SIGNIFICANCE:

Preventing Transmission of Contagious Pathogens in Healthcare Settings:

Healthcare-associated transmission of infectious pathogens can occur from numerous routes, including direct contact with infected patients, exposure to respiratory droplets in enclosed air spaces, and handling of contaminated objects within the patient environment.[1] The resultant healthcare-associated infections (HAIs) have a dramatic impact on the health and safety of patients. Awareness of the incidence of a number of these events has led to marked improvement in targeted outcomes through comparative measurement, visible reporting of performance, and accountability through financial incentives.[2,3] In contrast, awareness of the impact of these pathogens on the health and safety of the healthcare personnel (HCP) who care for patients infected with such pathogens is less well known. By nature of their occupation, HCP are at an increased risk of exposure to and subsequent infection by a variety of pathogens.[4-6] HCP also serve as vectors for pathogen transmission through their frequent contact with patients colonized or infected with these organisms.[7-9] Therefore, the prevention of transmission of these agents to HCP (a.k.a. "occupational infection prevention") is an important safety measure for both the individual HCP and his or her patients.

A foundational practice to prevent the spread of pathogens to HCP in healthcare settings is the use of transmission-based precautions. The basic concept of transmission-based precautions is using specific environmental controls and personal protective equipment (PPE) for pathogens based on their predominant mode of transmission. Used to augment Standard Precautions (i.e. core practices based on the principle that "all blood, body fluids, secretions, excretions except sweat, nonintact skin, and mucous membranes may contain transmissible infectious agents"[1]) that are applied to the care of all patients, transmission-based precautions include Contact, Droplet, and Airborne Precautions. Additional precautions include a combination of these three main types of precautions which are used for pathogens spread by multiple routes or that are highly contagious (Table 1).

A watershed event that elevated the importance of occupational infection prevention occurred last fall amid the largest-ever reported outbreak of Ebola Virus Disease (EVD). In October 2014, during the West Africa EVD outbreak, the first healthcare-associated acquisition of EVD among U.S. HCP occurred at a Dallas hospital.[10] This acquisition of EVD by two nurses created a groundswell of concern about how healthcare facilities protect their HCP from serious pathogens.[11,12] While the exact transmission route of EVD in these nurses is unclear and will never be identified, several major themes emerged in the dissection of this serious infection control failure. These included concerns about the type of PPE recommended for use when caring for EVD patients, the rapidly-evolving protocols for PPE and infection prevention in this setting, the misperceptions that "all healthcare facilities" could safely care for an Ebola-infected patient, and the lack of familiarity and comfort of the HCP with use of the recommended PPE and precautions. These transmission events rapidly triggered re-evaluation of all EVD protocols and PPE and led to a more detailed and robust set of expectations for infection prevention and PPE use.[13] Most striking was the understanding that safe care and treatment of EVD patients requires intensive preparation, HCP and leadership training and retraining, and an infrastructure that only a select set of healthcare facilities can provide.

While only two cases of healthcare-associated EVD-transmission have occurred in the U.S., the lessons learned and questions raised from these events are numerous and applicable to other infectious pathogens. For instance, while the PPE and protocols used for EVD infection prevention are extremely detailed due to that pathogen's ability to spread via exposure to infected blood and body fluids, the principles behind these protocols and the PPE utilized are implemented on a much wider scale each day in healthcare facilities across the world. Other pathogens that lead to considerable morbidly and mortality are spread similarly to Ebola (i.e. by direct contact with colonized or infected patients or with the contaminated patient environment), including *Clostridium difficile* and multidrug-resistant organisms (MDROs) like methicillin-

resistant *Staphylococcus aureus* (MRSA) and the carbapenem-resistant Enterobacteriaceae (CRE).[1]

Table 1: Summary of Transmission-Based Precaution Types and Components[1]

Type of Precautions	Type(s) of PPE Recommended						Negative Pressure Room	Examples of Pathogens for which Precaution Type is Used
	Gloves	Gown	Surgical Mask	N95 Respirator or PAPR	Eye Protection	Full Body Covering (e.g. Hood, Apron, Leg Covering)		
Contact	✓	✓						MDROs, *C. difficile*
Droplet			✓	✓*			✓*	Seasonal influenza, *B. pertussis*
Airborne				✓			✓	*M. tuberculosis*, measles
Novel Respiratory Pathogen	✓	✓		✓	✓		✓	Pandemic influenza, SARS-CoV, MERS-CoV
EVD Precautions	✓	✓	✓ or ✓*		✓	✓	✓*	Ebola, Other VHF Agents

PAPR = Powered Air Purifying Respirator; SARS-CoV = Severe Acute Respiratory Syndrome Coronavirus; MERS-CoV = Middle East Respiratory Syndrome Coronavirus; EVD = Ebola Virus Disease; VHF = Viral Hemorrhagic Fever * Use for aerosol-generating procedures (e.g. intubation, open suctioning of respiratory secretions, bronchoscopy)

The cases of HCP-acquired EVD have illuminated many important safety issues surrounding the use of transmission-based precautions and their associated PPE in healthcare facilities across the United States. When examining these issues, several key points are important to highlight:

- ***Transmission-based precaution utilization is common in acute care facilities.***
- ***HCP compliance with the PPE used for transmission-based precautions is suboptimal.***
- ***Exposure to patients with contagious pathogen infection or colonization even in the setting of PPE use can lead to pathogen contamination of HCP hands and the environment.***
- ***HCP can become infected with pathogens targeted by transmission-based precautions and can serve as vectors of patient transmission in healthcare facilities.***
- ***Factors that affect the appropriate use of PPE are numerous, complex, and not fully understood.***
- ***Formal competency training on the use of and routine auditing of compliance with PPE and transmission-based precaution practices is lacking at most healthcare***

facilities.

- ***Improving the effectiveness of PPE (through improved compliance) will require changing and hardwiring HCP behavior.***

Transmission-based precaution utilization is common in acute care facilities. Large-scale data on the number of patients placed in Contact or Droplet Precautions in U.S. healthcare facilities are lacking; however, an examination of the burden of several key pathogens for which such precautions are recommended can provide a surrogate measure of the burden of transmission-based precautions. Data from the Emerging Infections Program from the Centers for Disease Control and Prevention (CDC) estimated the national incidence of *C. difficile* infection of 48.2 per 100,000 people (453,000 cases), with an estimated burden of healthcare-associated *C. difficile* infection of 293,300 cases occurring in 2011.[14] For MRSA, the number of hospital-onset, healthcare-associated cases of invasive disease in 2012 was estimated at 12,901 for the U.S. population. Presumably, many of these cases were diagnosed and treated in an acute care facility where Contact Precautions would be reasonably expected to have been implemented following *C. difficile* or MRSA diagnosis. These are but two pathogens for which Contact Precautions are recommended, yet these statistics indicate a substantial burden of patients who require such precautions in acute care facilities.

HCP compliance with the PPE used for transmission-based precautions is suboptimal. While isolation precautions and the associated PPE are important interventions to prevent healthcare-associated pathogen transmission, lapses in their use are common. Although population-level data on PPE compliance are absent, smaller examinations of PPE use among HCP performing patient care activities in healthcare settings have noted a substantial, if not fairly consistent, rate of noncompliance. We collaborated with investigators from 11 academic medical centers in an analysis of Contact Precautions compliance among 1,013 HCP.[15] In this study, noncompliance with PPE components was 25.7% with use of gowns and 19.9% with use of gloves. Direct observation of Contact Precautions PPE use among 1,150 HCP in another study noted noncompliance with gown use by 24% of observed HCP.[16] Weber and colleagues noted a similar frequency of noncompliance at a tertiary-care hospital, with lapses in Contact Precautions PPE use occurring in 26.7% of observed instances.[17] Clock *et al* also identified similar noncompliance rates with glove (32.5% on room entry and 36.5% on room exit) and gown use (32.1% on entry and 22.9% on exit).[18] Lapses may be more frequent with performance of certain clinical activities. Chaing *et al* observed 44 episodes of cardiopulmonary resuscitation in Taiwan.[19] Using video analysis, frequent lapses in the use of recommended PPE were noted (e.g. 90% of HCP wore gloves but only 20% wore a gown). A total of 687 contamination events were identified, with a lack of a specific task assignment among HCP (44% of events) and inadequate preparation for procedures (42%) major factors in these breaches. The highest rate of events occurred among the nursing personnel.[19]

Exposure to patients with contagious pathogen infection or colonization even in the setting of PPE use can lead to pathogen contamination of HCP hands and the environment. The routine care of patients placed in Contact Precautions has been noted to result in the potential for HCP colonization and the subsequent transmission of contagious pathogens. Morgan *et al* examined the frequency of contamination of HCP hands and PPE components following the performance of nonemergent care of patients colonized or infected with an MDRO. Culture growth of MDROs occurred in 1.7-4.2% of HCP hand specimens, 10.0-29.3% of glove specimens, and 2.3-12.6% of gown specimens.[20] Overall 20.5% of HCP-patient interactions resulted in contamination of the HCP's gloves or gowns. This is concerning, as breaches in the use of this PPE could then contaminate the HCP's hands and the environment, leading to transmission to patients. The risk for contamination of PPE was significantly

increased with a HCP's duration in the room of at least 5 minutes, performance of a physical examination, and work in rooms with environmental contamination. Of equal concern, 8% of HCP room entries occurred with HCP who had colonization of a MDRO on their hands prior to room entry, emphasizing the role HCP can play in the transmission of these pathogens. While an audit for breaches in the use of PPE was not performed in this study, the frequency of PPE contamination and potential exposure risk in the event of PPE breaches is concerning. French investigators detected *C. difficile* spores on 25% of samples collected from the hands of HCP who had recently cared for a *C. difficile*-infected patient (compared to 0% in control HCP who were not exposed to *C. difficile* patients).[21] Patient contact without the use of gloves occurred in 7.8% of observations.

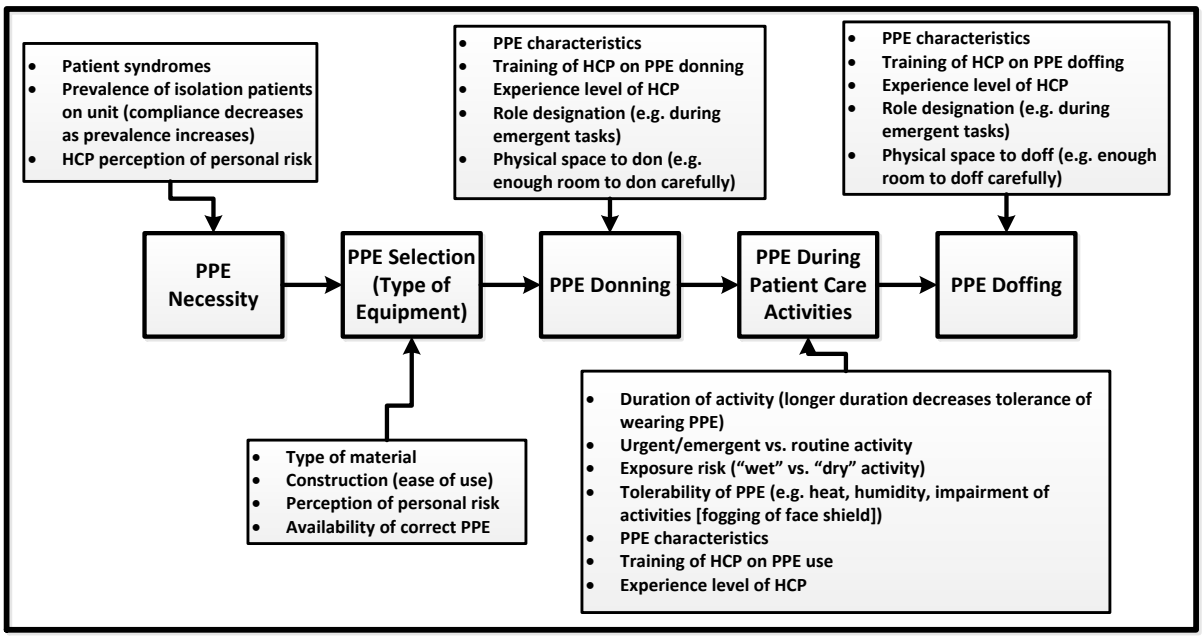
HCP can become infected with pathogens targeted by transmission-based precautions and can serve as vectors of patient transmission in healthcare facilities. Similar to the current aftermath following the acquisition of EVD among U.S. HCP, another major contagious disease outbreak that occurred over a decade ago affected HCP and triggered studies into the complexities of PPE use. In 2003, the emergence of the Severe Acute Respiratory Syndrome, or SARS, which was caused by a novel coronavirus (SARS-CoV), affected 29 countries, with over 8,096 cases and 780 deaths.[22] HCP were one of the primary populations affected by this disease. In Toronto, following an initial outbreak affecting 257 persons, a second wave of cases emerged, with nearly 40% (29 patients) occurring in HCP.[23] HCP exposure to pathogens such as MRSA, CRE, and *C. difficile* is far more common than exposure to EVD or SARS-CoV. Cases of HCP infected with these pathogens have been reported,[24,25] and the role of these personnel in pathogen transmission has been questioned.[26] Importantly, HCP have also been noted as potential sources of healthcare-associated outbreaks due to a variety of contagious infections, including, but not limited to, whooping cough,[27] measles,[28] mumps,[29] influenza,[30] and norovirus.[31]

Factors that affect the appropriate use of PPE are numerous, complex, and not fully understood. A deeper understanding of the factors that impact the use of PPE has emerged over the past 15 years, prompted to a degree by the SARS experience. Shigayeva and colleagues performed a retrospective cohort study of 795 HCP who cared for critically-ill SARS patients in the window surrounding patient intubation.[32] The HCP reported substantial breaches in the use of recommended barrier precautions (i.e. gloves, gown, masks, and eye protection), and the frequency of noncompliance declined over time, suggesting improvement as familiarity and comfort with the PPE increased. The following factors were significantly associated with an increased self-reported consistent compliance to PPE: recognition of patient as a SARS case (odds ratio [OR] 2.5, 95% confidence interval [CI] 1.5-4.5), recent infection control training (OR 2.7 for interactive training, 95% CI 1.7-4.4) and work in a SARS (OR 4.0, 95% CI 1.8-8.9) or intensive care (OR 4.3, 95% CI 2.0-9.0) unit. Conversely, provision of care of patients with higher Acute Physiology and Chronic Health Evaluation (APACHE) II scores (OR 0.4 for score ≥20, 95% CI 0.28-0.68) and work on shifts that required more than 6 room entries per shift (OR 0.5, 95% CI 0.32-0.86) were significantly associated with lower reported frequency of consistent compliance.

An in-depth assessment of 15 HCP who acquired SARS after implementation of isolation precautions during the 2003 outbreak identified several key issues.[33] Only 60% reported having received formal infection control training, 87% were unsure of proper PPE use, and 40% reused PPE and other items following their use for the care of a SARS patient. Strikingly, 54% reported an identified breach in the use of SARS infection control precautions during patient care. While the SARS-CoV is spread in a somewhat different fashion than pathogens like Ebola or MDROs (airborne vs. direct contact), the insights gained regarding the risk of PPE breaches greatly inform such risk for all types of PPE.

As guided by the studies noted above, the findings from events such as the outbreak of SARS among HCP and the HCP-acquired EVD cases, and the experience of healthcare epidemiologists and infection preventionists working in the field, there are likely many factors that can impact the effectiveness of PPE (Figure 1). Starting with determining the necessity of PPE use for a given patient care scenario and continuing through PPE selection, donning (or "putting on"), use, and doffing (removal), opportunities for breaches in PPE use and subsequent exposure of HCP to infectious pathogens are considerable.

Figure 1: Factors that may Impact the Effectiveness of PPE among HCP



Determining whether a specific patient requires placement into precautions upon entry to the healthcare facility is essential, and failure to recognize the need for precautions can lead to HCP exposure to pathogens of concern. The number of patients in a given unit may also impact PPE compliance. Vanderbilt investigators (Talbot) collaborated on the study by Dhar *et al* that noted a negative impact on compliance with PPE use (from 31.5% to only 6.5%) and hand hygiene (from 43.6% to 4.9%) as the proportion of patients on isolation precautions increased from less than 20% to greater than 60%.[15]

Once patients are placed into precautions, factors affecting PPE effectiveness include the availability of PPE, the perception of HCP risk (i.e. HCP belief of a specific patient's true likelihood of infection with the suspected pathogen), and the construction of the PPE (in terms of ease of use as well as underlying materials). Failure to don the PPE correctly, whether due to lack of HCP training on PPE use, the urgency of the patient care duty to be performed (i.e. emergent vs. routine), or physical constraints (i.e. enough space to don attire), also may impact PPE effectiveness. Patient factors (including clinical symptoms), details about the patient care tasks (i.e. duration, complexity), and tolerability of the PPE are also important. Finally, failure to doff PPE correctly can lead to contamination of HCP and the environment.

Formal competency training on the use of and routine auditing of compliance with PPE and transmission-based precaution practices is lacking at most healthcare facilities. Similar to many "basic" practices in healthcare, such as hand hygiene and the use of aseptic technique for wound care, HCP training on the appropriate use of PPE often occurs as part of "on-the-job" training, learned "on the fly" from supervisors or senior-level team members as a part of orientation to the HCP's specific clinical duties. Formal teaching and assessments of

competency in the proper use of PPE are rare at most healthcare facilities. The type of training, if present, may also have varying impact. In the study noted above of Toronto HCP who contracted SARS, those trained recently using passive methods (e.g. written instructions or video training) had a lower OR for report of consistent use of PPE compared to those who had undergone interactive training (e.g. face-to-face in-person sessions).[32] While programs to monitor and direct hand hygiene compliance by HCP are commonplace at many healthcare facilities,[34,35] routine audits of PPE use as a part of isolation precautions are less common. Standardized tools to monitor PPE use and assessments of breaches are clearly needed to assist healthcare facilities in improving compliance with PPE and, more importantly, protecting HCP and their patients. The World Health Organization's (WHO) process for hand hygiene measurement and training (a.k.a. the "Five Moments for Hand Hygiene" concept)[36] has provided a standardized process and template that has revolutionized how infection prevention and safety personnel track compliance with this important infection prevention behavior. The U.S. EVD experience highlights the importance of thorough training on the use of PPE to protect HCP and prevent healthcare-associated transmission of serious contagious pathogens, the need to measure compliance in order to drive improvement, and the importance of understanding the risk factors for breaches in PPE use. Simply put, an analogous "Five Moments for Safe PPE Use" is now needed.

Improving the effectiveness of PPE (through improved compliance) will require changing and hardwiring HCP behavior: Improving compliance with and reducing breaches during the use of PPE will likely require a multifaceted approach. Novel technology to improve PPE design and tolerability, better tools for monitoring compliance, and a clearer understanding of how pathogens are transmitted in various healthcare settings will all be important. Nonetheless, we must understand that decisions to utilize and then appropriately use recommended PPE are rooted in HCP behavior. Failure to develop interventions to drive expected behaviors surrounding PPE use will reduce the impact of advancements in PPE design. We have extensive experience in the creation and successful implementation of a program designed to change and hardwire HCP behavior surrounding another important infection prevention practice, hand hygiene.[34] This program, that partners standardized auditing of HCP practice with a foundation of data feedback, real-time peer-to-peer interventions to professionally redirect noncompliant behaviors, and performance accountability, resulted in marked improvement in hand hygiene compliance in a population of over 12,000 HCP.[34] Such a program will be important as we strive to improve the effectiveness of PPE to protect HCP and their patients.

Proposed Vanderbilt Epicenter for the Prevention of Healthcare-Associated Infections: As illustrated above, there remain gaps in understanding the reasons for lapses in PPE use, in the development of tools to improve PPE effectiveness, and, ultimately, and in the optimal manner to implement these precautions to reduce HCP harm and HAIs. In order to address the need for fully-powered, rigorous studies on HAIs and their prevention, the CDC developed the Epicenters network in 1998. Through the Epicenter program, a multitude of innovative and highly productive investigations have been conducted that have advanced our understanding of the detection, burden, and prevention of many major HAIs.[37-41] This network is ideally suited to examine the key questions surrounding the prevention of contagious pathogens spread through contact with infected patients and their environment, the barriers to successful PPE use by HCP, and the need to improve adherence to these important infection prevention strategies.

While not previously a member of the Epicenter network, Vanderbilt's Department of Infection Prevention has a robust history of successful and innovative infection prevention and healthcare epidemiology programs that have led to marked reductions in HAIs and have advanced the understanding of important infection prevention issues.[34,42-44] Importantly, members of the Department and the proposed Epicenter have been recognized as leading

experts in occupational infection prevention. Dr. Thomas Talbot (PI for the proposed Vanderbilt Epicenter) has conducted original research studies examining the risk of pathogen transmission from recipients of live and live-attenuated vaccines,[45,46] post-exposure management of HCP following *B. pertussis* exposures,[47] and prospective surveillance of respiratory virus shedding in asymptomatic and symptomatic HCP.[48] He is also an advocate for using occupational infection prevention strategies as important patient and HCP safety interventions.[34,49-52] Dr. William Schaffner (Advisory and Steering Committee Member) is an international authority on infection prevention and hospital epidemiology. His investigations into the burden of vaccine-preventable diseases and the importance of HCP immunization have been widely recognized.

Vanderbilt Epicenter investigators also have extensive research experience focused on other aspects of healthcare epidemiology and HAI prevention, including the epidemiology of MDROs,[53-57] the burden and prevention of vaccine-preventable diseases,[58-60] HAI outbreak detection and management,[57,61-63] and interventions to reduce HAIs.[34,42,44,64-67] In addition, they have coupled this experience with extensive work implementing and overseeing operational infection prevention programs. As a function of their roles as hospital epidemiologists at a variety of healthcare settings (academic, tertiary care medical center, community-based acute care facility, Veteran's Affairs hospital), several of the Vanderbilt Epicenter investigators and collaborators have extensive operational experience in HAI surveillance, outbreak investigation, and the epidemiology and burden of adverse events in healthcare facilities.

Epicenter Investigators and Collaborators: The Vanderbilt Epicenter's investigators, collaborators, and consultants comprise a diverse group of individuals with expertise in many key areas germane to healthcare epidemiology, occupational infection prevention, pathogen transmission, and HCP protection. They have served as successful collaborators, both in research and clinical care capacities, providing a rich infrastructure for multidisciplinary investigation. Through this group of skilled investigators, the Vanderbilt Epicenter will be uniquely positioned to conduct important and innovative clinical investigations into the use of PPE and the impact on HCP and environmental contamination, HCP compliance, and the impact on pathogen transmission.

Thomas R. Talbot, M.D., M.P.H. (Principal Investigator): Dr. Talbot is an Associate Professor of Medicine and Preventive Medicine at Vanderbilt University School of Medicine and also serves as the Chief Hospital Epidemiologist for Vanderbilt University Medical Center (VUMC). His clinical epidemiologic research has focused on occupational infection control,[44,48,59,68,69] including the use HCP vaccination as a means to reduce patient and HCP morbidity, secondary transmission from vaccinations,[45,46,70,71] and management of vaccinated HCP exposed to contagious infections. Clinical investigations include two NIH-funded studies examining the transmissibility of smallpox vaccination sites and the impact of site dressing on viral shedding and a CDC-funded study examining the effectiveness of post-exposure prophylaxis in Tdap-vaccinated HCP exposed to pertussis.[46,47,71] He served as the chair of the Society for Healthcare Epidemiology of America's (SHEA's) Task Force on Influenza Vaccination of Healthcare Personnel in 2005 and 2010 and was lead author on the SHEA Position Paper advocating for influenza vaccination as a condition of HCP employment.[51] More recently, his work has included the development of a hand hygiene improvement program as a tool for changing HCP behavior and driving a safe, accountable quality culture.[34] Dr. Talbot currently serves as a member of the CDC's Healthcare Infection Control Practices Advisory Committee (HICPAC), and recently served on the Board of Directors for SHEA. He also currently co-chairs the Tennessee Department of Health's multidisciplinary advisory group that oversees efforts focused on HAI prevention and reporting in the state. As a part of his role as the Chief Hospital Epidemiologist, he oversees the surveillance and prevention of HAIs at VUMC. He also was the physician lead for the extensive VUMC EVD planning and preparedness efforts last fall, which included PPE selection, clinical protocol development,

patient screening and triage processes, and HCP training. He also provided content expertise into the design of the Vanderbilt Communicable Disease Response Unit (CDRU), a dedicated unit for the evaluation and care of patients with highly-infectious diseases.

George Nelson, M.D. (Investigator): Dr. Nelson graduated from Princeton University in 2002 and Case Western Reserve School of Medicine in 2006. He completed residency training in Internal Medicine at Vanderbilt University and then served as an Epidemic Intelligence Service (EIS) officer at the CDC in the National Center for Immunization and Respiratory Diseases where he investigated transmission dynamics and control efforts during various outbreaks.[72-75] He was recognized for his contributions in outbreak control with the NCIRD Honor Award: Excellence in Public Health Protection. He has also served as PI on a large scale evaluation of over 9,500 invasive group A *Streptococcal* infections in the U.S. during a 7 year period (document currently in CDC clearance review). He then completed infectious diseases fellowship at Johns Hopkins Hospital. Dr. Nelson joined the faculty at Vanderbilt in 2014. He currently serves as the Associate Hospital Epidemiologist for VUMC and Associate Director of Antimicrobial Stewardship at Vanderbilt. His primary research interests focus on the prevention of MDRO infections and antimicrobial stewardship. He is currently overseeing an investigation in MDRO bacteremia and a substudy on MDRO colonization in India including more than 1,000 patients. Dr. Nelson was also heavily involved with VUMC EVD preparedness last fall, assisting on all aspects of EVD infection prevention planning, including PPE use and HCP training. He also serves on the Tennessee Antibiotic Resistance Task force and chairs the VUH *C. difficile* Task Force.

Steven S. Spires, M.D. (Investigator): Dr. Spires graduated from Mercer University School of Medicine in 2009. He completed residency training in Internal Medicine and fellowship training in Infectious Diseases at Vanderbilt University. He joined the faculty at Vanderbilt in 2014. He currently serves as the Hospital Epidemiologist at both Williamson Medical Center and the Tennessee Valley VA Healthcare System. He recently led an investigation into a healthcare-associated respiratory viral illness outbreak in a geriatric long term care unit. He also served as the regional clinical lead for the Ebola Preparation Taskforce for the VA Mid South Healthcare Network. His primary research interests are focused on the prevention of outpatient central line-associated bloodstream infections, the increased healthcare utilization associated with outpatient central lines, and HAI prevention in a community hospital setting.

Arna Banerjee, M.D. (Investigator): Dr. Banerjee is an Associate Professor of Anesthesiology and Critical Care Medicine at Vanderbilt University School of Medicine and Assistant Dean for Simulation in Medical Education. She directs the Center for Experiential Learning and Assessment (CELA). Her research interests include the use of high-fidelity simulation-based training and clinical performance assessment as educational tools.[76,77] She has served as the VUMC Anesthesiology Resident's Simulation Director and is currently the Director for the Simulation Program for the American Society of Anesthesiology Maintenance of Certification in Anesthesiology courses conducted at VUMC.

Epicenter Collaborators:

Gerald B. Hickson, M.D.: Dr. Hickson is the Senior Vice President of Quality, Safety and Risk Prevention, Assistant Vice Chancellor for Health Affairs, and Joseph C. Ross Chair of Medical Education and Administration at Vanderbilt University School of Medicine. Since 1990, Dr. Hickson's research has focused on why families choose to file suit, why certain physicians attract a disproportionate share of claims and how to identify and intervene with high-risk physicians. His work has resulted in over 150 peer review articles and chapters; several educational initiatives to promote disclosure of medical errors and address behaviors that undermine a culture of safety; and the development of PARS® (Patient Advocacy Reporting System), a program that uses unsolicited patient complaint data as the basis for tiered interventions on high-risk peer colleagues and has been implemented in more than 70 hospitals

and health systems nationwide. In this operational role as Senior Vice President of Quality, Safety and Risk Prevention, Dr. Hickson is charged with bringing greater alignment among VUMC's efforts to improve quality and the patient experience through collaborations spanning the institution with informatics, hospital operations, learning initiatives, and the Vanderbilt Health Affiliated Network. Dr. Hickson currently serves as Chair of the Board of Directors of the National Patient Safety Foundation (NPSF) and as Chair of the Board of Professionals in Patient Safety (CBPPS). The Department of Infection Prevention reports directly to Dr. Hickson, and he will serve as the Epicenter liaison to VUMC operations and administration to help ensure successful completion of the Vanderbilt Epicenter projects.

Greg Wilson, M.D.: Dr. Wilson graduated from Johns Hopkins School of Medicine in 1987. He completed residency training in Pediatrics and fellowship training in Pediatric Infectious Diseases at the Monroe Carell Jr. Children's Hospital at Vanderbilt (MCJCHV). He joined the faculty at Vanderbilt in 1996. As the Chief Hospital Epidemiologist for the MCJCHV, he directs efforts focused on the prevention HAIs in pediatric patients. Dr. Wilson will serve as the Epicenter liaison for any projects targeted in pediatric healthcare settings.

Vanderbilt Epicenter Advisory and Steering Committee: An advisory and steering committee comprised of individuals with expertise regarding various aspects of infection prevention, pathogen transmission, occupational health, HCP protection, use of PPE, and environmental safety will be created to guide the Epicenter's research program. Facilitated by the Vanderbilt Epicenter program coordinator, this committee will meet quarterly to assess progress on the epicenter projects, advise the development of new study protocols, review responses to new call for proposals set forth to the epicenter network, and assess barriers to study completion. We will invite and encourage CDC Epicenter leader participation at these sessions to ensure tight communication with and guidance from these partners. The following individuals have agreed to serve as initial members of the Vanderbilt Epicenter Advisory and Steering Committee:

C. Buddy Creech, M.D., M.P.H.: Dr. Creech is an Assistant Professor of Pediatrics and is board-certified in Pediatric Infectious Diseases. He also serves as the Associate Director of the Vanderbilt Vaccine Research Program (VVRP) and as Co-PI of the NIH-sponsored Vanderbilt Vaccine and Treatment Evaluation Unit (VTEU). Dr. Creech has conducted clinical and translational research for the past fifteen years, focusing on the epidemiology of bacterial infections and vaccine-preventable diseases.[64,78-84] His primary focus has been on defining the clinical and molecular epidemiology of *S. aureus* disease, in particular, MRSA in children and adolescents. In his role as Co-PI of the VTEU, he has conducted numerous Phase I-IV clinical trials of vaccines in infants, children, and adults. As a result of his knowledge of clinical research and collaborations in place with other investigators at Vanderbilt, he is uniquely positioned to combine expertise in clinical epidemiology, molecular epidemiology, and human immunology to answer fundamental questions regarding bacterial and viral diseases in children and pediatric healthcare settings. In July 2015, he will transition to the role of Director of the VVRP and Principal Investigator of the VTEU. Dr. Creech also leads the VVRP Laboratory, a translational science laboratory with expertise in molecular epidemiology of gram-positive organisms (e.g., streptococci and staphylococci) and human immunology, including functional assessment of human antibodies. The work of the laboratory includes experiments designed to answer questions regarding staphylococcal colonization in infants, children, and adults.

Marion Kainer, M.D., M.P.H.: Dr. Kainer is an infectious diseases physician and serves as the Director of the Hospital Infections and Antimicrobial Resistance Program for the Tennessee Department of Health (TDH). She has over 20 years of experience in infection control, hospital epidemiology and antimicrobial stewardship.[55,85-90] She was an EIS officer in the Division of Healthcare Quality Promotion (DHQP), CDC from 2000-2002. She is the chair of the HAI subcommittee, and co-chairs the HAI data standards committee for the Council of State and

Territorial Epidemiologists (CSTE). She also co-chairs the CDC's National Healthcare Safety Network (NHSN) steering working group and is a liaison to the NHSN change control board. She is a member of the CDC/CSTE antimicrobial resistance surveillance taskforce which was formed in response to CSTE position statement 13-SI-01 on strengthening antimicrobial resistance surveillance; Dr. Kainer was the submitting of author of that position statement. She was honored by the White House as a Champion of Change for Prevention and Public Health in 2013. Dr. Kainer was a member of the antibiotic resistance work group for the President's Council of Advisors in Science and Technology (PCAST) that issued its report in September 2014 and was accompanied by the President's Executive Order on Combating Antimicrobial Resistant Bacteria. Dr. Kainer has been nominated by CSTE to be a member of the Presidential Advisory Council for Combating Antimicrobial Resistant Bacteria. Dr. Kainer also is a member of the TDH mission coordination group for Ebola response and many of her staff hold key leadership roles under incident command structure (ICS) at the TDH State Health Operations Center.

William Schaffner, M.D.: Dr. Schaffner is a Professor of Preventive Medicine in the Department of Health Policy, Professor of Medicine in the Division of Infectious Diseases, and Associate Hospital Epidemiologist at VUMC. He has been a leading expert in the field of healthcare epidemiology for over 40 years. He served in the U.S. Public Health Service as an EIS Officer with the CDC from 1966 to 1968. He then returned to Vanderbilt and established a close collaboration with the TDH that continues to the present. He has authorized or coauthored many peer-reviewed articles on important infection control and public health topics, including antibiotic resistance, outbreaks of nosocomial infections, immunization practices and infection control for patients infected with HIV.[56,57,60,62,91-96] He has served as President of SHEA (1983) and the National Foundation for Infectious Diseases (2010-12); he has served on the Board of Directors of the International Federation of Infection Control (1985-90) and twice on the elected Board of the Infectious Diseases Society of America (2000-3; Secretary 2007-10). He is a Senior Associate Editor of *Infection Control and Hospital Epidemiology* and Associate Editor of the *Journal of Infectious Diseases*. He has written over 480 scientific articles and textbook chapters and is a consultant in public health policy and communicable disease control for numerous local, national, and international institutions, including the CDC and the WHO among others. He also serves as co-Principal Investigator for the Tennessee Emerging Infections Program which conducts studies of community and hospital-onset MRSA, *C. difficile* and influenza infections and other pathogens. He served as the Hospital Epidemiologist at Vanderbilt for over 35 years until 2006, where under his direction, the Department became a major influence in the prevention of HAIs throughout the region.

Melanie Swift, M.D.: Dr, Swift, the Medical Director of the Vanderbilt Occupational Health Clinic, joined the Vanderbilt faculty in 1995 after a residency in Internal Medicine at Brown University. She attained her MD from the University of Tennessee in Memphis. Dr. Swift provides oversight to all occupational health programs and clinics serving approximately 26,000 employees of Vanderbilt University and VUMC. Dr. Swift is past president of the Tennessee College of Occupational Environmental Medicine and is currently the Chair of American College of Occupational and Environmental Medicine (ACOEM) Medical Center Occupational Health Section. Through her leadership, the VUMC Occupational Health Clinic oversees all aspects of the employee health and safety program, including new employee evaluations, annual influenza vaccination and tuberculin skin testing, work-related illnesses or injuries, and exposures to contagious diseases. She has also been an active member of the VUMC EVD preparedness team, particularly regarding PPE selection and use protocols and HCP monitoring post-EVD exposure.

Patty W. Wright, M.D.: Dr. Wright serves as the Associate Vice Chair for Clinical Affairs in the Department of Medicine and is the Associate Director for Clinical Affairs in the Division of Infectious Diseases. She graduated from the University of Alabama School of Medicine in

Birmingham. She completed her residency in Internal Medicine and her fellowship in Infectious Diseases, both at the University of Alabama at Birmingham. Dr. Wright has chaired the Antibiotic Subcommittee of the VUMC Pharmacy and Therapeutics Committee since 2003 and has led the development of the Vanderbilt Antibiotic Stewardship Program since its inception. She has also been an active member of the VUMC EVD preparedness team, particularly in the areas of physician staffing and training.

Mary Yarbrough, M.D., M.P.H: As the Executive Director of Vanderbilt's Faculty/Staff Health and Wellness Programs, Dr. Yarbrough has responsibility for engaging employees of Vanderbilt and other Mid-South employers in innovative programs that maximize well-being and productivity. Dr. Yarbrough joined the Vanderbilt faculty following a career in preventive medicine at the state, national and international levels. She translated these experiences into an integrative occupational model that integrates workplace, personal, and psychosocial services to influence health and safety.[97,98] Prior to coming to Vanderbilt, Dr. Yarbrough served as the Director of Environmental Epidemiology for the State of Tennessee where her responsibilities included oversight of a multimillion U.S. Department of Energy grant evaluating the impact of historical offsite contaminant releases from the Oak Ridge Nuclear Reservation. Her international experiences have included community development in Africa and work with the Flying Doctor helicopter service in the jungles of Southeast Asia. She has served as a consultant to the WHO. Dr. Yarbrough was Principle Investigator in a series of contracts to develop a blueprint for a national surveillance system to monitor PPE for the CDC. Her preventive medicine programming at Vanderbilt has received national and international recognition, including the ACOEM Corporate Health Achievement Award and the prestigious C. Everett Koop Award in health promotion.

Specific Aims of the Vanderbilt Epicenter Research Plan:

The proposed Vanderbilt Epicenter research plan outlined below is designed to examine several important issues surrounding pathogen transmission, use and misuse of PPE, and methods to improve the protection of HCP and their patients. The proposed studies also harness Vanderbilt's expertise in the use of simulation training and tools (Aim I),[76] monitoring and feedback of practice compliance using a model of shared accountability (Aim II),[34,99] and the performance of quasi-experimental studies of infection prevention interventions in an operational setting (Aim III).[65] Successful completion of the proposed studies will improve the capacity to prevent and control the spread of EVD, MDROs, *C. difficile* and other infectious pathogens with similar modes of transmission in healthcare settings, thereby helping to prevent and control both current and future outbreaks.

Specific Aim I: *To examine risk factors for HCP self-contamination with the donning, use, and doffing of PPE used for Contact, Droplet, and EVD-Specific Precautions using simulation laboratory techniques.*
Specific Aim II: *To evaluate in a variety of clinical care settings the effectiveness of a standardized PPE compliance auditing tool coupled with a tiered accountability framework.*
Specific Aim III: *To investigate the impact of preemptive Contact Precautions for residents of long-term care facilities admitted to acute care units, including the impact on the rate of hospital acquisition of MDRO and C. difficile and unintended consequences (e.g. frequency of HCP contacts, patient falls) due to this isolation strategy.*

Specific Aim I: To examine risk factors for HCP self-contamination with the donning, use, and doffing of PPE used for Contact, Droplet, and EVD-Specific Precautions using simulation laboratory techniques.

SIGNIFICANCE: This project will use simulation to evaluate and examine risk factors for HCP self-contamination with the donning, use, and doffing of PPE used for Contact, Droplet, and EVD-Specific Precautions. Several studies suggest that PPE training maybe inadequate and may vary by type of HCP and clinical area.[100,101] In examining issues with PPE effectiveness, it is important to evaluate PPE use under a variety of clinical circumstances. Conducting such investigations using HCP engaged in actual patient care can be very challenging. As such, recent studies have investigated PPE use and the risk of self and environmental contamination using simulation assessments. Using a non-pathogenic bacteriophage (MS2) and simulation training, Casanova *et al* examined the risk of contamination and breaches with the use PPE among 10 volunteers.[102] Following the donning of PPE (gown, gloves, eye protection, and an N95 particulate respirator) that were contaminated with MS2 at strategic locations, the study subjects measured blood pressure on a simulation manikin and then doffed the PPE components. Bacteriophage contamination of the hands and underlying clothing of the volunteers occurred in a majority of instances (hand contamination 70-90%, clothing 75-100% of instances).

Investigators at the University of Nebraska Medical Center also employed simulation assessment to examine donning, use, and doffing of the PPE used with Contact (i.e. gown and gloves) and Airborne (i.e. N95 respirator) Precautions.[103] Ten HCP volunteers were observed using video monitoring for breaches in recommended practices while performing a simulated patient care scenario. These breaches were assessed independently by three study investigators. Fluorescent markers (Glo Germ™ powder) were also placed on strategic locations in the simulation room, including on the patient's gown front and arms, the bedside table, and the bed handrails. Following PPE doffing, each subject was examined for self-contamination of the fluorescent powder. Every participant committed at least one breach in PPE use, including touching unprotected areas of the body with contaminated PPE and unnecessary touching of surfaces in the room. Contamination with the fluorescent powder was detected on 80% of the subjects.

In a follow up investigation, this team examined compliance with isolation practices among 24 nurses using a simulated patient care setting.[104] Using methods similar to those noted above, poor compliance with PPE donning, in-room PPE use, and PPE doffing was noted. Example breaches included failure to tie gowns at the neck, touching of the face or other nonprotected areas with contaminated gloves, and failure to doff PPE as per recommendations.

Casanova *et al* compared the use of single vs. double gloving while performing a vital signs assessment on a simulation manikin and the risk of MS2 nonpathogenic bacteriophage contamination of the PPE components and participant hands.[105] Among the 18 HCP volunteers, hand contamination with MS2 was significantly more frequent with the use of a single pair of gloves (occurring in 78% of volunteers vs. only 28% of volunteers when double gloving was utilized, $p = 0.006$). Errors in PPE removal were frequent in both scenarios (72% with any error in double gloving scenarios; 67% in the single gloving scenario). Importantly, contamination occurred even with a visible PPE removal protocol present for reference during the scenario, suggesting the need for additional strategies to improve compliance along with these "just-in-time" reminders.

Lai *et al* examined the risk of contamination with different glove removal techniques using a fluorescent solution. Glove removal using any technique led to environmental contamination.[106] Wong and colleagues identified a variable risk of HCP contamination between different types of PPE (gowns or aprons) using simulated respiratory secretion exposure with a fluorescein solution.[107] A randomized crossover study of 50 subjects wearing novel respiratory pathogen precautions PPE (gloves, gown, N95 particulate respirator, face shield, and hair cover with and without a powered air-purifying respirator [PAPR]) also used fluorescein solution to assess contamination with PPE use. The solution was atomized onto the HCP while in the PPE,

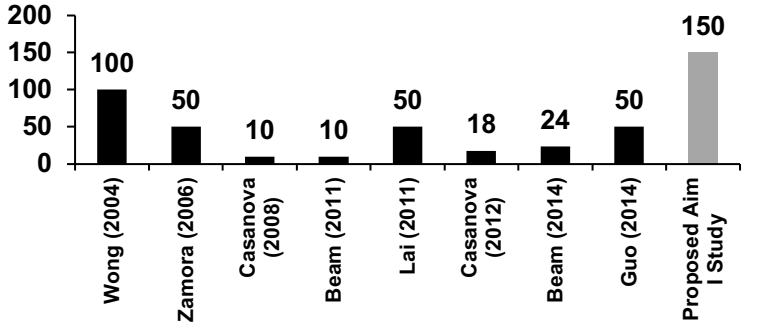
mimicking exposure to respiratory droplets. Contamination was greater in those who did not wear the PAPR, with the anterior neck, forearms, wrists and hands the most common areas of contamination.[108]

Finally, Guo *et al* examined the risk of breaches and environmental contamination with the use of three types of protective gowns and two different recommended strategies of gown removal.[109] Contamination was assessed using a fluorescent lotion (detected by ultraviolet units) mixed with olive oil and water to mimic infectious aerosol particles. Subjects received video training on the use of PPE and, once PPE was donned, were exposed to a spray of lotion on the upper torso. PPE was then doffed in a separate area. Environmental contamination was significantly lower when using a gown removal method that pulled the gown away from the wearer during doffing. The researchers also noted that hand contamination was significantly higher among subjects who had at least 16 years of clinical experience (perhaps due to a false sense of competency with PPE use), while nurses had a higher rate of shoe contamination when compared to other provider types. A cotton gown was associated with lower contamination of the environment when compared to a water-resistant gown and a disposable plastic apron; however, undergarment contamination was increased with use of the cotton gown.

While these studies are advancements in the understanding of and risk for breaches in PPE use, there are several key limitations. First, the number of HCP studied was relatively limited, in part due to the complexities and costs of simulation assessments (Figure 2). Second, the simulation scenarios involved single patient care tasks (e.g. blood pressure assessment) rather than a more complex patient interaction than is common during patient care. Finally, the duration of the scenarios were short and may not have captured issues and risk factors associated with more prolonged PPE use.

For this study Aim, we will utilize the expertise of investigators from the Vanderbilt Center for Experiential Learning and Assessment (CELA).[77,110-112] Directed by Arna Banerjee (an Epicenter Investigator), CELA is an advanced facility with of several interrelated programs, including human simulation using standardized patients and technical simulation utilizing state-of-the-art manikins. CELA optimizes the benefits of simulation by means of deliberate practice and multiple layers of thoughtful feedback and assessment, with a view towards enhancing professional communication skills and the mitigation of human error in the delivery of patient care. We aim to assess the frequency of and risk factors for PPE breaches using a larger study population and more complex scenarios that mimic typical patient care activities during which PPE is used.

Figure 2: Total Number of Subjects in Studies Examining PPE Breaches Using Simulation Tools



INNOVATION: The main innovation of this study Aim is that the majority of prior studies were on single evaluations of PPE breaches (double vs single gloves as example), where the current study will be comprehensive and employ longer and more complex scenarios that mirror actual HCP activities. In addition, 3 different precaution scenarios will be assessed. We will also use a cohort of HCP that is larger than in published investigations of this issue. We believe that patient care settings will not provide this opportunity because such activities usually occur in time-pressed, uncontrolled environments where patients must take precedence. Simulation has been

widely touted as a tool to improve clinical care and patient safety. It is a broad construct that ranges from role-playing to full-scale manikin-based Realistic Patient Simulation (RPS) and includes standardized patients (SP) and partial task trainers of varying sophistication. Realistic Patient Simulations can involve fully interactive simulation environments containing all clinical equipment and cues found in the patient care environment.[113] The manikin to be used in this project (SimMan™) is a computer-controlled plastic patient that generates or emulates physiological findings (e.g. ECG, invasive and non-invasive blood pressure, lung sounds, palpable pulses). The manikin's head contains a speaker so that the participant can converse with the 'patient' when contextually appropriate. The manikin responds to clinical interventions just as a patient would. Thus, participants interact with a realistic cognitive and physical representation of the full acute care environment and thereby experiences emotional and physiologic responses similar to those experienced in real situations.[114]

We will also use Standardized Patients (SP). SPs are persons recruited and trained to simulate an individual with a specific clinical story and respond accurately and reliably to questions regarding the medical condition or illness portrayed during a clinical encounter. SPs are trained to communicate emotional or contextual aspects of the scenario. The concept of SP has been applied to a wide range of training and assessment exercises that now include standardized family members, clients, standardized examinees and members of healthcare teams. In this study, we will use SPs as well as Simulated Clinicians (SC) who as team members will enhance the realism of the scenario. SPs have been effectively used in healthcare research, including clinician training, quality improvement and patient safety.[77] Successful completion of this Aim will result in an in depth-understanding of the frequency of and risks for lapses in PPE use and will inform the development of a standardized PPE compliance audit tool for use in a wide array of healthcare settings. Implementation of this tool will be the focus of Aim II. This may also lead to further studies on the use of these tools and infrastructure to train HCP on appropriate PPE use.

APPROACH:

RESEARCH DESIGN AND METHODS:

Study design: High-fidelity simulation experiments performed using three transmission-based precaution scenarios.

Study eligibility: HCP will be recruited for participation in the experimental assessments. The target sample size is 150 subjects with an explicit goal for a diversity of HCP types (i.e. physicians, nurses, and house staff). Eligible subjects must be currently working in a healthcare setting. Because the intricacies of EVD-specific precautions, for the scenarios focused on this type of precautions, volunteers will be recruited from members of the Vanderbilt Communicable Disease Response Team (CDRT). The CDRT consists of HCP from the following disciplines: nurses, physicians (including Epicenter Investigators Talbot and Nelson), paramedics, and educators. Each team member possesses knowledge and/or skills necessary to care for patients who require intensive medical care. Each volunteer also receives intensive periodic (quarterly) training in the care of patients with highly communicable, serious infectious diseases. Training includes specific disease pathology, PPE use, and EVD infection prevention protocols. Participants will be paid for participation in this study.

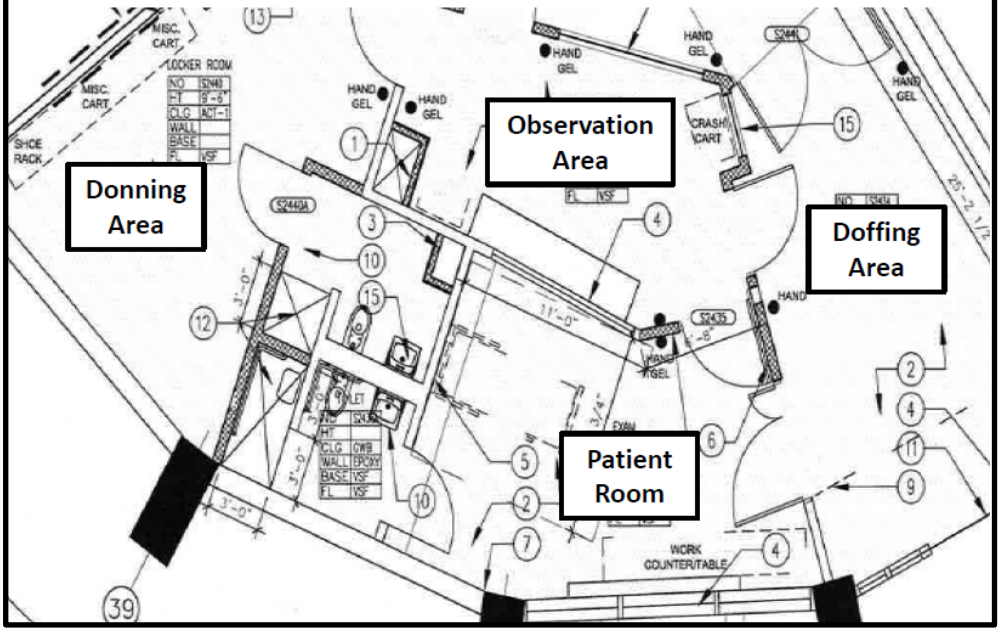
Study locations:

Center for Experiential Learning and Assessment (CELA): Most of the experiments will occur in the Vanderbilt CELA. This is an 11,000+ sq. ft. facility that includes a 1,100 sq. ft. simulation suite for manikin-based simulation. This structure allows two separate simulations to run simultaneously, configured jointly as a six-bed ED, four-bed ICU or PACU, or a combination of these, or to be a large single simulation suite that can be used for simulations. The suite also has a virtual reality training room, available 24/7, equipped with the latest in virtual reality simulators and partial task trainers designed to train advanced medical procedures.

Another core program involves the use of SP in simulations. This program is housed in a 7000 sq. ft. suite which consists of 12 fully equipped exam rooms, with the latest audiovisual and computer capabilities and one-way viewing mirrors into the exam rooms. Additional facilities are a designated student orientation room equipped with full audiovisual capabilities, a private observation room with monitors to watch student encounters and provide feedback through a software interface, two control rooms for operating the center's audio visual and software components, and a standardized patient lounge for use during events as well as a dedicated conference room for SP training and overflow during full capacity.

Communicable Disease Response Unit (CDRU): For the EVD-Precautions scenarios, we will also utilize the Vanderbilt CDRU. The CDRU (Figure 3) is a state-of-the-art facility designed for the care of a patient with a rare or unknown, highly communicable disease, such as EVD or MERS-CoV. The unit consists of several distinct areas: patient room, anteroom, PPE doffing area, and nurse's station. It provides a safe environment to care for patients while protecting staff, other patients, and the local community. Patient is care is provided by the CDRT.

Figure 3: Blueprint Layout of Vanderbilt Communicable Disease Response Unit (CDRU)



Study procedures: Three transmission-based precaution scenarios will be utilized (Table 2). These will involve Contact Precautions (PPE: gown and gloves), Droplet Precautions (PPE: surgical mask), and EVD-Precautions (PPE: PAPR, eye protection, hood, gown, double gloves, leg coverings, and apron). For the Contact Precautions scenario, subjects will perform a brief history and abbreviated physical exam along with a simulated wound dressing change. For the Droplet Precautions scenario, subjects will perform a brief history and abbreviated physical examination along with management of a urinary catheter (including emptying of collection bag). For the EVD-Precautions scenario, subjects will perform a brief history and abbreviated physical exam along with medication administration through an intravenous catheter. Non-CDRT personnel will participate in both the Contact and Droplet scenarios (A-D in Table 2), while only CDRT members will participate in the EVD-Precautions scenario (E & F in Table 2). Each scenario will have a standard 10 minute duration and a prolonged 20 minute duration (in which the exam is a standard physical exam) to assess the impact of prolonged PPE use on compliance.

Table 2: Simulation Scenarios for Aim I

Scenario	Standard Duration (10 mins)	Prolonged Duration (20 mins)
Contact Precautions	**A**	**B**
Droplet Precautions	**C**	**D**
EVD-Precautions	**E**	**F**

Using a fluorescent compound to reproduce contaminants in assessing

contamination rate is effective and can be utilized for comparison with body and environmental contamination levels.[106-108] A fluorescent powder (Glo Germ Co, Moab, UT)[115] especially developed for determining hand hygiene compliance will be used in this study. The powder will be applied in standardized amounts at locations surrounding and on the simulated patient (on patient's upper torso and arms, within the simulated wound for scenarios A & B, on the urinary collection bag for scenarios C & D, on the peripheral IV hub in scenarios E & F, on both bed rails, and on the patient's bedside table) prior to the scenario start. Subjects will be blinded to the locations of powder placement.

Study outcomes and assessment:

1) Lapses in PPE use: These will be captured via video monitoring and recording of each subject experiment from PPE donning through PPE doffing. Two independent investigators will review every scenario and note the frequency and type of breaches in the use of PPE. Investigators will be trained on a standardized method for reviewing each scenario and will use a standardized abstraction tool. The time of the lapse in relation to scenario start will be captured to examine the impact of the duration of PPE use.

2) HCP and environmental contamination: Contamination will be assessed using ultraviolet light inspection of the subjects following doffing of PPE and of the simulation room environment to assess for the number of contamination events during each scenario. The rooms will be cleaned prior to each experiment to avoid cross-contamination.

Analysis: A descriptive analysis of the frequency (number per minute of scenario time), number, and types of lapses in PPE use will be performed. The number of self and environmental contamination events (defined as an identified patch of fluorescent powder located in these areas) will also be described as a quantitative number and an event rate per minute of scenario time. Lapse and contamination rates will be compared between each scenario type (Contact, Droplet, and EVD), scenario duration (standard vs. prolonged), and HCP type (physician, nurse, other) using Student's t-test or Wilcoxon Rank Sum test (for duration comparison) and ANOVA or Kruskal-Wallis analysis (for precaution type and HCP type comparison given >2 study groups). For categorical outcomes (e.g. the number of lapses) Fisher's Exact Test will used for comparisons.

Limitations: Even with a larger study cohort, the sample size will limit the ability to examine nuanced details in patient care while wearing PPE that lead to lapses. Nonetheless, this will be one of the largest and most complex simulation experiments on PPE use published to date.

Specific Aim II: To evaluate in a variety of clinical care settings the effectiveness of a standardized PPE compliance auditing tool coupled with a tiered accountability framework.

SIGNIFICANCE: The lessons learned from hand hygiene improvement programs may be helpful when examining methods to audit and improve PPE compliance among HCP. Various innovative interventions to facilitate hand hygiene compliance have been developed over the past decade. These include visible and tactile monitors that alert the HCP to perform hand hygiene in real-time, user-friendly alcohol-based hand rub dispensers that provide easy access to hand hygiene materials, and enhanced monitoring tools.[116] These interventions not only incorporate the practice of hand hygiene into the workflow of HCP but also explicitly emphasize the importance of performing this essential infection prevention practice. Nonetheless, even with advancements in hand hygiene monitoring, messaging, and access to product, because the decision to perform hand hygiene is ultimately rooted in the behavior of the HCP, failure to develop interventions to drive expected behaviors will reduce the impact of these tools. PPE compliance is very similar, as even with advances in the PPE that may facilitate donning, use, and doffing, the underlying determinant of safe PPE utilization is rooted in HCP behavior.

Hand hygiene compliance monitoring has now become a central part of infection prevention programs at most healthcare facilities, and these data are being used on a large-scale as measures of healthcare quality.[117] In Australia, for example, the creation of the National Hand Hygiene Initiative in 2009 required the reporting of hand hygiene compliance in all Australian hospitals using a standardized methodology.[118] The development of a standardized measurement and education process for hand hygiene, the "Five Moments for Hand Hygiene" developed by the WHO, was a major advancement that provided healthcare facilities with a set of tools to improve hand hygiene compliance.[36] In contrast, standardized tools for auditing PPE compliance akin to the "Five Moments" methodology are absent. Ideally, these tools should be guided by data on practices that increase the risk for PPE breaches and the associated contamination of HCP and the environment.

As noted previously, we have extensive experience in the creation and successful implementation of a hand hygiene compliance improvement program that partners standardized, wide-scale auditing of HCP practice with a foundational structure of data feedback, real-time peer-to-peer interventions to professionally redirect noncompliant behaviors, and performance accountability.[34] Implemented in July 2009, the comprehensive program included extensive project planning, leadership buy-in and goal setting, financial incentives linked to performance, and use of a system-wide, shared accountability model. Compliance is monitored by direct observation of practice, and every inpatient and outpatient patient care area must designate a HCP to serve as an observer. Observers, once trained in the audit methodology, monitor locations other than their own on a monthly basis. This system has created an interdependence of unit leaders upon one another to provide important data to help drive improvement.

A central part of the program includes a formalized process for redirecting noncompliant behavior in real-time and a formal tiered accountability process that elevates units with compliance below institutional goals to receive more directed intervention. Using a tiered pyramid approach,[99] unit leaders with compliance rates below institutional goals are made aware of their performance compared to their peers, and if improvement is not noted, enhanced interventions occur. This program covers over 200 distinct clinical units (inpatient, outpatient, and procedural) and has captured over 250,000 observations of practice to date. It has resulted in significantly improved and sustained compliance rates (from 52% at program start to 96% for the current fiscal year), has been associated with reductions in HAIs, and, most importantly, has help drive a culture where monitoring and real-time correction of HCP behaviors is expected and accepted as an important safety intervention.[34] The success of this program was recognized in 2014 when the study manuscript was designated by SHEA as the year's top research paper published in the premier healthcare epidemiology journal, *Infection Control and Hospital Epidemiology*.[119]

We propose that ensuring compliance with transmission-based precautions and PPE must be driven by the same tenets and interventions used in improving hand hygiene compliance. While novel, more "user-friendly" types of PPE may be necessary to facilitate compliance, failure to hardwire practice through standardized process monitoring, shared accountability for performance, and professional real-time reminders will limit the effectiveness of improved equipment. This study Aim will examine the utilization and impact of a standard PPE compliance auditing tool folded into a shared accountability program model. Our hypothesis is that such a tool will aid in capturing PPE compliance in a diversity of healthcare settings and that the overriding process will result in a sustained improvement in practice.

INNOVATION: The primary innovations of this Aim are the development and evaluation of a standardized tool to audit PPE compliance and the creation of a structured program to hardwire expected behaviors surrounding safe PPE use. We anticipate that this tool and program

structure can be utilized to improve practice in a wide-array of healthcare facility types, similar to the impact the standardized hand hygiene compliance tools and programs.

APPROACH:

RESEARCH DESIGN AND METHODS:

Study Design: 1) Audit tool development and field testing; 2) Prospective quasi-experimental phased implementation study.

Tool Development and Initial Evaluation: For this Aim, we will first develop a PPE compliance audit tool based on learnings from the simulation experiments in Aim I. Information on the types of breaches in PPE use and the practices that led to these breaches will inform the tool. A review panel of experts in infection prevention, PPE use, and occupational infection prevention (consisting of some members of the Advisory and Steering Committee) will independently review the tool for content validity. An initial evaluation of the tool will then occur as members of the Vanderbilt Epicenter team will perform direct observation of practices using the tool. These observations will occur in a variety of healthcare facility types (including adult inpatient units at a tertiary academic medical center and at a community-based hospital, pediatric inpatient units, outpatient hemodialysis units, and an inpatient rehabilitation hospital). Feedback from these pilot observations, including time to complete and ease of use, will lead to revision of the tool for the second part of this Aim.

Implementation Study:

Study Population: The initial implementation will occur on acute care inpatient units at Vanderbilt University Hospital (VUH), the Monroe Carell Jr. Children's Hospital at Vanderbilt (MCJCHV), and Williamson Medical Center (WMC). The target number of units will be 6 VUH, 6 MCJCHV, and 2 WMC units. All HCP on study units will be included for observation of practice.

Study Procedures:

Study Outcomes: Overall compliance with PPE use for patients placed in transmission-based precautions.

Data Collection: Trained observers will utilize the revised audit tool to capture compliance. A target of 500 observations of individual HCP PPE use events will be collected per month per study unit. This will provide ~42,000 observations for each study period (500 observations/month/unit * 6 months * 14 units). These observers will be formal Vanderbilt Epicenter personnel as well as unit and clinic HCP, modeled after the Vanderbilt Hand Hygiene Program described above. Observers will be trained on the use of the tool in a standardized fashion.

Study Periods:

Baseline Monitoring Period: During this phase (6 months), PPE compliance will be audited by trained observers. Aggregate compliance reports with comparison to peer units will be fed back to unit leadership for dissemination among unit HCP.

Awareness and Accountability Period: Following the Baseline Monitoring Period an added facet of the program will be implemented with the intent of further improving PPE compliance. During this phase (6 months), PPE compliance will be audited using similar procedures to the baseline period. Two added measures will also be implemented: real-time reminders of lapses in PPE use by the trained observers and a tiered accountability model for feedback of compliance data (described below). Observers will be trained on how to provide professional feedback in real-time when lapses or noncompliance are identified.

Tiered Accountability Model for Feedback of Compliance Data: As a part of the observation process, tiered interventions that follow the model that has been used at Vanderbilt for several years to improve performance on multiple process and outcome measures, including hand hygiene, will be implemented. The tiered intervention model operates under the assumption that the vast majority of professionals will respond to data and improve

performance.[34,99,120,121] However, for some, additional interventions are needed to facilitate high performance. The steps of the tiered intervention (a.k.a. "accountability pyramid") are described in detail below (Figure 4).[99]

Monitoring and Feedback: This tier of the intervention will be implemented as part of the Baseline Monitoring period and continue into the Awareness and Accountability Period. During this phase, we will provide ongoing PPE compliance data to unit leader/quality management teams, including their performance relative to internal peers. We will reinforce their performance through positive messages from the study team and will ask them to share their best practices so that we may disseminate to other units for problem solving.

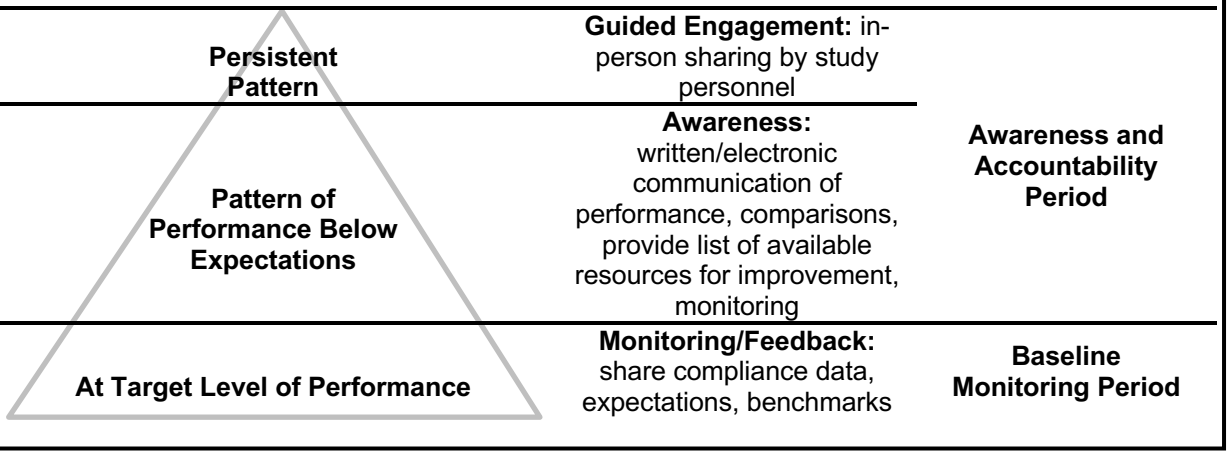
During the Awareness and Accountability Period, two additional tiers will be included.

1) Awareness: If a unit performs below target compliance goals for two or more periods, the unit leadership will receive written/electronic communication regarding the unit's below target performance (see *Sample Compliance Awareness Report*, Appendix) and will be provided information about resources available to improve performance, including local peers/units who are engaged in best practices. To allow units ample opportunity to demonstrate improvement, they may receive up to two awareness intervention visits before escalation to the next level.

2) *Guided Engagement:* If performance does not improve after two awareness interventions, units will receive a guided intervention, which includes in-person sharing of performance and meaningful comparisons delivered by trained study personnel.

Analysis: The aggregate rates of PPE compliance will be compared between both study periods, with a null hypothesis that compliance will not significantly improve from the Baseline Monitoring Period to the Awareness and Accountability Period. The primary analysis will examine the aggregate compliance in all study units, with an additional analysis stratified by acute care facility. In addition, a more robust interrupted time-series regression analysis with Newey-West standard errors will be performed using bimonthly compliance rates.

Figure 4: Tiered Accountability Model for Unit-Based PPE Compliance Performance



Limitations: Even with a robust observation program, the number of instances of HCP PPE use observed will be only a small proportion of the total number of these opportunities. Compliance measurements from the observed events may not be representative of the total, as there may be a Hawthorne Effect on HCP compliance based on the presence of an observer. We have encountered this issue with the hand hygiene program as well. Because these interventions and programs are designed to alter HCP behavior, we have found that even with the Hawthorne Effect of direct observation, the provision of regular observation and real-time feedback when lapses are noted has led to a hardwiring to expected behavior (based on other measures of hand hygiene compliance such as patient and embedded observer reports). We

anticipate a similar effect with the designed observation program. Finally, because the success of the hand hygiene program is due in part to the institutional culture at VUMC surrounding quality and to the shared goal of pursuing a robust and reliable quality and safety culture, any impact identified in our study will need to be examined in other settings, including those where such a culture is not as mature or robust.

Specific Aim III: To investigate the impact of preemptive Contact Precautions for residents of long-term care facilities admitted to acute care units, including the impact on the rate of hospital acquisition of MDRO and C. difficile and unintended consequences (e.g. frequency of HCP contacts, patient falls) due to this isolation strategy.

SIGNIFICANCE: One factor that may impact the effectiveness of the PPE used to prevent transmission of pathogens like MDROs and *C. difficile* centers upon the initial decision to implement these precautions. Specifically, patient selection for isolation precautions could lead to transmission if persons harboring these pathogens are not considered for placement into isolation. With the increasing prevalence of MDROs and *C. difficile*, specific patient populations at greater risk for infection and/or colonization with these organisms have been identified. One such patient population is residents of long term care facilities (LTCF).[122,123] LTCFs are important reservoirs of MDROs, including MRSA,[124] extended-spectrum beta lactamase (ESBL) producers,[125] MDR *Acinetobacter*,[126] and *C. difficile*.[127] A prospective cohort study evaluating transmission dynamics of MDR gram-negative bacteria (MDRGNB) among LTCF residents during one year of follow up found that 39% of residents acquired at least 1 MDRGNB.[128] A subsequent study evaluating 360 LTCF residents with advanced dementia demonstrated high rates of MDRO colonization at baseline (any MDRO = 45.6%, MDRGNB = 36.9%, MRSA = 12.8%). The proportion of all residents colonized at some point over a 12 month period was even higher: any MDRO, 66.9%; MDRGNB, 54.4%; and MRSA, 27.1%.[129]

When they are admitted to acute care facilities, these patients become an important source of MDRO and *C. difficile* transmission. In a study evaluating the inter- and intradissemination of MDRGNB among LTCF residents with advanced dementia, genetically-related MDRGNB strains were detected in residents of 82% (18/22) of LTCFs indicating interdissemination between these facilities. The authors concluded that MDRGNB are spread both within and between LTCFs among residents with advanced dementia and that infection control measures should target this high-risk group of residents.[130] A model of MRSA outbreaks in a LTCF demonstrated both direct and indirect effects of LTCF resident transfers on acute care facilities' MRSA prevalence indicating the role of transmission and need for hospitals to address LTCF in their infection control strategy.[131] CRE can be spread extensively throughout a diverse healthcare facility network, highlighted nicely by the involvement of 14 acute care hospitals, 2 long-term acute care facilities, and 10 LTCFs during an outbreak in a single community.[132] *C. difficile* shares similar risk factor and reservoir considerations as MDROs with the LTCF populations. Data suggest that *C. difficile* infection is endemic in LTCFs and remains largely uncontrolled despite numerous efforts to manage the issue.[133] The incidence rate (2.3 cases/10 000 resident-days) and recurrence rate (1.0 case/10 000 resident-days) of *C. difficile* infection in LTCFs is comparable to that of acute-care hospitals.[127]

At present, Contact Precautions are routinely employed in acute care facilities for patients colonized or infected with MDROs or *C. difficile*.[1] The decision to place a patient into these precautions is often based on the results of clinical or surveillance cultures positive for these pathogens. Notably, this practice may only identify patients at a time point after they have potentially exposed HCP, staff, and other patients. In addition, surveillance cultures obtained on patient admission is a controversial infection prevention strategy[134] and may not be performed in some hospitals. Even in those facilities that do perform such screening, testing for all important MDROs is rare and often not practical. Because of this, some have endorsed different

approaches to the identification of patients who may require Contact Precautions. As part of its Guidance for Control of CRE, the CDC noted that "extensive inter-facility sharing of patients across the continuum of care has the potential to facilitate widespread regional transmission of CRE." The guidelines then suggest as a supplementary practice to standard infection control practices the placement into preemptive Contact Precautions patients transferring from high-risk settings,[135] which may include LTCFs. Data are lacking to evaluate if this is a reasonable strategy. A review in *Clinical Microbiologic Review* stated, "[u]pon admission of patients at increased risk of CRE carriage (such as residency in an LTCF . . .), preemptive isolation while awaiting surveillance culture results can prevent early transmission events."[136] Preemptive Contact Precautions have been suggested for certain high risk groups[137] in extenuating circumstances for other pathogens such as MERS-CoV [138] with the understanding that targeting high risk populations could mitigate pathogen transmission.

Such an empiric isolation strategy, however, may have unintended consequences. Previous studies have demonstrated that patients placed into Contact Precautions may have more adverse events,[139] depression and delirium,[140] and potentially worse patient satisfaction and quality of care.[139,141-143] A prospective cohort study in four acute care facilities performing active surveillance for MRSA demonstrated that Contact Precautions were associated with activities likely to reduce transmission of MDROs such as fewer visits and better hand hygiene at exit, while simultaneously exposing patients to less HCP contact, less visitor contact and other unintended outcomes.[144] In contrast, a recent trial of universal gown and glove use in ICU settings assessed adverse event rates in these units and found patients were no more likely to experience adverse events than in control ICUs.[145]

For study Aim III, we will investigate the impact of preemptive Contact Precautions for residents of LTCFs admitted to acute care units on the rate of hospital acquisition of MDROs and *C. difficile*. We will also examine the potential for unintended consequences (e.g. frequency of HCP contacts, patient falls) due to this isolation strategy.

INNOVATION: Most Contact Precautions used in non-epidemic settings target patients with demonstrated MDRO or *C. difficile* infection or colonization detected through surveillance and/or clinical cultures. Our proposed study will preemptively target a population with a high risk exposure (LTCF residence). This approach has been suggested by CDC as a possible measure to reduce transmission of MDROs, but little evidence exists to support its use. A preemptive isolation approach would be logistically easy to implement operationally as there would be minimal delay in identifying patients who require isolation compared with the historical approach of culture-based practices. A preemptive isolation approach for high risk patients would be a horizontal infection control program, which would be a paradigm shift in terms of identifying those at risk and implementing control programs to reduce transmission. From a population-based perspective, horizontal infection control programs that substantially reduce all infections at a certain site is more impactful than a program than one that targets a single organism at that site.[146] Unintended consequences of Contact Precautions have been evaluated in several populations, but never specifically for LTCF residents. Any impact seen through a preemptive isolation strategy must be balanced with any unintended consequences. If this study demonstrates a decrease in hospital-onset (HO) MDRO/*C. difficile* infections **and** does not show an increase in non-infectious complications (i.e. patient falls), then it has the potential to be a new strategy for reducing pathogen transmission in acute care settings.

APPROACH:

Preliminary studies: The Vanderbilt Epicenter investigators have experience in the conduct of operational quasi-experimental studies. Specifically, we recently conducted a successful pragmatic cluster randomized, crossover study of 9,340 patients admitted to 5 adult ICUs from July 2012 through July 2013 to assess if daily chlorhexidine (CHG) bathing reduced HAIs.[65] The

primary prespecified outcome was a composite of central line-associated bloodstream infections (CLABSIs), catheter-associated urinary tract infections (CAUTIs), ventilator-associated pneumonia (VAP), and *C. difficile* infections. After adjusting for age, sex, race/ethnicity, unit of admission, time, comorbid conditions, and admission white blood cell count, no significant difference between groups in the rate of the primary outcome was detected. This study demonstrates Vanderbilt's capacity to support large-scale trials evaluating infection prevention interventions.

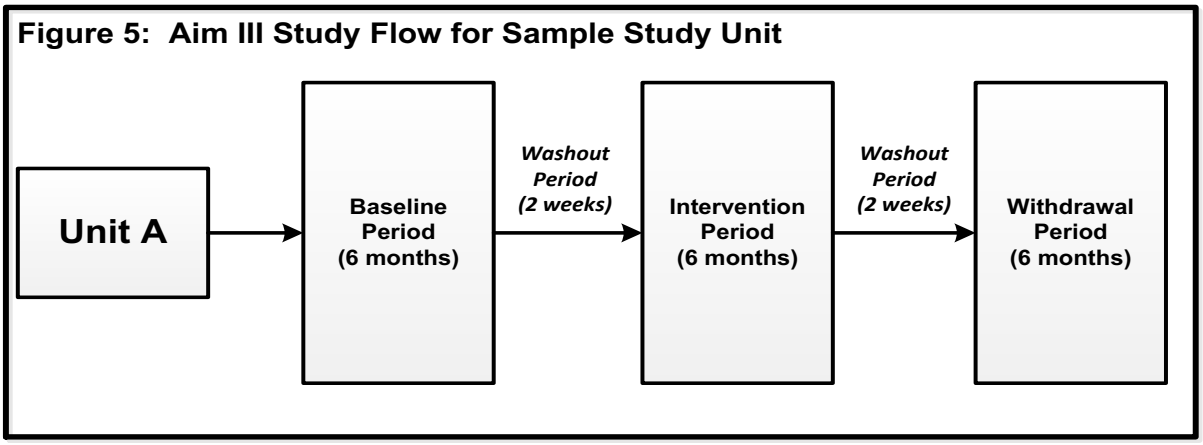
RESEARCH DESIGN AND METHODS:

Study design: Pre-post withdrawal quasi-experimental study using interrupted time series analysis.

Study sites: Six inpatient medical units within Vanderbilt University Hospital will serve as study units. These have been selected due to a higher rate of HO-MDRO/*C. difficile* incidence and/or a higher proportion of admissions comprising LCTF patients. The proposed acute care units have an average of 4,952 patient days per month with LTCF residents comprising 4.3-5.6% of unit admissions. This percentage is likely an underestimation because not all places of patient origin are documented and transfers between units within VUH are not included in this analysis. The HO-MDRO/*C. difficile* rate of these 6 units combined was 4.62 per 1,000 patient days for 2014.

Study procedures: After a 6 month baseline period, all units will be transitioned to a 6 month intervention period where all patients transferred onto the study units with LTCF origin prior to admission will be placed on preemptive Contact Precautions (Figure 5). Both patients admitted directly to a study unit as well as patients transferred from a non-study unit onto a study unit will be included under the policy. A washout period of 2 weeks will be introduced before a post-intervention withdrawal period of 6 months is implemented.

Figure 5: Aim III Study Flow for Sample Study Unit



Inclusion/exclusion criteria: All patients admitted to the unit will be included in the study. There will be no exclusion criteria.

Primary outcome - Rate of hospital-onset MDRO and *C. difficile* infections: Aggregate rates of all hospital-onset (HO)-MDRO infections (Table 3), including MRSA, *C. difficile*, VRE, ESBL+ GNB, CRE, and MDR *Acinetobacter*, on participating units will be calculated. As active surveillance for these pathogens is not performed at VUH, only culture specimens obtained for clinical decision making will be included. Specimens from any site (e.g. blood, urine, wound) will be included. These events will be captured daily using the Vanderbilt Infection Prevention Electronic Resource (VIPER), an HAI surveillance platform that monitors laboratory results in real time. Events will be classified as HO if the specimen was collected >3 days after admission to VUH (i.e. on or after day 4).

Secondary outcomes:

1) Unintended consequences:

a. Patient fall rates: All patient falls are reported and recorded as a part of the VUH quality program using the National Database of Nursing Quality Indicators (NDNQI) definitions and process.[147] As per NDNQI, a fall is defined as "an unplanned descent to the floor or other lower surface with or without injury to the patient that occurs in an eligible nursing unit."[147] All events are reviewed and categorized based on the degree of patient injury/harm, if any occurred. The fall rate per 1,000 patient days for the aggregate study unit population will be measured. In addition the rate of falls with harm (as defined by NDNQI) will also be assessed.

b. Fall events in patients placed in the preemptive intervention: In addition to the aggregate fall rates for the study units, the frequency and number of falls (as defined by NDNQI) that occur in patients placed into preemptive isolation will be captured.

c. HCP contact with patients placed in the preemptive intervention: Trained study personnel will audit HCP contact (time spent, # of encounters) for all patients placed into preemptive isolation as previously described.[145] As a proxy of HCP frequency of contact, the number of vital signs recorded per patient day will also be analyzed.

Table 3: Definitions of MDROs Included in Primary Study Outcome

MDRO Type	Defined as
MRSA	*Staphylococcus aureus* resistant to oxacillin or methicillin by standard susceptibility testing methods
VRE (vancomycin-resistant enterococci)	*Enterococcus faecalis*, *Enterococcus faecium*, or other *Enterococcus* species that is resistant to vancomycin
CRE (carbapenem-resistant Enterobacteriaceae)	Any *Escherichia coli*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, or *Enterobacter spp.* testing resistant to imipenem, meropenem, doripenem, or ertapenem by standard susceptibility testing methods OR by production of a carbapenemase (i.e., KPC, NDM, VIM, IMP, OXA-48) demonstrated using a recognized test (e.g., polymerase chain reaction).
MDR (multidrug resistant)-*Acinetobacter*	Any *Acinetobacter spp.* testing non-susceptible (i.e., resistant or intermediate) to at least one agent in three or more classes of antibiotics (excluding nitrofurantoin, tetracyclines, 1st and 2nd generation cephalosporins, and non-extended-spectrum penicillins)
ESBL + GNB (extended-spectrum beta-lactamase producing gram-negative bacillus)	Any *E. coli*, *K. pneumoniae* and *K. oxytoca* demonstrated to have ESBL activity based on results from BD Phoenix through microdilution methodology. The BD Phoenix performs ESBL testing using cephalosporins (ceftazidime/cefotaxime/ceftriaxone) + clavulanic acid.

2) Subgroup examinations of individual pathogen HO-infection rates for the overall study population and the aggregate HO-MDRO/*C. difficile* infection rate for each individual study unit

Covariates: Several factors may affect the impact of the intervention on the primary outcome. These will be measured and included in the analysis.

1) Hand hygiene compliance: Study unit compliance with hand hygiene as monitored by the Vanderbilt Hand Hygiene Program[34] will be included for analysis.

2) PPE compliance: Trained study personnel will perform audits of PPE use by HCP caring for patients placed into the preemptive intervention.

3) Antimicrobial utilization: Use of broad-spectrum antibiotics is currently tracked as a part of the VUMC Antibiotic Stewardship Program (Co-directed by Epicenter investigator Nelson). Because antibiotic use is a factor in the acquisition of MDROs and *C. difficile*, we will include a measure of broad-spectrum antimicrobial use in the analysis (measured as days of therapy [DOT]).

Analysis: The rates of the primary and secondary outcomes will be compared for the following phases, defined *a priori*: 6 month baseline period, 6 month intervention period, and 6 month withdrawal period. In addition, a more robust interrupted time-series regression analysis with Newey-West standard errors will be performed using bimonthly outcome rates (which will provide 12 separate time point measurements for each period).

Sample size considerations: Existing data were used to assess sample size adequacy. Using patient-days, the mean patient days per period will be 4,952 patient days/month for a total of 29,710/period. The rate of HO-MDROs on the units of interest is 4.6/1000 patient days for an average of 137 evaluable events per period. This study will have 80% power to detect a true difference in infection rates of 1.4/1000 patient days. That means a reduction by approximately 42 events in the intervention period. Nursing home admissions (those that will receive the intervention) are at least 4.3-5.6% on target units which is likely an underestimate given the current reporting system.

Safety: A data safety monitoring board (DSMB) will be created to oversee any potential adverse events that would require further assessment and intervention. At present 100% of falls, including all falls with harm, have an event review as part of the VUH quality program. The current fall rate on the four proposed units is 2.6 falls/month. The DSMB will review the event analysis of all falls on the unit on a quarterly basis with more in depth interim analysis of all falls stratified by study intervention. Due to the low rates of baseline falls, there is the potential for low case counts to cause large percentage increases, making a pre-defined threshold difficult for stopping the trial. If a sustained, significant increase in falls is seen and thought to be due to the Contact Precautions intervention, then the study will be halted.

Limitations and future directions: The evaluation of preemptive Contact Precautions for patients with LTCF exposure will be conducted in an academic, tertiary referral hospital with high rates of hand hygiene compliance. Preemptive isolation is a supplementary strategy and may not be generalizable to acute care hospitals with suboptimal hand hygiene compliance. If an impact on HO infections is seen during the intervention without unintended consequences, then there may be other high risk epidemiologic groups that could benefit from preemptive isolation. If this trial shows a reduction in HO-MDRO rates, this strategy may benefit from a larger-multicenter trial with randomization. This study has the potential to transform how isolation policies are implemented in acute care hospitals and could reduce the risk of pathogen transmission to other HCP and their patients.

Information Applicable to All Vanderbilt Epicenter Study Aims:

Regulatory Plans: Each individual research Aim project will be submitted to the Vanderbilt Institutional Review Board (IRB) for review prior to study onset. Vanderbilt has also developed IRBshare, a joint IRB review model for multisite studies that provides a mechanism to streamline IRB submission and the IRB review process at all phases of IRB review through the sharing of and reliance on IRB-approved documents between IRBs. This will be available for Vanderbilt Epicenter investigators for any multisite Epicenter research project. Volunteers for Aim I will undergo informed consent prior to study participation, although it is anticipated that the risks to subjects from participation in the simulation experiments will be minimal. For the Aim II audit and performance feedback project, we will request exemption from informed consent due to the minimal risk of observed subjects and the impact of obtaining informed consent on the validity of the observation data. Observers will be trained to note when significant breaches in PPE use occur that would warrant additional intervention above routine infection prevention practices such as hand hygiene. We will also request exemption from informed consent for study Aim III. Similar to the study of universal gown and glove use in the ICU (BUGG study),[145] this aim evaluates different infection prevention isolation policies. The BUGG study finding of no difference in adverse events among intervention subjects is reassuring regarding minimal

risk. We will have as an added measure, a formal safety monitoring group to investigate any increases in patient fall events among study subjects as a matter of added assurance.

Evaluation Plan: Several processes will be used to evaluate the Vanderbilt Epicenter program to ensure a research program that is innovative and up-to-date. Investigators will stay abreast of emerging issues and knowledge gaps related to the prevention of infectious pathogen transmission in healthcare settings through regular assessment of the medical literature and attendance at major scientific meetings in the field (i.e. IDWeek, SHEA Spring Scientific meeting). Vanderbilt Epicenter project findings will be submitted for publication in peer-review journals to disseminate this information to the healthcare epidemiology audience. Using the Advisory and Steering Committee, which will meet quarterly, the progress on the research plan in accordance to the timeline below will be tracked. Additional metrics will include the number of abstract presentations at scientific meetings, study-related publications, and creation of new study protocols in response to identified evidence gaps and CDC requests.

Timeline for Vanderbilt Epicenter Research Plan:

	Year 1				Year 2				Year 3			
Quarter	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**
Aim I												
Scenario development/planning												
Subject recruitment												
Experiments in simulation center												
Data analysis												
Presentation and publication of findings												
Aim II												
Audit tool development												
Observer training, study unit selection												
Baseline observation period												
Awareness/accountability period												
Data analysis												
Presentation and publication of findings												
Aim III												
Finalize study protocol/implementation												
Baseline period												
Intervention period												
Withdrawal period												
Data analysis												
Presentation and publication of findings												

Translation of Epicenter Findings/Future Directions: Successful completion of the Vanderbilt Epicenter projects will advance the understanding of various aspects of transmission-based precautions used to prevent pathogen spread in healthcare settings. This includes the development of tools to audit and train HCP on the appropriate and safe use of PPE, methods to hardwire such practices, novel strategies to evaluate new protocols (i.e. using simulation tools), and alternative strategies for use of these precautions. These results may direct future guidelines and policies surrounding safe use of PPE and should stimulate future hypothesis-generation for additional studies on these important issues.

Bibliography:

1. Siegel JD, Rhinehart E, Jackson M, Chiarello L, Health Care Infection Control Practices Advisory C. 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Health Care Settings. Am J Infect Control 2007;35:S65-164.
2. Marsteller JA, Hsu YJ, Weeks K. Evaluating the impact of mandatory public reporting on participation and performance in a program to reduce central line-associated bloodstream infections: evidence from a national patient safety collaborative. Am J Infect Control 2014;42:S209-15.
3. Centers for Disease C, Prevention. Vital signs: central line-associated blood stream infections--United States, 2001, 2008, and 2009. MMWR Morb Mortal Wkly Rep 2011;60:243-8.
4. Wright SW, Decker MD, Edwards KM. Incidence of pertussis infection in healthcare workers. Infect Control Hosp Epidemiol 1999;20:120-3.
5. Baba H, Iinuma Y, Imaizumi K, et al. Transmission of bacterial infections to healthcare workers during intubation and respiratory care of patients with severe pneumonia. Infect Control Hosp Epidemiol 2009;30:1019-21.
6. Kuster SP, Shah PS, Coleman BL, et al. Incidence of influenza in healthy adults and healthcare workers: a systematic review and meta-analysis. PLoS One 2011;6:e26239.
7. Sydnor E, Perl TM. Healthcare providers as sources of vaccine-preventable diseases. Vaccine 2014;32:4814-22.
8. Danzmann L, Gastmeier P, Schwab F, Vonberg RP. Health care workers causing large nosocomial outbreaks: a systematic review. BMC Infect Dis 2013;13:98.
9. Cimolai N. The role of healthcare personnel in the maintenance and spread of methicillin-resistant Staphylococcus aureus. J Infect Public Health 2008;1:78-100.
10. Liddell AM, Davey RT, Jr., Mehta AK, et al. Characteristics and Clinical Management of a Cluster of 3 Patients With Ebola Virus Disease, Including the First Domestically Acquired Cases in the United States. Ann Intern Med 2015.
11. Kliff S. How does an American nurse contract Ebola? With directions like these. Vox Accessed on May 21, 2015 at http://wwwvoxcom/2014/10/13/6968775/ebola-nurse-united-states-texas-directions-protocol-breach.
12. Edmond MB, Diekema DJ, Perencevich EN. Ebola virus disease and the need for new personal protective equipment. JAMA 2014;312:2495-6.
13. Centers for Disease Control and Prevention. Guidance on Personal Protective Equipment To Be Used by Healthcare Workers During Management of Patients with Ebola Virus Disease in U.S. Hospitals, Including Procedures for Putting On (Donning) and Removing (Doffing). Accessed on May 21, 2015 at http://www.cdc.gov/vhf/ebola/healthcare-us/ppe/guidance.html.
14. Lessa FC, Mu Y, Bamberg WM, et al. Burden of Clostridium difficile infection in the United States. N Engl J Med 2015;372:825-34.
15. Dhar S, Marchaim D, Tansek R, et al. Contact precautions: more is not necessarily better. Infect Control Hosp Epidemiol 2014;35:213-21.
16. Manian FA, Ponzillo JJ. Compliance with routine use of gowns by healthcare workers (HCWs) and non-HCW visitors on entry into the rooms of patients under contact precautions. Infect Control Hosp Epidemiol 2007;28:337-40.
17. Weber DJ, Sickbert-Bennett EE, Brown VM, et al. Compliance with isolation precautions at a university hospital. Infect Control Hosp Epidemiol 2007;28:358-61.
18. Clock SA, Cohen B, Behta M, Ross B, Larson EL. Contact precautions for multidrug-resistant organisms: Current recommendations and actual practice. Am J Infect Control 2010;38:105-11.

19. Chiang WC, Wang HC, Chen SY, et al. Lack of compliance with basic infection control measures during cardiopulmonary resuscitation--are we ready for another epidemic? Resuscitation 2008;77:356-62.
20. Morgan DJ, Rogawski E, Thom KA, et al. Transfer of multidrug-resistant bacteria to healthcare workers' gloves and gowns after patient contact increases with environmental contamination. Crit Care Med 2012;40:1045-51.
21. Landelle C, Verachten M, Legrand P, Girou E, Barbut F, Brun-Buisson C. Contamination of healthcare workers' hands with Clostridium difficile spores after caring for patients with C. difficile infection. Infect Control Hosp Epidemiol 2014;35:10-5.
22. Centers for Disease Control and Prevention. In the Absence of SARS-CoV Transmission Worldwide: Guidance for Surveillance, Clinical and Laboratory Evaluation, and Reporting Accessed on May 21, 2015 at http://www.cdc.gov/sars/surveillance/absence.html.
23. Centers for Disease C, Prevention. Update: severe acute respiratory syndrome--Toronto, Canada, 2003. MMWR Morb Mortal Wkly Rep 2003;52:547-50.
24. Arfons L, Ray AJ, Donskey CJ. Clostridium difficile infection among health care workers receiving antibiotic therapy. Clin Infect Dis 2005;40:1384-5.
25. Muder RR, Brennen C, Goetz AM. Infection with methicillin-resistant Staphylococcus aureus among hospital employees. Infect Control Hosp Epidemiol 1993;14:576-8.
26. Albrich WC, Harbarth S. Health-care workers: source, vector, or victim of MRSA? Lancet Infect Dis 2008;8:289-301.
27. Pascual FB, McCall CL, McMurtray A, Payton T, Smith F, Bisgard KM. Outbreak of pertussis among healthcare workers in a hospital surgical unit. Infect Control Hosp Epidemiol 2006;27:546-52.
28. Baxi R, Mytton OT, Abid M, et al. Outbreak report: nosocomial transmission of measles through an unvaccinated healthcare worker-implications for public health. J Public Health (Oxf) 2014;36:375-81.
29. Wharton M, Cochi SL, Hutcheson RH, Schaffner W. Mumps transmission in hospitals. Arch Intern Med 1990;150:47-9.
30. Chen LF, Dailey NJ, Rao AK, et al. Cluster of oseltamivir-resistant 2009 pandemic influenza A (H1N1) virus infections on a hospital ward among immunocompromised patients--North Carolina, 2009. J Infect Dis 2011;203:838-46.
31. Johnston CP, Qiu H, Ticehurst JR, et al. Outbreak management and implications of a nosocomial norovirus outbreak. Clin Infect Dis 2007;45:534-40.
32. Shigayeva A, Green K, Raboud JM, et al. Factors associated with critical-care healthcare workers' adherence to recommended barrier precautions during the Toronto severe acute respiratory syndrome outbreak. Infect Control Hosp Epidemiol 2007;28:1275-83.
33. Ofner-Agostini M, Gravel D, McDonald LC, et al. Cluster of cases of severe acute respiratory syndrome among Toronto healthcare workers after implementation of infection control precautions: a case series. Infect Control Hosp Epidemiol 2006;27:473-8.
34. Talbot TR, Johnson JG, Fergus C, et al. Sustained improvement in hand hygiene adherence: utilizing shared accountability and financial incentives. Infect Control Hosp Epidemiol 2013;34:1129-36.
35. Ellingson K, Haas JP, Aiello AE, et al. Strategies to prevent healthcare-associated infections through hand hygiene. Infect Control Hosp Epidemiol 2014;35:937-60.
36. Sax H, Allegranzi B, Uckay I, Larson E, Boyce J, Pittet D. 'My five moments for hand hygiene': a user-centred design approach to understand, train, monitor and report hand hygiene. J Hosp Infect 2007;67:9-21.
37. Evans RS, Wallace CJ, Lloyd JF, et al. Rapid identification of hospitalized patients at high risk for MRSA carriage. J Am Med Inform Assoc 2008;15:506-12.
38. Lin MY, Lolans K, Blom DW, et al. The effectiveness of routine daily chlorhexidine gluconate bathing in reducing Klebsiella pneumoniae carbapenemase-producing

Enterobacteriaceae skin burden among long-term acute care hospital patients. Infect Control Hosp Epidemiol 2014;35:440-2.
39. Mehta JM, Haynes K, Wileyto EP, et al. Comparison of prior authorization and prospective audit with feedback for antimicrobial stewardship. Infect Control Hosp Epidemiol 2014;35:1092-9.
40. Climo M, Diekema D, Warren DK, et al. Prevalence of the use of central venous access devices within and outside of the intensive care unit: results of a survey among hospitals in the prevention epicenter program of the Centers for Disease Control and Prevention. Infect Control Hosp Epidemiol 2003;24:942-5.
41. Sohn S, Climo M, Diekema D, et al. Varying rates of Clostridium difficile-associated diarrhea at prevention epicenter hospitals. Infect Control Hosp Epidemiol 2005;26:676-9.
42. Self WH, Speroff T, Grijalva CG, et al. Reducing blood culture contamination in the emergency department: an interrupted time series quality improvement study. Acad Emerg Med 2013;20:89-97.
43. St Jacques P, Sanders N, Patel N, Talbot TR, Deshpande JK, Higgins M. Improving timely surgical antibiotic prophylaxis redosing administration using computerized record prompts. Surg Infect (Larchmt) 2005;6:215-21.
44. Talbot TR, Wang D, Swift M, et al. Implementation of an enhanced safety-engineered sharp device oversight and bloodborne pathogen protection program at a large academic medical center. Infect Control Hosp Epidemiol 2014;35:1383-90.
45. Talbot TR, Crocker DD, Peters J, et al. Duration of virus shedding after trivalent intranasal live attenuated influenza vaccination in adults. Infect Control Hosp Epidemiol 2005;26:494-500.
46. Talbot TR, Ziel E, Doersam JK, LaFleur B, Tollefson S, Edwards KM. Risk of vaccinia transfer to the hands of vaccinated persons after smallpox immunization. Clin Infect Dis 2004;38:536-41.
47. Goins WP, Edwards KM, Vnencak-Jones CL, et al. A comparison of 2 strategies to prevent infection following pertussis exposure in vaccinated healthcare personnel. Clin Infect Dis 2012;54:938-45.
48. Esbenshade JC, Edwards KM, Esbenshade AJ, et al. Respiratory virus shedding in a cohort of on-duty healthcare workers undergoing prospective surveillance. Infect Control Hosp Epidemiol 2013;34:373-8.
49. Talbot TR. Improving rates of influenza vaccination among healthcare workers: educate; motivate; mandate? Infect Control Hosp Epidemiol 2008;29:107-10.
50. Talbot TR. Update on immunizations for healthcare personnel in the United States. Vaccine 2014;32:4869-75.
51. Talbot TR, Babcock H, Caplan AL, et al. Revised SHEA position paper: influenza vaccination of healthcare personnel. Infect Control Hosp Epidemiol 2010;31:987-95.
52. Talbot TR, Talbot HK. Influenza prevention update: examining common arguments against influenza vaccination. JAMA 2013;309:881-2.
53. Daniels TL, Deppen S, Arbogast PG, Griffin MR, Schaffner W, Talbot TR. Mortality rates associated with multidrug-resistant Acinetobacter baumannii infection in surgical intensive care units. Infect Control Hosp Epidemiol 2008;29:1080-3.
54. O'Neal CS, O'Neal HR, Daniels TL, Talbot TR. Treatment outcomes in patients with third-generation cephalosporin-resistant Enterobacter bacteremia. Scand J Infect Dis 2012;44:726-32.
55. Carpenter LR, Kainer M, Woron A, Schaffner W, Jones TF. Methicillin-resistant Staphylococcus aureus and skin infections among personnel at a pediatric clinic. Am J Infect Control 2008;36:665-7.

56. D'Agata EM, Green WK, Schulman G, Li H, Tang YW, Schaffner W. Vancomycin-resistant enterococci among chronic hemodialysis patients: a prospective study of acquisition. Clin Infect Dis 2001;32:23-9.
57. D'Agata EM, Thayer V, Schaffner W. An outbreak of Acinetobacter baumannii: the importance of cross-transmission. Infect Control Hosp Epidemiol 2000;21:588-91.
58. Devasia RA, Jones TF, Collier B, Schaffner W. Compliance with azithromycin versus erythromycin in the setting of a pertussis outbreak. Am J Med Sci 2009;337:176-8.
59. Goins WP, Schaffner W, Edwards KM, Talbot TR. Healthcare workers' knowledge and attitudes about pertussis and pertussis vaccination. Infect Control Hosp Epidemiol 2007;28:1284-9.
60. Jhung MA, D'Mello T, Perez A, et al. Hospital-onset influenza hospitalizations--United States, 2010-2011. Am J Infect Control 2014;42:7-11.
61. Carnevale RJ, Talbot TR, Schaffner W, Bloch KC, Daniels TL, Miller RA. Evaluating the utility of syndromic surveillance algorithms for screening to detect potentially clonal hospital infection outbreaks. J Am Med Inform Assoc 2011;18:466-72.
62. Haas DW, Milton S, Kreiswirth BN, Brinsko VL, Bifani PJ, Schaffner W. Nosocomial transmission of a drug-sensitive W-variant Mycobacterium tuberculosis strain among patients with acquired immunodeficiency syndrome in Tennessee. Infect Control Hosp Epidemiol 1998;19:635-9.
63. Pettit AC, Kropski JA, Castilho JL, et al. The index case for the fungal meningitis outbreak in the United States. N Engl J Med 2012;367:2119-25.
64. Creech CB, 2nd, Johnson BG, Alsentzer AR, Hohenboken M, Edwards KM, Talbot TR, 3rd. Vaccination as infection control: a pilot study to determine the impact of Staphylococcus aureus vaccination on nasal carriage. Vaccine 2009;28:256-60.
65. Noto MJ, Domenico HJ, Byrne DW, et al. Chlorhexidine bathing and health care-associated infections: a randomized clinical trial. JAMA 2015;313:369-78.
66. Self WH, Mickanin J, Grijalva CG, et al. Reducing blood culture contamination in community hospital emergency departments: a multicenter evaluation of a quality improvement intervention. Acad Emerg Med 2014;21:274-82.
67. Dortch MJ, Fleming SB, Kauffmann RM, Dossett LA, Talbot TR, May AK. Infection reduction strategies including antibiotic stewardship protocols in surgical and trauma intensive care units are associated with reduced resistant gram-negative healthcare-associated infections. Surg Infect (Larchmt) 2011;12:15-25.
68. Talbot TR, Dellit TH, Hebden J, Sama D, Cuny J. Factors associated with increased healthcare worker influenza vaccination rates: results from a national survey of university hospitals and medical centers. Infect Control Hosp Epidemiol 2010;31:456-62.
69. Talbot TR, May AK, Obremskey WT, Wright PW, Daniels TL. Intraoperative patient-to-healthcare-worker transmission of invasive group A streptococcal infection. Infect Control Hosp Epidemiol 2011;32:924-6.
70. Talbot TR, Peters J, Wright PF, Edwards KM. Absence of pharyngeal shedding of vaccinia following smallpox vaccination. Am J Infect Control 2007;35:486-8.
71. Talbot TR, Peters J, Yan L, Wright PF, Edwards KM. Optimal bandaging of smallpox vaccination sites to decrease the potential for secondary vaccinia transmission without impairing lesion healing. Infect Control Hosp Epidemiol 2006;27:1184-92.
72. Mahamud A, Fiebelkorn AP, Nelson G, et al. Economic impact of the 2009-2010 Guam mumps outbreak on the public health sector and affected families. Vaccine 2012;30:6444-8.
73. Nelson GE, Aguon A, Valencia E, et al. Epidemiology of a mumps outbreak in a highly vaccinated island population and use of a third dose of measles-mumps-rubella vaccine for outbreak control--Guam 2009 to 2010. Pediatr Infect Dis J 2013;32:374-80.
74. Nelson GE, Gershman KA, Swerdlow DL, Beall BW, Moore MR. Invasive pneumococcal disease and pandemic (H1N1) 2009, Denver, Colorado, USA. Emerg Infect Dis 2012;18:208-16.

75. Centers for Disease C, Prevention. Legionellosis --- United States, 2000-2009. MMWR Morb Mortal Wkly Rep 2011;60:1083-6.
76. Semler MW, Keriwala RD, Clune JK, et al. A randomized trial comparing didactics, demonstration, and simulation for teaching teamwork to medical residents. Ann Am Thorac Soc 2015;12:512-9.
77. Weinger MB, Slagle JM, Kuntz AH, et al. A Multimodal Intervention Improves Post-Anesthesia Care Unit Handovers. Anesth Analg 2015.
78. Aston JL, Dortch MJ, Dossett LA, Creech CB, May AK. Risk factors for treatment failure in patients receiving vancomycin for hospital-acquired methicillin-resistant Staphylococcus aureus pneumonia. Surg Infect (Larchmt) 2010;11:21-8.
79. Creech CB, 2nd, Kernodle DS, Alsentzer A, Wilson C, Edwards KM. Increasing rates of nasal carriage of methicillin-resistant Staphylococcus aureus in healthy children. Pediatr Infect Dis J 2005;24:617-21.
80. Creech CB, Litzner B, Talbot TR, Schaffner W. Frequency of detection of methicillin-resistant Staphylococcus aureus from rectovaginal swabs in pregnant women. Am J Infect Control 2010;38:72-4.
81. Creech CB, Saye E, McKenna BD, et al. One-year surveillance of methicillin-resistant Staphylococcus aureus nasal colonization and skin and soft tissue infections in collegiate athletes. Arch Pediatr Adolesc Med 2010;164:615-20.
82. House DL, Chon CH, Creech CB, Skaar EP, Li D. Miniature on-chip detection of unpurified methicillin-resistant Staphylococcus aureus (MRSA) DNA using real-time PCR. J Biotechnol 2010;146:93-9.
83. Jimenez-Truque N, Tedeschi S, Saye EJ, et al. Relationship between maternal and neonatal Staphylococcus aureus colonization. Pediatrics 2012;129:e1252-9.
84. Nicholson MR, Thomsen IP, Slaughter JC, Creech CB, Edwards KM. Novel risk factors for recurrent Clostridium difficile infection in children. J Pediatr Gastroenterol Nutr 2015;60:18-22.
85. Cardo D, Dennehy PH, Halverson P, et al. Moving toward elimination of healthcare-associated infections: a call to action. Infect Control Hosp Epidemiol 2010;31:1101-5.
86. Chang DC, Grant GB, O'Donnell K, et al. Multistate outbreak of Fusarium keratitis associated with use of a contact lens solution. JAMA 2006;296:953-63.
87. Duffy J, Sievert D, Rebmann C, et al. Effective state-based surveillance for multidrug-resistant organisms related to health care-associated infections. Public Health Rep 2011;126:176-85.
88. Kainer MA, Devasia RA, Jones TF, et al. Response to emerging infection leading to outbreak of linezolid-resistant enterococci. Emerg Infect Dis 2007;13:1024-30.
89. Kainer MA, Linden JV, Whaley DN, et al. Clostridium infections associated with musculoskeletal-tissue allografts. N Engl J Med 2004;350:2564-71.
90. Kainer MA, Reagan DR, Nguyen DB, et al. Fungal infections associated with contaminated methylprednisolone in Tennessee. N Engl J Med 2012;367:2194-203.
91. Schaffner W. Surgeons with HIV infection: the risk to patients. J Hosp Infect 1991;18 Suppl A:191-6.
92. D'Agata EM, Mount DB, Thayer V, Schaffner W. Hospital-acquired infections among chronic hemodialysis patients. Am J Kidney Dis 2000;35:1083-8.
93. Heavrin BS, Jones TF, Shavor T, Schaffner W. The changing epidemiology of HIV/AIDS in Tennessee. Tenn Med 2004;97:357-60.
94. Devasia RA, Jones TF, Kainer MA, et al. Two community hepatitis B outbreaks: an argument for vaccinating incarcerated persons. Vaccine 2006;24:1354-8.
95. Su S, Chaves SS, Perez A, et al. Comparing clinical characteristics between hospitalized adults with laboratory-confirmed influenza a and B virus infection. Clin Infect Dis 2014;59:252-5.

96. Lindegren ML, Griffin MR, Williams JV, et al. Antiviral Treatment among Older Adults Hospitalized with Influenza, 2006-2012. PLoS One 2015;10:e0121952.
97. Birdee GS, Byrne DW, McGown PW, et al. Relationship between physical inactivity and health characteristics among participants in an employee-wellness program. J Occup Environ Med 2013;55:514-9.
98. Byrne DW, Goetzel RZ, McGown PW, et al. Seven-year trends in employee health habits from a comprehensive workplace health promotion program at Vanderbilt University. J Occup Environ Med 2011;53:1372-81.
99. Hickson GB, Pichert JW, Webb LE, Gabbe SG. A complementary approach to promoting professionalism: identifying, measuring, and addressing unprofessional behaviors. Acad Med 2007;82:1040-8.
100. Conly JM. Personal protective equipment for preventing respiratory infections: what have we really learned? CMAJ 2006;175:263.
101. Sax H, Perneger T, Hugonnet S, Herrault P, Chraiti MN, Pittet D. Knowledge of standard and isolation precautions in a large teaching hospital. Infect Control Hosp Epidemiol 2005;26:298-304.
102. Casanova L, Alfano-Sobsey E, Rutala WA, Weber DJ, Sobsey M. Virus transfer from personal protective equipment to healthcare employees' skin and clothing. Emerg Infect Dis 2008;14:1291-3.
103. Beam EL, Gibbs SG, Boulter KC, Beckerdite ME, Smith PW. A method for evaluating health care workers' personal protective equipment technique. Am J Infect Control 2011;39:415-20.
104. Beam EL, Gibbs SG, Hewlett AL, Iwen PC, Nuss SL, Smith PW. Method for investigating nursing behaviors related to isolation care. Am J Infect Control 2014;42:1152-6.
105. Casanova LM, Rutala WA, Weber DJ, Sobsey MD. Effect of single- versus double-gloving on virus transfer to health care workers' skin and clothing during removal of personal protective equipment. Am J Infect Control 2012;40:369-74.
106. Lai JY, Guo YP, Or PP, Li Y. Comparison of hand contamination rates and environmental contamination levels between two different glove removal methods and distances. Am J Infect Control 2011;39:104-11.
107. Wong TK, Chung JW, Li Y, et al. Effective personal protective clothing for health care workers attending patients with severe acute respiratory syndrome. Am J Infect Control 2004;32:90-6.
108. Zamora JE, Murdoch J, Simchison B, Day AG. Contamination: a comparison of 2 personal protective systems. CMAJ 2006;175:249-54.
109. Guo YP, Li Y, Wong PL. Environment and body contamination: a comparison of two different removal methods in three types of personal protective clothing. Am J Infect Control 2014;42:e39-45.
110. Anders S, Miller A, Joseph P, et al. Blood product positive patient identification: comparative simulation-based usability test of two commercial products. Transfusion 2011;51:2311-8.
111. Saied N, Booker R, Weinger M. Misassembled bellows housing leading to failure of mechanical ventilation during general anesthesia. Simul Healthc 2012;7:380-9.
112. Weinger MB. The pharmacology of simulation: a conceptual framework to inform progress in simulation research. Simul Healthc 2010;5:8-15.
113. Holzman RS, Cooper JB, Gaba DM, Philip JH, Small SD, Feinstein D. Anesthesia crisis resource management: real-life simulation training in operating room crises. J Clin Anesth 1995;7:675-87.
114. DeAnda A, Gaba DM. Unplanned incidents during comprehensive anesthesia simulation. Anesth Analg 1990;71:77-82.

115. Glo Germ Company. Glo Germ. Accessed on May 21, 2015 at http://www.glogerm.com/index.html.
116. Jarrin Tejada C, Bearman G. Hand hygiene compliance monitoring: the state of the art. Curr Infect Dis Rep 2015;17:470.
117. Healthcare-Associated Infections Advisory Committee and its Hand Hygiene and Infection Prevention Subcommittee. Report and Recommendations on Implementation of a Statewide Hospital Hand Hygiene Campaign2009.
118. Grayson ML, Russo PL, Cruickshank M, et al. Outcomes from the first 2 years of the Australian National Hand Hygiene Initiative. Med J Aust 2011;195:615-9.
119. Society for Healthcare Epidemiology of America. SHEA Award Winners. Accessed on May 21, 2015 at http://www.shea-online.org/About/SHEAAwardWinners.aspx.
120. Pichert JW, Moore IN, Karrass J, et al. An intervention model that promotes accountability: peer messengers and patient/family complaints. Jt Comm J Qual Patient Saf 2013;39:435-46.
121. Swiggart WH, Dewey CM, Hickson GB, Finlayson AJ, Spickard WA, Jr. A plan for identification, treatment, and remediation of disruptive behaviors in physicians. Front Health Serv Manage 2009;25:3-11.
122. Richards CL, Jr. Infections in long-term-care facilities: screen or clean? Infect Control Hosp Epidemiol 2005;26:800-1.
123. Strausbaugh LJ, Sukumar SR, Joseph CL. Infectious disease outbreaks in nursing homes: an unappreciated hazard for frail elderly persons. Clin Infect Dis 2003;36:870-6.
124. Bradley SF. Staphylococcus aureus infections and antibiotic resistance in older adults. Clin Infect Dis 2002;34:211-6.
125. Rooney PJ, O'Leary MC, Loughrey AC, et al. Nursing homes as a reservoir of extended-spectrum beta-lactamase (ESBL)-producing ciprofloxacin-resistant Escherichia coli. J Antimicrob Chemother 2009;64:635-41.
126. Sengstock DM, Thyagarajan R, Apalara J, Mira A, Chopra T, Kaye KS. Multidrug-resistant Acinetobacter baumannii: an emerging pathogen among older adults in community hospitals and nursing homes. Clin Infect Dis 2010;50:1611-6.
127. Pawar D, Tsay R, Nelson DS, et al. Burden of Clostridium difficile infection in long-term care facilities in Monroe County, New York. Infect Control Hosp Epidemiol 2012;33:1107-12.
128. O'Fallon E, Kandel R, Schreiber R, D'Agata EM. Acquisition of multidrug-resistant gram-negative bacteria: incidence and risk factors within a long-term care population. Infect Control Hosp Epidemiol 2010;31:1148-53.
129. Mitchell SL, Shaffer ML, Loeb MB, et al. Infection management and multidrug-resistant organisms in nursing home residents with advanced dementia. JAMA Intern Med 2014;174:1660-7.
130. D'Agata EM, Habtemariam D, Mitchell S. Multidrug-Resistant Gram-Negative Bacteria: Inter- and Intradissemination Among Nursing Homes of Residents With Advanced Dementia. Infect Control Hosp Epidemiol 2015:1-6.
131. Lee BY, Bartsch SM, Wong KF, et al. The importance of nursing homes in the spread of methicillin-resistant Staphylococcus aureus (MRSA) among hospitals. Med Care 2013;51:205-15.
132. Won SY, Munoz-Price LS, Lolans K, et al. Emergence and rapid regional spread of Klebsiella pneumoniae carbapenemase-producing Enterobacteriaceae. Clin Infect Dis 2011;53:532-40.
133. Laffan AM, Bellantoni MF, Greenough WB, 3rd, Zenilman JM. Burden of Clostridium difficile-associated diarrhea in a long-term care facility. J Am Geriatr Soc 2006;54:1068-73.
134. Talbot TR. Two studies feed the debate on active surveillance for methicillin-resistant Staphylococcus aureus and vancomycin-resistant enterococci carriage: to screen or not to screen? J Infect Dis 2007;195:314-7.

135. Centers for Disease Control and Prevention. Guidance for Control of Carbapenem-resistant Enterobacteriaceae (CRE): 2012 CRE Toolkit. Accessed on May 23, 2015 at http://www.cdc.gov/hai/organisms/cre/cre-toolkit/f-level-prevention-supmeasures.html. 2012.
136. Tzouvelekis LS, Markogiannakis A, Psichogiou M, Tassios PT, Daikos GL. Carbapenemases in Klebsiella pneumoniae and other Enterobacteriaceae: an evolving crisis of global dimensions. Clin Microbiol Rev 2012;25:682-707.
137. Saidel-Odes L, Borer A. Limiting and controlling carbapenem-resistant Klebsiella pneumoniae. Infect Drug Resist 2013;7:9-14.
138. Cunha BA, Dumont M, Abruzzo E. An Adult Returned Traveler from Dubai Hospitalized with an Influenza-Like Illness (ILI): Middle East Respiratory Syndrome (MERS) or Influenza? Infection Control Implications from a Near MERS Case. Infect Control Hosp Epidemiol 2015:1-3.
139. Stelfox HT, Bates DW, Redelmeier DA. Safety of patients isolated for infection control. JAMA 2003;290:1899-905.
140. Day HR, Perencevich EN, Harris AD, et al. Association between contact precautions and delirium at a tertiary care center. Infect Control Hosp Epidemiol 2012;33:34-9.
141. Morgan DJ, Diekema DJ, Sepkowitz K, Perencevich EN. Adverse outcomes associated with Contact Precautions: a review of the literature. Am J Infect Control 2009;37:85-93.
142. Morgan DJ, Day HR, Harris AD, Furuno JP, Perencevich EN. The impact of Contact Isolation on the quality of inpatient hospital care. PLoS One 2011;6:e22190.
143. Gasink LB, Singer K, Fishman NO, et al. Contact isolation for infection control in hospitalized patients: is patient satisfaction affected? Infect Control Hosp Epidemiol 2008;29:275-8.
144. Morgan DJ, Pineles L, Shardell M, et al. The effect of contact precautions on healthcare worker activity in acute care hospitals. Infect Control Hosp Epidemiol 2013;34:69-73.
145. Harris AD, Pineles L, Belton B, et al. Universal glove and gown use and acquisition of antibiotic-resistant bacteria in the ICU: a randomized trial. JAMA 2013;310:1571-80.
146. Wenzel RP. Minimizing surgical-site infections. N Engl J Med 2010;362:75-7.
147. Bouldin EL, Andresen EM, Dunton NE, et al. Falls among adult patients hospitalized in the United States: prevalence and trends. J Patient Saf 2013;9:13-7.