hospital settings, approximately one in four patients experience at least one adverse event.[28] Adverse events may result in temporary harm, prolonged hospitalization, permanent disability, or death.[5,10,11] The Office of the Inspector General reported that 27% of Medicare patients experienced an adverse event.[13] An estimated 15,000 Medicare patients per month will experience an adverse event that contributes to their death.[13] In addition, preventable adverse events cost the U.S. $6.7 billion each year.[14]

The Centers for Disease Control and Prevention (CDC) recommend use of Contact Precautions (glove and gown use prior to patient room entry) for patients colonized or infected with antibiotic-resistant bacteria to reduce transmission of these bacteria and subsequent HAIs.[35] However, Contact Precautions may increase the frequency of adverse events.[42,44] Healthcare workers visit patients on Contact Precautions less often than other patients.[46,48,50] When Contact Precautions are used for all patients, the practice is called universal glove and gown use. Differences between Contact Precautions and universal glove and gown are few but include Contact Precautions causing delays in hospital admission from the emergency room or discharge from the hospital to a nursing home because of the need for a private room.[62-64] A cluster randomized trial among intensive care units (Benefits of Universal Gloving and Gowning, BUGG) found that

universal use of gloves and gowns decreased acquisition of methicillin resistant Staphylococcus aureus (MRSA) by 40% without impacting vancomycin-resistant enterococci (VRE) acquisition rates.[46]

Contact Precautions may cause psychological harm to patients[37,38] but physical harm remains unresolved. In a retrospective study, Stelfox et al. reported twice the rate of overall adverse events and seven times as many preventable adverse events in patients on Contact Precautions compared to patients not on Contact Precautions.[42] Within the ICU setting, Zahar et al. reported a 1.5 times increase in rates of hypo- and hyperglycemia among patients on Contact Precautions.[43] In contrast, a recent case-crossover study on the use of Contact Precautions for patients with VRE found no overall difference in adverse events.[44]

A major limitation of these studies is that they could not completely account for greater severity of illness among patients on Contact Precautions. Patients identified with MRSA or VRE generally are more severely ill,[52,53] which increases overall risk of adverse events. Further, some studies used unconventional definitions of adverse events including electrolyte imbalances or select types of events.[42,43,45] Thus, the role of Contact Precautions in patient adverse events remains unclear.

Within a cluster randomized trial of universal glove and gown use (universal use of Contact Precautions) we examined whether universal glove and gown use increased the rate of patient adverse events compared to usual care.

Methods

Study Design

This was a secondary analysis of a 20-site cluster randomized trial in adult (≥18 years of age) ICUs across the United States (BUGG) with institutional review board approval.[46] Healthcare workers in ICUs randomized to the intervention donned gloves and gowns prior to all patient contact, while healthcare workers randomized to the control arm (usual care) did this only for patients known to be colonized or infected with antibiotic-resistant bacteria, per CDC guidelines.[35] Hospitals were recruited via the Society for Healthcare Epidemiology Research Network. The study period was January 2012 to October 2012. The ICUs were pair-matched on three-month baseline composite acquisition of MRSA or VRE and randomized to intervention or control group within pair-matches. During the study period, 10 to 14 patient charts per site were randomly selected (via random number generator) each month for review for adverse events (90 patients per site and 1800 patients overall). No historical data on adverse event rates was available.

Recruitment and Eligibility Criteria

Individual patient charts were eligible for sampling and review if the patient stayed in the study ICU for at least 24 hours. Rates of adverse events seen in patients in the control arm (those not colonized or infected with antibiotic-resistant bacteria on ICU admission and not on Contact Precautions at any point in stay) were compared to rates for patients in the intervention arm (also not colonized or infected with antibiotic-resistant

bacteria but on universal glove and gown). This allowed a randomized method to assess the effect of Contact Precautions on patients with similar characteristics.

Outcomes

The primary outcomes were counts of noninfectious and infectious adverse events. Adverse events were defined as "unintended physical injury resulting from or contributed to by medical care that requires additional monitoring, treatment, or hospitalization or that results in death," according to the Institute for Healthcare Improvement (IHI) Global Trigger Tool.[1] Events due to the patient's underlying condition were not recorded as adverse events. Infectious adverse events were defined as infections that occurred in the ICU but were not present or incubating on patient ICU admission (hospital-acquired infections). Infectious events were determined by two infectious disease physicians (D.J.M. and A.D.H.) by applying CDC National Healthcare Safety Network criteria. All other adverse events were classified as noninfectious. Rates of adverse events were expressed as the number of a specific ICU adverse event type divided by total person-time at-risk (patient-specific ICU length of stay in days).

Adverse events were identified using the IHI Global Trigger Tool to conduct structured patient chart reviews,[1] which is designed for completion of chart review within twenty minutes. Ninety patient charts were reviewed at each site by a primary reviewer. Primary site reviewers were clinical research staff unaffiliated with study ICUs who were unaware of the secondary study question and hypothesis. Site reviewers received standardized in-person and webinar training on the IHI Global Trigger Tool. Prior to study period data collection, site reviewers received training with 10 standardized sample charts and an additional 10 reviews on patient charts from their own institution.

Personalized feedback on training chart reviews was provided (by D.J.M) to each of the site reviewers. Landrigan and colleagues have reported 81% agreement between reviewers and "gold standard" experienced reviewers[23] and Sharek et al. have reported inter-reviewer kappas ranging from 0.64 to 0.93 when the IHI Global Trigger Tool is used to identify adverse events.[32]

Secondary outcomes included rates of severe and preventable adverse events and type of harm categorized by physiological system affected.[23] Severity of adverse events was measured with a five-point Likert scale (minimal, clinically significant, serious, life-threatening, fatal) as modified from the National Coordinating Council for Medication Error Reporting and Prevention severity index.[1,54] Best fit to a category was assigned by final physician reviewers.

Site reviewers examined patient charts for adverse events and recorded events, severity and preventability ratings, a short description of the event(s), and discharge summary on a standardized, de-identified data extraction sheet sent to the study coordinator at the University of Maryland. Records were received, blinded to site identity, and two physician reviewers (A.D.H and D.J.M) independently reviewed the discharge summaries. Physician reviewers met to discuss and come to consensus on disagreements for occurrence of an adverse event (inter-physician reviewer percent agreement 89.5% prior to consensus). Reviewers determined whether each adverse event initially began before, during, or after the admission of interest. Analysis was restricted to adverse events which began during the index admission only as events that began prior to or after the admission would not be the result of exposure to universal glove and gown.

Covariates

Covariates considered in the analysis included: type of ICU (medical, surgical, or combined), hospital type (academic hospital with a medical school versus non-academic), and size of ICU (continuous number of beds). In addition, as a measure of severity of illness, the Centers for Medicare and Medicaid (CMS) case-mix index (CMI) for each hospital was obtained for the fiscal year prior to randomization (2011). The CMI is a measure of average patient acuity of a hospital.[57,58] Studies of risk of patient falls among ICU patients have previously used hospital level CMS CMI as a measure of average patient acuity.[65]

Statistical Power

We used a previously reported effect size for increase in adverse events due to Contact Precautions for an incidence rate ratio (IRR) of 2.4 among patients in universal glove and gown ICUs compared to patients in control ICUs.[42] We accounted for ICU level clustering using an intraclass correlation coefficient of 0.001.[59] For a two-sided test with 5% type I error, with 900 patients in each arm of the study, we had 91% power to detect a 2.4 times higher rate of adverse events among patients in intervention ICUs compared to control ICUs.

Statistical Analysis

Randomization and the intervention occurred at the ICU level. Analysis of adverse events was conducted at the patient level, accounting for clustering by study site. Outcomes for this secondary analysis were unrelated to treatment allocation so pair-

matching by baseline MRSA and VRE was not maintained for this study analysis. Noninfectious, infectious, preventable, and severe adverse event rates were modeled using Poisson mixed effects, random-intercept models with ICU site included as the clustering variable and a compound symmetry covariance structure. The model offset was the log of patient ICU length of stay. Models of severe and preventable adverse event rates were constructed only for noninfectious adverse events. Covariates that meaningfully changed the log rate ratio estimate for universal glove and gown by approximately 10% or more owing to chance imbalances were included in the model. The covariates meeting this criterion included type of ICU, CMI, academic setting, and ICU bed size. Effect modification by biologically plausible variables such as CMI, academic hospital setting, and ICU bed size was considered by introducing interaction terms into the model and testing for statistical significance.

The analysis of harm by physiological system affected was descriptive in nature. Counts of adverse events by intervention group were recorded and a bivariate analysis that did not account for clustering by ICU was performed using a chi-square test.

Results

Patients from intervention and control ICUs were similar with respect to ICU characteristics (Table 4). However, patients in the intervention group were more likely to be admitted to medical ICUs (MICUs) and combined medical-surgical ICUs (MICU-SICUs) (60.0% and 30.0%, respectively) compared to control patients (50.0% in MICUs and 10.0% in MICU-SICUs). Within the larger BUGG randomized trial, compliance with universal use of Contact Precautions on room entry was high in intervention ICUs (86.2% for gloves and 85.1% for gowns).[46]

Table 4. Patient and Hospital Characteristics of Adverse Event Review in Intensive Care Units (ICUs) Randomized to Universal Glove and Gown Use vs. Usual Care.

Characteristic	Universal glove and gown ICUs N=900	Control ICUs N=900
ICU size (# of beds), mean (SD)	19.00 (4.8)	18.3 (7.7)
ICU type, N (%)		
MICU	540 (60.0)	449 (50.0)
SICU	90 (10.0)	361 (40.0)
MICU/SICU	270 (30.0)	90 (10.0)
CMS CMI [a]	1.88 (1.75-2.01)	1.83 (1.77-2.07)
Hospital Setting		
Non-academic	180 (20.0)	270 (30.0)
Academic	720 (80.0)	630 (70.0)
ICU average length of stay (days) [a]	4.62 (3.98-4.70)	3.93 (3.78-5.06)
Region		
Midwest/West	450 (50.0)	180 (20.0)
South	270 (30.0)	269 (29.9)
East	180 (20.0)	451 (50.1)
Number of noninfectious adverse events	212	274
Number of patient-days at risk	4582	4846
Unadjusted noninfectious adverse event rate [b, c]	46.3	56.5

Abbreviations: ICU, intensive care unit; SD, standard deviation; MICU, medical intensive care unit; SICU, surgical intensive care unit; CMS CMI, Center for Medicare Services case-mix index.

[a] median (interquartile range).

[b] Unadjusted adverse event rate calculated as number of noninfectious adverse events/1000 patient-days at risk.

[c] Due to chance imbalance in ICU type between study arms, the effect of excluding surgical events from unadjusted analysis of noninfectious adverse events was investigated. Direction of effect remained the same (40.6 noninfectious adverse events per 1000 patient-days among universal glove and gown ICU patients versus 45.4 per 1000 patient-days among control ICU patients).

In unclustered, descriptive analyses that did not examine rates given small absolute numbers of adverse events in each category, there was no significant increase in adverse events among intervention ICU patients for any physiological system (Table 5). However, there were significantly fewer cardiovascular and surgical adverse events among intervention ICU patients. For example, 21 adverse events affecting the cardiovascular system of patients in intervention ICUs occurred versus 39 in control ICU patients ($p=0.02$). Patients in intervention ICUs experienced 26 surgery-related adverse events versus 54 such events among patients in control ICUs ($p=0.001$).

Table 5. Frequency of Specific Adverse Events in Patients in Universal Glove and Gown Intensive Care Units (ICUs) Compared to Control ICUs.[a]

Type of Adverse Event	Total Events	Universal Glove and Gown ICUs N=900	Control ICUs N=900	P value
Infectious adverse event	**149**	**54**	**95**	**<0.001**
Central venous catheter-related bloodstream infection	11	5	6	
Ventilator-associated pneumonia	34	10	24	
Nosocomial pneumonia, not ventilator-related	32	15	17	
Urinary tract infection	28	8	20	
Surgical site infection	14	6	8	
Clostridium difficile colitis	13	5	8	
Other hospital-acquired infection [b]	17	5	12	
Cardiovascular system	**60**	**21**	**39**	**0.02**
Cardiac arrest	7	4	3	
Hypotension	23	6	17	
Arrhythmias or conduction abnormality	21	7	14	
Myocardial ischemia/infarction	9	4	5	
Respiratory system	**78**	**31**	**47**	**0.06**
Acute respiratory failure	32	14	18	
Pneumothorax	8	1	7	
Atelectasis	4	1	3	
Aspiration	17	9	8	
Pulmonary embolus	3	2	1	
Need for reintubation	11	4	7	
Other respiratory event [c]	3	0	3	
Renal or endocrine system	**86**	**49**	**37**	**0.18**
Fluid overload	7	4	3	
Acute renal failure	33	18	15	
Metabolic acidosis	1	1	0	
Hyperglycemia	7	2	5	
Hypoglycemia	28	22	6	
Hyperkalemia	2	0	2	
Other renal or endocrine event [d]	8	2	6	
Hematologic system	**58**	**27**	**31**	**0.59**
Hemorrhage	21	11	10	
Thromboembolic venous event	29	11	18	
Hematoma	3	2	1	
Other hematologic event [e]	5	3	2	
Gastrointestinal system	**25**	**10**	**15**	**0.31**
Nausea or vomiting	8	4	4	
Diarrhea	5	2	3	
Constipation	2	1	1	
Pancreatitis	1	0	1	
Ileus	6	1	5	
Other gastrointestinal event [f]	3	2	1	

Table 5. Frequency of Specific Adverse Events in Patients in Universal Glove and Gown Intensive Care Units (ICUs) Compared to Control ICUs.[a] (continued)

Type of Adverse Event	Total Events	Universal Glove and Gown ICUs N=900	Control ICUs N=900	P value
Neurologic system	**58**	**30**	**28**	**0.79**
Oversedation	11	8	3	
Delirium or encephalopathy	36	18	18	
Seizure	1	0	1	
Stroke or intracerebral hemorrhage	4	2	2	
Inadequate analgesia	4	0	4	
Other neurologic event[g]	2	2	0	
Surgical event	**80**	**26**	**54**	**0.001**
Postoperative hemorrhage	26	13	13	
Postoperative hematoma	10	4	6	
Laceration or other organ injury	6	2	4	
Vascular injury	9	1	8	
Surgical anastomosis failure	2	1	1	
Wound dehiscence	2	0	2	
Failed procedure	11	2	9	
Unplanned return to surgery	8	1	7	
Other event[h]	6	2	4	
Other types of harm	**41**	**18**	**23**	**0.43**
Allergic reaction	10	4	6	
Fall	1	1	0	
Pressure ulcer	23	10	13	
Rash	1	0	1	
Catheter complication	5	3	2	
Other[i]	1	0	1	
Severe noninfectious events[j,l]	**303**	**130**	**173**	**0.007**
Preventable noninfectious events[k,l]	**211**	**98**	**113**	**0.27**

[a] 635 total adverse events occurred (266 in universal glove and gown; 369 in control ICUs).

[b] Other hospital-acquired infection events include: bronchitis; sinusitis secondary to nasal intubation; peritonitis; tracheobronchitis, some requiring intubation; tracheitis; ventriculoperitoneal shunt infection; cellulitis; peripheral vein IV site cellulitis.

[c] Other respiratory events include: failure to reposition or need to exchange endotracheal tube (ETT); hypoxia.

[d] Other renal or endocrine events include: postoperative urinary retention; patient removal of Foley catheter resulting in trauma and hematuria; catheter-related trauma on Coumadin requiring blood transfusion; multiple electrolyte abnormalities secondary to medical management; hyponatremia due to fluid resuscitation.

[e] Other hematologic events include: heparin-induced thrombocytopenia.

[f] Other gastrointestinal events include: mucositis requiring parenteral nutrition; medication-related impaired liver function; dysphagia.

[g] Other neurologic events include: hospital or ICU myopathy.

[h] Other surgical events include: delayed extubation postoperatively; failed placement of nasogastric tube, becoming stuck on removal attempt; bladder dysfunction following spine surgery; postoperative transplant rejection.

[i] Other type events include: gout.

[j] Severe events include: adverse events which are serious (organ dysfunction); life-threatening (death possible without therapy within a few hours); death.

[k] Preventable events are adverse events considered probably or definitely preventable by current practice standards, knowledge, and/or technology.

[l] Not included in total events count for the rest of the table as these events are not mutually exclusive of physiological system affected.

There was no statistically significant difference in unadjusted rate of noninfectious adverse events between patients in intervention ICUs compared to control ICU patients (46.3 per 1000 patient-days versus 56.5 per 1000 patient-days; IRR= 0.81; 95% confidence interval [CI], 0.48-1.36; p=0.42). In unadjusted analysis, there was also no significant difference in infectious adverse events among patients in intervention ICUs (IRR= 0.57; 95% CI, 0.31-1.04; p=0.07). No evidence of effect modification was found among covariates investigated.

Adjusted for type of ICU, CMS case-mix index, hospital setting, and ICU bed size, the rate of noninfectious adverse events among patients in intervention ICUs did not significantly differ from the rate of adverse events among patients in control ICUs (IRR= 0.91; 95% CI, 0.59-1.42; p=0.68; Table 6). Similarly, we found no statistically significant difference in the rate of infectious adverse events (IRR= 0.75; 95% CI, 0.47-1.21; p=0.24) when adjusted for clustering and confounding (Table 6). Severe noninfectious adverse events were less common among patients in intervention ICUs than among patients in control ICUs, but the finding was not statistically significant (IRR= 0.82; 95% CI, 0.42-1.59; p=0.56) after adjustment for the same covariates (Figure 2). Universal glove and gown use was not significantly associated with preventable noninfectious adverse events (IRR= 1.26; 95% CI, 0.69-2.30; p=0.46) (Figure 2).

Table 6. Adjusted Rates of Noninfectious and Infectious Adverse Events Among Patients in Intensive Care Units (ICUs) Randomized to Universal Glove and Gown Use vs. Usual Care.

Characteristic	Rate Ratio	95% Confidence Interval [a]	P value
Noninfectious adverse events [b, c]			
Patients in universal glove and gown ICUs vs. control ICU patients	0.91	(0.59, 1.42)	0.68
Type of ICU			
MICU/SICU	0.94	(0.55, 1.60)	0.82
SICU	1.23	(0.71, 2.12)	0.46
MICU	1.00	[Reference]	
CMI <1.83 [d]	0.77	(0.48, 1.25)	0.29
Non-academic hospital setting	1.01	(0.58, 1.75)	0.97
ICU size (per bed)	1.03	(1.00, 1.06)	0.06
Infectious adverse events [e]			
Patients in universal glove and gown ICUs vs. control ICU patients	0.75	(0.47, 1.21)	0.24
Type of ICU			
MICU/SICU	0.49	(0.22, 1.10)	0.08
SICU	1.65	(1.05, 2.61)	0.03
MICU	1.00	[Reference]	
CMI <1.83 [d]	1.20	(0.83, 1.73)	0.33
Non-academic hospital setting	0.93	(0.52, 1.67)	0.81
ICU size (per each additional bed)	1.00	(0.97, 1.04)	0.85

Abbreviations: ICU, intensive care unit; MICU, medical intensive care unit; SICU, surgical intensive care unit; MICU/SICU, combined medical-surgical intensive care unit; CMI, case-mix index.

[a] 95% confidence intervals were produced using sandwich estimator robust variances to account for excess zeroes

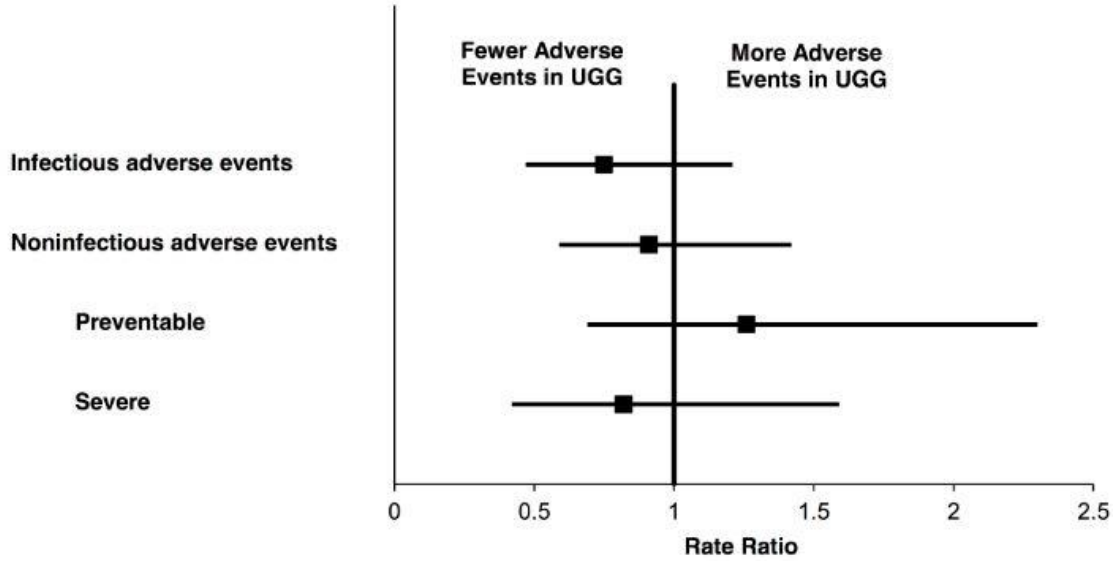
[b] Noninfectious adverse events were also modeled using the negative binomial which produced comparable results to the Poisson mixed effects model presented here.

[c] intraclass correlation coefficient= 0.018

[d] median split of hospital CMS CMI

[e] intraclass correlation coefficient=0.006

Figure 2. Adjusted Rate of Adverse Events[a] Among 900 Patients in Universal Glove and Gown (UGG) Use Compared With 900 Patients in Control ICUs by Subtype of Adverse Event.[b]



[a]each adverse event model is adjusted for: ICU type (combined medical-surgical ICU [MICU-SICU], SICU only [reference: MICU only]), case-mix index ≤ 1.83, non-academic hospital setting, ICU bed size

[b]boxes represent rate ratio point estimate and lines represent 95% confidence intervals

Discussion

We found that universal glove and gown use did not have an impact on overall rate of adverse events, including subtypes of infectious, noninfectious, preventable or severe adverse events. We also observed fewer adverse events among patients in universal glove and gown ICUs for surgical and cardiovascular systems.

Previous observations of healthcare worker (HCW) behavior found that HCWs visit patients on Contact Precautions less often than those not on Contact Precautions.[46,48,50] However, despite observing one less HCW visit per hour in universal glove and gown ICUs (universal use of Contact Precautions),[46] we found no evidence of increased risk of adverse events. Other changes to hospital flow with Contact Precautions but not universal glove and gown use (delayed admission or discharge) could still contribute to patients on Contact Precautions having more adverse events.[62-64]

To our knowledge, this is the first study to examine risk of adverse events in patients randomly exposed to universal glove and gown use. Past observational studies of Contact Precautions and adverse events have reported mixed results. Stelfox et al. completed a retrospective cohort study of general medicine and congestive heart failure patients, finding 2.2 times as many adverse events and 7.0 times as many preventable adverse events among patients on Contact Precautions.[42] This difference may be explained by greater severity of illness among patients on Contact Precautions. Patients identified with MRSA or VRE generally have a greater severity of illness[52,53] which increases risk of adverse events. In contrast, our study excluded patients who would be on Contact Precautions to better examine the effect of universal glove and gown use, separate from severity of illness. Furthermore, the non-standard definition of adverse

event used by Stelfox et al. included fluid and electrolyte imbalances as adverse events (without requirement for harm). Similar to our results, two studies that had more closely matched control groups reported no overall difference in the rate of adverse events.[44,45]

The observation that universal glove and gown use may result in fewer adverse events was unanticipated. Universal glove and gown use could potentially have led to a decrease in healthcare-associated infections by serving as a barrier to acquiring new bacteria both through physical use of gloves and gowns as well as fewer healthcare worker visits and better hand hygiene. A suggestion of improvement in noninfectious adverse events in patients cared for by universal glove and gown use would not be an obvious result of the physical use of gloves and gowns and, if real, would likely be due to a change in healthcare worker behavior during the intervention (bundling activities or different level of attention to care). That noninfectious adverse events which were less common with gown and glove use were not considered preventable, raises the question of whether the trend towards fewer adverse events with gown and glove was the result of random variation (as absolute number of preventable adverse events trended in the opposite direction). In contrast, our finding of no significant change in infectious adverse events is compatible with the primary BUGG study result of no significant reduction in composite VRE or MRSA despite the significant decrease reported for MRSA acquisition alone.[46] In addition, MRSA represents only one kind of infectious adverse event and contaminated healthcare personnel clothing and hands may have a larger role in transmission of MRSA than for other organisms.

This study has some limitations. First, our study was powered to detect at least twice the rate of adverse events with universal glove and gown use, similar to the increase reported by Stelfox et al.[42] Despite having four times as many patients as Stelfox et al.,[42] the study was not powered to detect a smaller increase in adverse events because of accounting for clustering at different sites. Clustering occurs when patients in the same ICU are more similar to one another than to patients in the other ICUs and results in a marked decrease in statistical power. However, our findings of lower or similar rates of adverse events suggest that there is no increased risk of adverse events from universal glove and gown use. Second, despite standardized training and two-physician blinded review for final counts, differences in initial site chart review could have occurred. These differences would likely have been nondifferential in nature as site reviewers were unaware of adverse event reporting by other sites. Finally, despite being the gold standard for adverse event detection, the IHI Global Trigger Tool may have led to nondifferential underreporting of less severe adverse events.[23] These adverse events also would have been all-cause harms and not limited to those plausibly resulting from universal glove and gown use.

Our study has strengths including using a random sample of patient charts from a cluster randomized trial comparing universal glove and gown use to usual care. This, combined with exclusion of patients known to have antibiotic-resistant bacteria, helps minimize uncontrolled confounding that occurred in past observational studies on Contact Precautions. We also used a standard definition of adverse events and final physician reviewers were blinded to the exposure status of patients during chart review for adverse events.

Patients in ICUs where healthcare workers donned gloves and gowns for all patient contact were no more likely to experience noninfectious or infectious adverse events than when healthcare workers did not use gloves and gowns. In fact, patients in universal glove and gown ICUs had fewer overall adverse events. Concerns that universal glove and gown use could contribute to adverse events should not be a limiting factor for implementation.

IV. DIFFERENCES BETWEEN ICU VERSUS GENERAL WARD PATIENTS AND UNIVERSAL GLOVE AND GOWN VERSUS CONTACT PRECAUTIONS

A. Differences Between ICU and General Ward Patients

As was discussed in detail earlier, there are marked differences between ICUs and general wards. This is apparent both in the types of patients and care needs of patients as well as the frequency and types of adverse events that occur in each location. Patients in ICUs are often reliant on artificial support for respiratory, renal, or cardiovascular needs, are frequently sedated or otherwise unaware of their surroundings and rarely are ambulatory or able to attend to their own needs. In contrast, on a general ward, patients tend to be more mobile and alert and are better able to communicate with healthcare personnel about their care. Rather than oversedation or pressure ulcers such as might be more common among ICU patients, general ward patients may be at increased risk of mobility-related harms such as falls in a way ICU patients may not be. Further, patients in general ward locations require a differing intensity of care from ICU patients, altering the type and frequency of care they receive as well as the dynamic of how healthcare workers interact with the patients. Within the ICU, nurse to patient staffing ratios tend to be 2:1 or even 1:1 so a nurse may be caring for fewer patients but case complexity is higher and closer monitoring as well as a greater number of interventions are more likely among ICU patients than floor patients.

Additionally, the types of adverse events that occur differ in these very different areas of the hospital both in the frequency and severity of adverse events based on whether patient care occurs in the intensive care unit or in a non-ICU location

(approximately 5.0 adverse events per 100 patient-days versus 1.5 adverse events per 100 patient-days).[10] Death or disability as the result of an adverse event occurs twelve times more often among ICU patients compared to internal medicine patients (4.9% of adverse events vs. 0.4% of adverse events). Furthermore, surgical or procedural complications and hospital-acquired infections account for the majority of adverse events experienced by ICU patients while adverse drug events are the most common type of adverse event among ward patients.[10] Some have argued that there are many unique aspects to care in the ICU and how it is delivered and that this may be responsible for the differences observed in adverse event rate between ICU and non-ICU settings.[33] Adverse event frequency, outcome, and major types of adverse events differ between the two settings. In addition, Contact Precautions are hypothesized to affect adverse event occurrence based on how its use impacts delivery of care, something which already differs between ICU and floor locations regardless of Contact Precautions exposure. Thus, it is important to separately examine the potential association between Contact Precautions use and adverse event occurrence in both the ICU and general ward environments.

B. Universal Glove and Gown versus Contact Precautions

In addition to the need to investigate the association between Contact Precautions and adverse events in both ICU and non-ICU settings, the second study of this dissertation focuses on the role for Contact Precautions rather than universal glove and gown use in adverse event occurrence. Universal gloving and gowning for all patient contact regardless of patient colonization with a resistant organism is a high intensity use of Contact Precautions which is used in a limited number of circumstances. In contrast,

Contact Precautions require gown and glove use for patient contact only for patients known to be colonized or infected with antibiotic resistant organisms (approximately 10-30% of patients) rather than for all patients. Contact Precautions are used in nearly all US hospitals and thus potential harms associated with Contact Precautions use are more useful for informing current policy debates than the infrequently used universal gowning and gloving.

Additionally, since all patients in universal gloving and gowning setting are cared for similarly, differential wait times or other hospital flow factors that may impact occurrence of adverse events may not occur as might be the case with Contact Precautions. For example, some studies have suggested that patients with a history of colonization with MRSA[66] or any multidrug resistant organism[64] have significantly longer wait times for admission from the emergency department than patients who are not similarly colonized. As differences in the delivery of care are a possible mechanism for how Contact Precautions could result in adverse events it is important to examine the potential association between Contact Precautions and adverse events separate from universal glove and gown use.

C. Conclusion

Due to these differences among patients between floor and ICU locations and in intensity of exposure between universal glove and gown use and Contact Precautions, the second study was necessary to examine any association between Contact Precautions and adverse events among non-ICU patients.

V. THE EFFECT OF CONTACT PRECAUTIONS ON FREQUENCY OF HOSPITAL ADVERSE EVENTS[1]

Abstract

OBJECTIVE. To determine whether use of Contact Precautions on hospital ward patients is associated with patient adverse events.

DESIGN. Individually-matched prospective cohort study.

SETTING. The University of Maryland Medical Center, a tertiary care hospital in Baltimore, Maryland.

METHODS. A total of 296 medical or surgical inpatients admitted to non-intensive care unit hospital wards were enrolled at admission from January to November 2010. Patients on Contact Precautions were individually matched by hospital unit after an initial 3-day length of stay to patients not on Contact Precautions. Adverse events were detected by physician chart review and categorized as noninfectious, preventable and severe noninfectious, and infectious adverse events during the patient's stay using the standardized Institute for Healthcare Improvement's Global Trigger Tool.

[1]Lindsay D. Croft, Michael Liquori, James Ladd, Hannah Day, Lisa Pineles, Elizabeth Ramos, Ryan Arnold, Preeti Mehrotra, Jeffrey C. Fink, Patricia Langenberg, Linda Simoni-Wastila, Eli Perencevich, Anthony D. Harris, Daniel J. Morgan. Submitted to: *Infection Control and Hospital Epidemiology*. 2015.

RESULTS. 148 patients on Contact Precautions at admission were matched to 148 patients not on Contact Precautions. Of the total 296 subjects, 104 (35.1%) experienced at least one adverse event during their hospital stay. Contact Precautions were associated with fewer noninfectious adverse events (rate ratio [R_tR], 0.70; 95% confidence interval [CI], 0.51-0.95; p=0.02) and non-statistically significant fewer severe adverse events (R_tR, 0.69; 95% CI, 0.46-1.03; p=0.07). Preventable adverse events (R_tR, 0.85; 95% CI, 0.59-1.24; p=0.41) did not significantly differ between patients on Contact Precautions compared to unexposed patients.

CONCLUSIONS. Hospital ward patients on Contact Precautions were less likely to experience noninfectious adverse events during their hospital stay than patients unexposed to Contact Precautions.

Introduction

Adverse events are unintentional injuries related to medical or surgical care not due to an underlying condition.[1] Adverse events include healthcare-associated infections (HAIs) as well as delirium, falls, renal injury, and other noninfectious adverse events.[23] One to 2.4 million hospital adverse events are estimated to occur each year in the US[14] and contribute to 98,000 inpatient deaths annually.[6] In the United States, preventable adverse events are estimated to cost between $17 and $29 billion per year.[6]

Contact Precautions are a transmission-based infection control method recommended by the Centers for Disease Control and Prevention (CDC). Contact Precautions require donning gowns and gloves prior to room entry for patients known to be colonized or infected with antibiotic resistant organisms, in addition to cohorting or placing the patient in a single room.[35]

There may be unintended consequences of Contact Precautions. For example, healthcare personnel have consistently been shown to visit patients on Contact Precautions significantly less often than patients unexposed to Contact Precautions.[48,49,62] In addition, adverse events may occur more frequently among patients on Contact Precautions. Stelfox and colleagues reported that patients on Contact Precautions experienced more than twice the rate of adverse events of patients unexposed to Contact Precautions and experienced seven times more preventable adverse events.[42] However, a case-crossover study found no significant difference in adverse events when patients on Contact Precautions were compared to the same patients in an earlier time period when Contact Precautions were not used.[44] Other studies have reported significant associations

only between Contact Precautions and very specific subtypes of adverse events such as hyperglycemia.[43]

Past studies of the adverse effects associated with Contact Precautions have been limited by use of non-standard definitions of adverse events (for example, electrolyte imbalances or very specific subtypes of events).[42,43] Whether Contact Precautions are associated with the occurrence of any adverse events remains unresolved.

To investigate whether Contact Precautions are associated with the occurrence of adverse events, we conducted a prospective cohort study of patients on Contact Precautions matched to patients unexposed to Contact Precautions.

Methods

Study Design

The study was a prospective cohort of general medical and surgical patients recruited at the University of Maryland Medical Center, an academic tertiary care hospital. The patients in this study were initially recruited between January 2010 and November 2010 for a prospective study of the relationship between Contact Precautions and depression, anxiety, and patient satisfaction.[40,67] Patients on Contact Precautions were individually matched to patients unexposed to Contact Precautions by a minimum three-day hospital length of stay and by admission service (to limit bias related to patients on Contact Precautions having longer length of stay and more severe illness). Study participants on Contact Precautions remained on Contact Precautions for the duration of their hospital stay and patients unexposed to Contact Precautions also did not change Contact Precautions exposure status during the study period. This study was approved by the Institutional Review Board of the University of Maryland, Baltimore.

Measurements and Outcomes

Demographic data such as age, gender, education, minority status (Hispanic and/or non-white race) and marital status were collected at study enrollment, while Charlson comorbidity score and length of stay were obtained from the hospital central data repository. We defined adverse events as "unintended physical injury resulting from or contributed to by medical care that requires additional monitoring, treatment, or hospitalization or that results in death" as used by the Institute for Healthcare Improvement (IHI) Global Trigger Tool.[1] We did not consider events due to the patient's

underlying condition as adverse events. Adverse events were identified using the IHI Global Trigger Tool which is a standardized method for completion of structured medical record reviews within approximately 20 minutes.[1] The trigger tool detects more adverse events than approaches such as the Agency for Healthcare Research and Quality (AHRQ) Patient Safety Indicators or hospital reporting systems.[22,28] Three initial reviewers used the trigger tool to review the patient charts of all members of the cohort for adverse events. One initial reviewer (L.D.C.) reviewed the records of all 296 cohort members and two initial physician reviewers (M.L. and J.L.) each reviewed half (N=148) of the cohort. A final physician reviewer (D.J.M.) adjudicated any disagreements on adverse event occurrence between initial reviewers, per the IHI Global Trigger Tool method.[1] All reviewers received training on using the IHI Global Trigger Tool and practiced with standardized sample charts.[46] Reviewers determined whether each adverse event initially began before, during, or after the admission of interest. Analysis was restricted to adverse events which began during the index admission only as events that began prior to or after the admission may not be the result of exposure to Contact Precautions.

Our primary outcomes were noninfectious and infectious adverse event rates considered separately and the secondary study outcomes were preventable and severe noninfectious adverse events. Infectious adverse events were defined as infections that occurred in the hospital that were not present or incubating on admission while noninfectious adverse events that occurred in the hospital were all adverse events with infectious events excluded. We rated adverse event severity using a 5-point Likert scale (minimal, clinically significant, serious, life-threatening, fatal) using a severity index modified from the National Coordinating Council for Medication Error Reporting and

Prevention.[1,54] Adverse events that were serious (e.g., organ dysfunction), life-threatening (death possible within a few hours without intervention), or fatal were classified as severe events. Similarly, preventability was measured on a 4-point Likert scale (definitely, probably, probably not, or definitely not preventable) as has been used previously.[23,32,33] Preventability was determined based on whether the event was considered preventable by current knowledge, practice standards or technology.[33] Finally, adverse events were also categorized by the primary physiological system affected (cardiovascular, respiratory, renal or endocrine, hematologic, gastrointestinal, neurologic, hospital-acquired infection, and surgical).[23] Rates of adverse events were calculated as the number of a specific adverse event type divided by total person-time at risk (patient-specific hospital length of stay in days).

Statistical Analysis

Distribution of demographic variables, such as age or gender, by exposure to Contact Precautions was analyzed using t-tests for continuous variables and chi-square tests for categorical variables. An initial multivariable, scaled deviance Poisson regression model for noninfectious adverse events was constructed by including Contact Precautions exposure status and adjusting for the matching variable of admission service (grouped as oncology, general medicine, or surgery). More than one adverse event was allowed per patient. The model offset was the log of patient length of stay. An adjusted model was constructed by adding covariates one at a time to the initial model in order of the greatest magnitude change produced in the log rate ratio of the Contact Precautions estimate until no meaningful change (less than 10%) occurred with the addition of new

covariates. As no covariates meaningfully changed the coefficient, we included biologically plausible variables such as age and Charlson comorbidity score. Models of severe and preventable adverse events were constructed for noninfectious adverse events only. Model building for preventable noninfectious adverse events followed the same approach as for noninfectious adverse events. Due to few severe noninfectious adverse events, we constructed a model for severe adverse events adjusted only for matching. For each physiological system, counts of adverse events by Contact Precautions exposure status were recorded and bivariate analysis was conducted using chi-square or Fisher's exact test, as appropriate. All analyses were conducted using SAS version 9.3 (SAS Institute, Cary, NC).

Power Calculation

Applying a previously reported frequency of adverse events among general medical inpatients (25 adverse events per 100 admissions)[23] to the average length of stay among the current study's patients unexposed to Contact Precautions, the expected rate of adverse events among unexposed patients was 53.2 adverse events per 1000 patient-days. For a two-sided test and α=0.05, we had 84% power to detect an 80% increase in adverse event rate among patients on Contact Precautions compared to patients unexposed to Contact Precautions.

Results

Of the 296 patients in the cohort, 35.1% (104/296) experienced at least one adverse event (49 patients on Contact Precautions and 55 patients unexposed to Contact Precautions). There were 77.3 adverse events per 1000 patient-days within the entire cohort (62.8 events per 1000 patient-days among patients on Contact Precautions and 92.8 per 1000 patient-days among unexposed patients). Patients on Contact Precautions did not significantly differ from patients unexposed to Contact Precautions with respect to age, gender, Charlson comorbidity score (Table 7). However, patients on Contact Precautions were less likely to have at least some college education (37.8%) compared to patients unexposed to Contact Precautions (57.4%), $p<0.001$. In descriptive analysis, we observed a trend toward a fewer number of adverse events among patients on Contact Precautions for all physiological systems except respiratory, neurologic, and renal or endocrine (Table 8). We examined the trigger tool reviews of the thirteen patients with postoperative hemorrhage in depth as it event type driving a significant reduction in surgical adverse events among patients on Contact Precautions. There was an even distribution of patients experiencing postoperative hemorrhage by enrollment location (6 general medicine locations and 7 surgery or transplant locations). The majority of these adverse events were decreases in hemoglobin or hematocrit values during or immediately following surgery which required transfusion rather than harms caused during postoperative care.

Table 7. Demographic Characteristics for Patients on Contact Precautions vs. Patients Unexposed to Contact Precautions.

Characteristic	Contact Precautions Yes N=148	Contact Precautions No N=148	P
Age (years), mean ± SD	52.0 ±13.8	52.3 ± 14.6	0.87
Male	86 (53.4)	75 (46.6)	0.20
Education (some college)	56 (37.8)	85 (57.4)	0.001
Married or living with partner	57 (38.5)	74 (50.0)	0.05
Minority	82 (55.4)	62 (41.9)	0.02
Charlson comorbidity score ≥2	73 (49.3)	63 (42.6)	0.24
Admission to ICU during hospitalization	8 (5.4)	14 (9.5)	0.18
Prior hospital stay in past 30 days	50 (58.8)	35 (41.2)	0.05
Enrollment location			-
General medicine	96	96	
Surgery/Transplant	34	34	
Oncology	18	18	
Length of hospital stay (days), median (IQR)	4.7 (3.3-7.1)	5.5 (3.7-8.1)	0.16

NOTE. Data are no. (%) of patients, unless otherwise indicated. SD, standard deviation; IQR, interquartile range; ICU, intensive care unit.

Table 8. Frequency of Specific Adverse Events in Patients on Contact Precautions vs. Patients Unexposed to Contact Precautions[a]

Type of Adverse Event	Total Events	Contact Precautions		P [b]
		Yes N=148	No N=148	
Infectious adverse event	**16**	**6**	**10**	**0.30**
Central venous catheter-related bloodstream infection	3	2	1	
Ventilator-associated pneumonia	0	0	0	
Nosocomial pneumonia, not ventilator-related	1	1	0	
Urinary tract infection	3	0	3	
Surgical site infection	2	0	2	
Clostridium difficile colitis	5	3	2	
Other hospital-acquired infection [c]	2	0	2	
Cardiovascular system	**9**	**3**	**6**	**0.50[d]**
Cardiac arrest	0	0	0	
Hypotension	6	3	3	
Arrhythmias or conduction abnormality	3	0	3	
Myocardial ischemia/infarction	0	0	0	
Respiratory system	**8**	**4**	**4**	**1.00 [d]**
Acute respiratory failure	1	0	1	
Pneumothorax	2	2	0	
Atelectasis	1	0	1	
Aspiration	1	1	0	
Pulmonary embolus	0	0	0	
Need for reintubation	0	0	0	
Renal or endocrine system	**22**	**14**	**8**	**0.27**
Fluid overload	3	2	1	
Acute renal failure	5	3	2	
Metabolic acidosis	0	0	0	
Hyperglycemia	5	3	2	
Hypoglycemia	8	5	3	
Hyperkalemia	0	0	0	
Other renal or endocrine event [e]	1	1	0	
Hematologic system	**10**	**1**	**9**	**0.02**
Hemorrhage	2	0	2	
Thromboembolic venous event	2	0	2	
Hematoma	2	0	2	
Other hematologic event [f]	4	1	3	

Table 8. Frequency of Specific Adverse Events in Patients on Contact Precautions vs. Patients Unexposed to Contact Precautions[a] (continued)

Type of Adverse Event	Total Events	Contact Precautions		P [b]
		Yes N=148	No N=148	
Gastrointestinal system	**46**	**20**	**26**	**0.33**
Nausea or vomiting	39	17	22	
Diarrhea	3	2	1	
Constipation	3	3	3	
Pancreatitis	0	0	0	
Ileus	0	0	0	
Other gastrointestinal event [g]	1	1	0	
Neurologic system	**8**	**6**	**2**	**0.28 [d]**
Oversedation	6	6	0	
Delirium or encephalopathy	2	0	2	
Seizure	0	0	0	
Stroke or intracerebral hemorrhage	0	0	0	
Inadequate analgesia	0	0	0	
Surgical event	**19**	**3**	**16**	**0.002**
Postoperative hemorrhage	13	1	12	
Postoperative hematoma	1	1	0	
Laceration or other organ injury	1	0	1	
Vascular injury	0	0	0	
Surgical anastomosis failure	0	0	0	
Wound dehiscence	0	0	0	
Failed procedure	0	0	0	
Unplanned return to surgery	1	1	0	
Other event [h]	3	0	3	
Other types of harm	**24**	**11**	**13**	**0.67**
Allergic reaction	11	5	6	
Pyrexia	1	1	0	
Fall	1	1	0	
Pressure ulcer	2	1	1	
Rash	1	1	0	
Catheter complication	2	1	1	
Other [i]	6	1	5	
All noninfectious events [j]	**146**	**62**	**84**	**0.01**
Severe noninfectious events [j, k]	**47**	**20**	**27**	**0.27**
Preventable noninfectious events [j, l]	**78**	**37**	**41**	**0.60**

[a] 162 total adverse events occurred (68 among patients on Contact Precautions; 94 among patients unexposed to Contact Precautions)

[b] Pearson chi-square test unless otherwise indicated

[c] Other hospital-acquired infection events include: bronchitis; oral Candida albicans

[d] Fisher's exact test

[e] Other renal or endocrine events include: hyponatremia and hypovolemia due to diuresis

[f] Other hematologic events include: chemotherapy-induced thrombocytopenia; chemotherapy-related decrease in white blood cell count; thrombophlebitis from IV requiring vein excision; postoperative thrombophlebitis

[g] Other gastrointestinal events include: medication-related gastrointestinal upset

[h] Other surgical events include: postoperative itching and insomnia; intraoperative anesthesia-induced increases in transaminases and bilirubin; acute on chronic pancreatitis secondary to ERCP

[i] Other type events include: graft versus host disease and nausea/vomiting; medication-induced restless leg; chemotherapy related mucositis, nausea/vomiting, and acute renal failure; itching due to pain medication; itching at patch site

[j] Not included in total events count for the rest of the table as these events are not mutually exclusive of physiological system affected

[k] Severe events include: adverse events which are serious (organ dysfunction); life-threatening (death possible without therapy within a few hours); death

[l] Preventable events are adverse events considered probably or definitely preventable by current practice standards, knowledge, and/or technology

In unadjusted analyses, Contact Precautions were significantly associated with a lower rate of noninfectious adverse events (rate ratio [R_tR], 0.69; 95% confidence interval [CI], 0.51-0.94; p=0.02) and a lower rate of infectious adverse events (rate ratio [R_tR], 0.56; 95% confidence interval [CI], 0.34-0.94; p=0.03). There was a trend toward fewer severe noninfectious adverse events (R_tR, 0.69; 95% CI, 0.46-1.03; p=0.07). Unadjusted results did not differ when adjusted for matching. Adjusted for gender, prior hospitalization, and Charlson comorbidity score, there was a significant 30% relative reduction in rate of noninfectious adverse events with exposure to Contact Precautions (R_tR, 0.70; 95% CI, 0.51-0.95; p=0.02; Table 9). There was no significant association between Contact Precautions and preventable noninfectious adverse events (R_tR, 0.85; 95% CI, 0.59-1.24 p=0.41) after adjusting for gender and Charlson comorbidity score. Males were 27% less likely to experience an adverse event compared to females (R_tR, 0.73; 95% CI, 0.54-0.99).

Table 9. Adjusted Rates of Noninfectious Adverse Events Among Patients on Contact Precautions vs. Patients Unexposed to Contact Precautions.

Type of adverse event	R_tR (95% CI)	P
Noninfectious adverse events*		
Patients on Contact Precautions vs. unexposed to Contact Precautions	0.70 (0.51, 0.95)	0.02
Prior hospitalization in previous 30 days	1.22 (0.87, 1.70)	0.25
Charlson comorbidity score ≥2	1.04 (0.75, 1.45)	0.80
Male gender	0.73 (0.54, 0.99)	0.05
Preventable noninfectious adverse events*		
Patients on Contact Precautions vs. unexposed to Contact Precautions	0.85 (0.59, 1.24)	0.41
Male gender	0.67 (0.46, 0.98)	0.04
Charlson comorbidity score ≥2	0.89 (0.60, 1.33)	0.57

NOTE. *Adjusted for matching by unit of enrollment (surgery/transplant; oncology; general medicine). R_tR, rate ratio; CI, confidence interval.

Discussion

In our prospective cohort study, we found significantly fewer noninfectious adverse events for patients exposed to Contact Precautions compared to patients unexposed to Contact Precautions. Our findings should be interpreted relative to past studies. Stelfox and colleagues conducted a prospective cohort study of adverse events and Contact Precautions in general medicine and congestive heart failure patients.[42] They reported that patients on Contact Precautions experienced more than twice the rate of adverse events as patients unexposed to Contact Precautions and seven times the rate of preventable adverse events. However, that study used a non-standard definition of adverse events which included abnormal laboratory values without requirement for harm (the majority of adverse events observed by Stelfox et al. belonged to this adverse event subtype) and likely had confounding by inappropriate matching. We identified an opposite effect.

More recent studies found a smaller impact of Contact Precautions. A case-crossover study by Karki et al. compared patients on Contact Precautions for vancomycin-resistant enterococci to earlier time periods when each patient was not on Contact Precautions. They observed no increase in adverse events during the periods of Contact Precautions use (R_tR 1.04; p=0.70).[44] Another study using patients matched on admission diagnosis found no significant difference in the mean number of complications per patient when patients on Contact Precautions were compared to unexposed patients.[45] Similarly, the safety analysis for a cluster randomized trial of universal glove and gown use in intensive care units (universal use of Contact Precautions for all patient contact) found no significant association with adverse events, although there was a consistent

trend towards fewer adverse events with universal Contact Precautions.[46] This randomized trial used the same definition of adverse events and the same data collection tool, the IHI Global Trigger Tool, as in the current study.

This study has limitations. Chart reviews using the IHI Global Trigger Tool may fail to identify less severe adverse events. However, each patient chart was reviewed by two trained reviewers to help ensure all possible adverse events were identified. The IHI Global Trigger Tool has also been shown to identify more adverse events than other methods for measuring adverse events.[22,31] We had limited ability to control for severity of illness because measures such as the Acute Physiology and Chronic Health Evaluation tool were unavailable for these patients outside of the intensive care setting. However, we did match study participants on admission service, as well as using the Charlson score to control for comorbidities. Furthermore, residual confounding from severity of illness would be expected to inflate risk estimates of the association between Contact Precautions and adverse events rather than result in a lower rate of adverse events as was observed in this study since patients indicated for Contact Precautions are more severely ill[52] and more severely ill patients are more likely to experience adverse events.[19,21]

The observed effect of Contact Precautions was unexpected and in the opposite direction of our hypothesized increase in risk. It remains unclear why hematologic and surgical adverse events, as well as noninfectious adverse events overall, might be lower in those patients on Contact Precautions. Patients on Contact Precautions appear to consistently receive fewer healthcare personnel visits.[48,49] Fewer adverse events in this isolated group may reflect a protective effect from fewer healthcare personnel visits. Less healthcare personnel contact has been proposed to improve patient care and satisfaction.[68]

Alternatively, the cognitive process required for considering room entry with Contact Precautions may have prompted more thoughtful assessment of patient needs resulting in the observed reduction in noninfectious adverse events.

Our study is a sizeable matched cohort with 148 patients in each group and Contact Precautions exposure was known to precede occurrence of adverse events. Additionally, our study used a standard definition of adverse event[1] which aids in interpretation of our results and comparison with the existing literature. Finally, we identified adverse events using a standardized and validated data collection tool.[24,28,32]

Hospital ward patients on Contact Precautions for antibiotic resistant organisms were less likely to experience noninfectious adverse events than patients unexposed to Contact Precautions and do not experience significant changes in preventable or severe noninfectious adverse events. Concerns that use of Contact Precautions may result in adverse events should not limit their implementation.

VI. DISCUSSION

This dissertation involved two separate studies, one a cluster randomized trial and the other a prospective cohort, to investigate the association between Contact Precautions and the occurrence of hospital adverse events. For the cluster randomized trial, the exposure was universal use of Contact Precautions (i.e. universal glove and gown use for all patient contact), whereas in the cohort study Contact Precautions was used in a traditional sense for patients colonized with MDROs. The cluster randomized trial identified no difference in rate of adverse events with patient exposure to universal glove and gown use (a statistically non-significant trend toward fewer adverse events was noted in patients on universal gowning and gloving). The cohort study found a significant reduction in noninfectious adverse events with Contact Precautions exposure. These results are consistent and both reject the hypothesis that Contact Precautions lead to more adverse events.

A. Universal Glove and Gown Use (Universal Contact Precautions) is Not Associated With Rate of Adverse Events Among ICU Patients

No randomized studies have examined the effect of Contact Precautions or universal glove and gown use on the occurrence of adverse events among hospitalized adult patients. Given that patients normally placed on Contact Precautions for antibiotic resistant organisms have a greater severity of illness and severity of illness is itself associated with adverse event occurrence, many previous observational studies of Contact Precautions and adverse events may have been confounded by this non-random

exposure to Contact Precautions. Conversely, in our study, we examined the effect of random allocation of universal glove and gown use at the ICU level on rate of patient adverse events. To isolate the effect of Contact Precautions, we only included patients not indicated for Contact Precautions use due to colonization or infection with antibiotic resistant organisms.

In this study, we observed that almost one-quarter (24.8%) of all ICU patients experienced at least one adverse event that began in the ICU. However, when the frequency of adverse events was compared based on exposure to universal glove and gown use, patients exposed to universal gloving and gowning had no difference in rate of noninfectious adverse events (IRR 0.91; 95% CI, 0.59-1.42; p=0.68). Similarly, the rates of infectious adverse events and preventable or severe noninfectious adverse events did not differ between patients in universal glove and gown use ICUs and control ICUs. While not statistically significant, there was a consistent pattern of lower rates of adverse events among patients in universal glove and gown ICUs. These results suggest that ICU patients exposed to universal glove and gown use are not at an increased risk of experiencing adverse events during their hospital stay and universal glove and gown use should not be avoided due to concerns of patient harm. While universal gloving and gowning has different effects on hospital flow from traditional use of Contact Precautions, and as a result, is not an identical exposure, these findings might be relevant considerations for the traditional use of Contact Precautions among ICU patients as well.

B. Contact Precautions are Associated With Significantly Lower Rate of Adverse Events Among Hospital Ward Patients

Current evidence on the association between Contact Precautions and adverse events is mixed, with some authors reporting large increases in adverse events with exposure to Contact Precautions and other authors finding no association. In part, these different conclusions may be attributed to methodologic issues and use of non-standard measures and definitions of adverse events. We conducted a prospective cohort study of 296 patients at the University of Maryland Medical Center to determine whether hospital ward patients exposed to Contact Precautions experience a higher rate of adverse events compared to unexposed patients. Our study found a 30% significant reduction in noninfectious adverse event rate among patients on Contact Precautions compared to patients unexposed to Contact Precautions (IRR, 0.70; 95% CI, 0.51-0.95; p=0.02). However, there was no significant difference in the rate of preventable or severe noninfectious adverse events for patients exposed to Contact Precautions.

This second study also indicates Contact Precautions do not increase the risk of adverse events, so concerns regarding adverse events should not limit the implementation of Contact Precautions. Surprisingly, a decrease in noninfectious adverse events was observed with use of Contact Precautions. However, we conducted a conservative sensitivity analysis limiting each patient to only one adverse event and, while the reduction was no longer statistically significant due to the decrease in an already limited number of events, we observed a consistent result of fewer adverse events among patients on Contact Precautions. The subtypes of adverse events that were less common in patients on Contact Precautions were postoperative bleeding and hematologic events and

were considered non-preventable. There is no obvious reason why Contact Precautions would lead to fewer of these events.

C. National Level Changes Which Could Have Affected Study Results

Our findings that adverse event rate does not increase with Contact Precautions use were unexpected. It is possible that there were other concurrent changes in national patient safety policies or in the epidemiology of pathogens that commonly cause infectious adverse events and that these time effects contribute to the observed differences between early adverse event studies and more recent literature, including our studies. For example, in the past decade, there has been a substantial shift in the epidemiology of methicillin-resistant Staphylococcus aureus infection. Initially, MRSA was almost solely a hospital-acquired infection but now many infections with MRSA are community-acquired,[69] which is a generally healthier population than hospital patients. As MRSA is one of the primary organisms patients are indicated for Contact Precautions for in the United States, this shift in patients exposed to Contact Precautions could be meaningful. If patients on Contact Precautions for community-acquired MRSA are healthier than the hospital patient population indicated for Contact Precautions and severity of illness is associated with higher risk of adverse events,[16,17,21] it is possible that confounding by indication present in older studies is less of an issue in more recent studies. This is one potential explanation for our finding of no (or decreased) association of Contact Precautions with adverse events compared with older literature.

In addition, policies at the national level that were targeted at decreasing specific types of adverse events may have affected the frequency of adverse event occurrence as

well as the associations observed in our studies with Contact Precautions compared to studies conducted in the early 2000's. For example, the CDC, Joint Commission, and AHRQ have all recommended the use of care checklists for prevention of central line-associated bloodstream infections.[70-72] However, the use of checklists to prevent this type of infection began in the mid-2000's[73] and only recently became more widespread in use.[72] Compliance with hand hygiene was also a continuing focus of the Joint Commission over these time periods.[74] Also over this period of time, there was an increasing awareness of the role that environment plays in the transmission of antibiotic resistant organisms in the hospital setting[75-77] and that improved environmental cleaning practices potentially decrease rates of hospital-acquired infections.[78] Further, the practice of chlorhexidine bathing[79,80] was introduced and became widely adopted in recent years.

All of these national level interventions and policies were targeted at decreasing transmission of antibiotic resistant organisms, as Contact Precautions are also intended to do. It is possible that these approaches for decreasing infectious adverse events and similar policy changes for other adverse event types impacted the frequency of adverse events, contributing to the differences observed between our studies and older work. However, these changes occurred on a national level and were not targeted specifically to patients on Contact Precautions. Thus, a differential effect in decreasing adverse event occurrence among only patients exposed to Contact Precautions would not be expected but would be necessary to observe the results our studies report. Further, all of these interventions were designed to reduce adverse events but our unadjusted adverse event rates were higher than those reported in the 2003 Stelfox study.[42] This higher event rate is likely due to the higher sensitivity of the trigger tool in detecting adverse events than

other methods[22,28] and is similar to rates previously reported by Landrigan and colleagues using the IHI Global Trigger Tool.[23] Finally, studies of adverse events suggest no change in rates between the early time period of prior studies and 2010 (the time period patients in our second study were assessed for adverse events).[23] Therefore, it is unlikely that national level period effects explain our findings of no increase in adverse events and Contact Precautions use.

D. Potential Reasons for No Increase in Adverse Events with Contact Precautions (and Possibly Fewer Adverse Events)

As previously stated, our finding of no increase in the rate of adverse events with universal gloving and gowning or traditional Contact Precautions was unexpected. While in the study of universal glove and gown use there was no significant reduction in overall rate of noninfectious adverse events, there were significantly fewer cardiovascular events (primarily hypotension and arrhythmias or conduction abnormalities), surgical events, respiratory events, and severe noninfectious events among patients in universal glove and gown use ICUs. Within the cohort study of floor patients, significantly fewer noninfectious adverse events occurred among patients on Contact Precautions. By subtype, there were significantly fewer hematologic and surgical events (primarily postoperative hemorrhage), although there were small numbers of hematologic events. Notably, within both studies there were significantly fewer surgical noninfectious adverse events with exposure to either universal glove and gown use or traditional Contact Precautions than among unexposed patients. It is not readily apparent what mechanism

could plausibly result in a significant reduction of surgical events with universal glove and gown or Contact Precautions use.

However, with respect to the other types of adverse events, the finding that Contact Precautions do not increase the rate of adverse events might be explained by how Contact Precautions use modifies healthcare worker behavior rather than by glove and gown use itself. As has been previously reported, the cluster randomized study from which the data for the first aim of this dissertation was obtained, observed a significant reduction in frequency of healthcare worker visits (a decrease of approximately one visit per hour) among patients in ICUs randomized to universal glove and gown use.[46] Similarly, in a study including patients at the University of Maryland Medical Center, there were significantly fewer healthcare worker visits and shorter contact time each hour among patients on Contact Precautions.[49]

It is possible that our primary results of either no increase or a significant reduction in noninfectious adverse events with Contact Precautions use may be explained by this decrease in visits from healthcare personnel. Both of our studies and the trigger tool instrument itself[1] were designed to measure errors of commission; that is, active harms from delivered care rather than harm due to care that should have been delivered and was not. Fewer visits from healthcare workers may translate into fewer interventions, overmedication, or unnecessary tests for patients on Contact Precautions and thus fewer encounters where patients are at risk of an active harm. Less healthcare worker contact has been proposed to improve patient care and satisfaction.[68]

Conversely, while fewer visits to patients on Contact Precautions may have either no effect or significantly decrease the risk of harm due to errors of commission, a

decrease in visits from healthcare personnel may increase the risk of events due to errors of omission (care a patient should have received but did not). For example, much of the increase in adverse events reported by Stelfox et al. were pressure ulcers,[42] which is more an indication of repeated failure to change a patient's positioning than an actively caused harm. Similarly, Karki and colleagues reported no increase in overall adverse events for periods of Contact Precautions exposure compared to earlier unexposed time periods.[44] However, they did observe a more than three times increase in rate of injuries from falls or self-harm during periods of Contact Precautions exposure. Finally, a study of adverse events among ICU patients found an increase in only hypo- and hyper-glycemic adverse events among patients on Contact Precautions, which could be related to less frequent care and monitoring, but the authors did not observe increases in other types of adverse events (i.e., harms due to errors of commission).[43]

Aside from Contact Precautions exposure resulting in fewer visits from healthcare workers, which may decrease the risk of harms due to errors of commission, our findings of no increase or fewer noninfectious adverse events may be driven by another unknown effect of gown and glove use on healthcare worker behavior.

E. Strengths and Limitations

1. Limitations

In Aim 1 examining the effect of universal glove and gown use on rate of adverse events, the study was powered to detect a significant increase in rate of adverse events and not a statistically significant decrease. However, the inability to determine whether

universal glove and gown use is associated with fewer adverse events in the absence of a plausible mechanism for its reduction of surgical adverse events, may not be as important as not observing an increase in adverse events. Further, the key question surrounding current policy debates is whether gown and glove use significantly increases risk of adverse events. Our study is able to address this clinically relevant question and found no increase in adverse event rate with universal glove and gown use. Also, by chance, slightly fewer surgical intensive care units were randomized to universal glove and gown use than control which could have impacted the lower number of surgical events reported among patients exposed to universal glove and gown use. However, the prospective cohort matched patients based on enrollment location (including surgery or transplant service). After this matching and an adjusted analysis which accounted for the enrollment location, the cohort study still found a significant reduction in surgical events with Contact Precautions exposure. This consistency with the results of the prospective cohort lends credence to the result of the universal glove and gown study.

In both of our studies, there is the potential for differences in how initial reviewers identified adverse events, however all reviewers received standardized training and feedback on practice medical records and were blinded to use of contact precautions. Also, the final determination in adverse event occurrence was made by the same physician reviewer and only adverse events confirmed in final review were used for analysis. If misclassification of events did occur, it was likely to be nondifferential in nature since final reviewers in the study of universal glove and gown use were blinded to exposure status of patients and this also would not explain a significant reduction in rate of adverse events in the second study, contrary to our hypothesis of increased risk. In

addition, within the prospective cohort study, inter-reviewer agreement between initial reviewers was high (reviewer 1-reviewer 2 agreement: 74.3%; reviewer 1-reviewer 3 agreement: 75%).

As discussed in the manuscripts above, there is the possibility of nondifferential underreporting of less severe adverse events as the IHI Global Trigger Tool is not designed to detect every event and it is possible that not all adverse events were recorded in a patient's medical record. However, the IHI Global Trigger Tool is still the current gold standard for event detection, as the tool detects more adverse events than other approaches, such as the AHRQ Patient Safety Indicators or hospital reporting systems.[22,31]

Finally, in the prospective cohort study, there was a limited ability to control for severity of illness of patients as most severity of illness measures such as the Acute Physiology and Chronic Health Evaluation tool are unavailable for patients outside of the intensive care setting. While they are imperfect surrogates for severity of illness, patients were matched on ward location and adjusted for both location the patient was enrolled on and Charlson comorbidity score. Further, residual confounding from severity of illness would be expected to introduce an increase in rate of adverse events and would not explain the significant reduction in noninfectious adverse events identified in the study.

2. Strengths

Beyond the limitations just discussed, our studies have several strengths. To our knowledge, the study of universal glove and gown use is one of the largest studies of adverse events and gown and glove use to-date. The study also observed significantly fewer healthcare worker visits[46] which is consistent with prior literature.[48,49,51] This

reproduction of prior findings for associations with Contact Precautions adds to our confidence that our findings of no increased risk of noninfectious adverse events are real and not an artifact of the study population or design.

A key strength of the universal glove and gown study is that patients indicated for Contact Precautions (patients with antibiotic resistant organisms) were excluded from both arms of the study to better examine the effect of universal glove and gown use on adverse event occurrence, separate from the effect of severity of illness which is interlinked with colonization or infection with antibiotic resistant organisms. Further addressing this issue, the exposure of universal glove and gown use was randomized and within the larger study, a random sample of patients were selected for review for adverse events at each site, further limiting the effect that selecting patients based on individual characteristics would have had. An additional strength of excluding patients indicated for Contact Precautions from both arms of the study was that this permitted blinding of the final physician reviewers so that adverse event determination occurred while masked to universal glove and gown exposure status.

More generally, both of our studies employed a standard definition of adverse event which aids in evaluating our work in the context of prior studies as well as the relevance of the types of adverse events measured. This definition also permitted the examination of a wider range of adverse events of concern, unlike prior studies which selected small subsets of event types such as hypoglycemia and hemorrhage,[43] which may not be representative of the full effect (or lack of effect) of Contact Precautions on adverse event occurrence. Moreover, both of our studies of adverse events utilized a

standardized and validated measurement tool rather than relying on subjective reviews and definitions encountered with the traditional, unstructured chart review.

F. Contribution of Current Work to Ongoing Debate over the Use of Contact Precautions

Currently within the field of hospital epidemiology and infection control, a debate is occurring over the role for Contact Precautions in infection prevention, especially over whether it should be implemented for endemic MRSA and VRE. This ongoing policy discussion affects a large number of hospital patients. The most basic detection and implementation effort for MRSA or VRE results in 5-10% of patients being placed onto Contact Precautions and that increases to 20-25% of inpatients when more expansive active surveillance methods are followed.[81] Despite the large numbers of inpatients placed onto Contact Precautions, there is limited evidence that even universal glove and gown use, a "maximum" type of Contact Precautions,[81] successfully prevents transmission of VRE, with only slightly more evidence for MRSA.[46,82]

In addition, some have begun arguing for replacing Contact Precautions for MRSA and VRE with other infection control methods and focusing on other horizontal prevention approaches, such as improving hand hygiene.[83] Others argue for restricting Contact Precautions to certain limited situations.[81,84] This argument has been augmented by reports of Contact Precautions for MRSA and VRE being discontinued without any subsequent increase in rates of these organisms.[47,83] Currently, more than 30 major US hospitals do not use Contact Precautions for endemic MRSA or VRE[81,85] and this decision

is partly attributed to concerns about increases in the risk of adverse events influencing the risk-benefit assessment of Contact Precautions use.[81,84,85]

The results of both of our studies, that Contact Precautions and universal glove and gown use do not increase adverse event rates, are important findings for informing accurate assessments of the risk-benefit comparison when deciding Contact Precautions policy. It is unclear in our prospective cohort study whether there are truly significantly fewer adverse events with Contact Precautions exposure since a plausible mechanism for this finding has not yet been identified. However, both of our studies provide consistent results with respect to no increased risk of adverse events with traditional or universal Contact Precautions use. Prior to questions of increased risk of physical injury with Contact Precautions, concern focused on the psychological impacts of Contact Precautions, specifically whether exposure to gowning and gloving resulted in depression and anxiety among isolated patients.[36,38] Recently, a prospective cohort study using the same cohort as Aim 2 of this study, established that while patients on Contact Precautions are admitted with more depression and anxiety, exposed patients did not develop depression or anxiety during hospitalization any more often than patients unexposed to Contact Precautions.[40] Similarly, our studies use sound methodology and clearly establish that Contact Precautions (or universal glove and gown use) are not associated with an increase in adverse events.

Additional concerns about the effects of Contact Precautions still exist. These concerns range from the effect Contact Precautions have on hospital flow by increasing time to bed assignment,[63-64] time to receive computer-aided tomography scans,[86] and time to discharge to an extended care facility[87] to negative impacts on patient satisfaction with

care.[67] These concerns are part of the ongoing Contact Precautions policy discussion. However, the findings of the studies included in this dissertation consistently found that Contact Precautions are not associated with increased risk of adverse events. These results should limit future concerns about adverse events as the debate surrounding Contact Precautions continues.

VII. APPENDIX 1: MODIFIED IHI GLOBAL TRIGGER TOOL DATA COLLECTION TOOL

DATE OF REVIEW: ____/____/_____ SUBJECT ID # (from UM) _____

Instructions for reviewer:

1. Briefly review chart with aid such as discharge summary—provide patient summary without any patient identifiers (MRN, name, date).
2. Look for each trigger using the discharge summary, MAR, order sheet, laboratory system and progress notes as necessary. If trigger is present, in Table 1 place a **+** mark next to trigger and record the date the trigger occurred.
3. For each trigger, describe the trigger in Table 2 below.

Patient Summary: (Please provide a brief summary of the admission)

The guide below is an example to highlight specific information that would be helpful to include in your summary:

(XX) yo patient admitted to (ward/ICU) for (admitting diagnosis). Was treated with (include any key therapies). Remained inpatient for (XX) days. Hospital days (X-XX) were spent in the study ICU. Was transferred to the ICU for (include reason). Was discharged after management of (give all issues addressed during ICU stay and during hospitalization). Had the following possible complications of therapy: _____

How aggressively was this patient managed? *_____1 -10 (1= very conservative, hospice or equivalent, 5=guideline based care but nothing extra, 10 very aggressive, experimental type therapy)*

Did any AEs result from possibly unnecessary care? *____Y/N (if Y, which AEs and unnecessary care?):*

Did any AEs result from lack of possibly necessary care? *____Y/N:*

VII. APPENDIX 1: MODIFIED IHI GLOBAL TRIGGER TOOL DATA COLLECTION TOOL (CONTINUED)

DATE OF REVIEW: ____ / ____ / ____ SUBJECT ID # (from UM) _____

Table 1: Worksheet of trigger tools for identifying adverse events (adapted from IHI Global Trigger Tool)

Cares Module Triggers		**+**	**Date**
C1	Transfusion or use of blood products		
C2	Any code or arrest		
C3	*New* need for dialysis		
C4	Positive blood culture		
C5	US or CT for PE/DVT		
C6	Drop >25% in Hb or HCT		
C7	Patient Fall (Head CT)		
C8	Pressure ulcers		
C9	Readmission within 30 days		
C10	Restraint use		
C11	Healthcare-associated infection of any kind		
C12	In-hospital stroke		
C13	Any procedure complication		
C14	Other		
Medication Module Triggers		**+**	**Date**
M1	*(removed)*		
M2	Partial thromboplastin time (PTT) >100 seconds		
M3	Internationalized normalized ratio (INR) >5		
M4	Glucose <50 mg/dl		
M5	Rising BUN or serum creatinine >2x baseline		
M6	Vitamin K administration*		
M7	Diphenhydramine use*		
M8	Flumazenil use*		
M9	Narcan (naloxone) use*		
M10	Anti-emetic use*		
M11	Over-sedation/ hypotension		
M12	Abrupt medication stop*		
M13	Other		

Surgical Module Triggers		**+**	**Date**
NOTE: Did a surgical procedure occur? (if NO, stop)			
S1	Return to Surgery		
S2	Change in procedure		
S3	Unexpected admission to ICU post-operatively		
S4	Intubation, re-intubaiton or use of BiPap in PACU*		
S5	X-ray intraop or in PACU*		
S6	Intra-op or post-op death		
S7	Mechanical ventilation >24 h post-op		
S8	Intra-op epinephrine, norepinephrine, naloxone, romazicon		
S9	Post-op troponin elevation		
S10	Change of anesthetic during surgery*		
S11	Consult requested in PACU*		
S12	Pathology report normal or unrelated to diagnosis*		
S13	Insertion of arterial or central venous line during surgery*		
S12	Operative time >6 hours		
S14	Removal/injury or repair of organ		
S15	Any operative complication		
Intensive Care Module Triggers		**+**	**Date**
I1	Pneumonia starting in the ICU		
I2	Readmission to ICU		
I3	In-unit procedure		
I4	Intubation/reintubation		

*look for these triggers last, if time remains

VII. APPENDIX 1: MODIFIED IHI GLOBAL TRIGGER TOOL DATA COLLECTION TOOL (CONTINUED)

NOTE—for triggers without injury due to care (Column A) only need to complete column F. (leave shaded sections blank unless mark "yes" in column A)

TABLE 2

Trigger	**A**	**C**	**D**	**E**	**F**	**G**	**H**
From Table 1	***Injury due to care***	***Preventability***	***Severity****	***Confidence AE occurred***	***Description of event (use additional page if necessary)***	***Consequence for patient***	***When event started***
example: C1	Yes or No (*if No, only complete description of event*)	1 - Definitely 2 - Probably 3 - Probably not 4 - Definitely not	1 - Death 2 - Life threatening 3 - Serious 4 - Significant 5 - Minimal	(≥ 4 required for AE)	Include diagnosis: meds (own or hosp), surgery, tests, etc. Was there any way to prevent this event from occurring (e.g., closer monitoring, patient/staff education, team training, IT intervention)?	1 - Death 2 - Permanent 3 - Temporary 4 - Prolonged 5 - Limited	0 – prior to admit 1 – during admission 2-after admission
	☐ Yes ☐ No	☐ 1 ☐ 2 ☐ 3 ☐ 4	☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5	☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6		☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5	☐ 0 ☐ 1 ☐ 2
	☐ Yes ☐ No	☐ 1 ☐ 2 ☐ 3 ☐ 4	☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5	☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6		☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5	☐ 0 ☐ 1 ☐ 2 ☐ 3
	☐ Yes ☐ No	☐ 1 ☐ 2 ☐ 3 ☐ 4	☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5	☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6		☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5	☐ 0 ☐ 1 ☐ 2 ☐ 3
	☐ Yes ☐ No	☐ 1 ☐ 2 ☐ 3 ☐ 4	☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5	☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6		☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5	☐ 0 ☐ 1 ☐ 2 ☐ 3
	☐ Yes ☐ No	☐ 1 ☐ 2 ☐ 3 ☐ 4	☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5	☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6		☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5	☐ 0 ☐ 1 ☐ 2 ☐ 3

***Severity coding**	**1 = Death**	**2 = Life Threatening**	**3 = Serious**	**4 = Clinically Significant**	**5 = Minimal or Trivial**
Description	Death	(death possible without therapy in few hours—e.g intubation, pressor medications)	(organ dysfunction like delirium, PE, MI, CVA)	(usually symptoms or lab abnormalities. Panic lab values or Common Toxicity Criteria)	Minimal or trivial

VIII. APPENDIX II: LIST OF SPECIFIC ADVERSE EVENT CATEGORIES

Cardiovascular system
Cardiac arrest
Hypotension
Hypertension
Shock
Arrhythmias or conduction abnormality
Myocardial ischemia
Other cardiovascular event

Respiratory system
Acute respiratory failure
Respiratory distress, not acute failure
Pneumothorax
Atelectasis
Bronchospasm
Aspiration
Pulmonary embolus
Need for re-intubation
Other respiratory event

Renal or endocrine system
Fluid overload
Dehydration or oliguria
Acute renal failure
Metabolic acidosis
Hyperglycemia
Hypoglycemia
Hyperkalemia
Other renal or endocrine event

Hematologic system
Hemorrhage
Thromboembolic venous event
Hematoma
Other hematologic event

Gastrointestinal system
Nausea or vomiting
Diarrhea
Constipation
Gastric distension
Pancreatitis
Ileus
Other gastrointestinal event

Neurologic system
Oversedation
Delirium or encephalopathy
Seizure
Stroke or intracerebral hemorrhage
Inadequate analgesia
Withdrawal symptoms
Other neurologic event

Hospital-acquired infection
Catheter-related bloodstream infection
Sepsis or bacteremia unrelated to catheter
Ventilator-associated pneumonia
Nosocomial pneumonia, not ventilator-related
Urinary tract infection
Surgical-site infection
Endometritis
Clostridium difficile colitis
Other hospital-acquired infection

Surgical event
Postoperative hemorrhage
Postoperative hematoma
Laceration or other organ injury
Unplanned removal of organ after intraoperative injury
Vascular injury
Nerve injury
Surgical anastomosis failure
Wound dehiscence
Failed procedure
Unplanned return to surgery
Other surgical event

Other types of harm
Hypothermia
Pyrexia
Alcohol or drug withdrawal
Allergic reaction
Fall
Pressure ulcer
Rash
Catheter complication

IX. APPENDIX III: ADMISSION SERVICES OF PATIENTS FOR AIM 2

CANCER CENTER-BMT
CANCER CNTR ONCOLOG
CARDIAC SURGERY
CARDIOLOGY
DAS HOSPITALIST
FAMILY MEDICINE
GENERAL SURGERY
GENERL INTERNAL MED
HOSPITALIST SERVICE
MED
MEDICAL SUBSPECIAL
MEDICINE TRANSPLANT
NEPHROLOGY
NEUROLOGY
NEUROSURGERY
OBSTETRICS
ORGAN TRANSPLANT
ORTHOPEDIC
SHOCK TRAUM-TEAM A
SHOCK TRAUMA-TEAM B
SHOCK TRAUMA-TEAM C
SOFT TISSUE STC
SURGICAL ONCOLOGY
THORACIC SURGERY
VASCULAR
VIROLOGY

X. GLOSSARY

Adverse event (adverse safety event): unintended physical injury resulting from or contributed to by medical or surgical care and not due to a patient's underlying condition

Adverse drug event: subtype of adverse event resulting from medical intervention with a medication

Death: subtype of severe adverse event which results in (or contributes to) patient death

Infectious adverse event: subtype of adverse event that is a hospital-acquired infection (an infection that occurs in the hospital setting but that was not present or incubating on admission)

Life-threatening adverse event: subtype of severe adverse event which could result in death within a few hours without treatment

Preventable adverse event: subtype of adverse event that is considered probably or definitely preventable by current practice standards, technology, and knowledge

Preventable adverse drug event: subtype of adverse drug event which is considered probably or definitely preventable by current practice standards, technology, and knowledge

Serious adverse event: subtype of severe adverse event which results in organ dysfunction (e.g. delirium, pulmonary embolism, myocardial infarction)

Severe adverse event: subtype of adverse event which results in death, life-threatening, or serious harm to the patient

XI. REFERENCES

1. Griffin F, Resar R. Institute for Healthcare Improvement. IHI global trigger tool for measuring adverse events. Institute for Healthcare Improvement Innovation Series White Paper, 2009. http://www.ihi.org/knowledge/pages/IHIWhitePapers/IHIGlobalTriggerToolWhitePaper.aspx. Accessed March 2014.

2. Szekendi MK, Sullivan C, Bobb A, Feinglass J, Rooney D, Barnard C, Noskin GA. Active surveillance using electronic triggers to detect adverse events in hospitalized patients. *Qual Saf Health Care,* 2006;15(3):184-190.

3. Kirkendall ES, Kloppenborg E, Papp J, et al. Measuring adverse events and levels of harm in pediatric inpatients with the Global Trigger Tool. *Pediatrics*, 2012;130(5):e1206-e1214. doi: 10.1542/peds.2012-0179

4. Giraud T, Dhainaut JF, Vaxelaire JF, et al. Iatrogenic complications in adult intensive care units: a prospective two-center study. *Crit Care Med*, 1993;21(1):40-51.

5. Brennan TA, Leape LL, Laird NM, et al. Incidence of adverse events and negligence in hospitalized patients. Results of the Harvard Medical Practice Study I. *N Engl J Med*, 1991;324(6):370-376.

6. Kohn LT, Corrigan JM, Donaldson MS, eds.; Committee on Quality of Health Care in America, Institute of Medicine. To err is human: building a safer health system. *Washington DC: National Academy Press, 2000*; Available at: www.iom.edu/Reports/1999/to-err-is-human-building-a-safer-health-system.aspx. Accessed March 2014.

7. McDonald CJ, Weiner M, Hui SL.. Deaths due to medical errors are exaggerated in Institute of Medicine report. *JAMA*, 2000;284(1):93-95.

8. Leape LL. Institute of Medicine medical error figures are not exaggerated. *JAMA*, 2000;284(1):95-97.

9. Sox CH, Woloshin S. How many deaths are due to medical error? Getting the number right. *Effective clinical practice*, 2000;3(6):277-283.

10. Forster AJ, Worthington JR, Hawken S, Bourke M, Rubens F, Shojania K, van Walraven C. Using prospective clinical surveillance to identify adverse events in hospital. *BMJ Qual Saf*, 2011;20(9):756-763.

11. de Vries EN, Ramrattan MA, Smorenburg SM, Gouma DJ, Boermeester MA. The incidence and nature of in-hospital adverse events: a systematic review. *Qual Saf Health Care*, 2008;17(3):216-223. doi:10.1136/qshc.2007.023622

12. Long SJ, Brown KF, Ames D, Vincent C. What is known about adverse events in older medical hospital inpatients? A systematic review of the literature. *Int J Qual Health Care*, 2013;25(5):542-554. doi: 10.1093/intqhc/mzt056.

13. Levinson DR. Adverse events in hospitals: National incidence among Medicare beneficiaries. OEI-06-09-00090, 2010. Available at: https://oig.hhs.gov/oei/reports/oei-06-09-00090.pdf.

14. Goodman JC, Villarreal P, Jones, B. The social cost of adverse medical events, and what we can do about it. *Health Aff*, 2011; 30(4):590-5. doi: 10.1377/hlthaff.2010.1256.

15. Tsang C, Bottle A, Majeed A, Aylin P. Adverse events recorded in English primary care: observational study using the General Practice Research Database. *Br J Gen Pract*, 2013;63(613):e534-e542. doi: 10.3399/bjgp13X670660.

16. Beckmann U, Bohringer C, Carless R, et al. Evaluation of two methods for quality improvement in intensive care: facilitated incident monitoring and retrospective medical chart review. *Crit Care Med*, 2003;31(4):1006-1011. doi: 10.1097/01.CCM.0000060016.21525.3C.

17. Rubins HB, Moskowitz MA. Complications of care in a medical intensive care unit. *J Gen Intern Med*, 1990;5(2):104-109.

18. Kopp BJ, Erstad BL, Allen ME, Theodorou AA, Priestley G. Medication errors and adverse drug events in an intensive care unit: direct observation approach for detection. *Crit Care Med*, 2006;34(2):415-425. doi: 10.1097/01.CCM.0000198106.54306.D7.

19. Dequito A, Mol PGM, van Doormaal JE, et al. Preventable and non-preventable adverse drug events in hospitalized patients: a prospective chart review in the Netherlands. *Drug saf*, 2011;34(11):1089-1100.

20. Classen DC, Pestotnik SL, Evans RS, Lloyd JF, Burke JP. Adverse drug events in hospitalized patients. Excess length of stay, extra costs, and attributable mortality. *JAMA*, 1997;277(4):301-306.

21. Baines RJ, Langelaan M, de Bruijne MC, et al. Changes in adverse event rates in hospitals over time: a longitudinal retrospective patient record review study. *BMJ Qual Saf* 2013;22(4):290-298.

22. Classen DC, Resar R, Griffin F, Federico F, et al. 'Global trigger tool' shows that adverse events in hospitals may be ten times greater than previously measured. *Health Aff* 2011;30(4):581-589.

23. Landrigan C, Parry G, Bones C, Hackbarth A, Goldmann D, Sharek P. Temporal trends in rates of patient harm resulting from medical care. *N Engl J Med* 2010;363(22):2124-2134.

24. Classen DC, Lloyd RC, Provost L, Griffin FA, Resar R. Development and evaluation of the Institute for Healthcare Improvement global trigger tool. *J Patient Saf* 2008;4(3):169-177.

25. Sharek P, Horbar J, Mason W, et al. Adverse events in the neonatal intensive care unit: development, testing, and findings of an NICU-focused trigger tool to identify harm in North American NICUs. *Pediatrics*, 2006;118(4):1332-1340.

26. Good V, Saldana M, Gilder R, Nicewander D, Kennerly D. Large-scale deployment of the Global Trigger Tool across a large hospital system: refinements for the characterisation of adverse events to support patient safety learning opportunities. *BMJ Qual Saf*, 2011;20(1):25-30.

27. Resar R, Rozich JD, Simmonds T, Haraden CR. A trigger tool to identify adverse events in the intensive care unit. *J Qual Patient Saf*, 2006;32(10):585-590.

28. Naessens JM, O'Byrne TJ, Johnson MG, Vansuch MB, McGlone CM, Huddleston JM. Measuring hospital adverse events: Assessing inter-rater reliability and trigger performance of the global trigger tool. *Int J Qual Health Care* 2010;22(4): 266-74. doi: 10.1093/intqhc/mzq026.

29. Unbeck M, Schildmeijer K, Henriksson P, et al. Is detection of adverse events affected by record review methodology? An evaluation of the "Harvard Medical Practice Study" method and the "Global Trigger Tool". *Pat Saf Surg* 2013;7(1):10-10.

30. Jha AK, Kuperman GJ, Teich JM, et al. Identifying adverse drug events: development of a computer-based monitor and comparison with chart review and stimulated voluntary report. *J Am Med Inform Assoc*, 1998;5(3):305-314. doi: 10.1136/jamia.1998.0050305.

31. Naessens J, Campbell C, Huddleston J, et al. A comparison of hospital adverse events identified by three widely used detection methods. *Int J Qual Health Care* 2009;21(4):301-307. doi: 10.1093/intqhc/mzp027.

32. Sharek PJ, Parry G, Goldmann D, et al. Performance characteristics of a methodology to quantify adverse events over time in hospitalized patients. *Health Serv Res 2011*;46(2): 654-78. doi: 10.1111/j.1475-6773.2010.01156.x.

33. Rothschild J, Landrigan C, Cronin J, et al. The Critical Care Safety Study: The incidence and nature of adverse events and serious medical errors in intensive care. *Crit Care Med*, 2005;33(8):1694-1700.

34. Cullen DJ, Sweitzer BJ, Bates DW, Burdick E, Edmondson A, Leape LL. Preventable adverse drug events in hospitalized patients: a comparative study of intensive care and general care units. *Crit Care Med*, 1997;25(8):1289-1297.

35. Siegel J, Rhinehart E, Jackson M, Chiarello L; Health Care Infection Control Practices Committee. 2007 guideline for isolation precautions: preventing transmission of infectious agents in health care settings. *Am J Infect Control*, 2007;35(10 Suppl 2):S65-164.

36. Gammon J. The psychological consequences of source isolation: a review of the literature. *J Clin Nurs*, 1999;8(1):13-21.

37. Tarzi S, Kennedy P, Stone S, Evans M. Methicillin-resistant staphylococcus aureus: Psychological impact of hospitalization and isolation in an older adult population. *J Hosp Infect*, 2001;49(4): 250-4.

38. Catalano G, Houston SH, Catalano MC, et al. Anxiety and depression in hospitalized patients in resistant organism isolation. *South Med J*, 2003;96(2): 141-5.

39. Lupión-Mendoza C, Antúnez-Domínguez MJ, González-Fernández C, Romero-Brioso C, Rodriguez-Bano J. Effects of isolation on patients and staff. *Am J Infect Control*, 2015;43(4):397-399. doi: 10.1016/j.ajic.2015.01.009.

40. Day H, Perencevich E, Harris A, et al. Depression, anxiety, and moods of hospitalized patients under contact precautions. *Infect Control Hosp Epidemiol*, 2013;34(3):251-258.

41. Seibert DJ, Speroni KG, Oh KM, DeVoe MC, Jacobsen KH. Preventing transmission of MRSA: A qualitative study of health care workers' attitudes and suggestions. *Am J Infect Control*, 2014;42(4):405-411.

42. Stelfox H, Bates D, Redelmeier D. Safety of patients isolated for infection control. *JAMA*, 2003;290(14):1899-1905.

43. Zahar JR, Garrouste-Orgeas M, Vesin A, et al. Impact of contact isolation for multidrug-resistant organisms on the occurrence of medical errors and adverse events. *Intensive Care Med*, 2013;39(12):2153-2160.

44. Karki S, Leder K, Cheng AC. Patients under contact precautions have an increased risk of injuries and medication errors: a retrospective cohort study. *Infect Control Hosp Epidemiol*, 2013;34(10):1118-1120.

45. Masse V, Valiquette Louis, Boukhoudmi S, et al. Impact of methicillin resistant staphylococcus aureus contact isolation units on medical care. *PLoS One*, 2013;8(2): e57057. doi: 10.1371/journal.pone.0057057.

46. Harris AD, Pineles L, Belton B, et al; Benefits of Universal Glove and Gown (BUGG) Investigators. Universal glove and gown use and acquisition of antibiotic-resistant bacteria in the ICU: a randomized trial. *JAMA* 2013;310(15):1571-1580.

47. Gandra S, Barysauskas C, Mack D, Barton B, Finberg R, Ellison R. Impact of contact precautions on falls, pressure ulcers and transmission of MRSA and VRE in hospitalized patients. *J Hosp Infect*, 2014;88(3):170-176.

48. Kirkland KB, Weinstein JM. Adverse effects of contact isolation. *Lancet* 1999;354(9185):1177-1178.

49. Morgan DJ, Pineles L, Shardell M, et al. The effect of contact precautions on healthcare worker activity in acute care hospitals. *Infect Control Hospital Epidemiol*, 2013;34(1):69-73.

50. Saint S, Higgins LA, Nallamothu BK, Chenoweth C. Do physicians examine patients in contact isolation less frequently? A brief report. *Am J Infect Control*, 2003;31(6): 354-356.

51. Evans H, Shaffer M, Hughes M, et al. Contact isolation in surgical patients: a barrier to care? *Surgery*, 2003;134(2):180-188.

52. Ho PL; Hong Kong Intensive Care Unit Antimicrobial Resistance Study (HK-ICARE) Group. Carriage of methicillin-resistant staphylococcus aureus, ceftazidime-resistant gram-negative bacilli, and vancomycin-resistant enterococci before and after intensive care unit admission. *Crit Care Med*, 2003;31(4):1175-82. doi: 10.1097/01.CCM.0000059437.01924.97.

53. McKinnell JA, Miller LG, Eells SJ, Cui E, Huang SS. A systematic literature review and meta-analysis of factors associated with methicillin-resistant staphylococcus aureus colonization at time of hospital or intensive care unit admission. *Infect Control Hosp Epidemiol*, 2013;34(10):1077-86. doi: 10.1086/673157.

54. National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) Index for Categorizing Medication Errors, 2001. Available at: http://www.nccmerp.org/medErrorCatIndex.html. Accessed 14 June 2014.

55. Weissman JS, Schneider EC, Weingart SN, et al. Comparing patient-reported hospital adverse events with medical record review: do patients know something that hospitals do not? *Ann Intern Med*, 2008;149(2):100-108.

56. Weingart SN, Toth M, Eneman J, et al. Lessons from a patient partnership intervention to prevent adverse drug events. *Int J Qual Health Care*, 2004;16(6):499-507.

57. State of California Office of Statewide Health Planning and Development. Case mix index. Available at: http://www.oshpd.ca.gov/HID/Products/PatDischargeData/CaseMixIndex/. Accessed 18 June 2014.

58. State of California Office of Statewide Health Planning and Development. Calculation of the Office of Statewide Health Planning and Development's (OSHPD) Case Mix Index (CMI). Available at: http://www.oshpd.ca.gov/HID/Products/PatDischargeData/CaseMixIndex/CMI/ExampleCalculation.pdf. Accessed 18 June 2014.

59. Platt R, Takvorian SU, Septimus E, et al. Cluster randomized trials in comparative effectiveness research: Randomizing hospitals to test methods for prevention of healthcare-associated infections. *Med Care*, 2010;48(6 Suppl): S52-7. doi: 10.1097/MLR.0b013e3181dbebcf.

60. Lynn HS, McCulloch CE. When does it pay to break the matches for analysis of a matched-pairs design? *Biometrics*, 1992:397-409.

61. Magill SS, Edwards JR, Bamberg W, et al.; Emerging Infections Program Healthcare-Associated Infections and Antimicrobial Use Prevalence Survey Team. Multistate point-prevalence survey of health care-associated infections. *N Engl J Med*, 2014;370(13): 1198-1208. doi: 10.1056/NEJMoa1306801.

62. Morgan DJ, Diekema DJ, Sepkowitz K, Perencevich EN. Adverse outcomes associated with contact precautions: a review of the literature. *Am J Infect Control* 2009;37(2):85-93.

63. Shenoy ES, Walensky RP, Lee H, Orcutt B, Hooper DC. Resource burden associated with contact precautions for methicillin-resistant staphylococcus aureus and vancomycin-resistant enterococcus: The patient access managers' perspective. *Infect Control Hosp Epidemiol*, 2012;33(8):849-52. doi: 10.1086/666629.

64. McLemore A, Bearman G, Edmond MB. Effect of contact precautions on wait time from emergency room disposition to inpatient admission. *Infect Control Hosp Epidemiol*, 2011;32(3): 298-9. doi: 10.1086/658913.

65. Lake ET, Shang J, Klaus S, Dunton NE. Patient falls: association with hospital Magnet status and nursing unit staffing. *Res Nurs Health*, 2010;33(5):413-425.

66. Gilligan P, Quirke M, Winder S, Humphreys H. Impact of admission screening for meticillin-resistant Staphylococcus aureus on the length of stay in an emergency department. *J Hosp Infect*, 2010;75(2):99-102.

67. Mehrotra P, Croft L, Day H, Perencevich E, Pineles L, Harris A, Weingart S, Morgan D. Effects of contact precautions on patient perception of care and satisfaction: a prospective cohort study. *Infect Control Hospital Epidemiol*, 2013;34(10):1087-1093.

68. Kolata G. Doctors strive to do less harm. *New York Times* website. http://www.nytimes.com/2015/02/18/health/doctors-strive-to-do-less-harm-by-inattentive-care.html. Published February 17, 2015. Accessed February 18, 2015.

69. McCarthy NL, Sullivan PS, Gaynes R, Rimland D. Health care-associated and community-associated methicillin-resistant Staphylococcus aureus infections: a comparison of definitions. *Am J Infect Control*, 2010;38(8):600-606.

70. The Joint Commission. Preventing central line-associated bloodstream infections: A global challenge, a global perspective. 2012. Oak Brook, IL: Joint Commission Resources.

71. Centers for Disease Control and Prevention, Division of Healthcare Quality and Promotion. Checklist for prevention of central line associated blood stream infections. http://www.cdc.gov/HAI/pdfs/bsi/checklist-for-CLABSI.pdf. Updated 2012. Accessed 23 April 2015.

72. Sawyer M, Weeks K, Goeschel CA, et al. Using evidence, rigorous measurement, and collaboration to eliminate central catheter-associated bloodstream infections. *Crit Care Med*, 2010;38(8 Suppl):S292-8.

73. Pronovost P, Needham D, Berenholtz S, et al. An intervention to decrease catheter-related bloodstream infections in the ICU. *N Engl J Med*, 2006;355(26):2725-2732.

74. The Joint Commission. Sustaining and Spreading Improvements in Hand Hygiene Compliance. *J Qual Patient Saf*, 2015;41(1). http://www.jointcommission.org/assets/1/18/JQPS_1_15.pdf. Published 2015. Updated 2015. Accessed 23 April 2015.

75. Weber DJ, Anderson D, Rutala WA. The role of the surface environment in healthcare-associated infections. *Curr Opin Infect Dis*, 2013;26(4):338-344.

76. Chemaly RF, Simmons S, Dale C, et al. The role of the healthcare environment in the spread of multidrug-resistant organisms: update on current best practices for containment. *Ther Adv Infect Dis*, 2014;2(3-4):79-90. doi: 10.1177/2049936114543287.

77. Carling PC, Huang SS. Improving Healthcare Environmental Cleaning and Disinfection: Current and Evolving Issues. *Infect Control Hosp Epidemiol*, 2013;34(5):507-513.

78. Donskey CJ. Does improving surface cleaning and disinfection reduce health care-associated infections? *Am J Infect Control*, 2013;41(5):S12-S19.

79. Huang SS, Septimus E, Kleinman K, et al. Targeted versus universal decolonization to prevent ICU infection. *N Engl J Med*, 2013;368(24):2255-2265.

80. Morgan D, Pineles L, Shardell M, et al. Effect of chlorhexidine bathing and other infection control practices on the Benefits of Universal Glove and Gown (BUGG) trial: A subgroup analysis. *Infect Control Hosp Epidemiol*, 2015. [Epub ahead of print.] PMID: 25707404.

81. Morgan DJ, Kaye KS, Diekema DJ. Reconsidering isolation precautions for endemic methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant Enterococcus. *JAMA*, 2014;312(14):1395-1396.

82. Huskins WC, Huckabee CM, O'Grady NP, et al. Intervention to reduce transmission of resistant bacteria in intensive care. *N Engl J Med*, 2011;364(15):1407-1418.

83. Edmond M, Bearman G, Stevens M, Ober J. Impact of de-escalating contact precautions on MRSA infection rates in an academic medical center. IDWeek; October 8-12, 2014; Philadelphia, PA.

84. Anderson DJ, Weber DJ, Sickbert-Bennett E. On contact precautions: the good, the bad, and the ugly. *Infect Control*, 2014;35(03):222-224.

85. Edmond M, Pegues D. Should Contact Precautions be Eliminated? IDWeek; October 8-12, 2014; Philadelphia, PA.

86. Karki S, Leder K, Cheng A. Delays in accessing radiology in patients under contact precautions because of colonization with vancomycin-resistant enterococci. *Am J Infect Control*, 2013;41(11):1141-1142.

88. Goldszer RC, MBA ET, Shadick N, et al. A program to remove patients from unnecessary contact precautions. *JCOM*, 2002;9(10).