Title Page

PI

Lisa Casanova MS, PhD

Affiliation

Department of Population Health Sciences, School of Public Health, Georgia State University

contact information

P.O. Box 3995 Atlanta, GA 30302

404-413-1136

lcasanova@gsu.edu

institution to which the award was made (include full address)

Georgia State University

P.O Box 3999 Atlanta, GA 30302

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List of Terms and Abbreviations

HCP: healthcare provider
PPE: personal protective equipment
HFE: human factors engineering
FMEA: failure modes and effects analysis
FTA: fault tree analysis
PAPR: powered air purifying respirator

Abstract

Project title

Preventing Occupational Infections in Healthcare Professionals Using Risk Models

PI contact information

Lisa Casanova MS, Ph.D Phone: 404-413-1136 Email:lcasanova@gsu.edu

Occupational safety and health issues that were addressed

To prevent occupational infections spread by droplets, aerosols, and bodily fluids in healthcare professionals (HCP), practices and guidelines for personal protective equipment (PPE) need to be continually developed and improved. Research and adoption of best practices for PPE is a NIOSH priority, but there are few studies that demonstrate which practices reduce potential transmission of these occupational infections.

Worker group(s) or setting(s) studied

Our unique study population of HCP trained in Ebola PPE and patient care (some had cared for Ebola patients) used complex PPE in intensive care-type settings.

Approaches used

We developed a novel approach for designing exposure models, identifying unknown parameters, and integrating realistic simulations of patient care using volunteers, surrogate viruses, and human factors analysis (HFE) to produce models of exposure and risk. HCPs participated in simulations using virus-contaminated PPE, where processes, actions, and tasks were analyzed with HFE methods.

Significant and Key Findings

A key finding was that we could refine transmission models with simulation. Using simulations of Ebola PPE use across four hospitals, we determined parameters and values for risk models of transmission while using Ebola PPE. Using iterative simulations, we were able to estimate transfer of virus from PPE to HCP's hands, face, and clothing, and viral die-off rates on hands. Our models can be used to predict infection risks to HCPs using Ebola PPE, particularly the HFE modeling approaches of failure modes and effects analysis and fault tree analysis. Once modeling identified risk points and failure modes, we designed new simulations to mitigate risk. We can measure changes in risk when changes in wearing and removing PPE and design changes in the patient care environment were implemented. These methods can inform exposure assessments by following and quantifying viruses moving through different transmission routes. We worked in facilities with different environments, training, and protocols for Ebola PPE. We determined there are weaknesses in PPE practices that result in observable transfer of virus to hands and clothing during PPE doffing. We were able to identify the failure modes and high-risk tasks and actions that contributed to risk.

Translation to improvements for worker safety and health

We developed and refined models to identify key processes, actions, and failure modes creating transmission risks. We altered actions and processes to test mitigation measures. Interactive presentations to our facilities provided suggestions for improvement tailored to their environment and protocols. We provided suggestions to redesign the patient care environment to reduce risk, for constructing new environments and making simple changes to current environments. Our methods can be used in healthcare facilities where researchers and clinicians collaborate to improve PPE use. Our findings have resulted in changes to PPE doffing practices after patient care and redesign of the patient care environment in the high-risk pathogen patient care program where we conducted research. These methods can and have been adopted by healthcare facilities and researchers to evaluate PPE practices to protect HCP from infection. We are putting our methods into practice to respond to the SARS-CoV-2 pandemic to optimize PPE to protect HCP from this deadly disease during patient care.

Section 1: Key Findings, Research Products, and Outcomes

Significant and Key Findings

Specific Aim 1:

Build theoretical mathematical risk models that describe how HCPs can acquire occupational infection by pathways such as aerosols, hand contact, handling of contaminated objects, and removal of contaminated PPE, and the risks of infection associated with these pathways.

Key findings:

Building models begins with theoretical maps of potential transmission pathways, requiring granular understanding of events during PPE use, including donning, wearing during patient care, and doffing. My new collaborations gave access to a unique study population of HCP trained in Ebola PPE and patient care; some had cared for Ebola patients. With their expert input, we mapped possible transmission pathways from contaminated PPE to the HCP hands, face, and clothing. Our first key finding was that we could develop a novel system integrating human factors engineering (HFE), where we documented HCP during realistic simulated patient care with PPE using fixed cameras, wearable ones from the HCP's POV, and external ones from multiple perspectives.

Video was analyzed with HFE methods to identify, define, and code processes, actions, and tasks. Our second key finding was that we could significantly refine transmission models using this video data, including identifying events and parameters we had not previously considered.

Significant research products

Goals for this aim were to develop complete conceptual models describing distinct exposure scenarios for infection, determine parameters to build these models, and identify which of these parameters will be defined using data from experimental laboratory simulations. Two significant products: 1) A novel approach for designing exposure models, identifying parameters that lack data, and integrating realistic simulations of patient care using volunteers, surrogate viruses, and HFE to design experiments that fill data gaps and produce models of exposure and risk. 2) demonstration that these methods can inform exposure assessments by following transmission to the HCP and quantifying viruses moving through a particular transmission route.

Basic/applied, translational, and intervention related contributions

These methods can and have been adopted by healthcare facilities and researchers to evaluate PPE practices to protect HCP from high-risk pathogens. They resulted in changes to PPE doffing practices for the high-risk pathogen patient care program where we conducted our research.

Specific Aim 2:

Simulate and measure how HCPs become contaminated with viruses using realistic experimental laboratory simulations of patient care with human volunteers. 2a. Develop and test an aerosol system that simulates the spread of respiratory viruses by coughing, sneezing, and medical procedures, such as intubation and suctioning. 2b. Integrate this aerosol delivery system into simulations of HCPs using PPE. 2c. Using this experimental exposure assessment system, determine the values of undefined parameters in the mathematical risk models. Specifically, estimate the transfer of virus from a patient to the HCP's hands, face and clothing, as well as viral die-off rates on a HCP's hands, face and clothing during and after patient care.

Key finding:

Using our integrated simulation and HFE experimental exposure assessment system, we carried out 40 simulations of complex Ebola PPE use across four facilities designated as Ebola patient care centers. We recruited volunteers who were trained in this PPE use, and volunteers who had provided actual Ebola patient care. We determined previously unrecognized parameters and the values of undefined parameters in risk models of transmission while using complex Ebola PPE. Using iterative simulations, we were able to estimate 1) the transfer of virus from a patient to the HCP's hands, 2) transfer of viruses to the face, and 3) transfer of viruses to the clothing. Using separate simulations with an enveloped virus surrogate, we were able to estimate viral die-off rates on hands.

Significant research products

Our research took place in four facilities with different built environments, training protocols and practices, and protocols and practices for Ebola PPE use. With our integrated approach, we determined that there are weaknesses in Ebola PPE practices that result in observable transfer of virus to hands and clothing during PPE doffing. We were able to identify the failure modes and high-risk tasks and actions that contributed to risk.

Building a system in my laboratory was more challenging than anticipated and was not finished during the grant. I have now obtained a human breathing and cough simulator custom built by a NIOSH engineer, and am collaborating with colleagues on methods to protect HCP from respiratory exposures. The system is much more sophisticated than I originally envisioned and can be used in my laboratory and a patient care simulation facility at Emory.

Basic/applied, translational, and intervention related contributions

After completion of the project, we provided individual interactive presentations of results to each facility, with suggestions for improvement tailored to their environment and protocols.

Specific Aim 3.

Define the parameters of mathematical models with data from Aim 2 to predict infection risks to HCPs using PPE. Examine: 3a. Risk of infection from current PPE use practices. 3b. Changes in risk resulting from the adoption of alternative practices for wearing and removing PPE.

Significant research products

We defined model parameters with data to predict infection risks to HCPs using Ebola PPE. We used HFE modeling approaches: 1) failure modes and effects analysis (FMEA), a technique to identify, quantify risk of, and eliminate problems in a process ("failure modes"), and 2) fault tree analysis (FTA), which predicts the probability of an undesirable event (top of the "tree") based on the sequence and combinations of events at the bottom of the tree that are basic causes of the top event. Once FMEA and FTA identified risk points and failure modes, we designed new simulations to mitigate these risks. From these, we were able to measure changes in transmission risk when changes in wearing and removing PPE and design changes in the built patient care environment were implemented.

Basic/applied, translational, and intervention related contributions

After completion of the project, we provided individual interactive presentations of results to each facility, with suggestions for improvement tailored to their environment and protocols.

Translation of Findings

We focused on transmission of Ebola through body fluids while using complex PPE. We developed models, conducted simulations of virus transmission based on the models, and refined them by identifying key process points, actions, and possible failure modes that were high-risk for transmission. We designed more simulations to mitigate these risks where volunteers altered actions and processes to test mitigation measures we designed. For our participating facilities, we provided interactive presentations to each facility, with suggestions for improvement tailored to their environment and protocols. We provided generalized suggestions for all types of facilities to redesign the patient care environment to reduce exposure risks. This included suggestions for constructing new environments, as well as simple changes to current environments.

Research Outcomes/Impact

Potential outcomes

Potential outcomes are improvements in PPE use that protect HCP in other healthcare settings and systems. Our methods can be used in research programs that are integrated into healthcare facilities, where researchers, clinicians, and physician-scientists collaborate to improve PPE use.

Intermediate Outcomes

An intermediate outcome is they have resulted in concrete changes to 1) PPE doffing practices after patient care for and 2) redesign of the patient care environment to mitigate failure modes and risk points in the high-risk pathogen patient care program which we conducted the research.

Our work has not yet resulted in end outcomes. This is partly because there has (fortunately) not been a new need to protect HCP from Ebola in a large-scale outbreak. However, we have been invited by advisory bodies to contribute to new PPE guidelines to enhance preparedness for such outbreaks in the future.

Improvements in occupational safety and health

These methods can (and have) been adopted by healthcare facilities and researchers to evaluate PPE donning, doffing, and use practices to protect HCP from high-risk pathogens. We are currently putting our methods into practice to respond to the SARS-CoV-2 pandemic. We will use surrogate viruses, laboratory experiments, volunteer simulations, and HFE methods to optimize PPE to protect HCP from this deadly disease during patient care.

Section 2: Scientific Report

Background

Healthcare professionals (HCP) are at increased risk for acquiring potentially dangerous infections spread by droplets, aerosols, and bodily fluids on the job, including SARS CoV-1 and -2 seasonal and pandemic influenza, and Ebola. For well-recognized infections like seasonal and pandemic influenza, these infections occur despite well-publicized guidelines for the use of personal protective equipment (PPE) in healthcare settings. For emerging diseases and those where there is a much smaller body of patient care experience, new ways of using PPE must be developed, often right when they are needed. Research and adoption of best practices for PPE is a major NIOSH priority, but there are few studies that demonstrate which practices effectively reduce potential transmission of occupational droplet, aerosol, and body fluid-borne infection. The field lacks tools for determining what are the best practices for PPE use, to what extent current practices contribute to or attenuate HCPs' risk for infection, and what alternative prevention strategies work to maximize protection from PPE. Specifically, we lack evidence-based quantitative models for determining best practices in PPE use that demonstrate reductions in the risk of serious infections. I proposed to fill this gap using experimental laboratory simulations and quantitative risk models that can characterize and predict infectious agent exposure as well as mechanisms and determinants of transmission routes.

In my laboratory at Georgia State University, I have developed protocols where human volunteers contaminated with known quantities of harmless microorganisms simulate patient care activities. These simulations are designed to measure in a controlled fashion how a pathogen spreads from an infected patient to a HCP's hands, face, and clothing, and how varying use of PPE affects spread. Around the time that this project began, one of the largest outbreaks of Ebola in history significantly changed the trajectory of my research program.

As a result of my previous work with enveloped viruses and the use of simulations to understand PPE use, I was approached as a subject matter expert by guideline-creating bodies, and I was invited to multiple research collaborations to study healthcare worker PPE to protect against Ebola. This changed and expanded my research focus to encompass other enveloped viruses. Although it was beyond the period of this grant, this has continued with the emergence of the SARS-CoV2 pandemic. I did not expect at the beginning of this grant that I would develop a collaboration that would allow the integration of healthcare human factors engineering and analysis into my work. This has raised the level of capability and sophistication of both the simulations and modeling I am able to do. To better understand the precise characteristics of airborne and body fluid transmission in the setting of a range of PPE applications, I have developed methods and systems to deliver viruses, realistically simulating how viruses spread from an infected patient to a HCP. In a novel collaboration with human factors scientists, I have used these experimental scenarios to define the parameters relevant to mathematical models for predicting risk, such as efficiency of transfer from hands to objects, distribution of contamination of PPE during use and doffing, and survival of viruses on hands and objects, to fill critical gaps in our understanding of the infection risks associated with PPE use by HCPs.

Specific Aims

Specific Aim 1.

Build theoretical mathematical risk models that describe how HCPs can acquire occupational infectious agents through pathways such as aerosols, hand contact, and handling of contaminated objects, and the risks of infection associated with these pathways.

Specific Aim 2.

Simulate and measure how HCPs become contaminated with viruses using realistic experimental laboratory simulations of patient care with human volunteers.

Aim 2a. Develop and test a precision aerosol delivery system that simulates the spread of respiratory viruses by coughing, sneezing, and medical procedures, such as intubation and suctioning.

Aim 2b. Integrate this aerosol delivery system into simulations of HCPs using PPE. Using a non-pathogenic virus (bacteriophage Φ6) that simulates the behavior of human respiratory viruses, we will work with NIOSH and GSU Respiratory Therapy mentors who are experts in aerosol generation and delivery to simulate replicable dispersion patterns and doses of virus via the airborne route. The result will be an exposure assessment system where contamination can be measured during simulated patient care.

Aim 2c. Using this experimental exposure assessment system, determine the values of undefined parameters in the mathematical risk models. Specifically, we will estimate the transfer efficiency of virus from a patient to the HCP's hands, face and clothing, as well as viral die-off rates on a HCP's hands, face and clothing during and after patient care.

Specific Aim 3

Define the parameters of mathematical models (developed in Aim 1) with data from Aim 2 to predict infection risks to HCPs using PPE. Specifically, we will examine:

Aim 3a. Risk of infection from current PPE use practices.

Aim 3b. Changes in risk resulting from the adoption of alternative practices for wearing and removing PPE

Methodology

Specific Aim 1: Build theoretical mathematical risk models that describe how HCPs can acquire occupational infectious agents through pathways such as aerosols, hand contact, and handling of contaminated objects, and the risks of infection associated with these pathways.

As a result of my previous work with enveloped viruses and the use of simulations to understand PPE use, I was approached by a team of multiple research collaborators to study healthcare worker PPE to protect against Ebola. This included physician-scientists and nurses from Emory Healthcare, human factors engineers from the Georgia Institute of Technology, and healthcare built environment design experts from Georgia Tech. This changed and expanded my research focus to encompass other enveloped viruses, particularly Ebola. Therefore, I designed conceptual models of scenarios for occupational exposure to Ebola during patient care. Building on previous models of the spread of infectious diseases via the environment and hands, these conceptual models describe, step by step, the process by which viruses transfer from PPE to the HCP, and capture all of the routes by which a HCP is exposed to virus during patient care of an infected patient. The conceptual models can describe an exposure scenario with multiple possible branching events. The main conceptual model with theoretical parameters, shown in Figure 1, is for a patient care encounter where the HCP is wearing Ebola PPE, including scrubs, a Tyvek suit, A personal air purifying respirator, an impervious apron, and double gloves. The conceptual models include removal and handling of contaminated PPE, building on my previous work in collaboration with mentor Dr. David Weber.

Specific Aim 2: Simulate and measure how HCPs become contaminated with viruses using realistic experimental laboratory simulations of patient care with human volunteers.

Aim 2a: Develop and test a precision aerosol delivery system that simulates the spread of respiratory viruses by coughing, sneezing, and medical procedures, such as intubation and suctioning.

This aim ended up being exceptionally difficult. Building a system in my laboratory was more challenging than anticipated and was not finished during the grant. I have now obtained a human breathing and cough simulator custom built by a NIOSH engineer, and am collaborating with colleagues on methods to protect HCP from respiratory exposures. The system is much more sophisticated than I originally envisioned and can be used in my laboratory and a patient care simulation facility at Emory. This has allowed me to move forward with projects that are related to the original aims of this grant.

Given these obstacles and the new opportunities and direction provided by my collaborations, I decided to pivot the simulations to focus on the use of complex Ebola PPE. This changed the approach to a method that used suspensions of virus, to simulate small droplet contamination with body fluids at multiple sites on complex PPE during patient care. For the contamination method, after donning of PPE, a mixture of MS2 and Φ6 suspended in phosphate buffered saline containing a fluorescent tracer (GloGerm, Moab, UT) was applied to four sites: the palm of the dominant hand, the shoulder of the gown opposite the dominant hand, the top side of the PAPR opposite the dominant hand, and the toe of the shoe cover opposite the dominant hand. A total of 25μL was applied to each site in 5 drops of 5μL each to simulate small droplet body fluid exposure that the HCW may not be aware of Sites to be contaminated were chosen after consulting with clinicians with EVD patient care experience, who had observed PPE contamination in the patient care setting. The mean virus titer applied to each site in 25μL was 2.3×10^5 for Φ6 and 5.70×10^6 for MS2, based on reports of viral load in body fluids during acute phases of EVD,[1-3] as well as non-enveloped viruses such as norovirus that are shed in high titers in body fluids. There was no statistically significant difference between the inoculum of Φ6 and MS2 applied to each site ($p=0.19$). Both participant and observer were instructed to close their eyes during application so they were not aware of the exact location of contamination.

2b. Integrate this aerosol delivery system into simulations of HCPs using PPE. Using a non-pathogenic virus (bacteriophage Φ6) that simulates the behavior of human respiratory viruses, we will work with NIOSH and GSU Respiratory Therapy mentors who are experts in aerosol generation and delivery to simulate replicable dispersion patterns and doses of virus via the airborne route. The result will be an exposure assessment system where contamination can be measured during simulated patient care.

Initial simulations

The first set of human volunteer simulations were conducted in the dedicated patient care space reserved for patients with high risk pathogens at Emory University Hospital. All human volunteer simulation protocols were approved by the Emory University Institutional Review Board. Participants were members of the patient care team of a specialized biocontainment unit at a large tertiary care academic medical center. HCW were excluded as team members if they were pregnant, immunocompromised, trainees, allergic to latex, or had non-intact skin on their

hands or face. All participants had extensive training in the biocontainment unit in the donning, doffing, and use of EVD-specific PPE, and most had direct patient care experience with patients with confirmed EVD. All participants in this study, as a requirement of being a member of the biocontainment unit patient care team, had undergone quarterly training that included evaluation of their ability to don and doff their PPE.

The trained observer (TO) for all simulations was a physician who had provided direct care to patients with confirmed EVD. The TO had donned and doffed EVD PPE and observed the donning and doffing process for other providers multiple times during care of patients with EVD. The PPE doffing protocol used by the facility for care of patients with suspected or confirmed EVD (Table 1) was used in simulations.

Table 1. The Ebola-level personal protective equipment doffing protocol used at the facility for care of suspected or confirmed Ebola, and for all simulations. All steps indicating "sanitize" use alcohol-based hand rub.

Location	Step	Required Action
Patient room	Step 1	Remove apron.
Patient room	Step 2	Remove one bootie, then step onto chemical mat
Patient room	Step 3	Remove other bootie, then step onto chemical mat
Patient room	Step 4	Sanitize gloves
Patient room	Step 5	Remove outer gloves using the beaking method
Patient room	Step 6	Sanitize inner gloves.
Patient room	Step 7	Remove tape.
Patient room	Step 8	Sanitize inner gloves.
Patient room	Step 9	Remove biohazard coverall.
Patient room	Step 10	Sanitize inner gloves.
Patient room	Step 11	Enter anteroom
Anteroom	Step 12	Remove PAPR Hood.
Anteroom	Step 13	Sanitize inner gloves.
Anteroom	Step 14	Remove inner gloves using the beaking method
Anteroom	Step 15	Wash hands with soap and water.
Anteroom	Step 16	Remove belt, battery and motor.

Simulations took place in the anteroom and patient room of the biocontainment unit used for patient care, beginning with the donning process. First, the participant changed into disposable scrub shirt and pants and fluid-resistant shoes in the locker room, and then moved to the anteroom of the biocontainment unit. The TO then verbally guided them through the donning process using the biocontainment unit's checklist. When finished the participant wore a Tyvek® suit, fluid resistant apron, one pair of short inner gloves taped to the wrist of the Tyvek® suit, one pair of long outer gloves covering the wrist completely, a PAPR, a PAPR hood, and fluid-resistant shoe covers.

To simulate actual tasks done while wearing PPE, the HCW then entered the patient room and emptied a urinary catheter bag attached to a mannequin, disposing of the contents in the toilet according to the biocontainment unit's protocol. The HCW then cleaned the room according to the biocontainment unit's standard protocols, including using disinfectant wipes on surfaces and mopping floors. After room cleaning, they began the PPE doffing process, which started in the patient room and proceeded through a door into the anteroom for the final step of removing the PAPR hood and PAPR. The TO verbally and visually (with gestures) guided them through the doffing process using the checklist in Table 1. Hand hygiene was frequently performed using alcohol-based hand rub (ABHR) except for step 15, where soap and water is used. At the doffing step when inner gloves were removed (Step 14), they were collected for sampling. The facility's protocol uses the "beaking" method for removing gloves, a glove-in-glove technique that results in the gloves coming off one inside the other, so gloves were sampled together.

The entire simulation process was video recorded from multiple angles using 4 stationary cameras and 1 hand-held camera for human factors analysis. We recorded each simulation using 1 handheld and between 2 and 5 stationary cameras. Using these recordings (and the details of each site's doffing protocol), we determined the duration of doffing steps, the different ways each step can fail to accomplish its goal(s) (ie, failure modes [FMs], and the frequency of each FM. FMs were determined via an Failure Modes and Effects Analysis, which is a technique for identifying and quantifying the risk of failures in a process in order to prioritize interventions that mitigate their effects.

For each site, at least 2 human factors experts reviewed each simulation to identify FMs in the major doffing steps; judges considered elements such as knowledge of a site's doffing protocol, the PPE likely to be contaminated, as well as evident human factors missteps (eg, errors of execution). Two human factors experts independently identified similar FMs that occurred at either most or all of the sites (ie, common FMs); reliability was assessed with percentage agreement.

For each site, 2 raters independently tallied the frequency at which each FM occurred in the simulations using the Observer XT version 12.5 (Noldus Information Technology, Leesburg, VA). Raw frequencies were transformed into a 5-point frequency scale. At each site, human factors and subject matter experts (eg, infectious disease physicians and nurses experienced in donning and doffing) independently rated the severity of the effect(s) of each FM using a 5-point scale that ranged from 1 (negligible) to 5 (catastrophic). For each FM at a site, we then calculated a risk index by multiplying the average severity rating for that FM by its transformed frequency value. We assessed the reliability of coding the frequency and sequence of FMs with Cohen's kappa and the reliability of the average severity rating of FMs with an average measures intraclass correlation. Immediately after doffing, half of the HCWs at each site (n = 5) completed the NASA Task Load Index (NASA-TLX) for the major doffing steps at their facility. The NASA-TLX comprises 6 subscales of workload (mental demand, physical demand, temporal demand, performance, effort, and frustration) that are each rated on a 100-point scale, with larger values corresponding to greater amounts of perceived workload.

Expanded simulations

After the completion of 10 simulations at Emory, we expanded to three additional hospitals that were state-designated to receive potential Ebola patients. In total we performed 41 simulations across the 4 state-designated Ebola treatment centers in Georgia. During each simulation, a single HCW donned high-level PPE for serious communicable diseases in his or her biocontainment unit, performed a standardized task (changing a urinary catheter bag on a mannequin), and then doffed according to his or her institutional protocol.

Aim 2c: Using this experimental exposure assessment system, determine the values of undefined parameters in the mathematical risk models. Specifically, we will estimate the transfer efficiency of virus from a patient to the HCP's hands, face and clothing, as well as viral die-off rates on a HCP's hands, face and clothing during and after patient care.

After the doffing process concluded (Step 16), three sites were examined under ultraviolet light for fluorescent tracer and sampled for virus: bare hands, face, and scrubs worn under PPE. The face was swabbed on each cheek for virus using a polyester swab dipped in eluent. Hands were sampled for virus using whole-hand sampling. Scrubs were collected for sampling by complete immersion in eluent after removal. Samples were placed on ice and immediately transported back to the laboratory for analysis using previously described methods.[4] High touch surfaces in the patient room and doffing area were examined under ultraviolet light for the presence of fluorescent tracer, including door handles, toilet handles, and bedrails. Any sites that appeared to have any fluorescent tracer were sampled using macrofoam swabs. A 1 cm^2 surface surrounding the tracer was defined and swabbed 10 times in a back and forth motion. Swabs were eluted in 1.5% beef extract containing 0.1% Tween 80 by shaking at 100 rpm for 20 minutes. All samples were assayed for MS2 and Φ6 using the single agar layer (SAL) assay. Virus recovered from each site was expressed as plaque forming units (PFU).

For identifying previously unrecognized parameters, the entire simulation was video recorded from different angles using 4 stationary cameras and 1 hand-held camera. Video recordings were coded for frequency and duration of the major doffing steps (eg, remove apron), substeps (eg, roll apron into a ball before disposing), and frequency of FMs by 2 independent investigators using The Observer XT version 12.5 (Noldus Information Technology, Leesburg, Virginia). Interrater reliability was assessed with Cohen κ. Duration of doffing steps was assessed using box plots and compared using the Wilcoxon signed-rank test.

Iterative simulations

In collaboration with Emory scientists and scientists at the Georgia Institute of Technology, we used an iterative simulation approach to test possible risk mitigation measures incorporated into PPE protocols and into the patient care environment. Through a stepwise approach, in three phases we assessed how the physical environment can support the high-risk step of removing shoe covers, specifically evaluating four different stability aids (L-shaped stool, chair, horizontal bar, and vertical grab bar). Our objective was to assess the effectiveness of design improvements of the doffing area by comparing the results of Phase I (original layout) and Phase III (redesigned layout) on HCW performance, physical load and cognitive load. In the first phase, we analyzed the layouts of the biocontainment units

at the four state-designated Ebola treatment centers in Georgia and observed a series of simulations in all four BCUs. We conducted some of the simulations in one replicated high-fidelity BCU mockup that included walls, doors, windows, a bed and other realistic features built in the SimTigrate Design Lab at the Georgia Institute of Technology. This phase included 41 doffing HCWs (including nurses and physicians) and 15 trained observers (TOs), all of whom were trained on using Ebola-level PPE. Participants were asked to don the PPE, perform a simulated patient care task and then doff the PPE following the step-by-step protocol adopted by their hospital while the TO guided the HCWs through the doffing process.

In the second phase, we tested different balance aids (stool, L-shaped step stool, vertical grab bar and horizontal grab bar) and different levels of space flexibility with 31 undergraduate students with no PPE training (Phase IIA). Based on the framework from Phase I and our findings from Phase IIA, we designed two optimized layouts that we hypothesized would reduce physical and cognitive load and reduce the occurrence and number of observed risky behaviors. We built these layouts in the SimTigrate Design Lab's high-fidelity BCU mockup and tested with an additional nine students (Phase IIB). Using the input from the questionnaire administered to students, and results for performance, physical and cognitive load we selected one final layout (Figure 1). In the third phase, we tested the redesigned doffing area layout from Phase II in simulations with 10 trained HCWs and one TO.

Simulations were recorded using between two and five stationary cameras and an additional handheld camera for Phase I and III. We coded each video to identify the number of risky behaviors a HCW performed and tested for and achieved interrater reliability using Pearson 2-tailed correlation (0.89, $p = 0.001$). We define risky behaviors as actions that could increase the risk of self- and cross-contamination or occupational injury [5,6]. Based on our previous work, we identified 11 risky behaviors that are impacted by the built environment and defined their risk domain. We measured physical load at the moment of removing the disposable shoe covers, using the Rapid Entire Body Assessment (REBA) when participants were standing, and the Rapid Upper Limb Assessment (RULA) when participants were sitting. REBA (score range: 1-15) and RULA (score range: 1-13) are assessment tools that measure the physical load of a task and the risk of occupational injury by evaluating posture, with higher scores indicating higher physical load. The score quantifies the position, angle, and twist of upper and lower limbs, the neck and the trunk with regards to other body parts. We used the NASA Task Load Index (TLX), a questionnaire tool, to measure the perceived workload of a task on six different subscales (Mental Demand, Physical Demand, Temporal Demand, Frustration, Effort and Performance). The TLX scores for perceived workload range between 0 and 100, for all six subscales. Higher scores indicate higher perceived workload. Some participants in Phase I ($N = 19$) and all in Phase III provided their workload rating on each subscale and after each major task. We analyzed REBA/RULA scores by one-way ANOVA to determine if there were differences in physical load when participants used different balance aids. We compared the number of risky behaviors between Phase I and Phase III using the Mann U Whitney test; we determined the change in occurrence of specific behaviors by calculating the percentage change and tested for association between phase and the risky behaviors using Fischer's exact test. For Phase I, we excluded incomplete data from the analysis and data for three HCWs because the TO removed the shoe covers for those HCWs; in Phase II data was incomplete for seven participants; in Phase III data was excluded for one of the participants who did not use the balance aid.

Specific Aim 3

Define the parameters of mathematical models (developed in Aim 1) with data from Aim 2 to predict infection risks to HCPs using PPE. Specifically, we will examine:

Aim 3a. Risk of infection from current PPE use practices.

After the doffing process concluded (Step 16), three sites were examined under ultraviolet light for fluorescent tracer and sampled for virus: bare hands, face, and scrubs worn under PPE. The face was swabbed on each cheek for virus using a polyester swab dipped in eluent. Hands were sampled for virus using whole-hand sampling. Scrubs were collected for sampling by complete immersion in eluent after removal. Samples were placed on ice and immediately transported back to the laboratory for analysis using previously described methods.[4] High touch surfaces in the patient room and doffing area were examined under ultraviolet light for the presence of fluorescent tracer, including door handles, toilet handles, and bedrails. Any sites that appeared to have any fluorescent tracer were sampled using macrofoam swabs. A 1 cm^2 surface surrounding the tracer was defined and swabbed 10 times in a back and forth motion. Swabs were eluted in 1.5% beef extract containing 0.1% Tween 80 by shaking at 100 rpm for 20 minutes. All samples were assayed for MS2 and Φ6 using the single agar layer (SAL) assay. Virus recovered from each site was expressed as plaque forming units (PFU).

The entire simulation process was video recorded from multiple angles using 4 stationary cameras and 1 handheld camera for human factors analysis. We recorded each simulation using 1 handheld and between 2 and 5 stationary cameras. Using these recordings (and the details of each site's doffing protocol), we determined the duration of doffing steps, the different ways each step can fail to accomplish its goal(s) (ie, failure modes [FMs], and the frequency of each FM. FMs were determined via an Failure Modes and Effects Analysis, which is a technique for identifying and quantifying the risk of failures in a process in order to prioritize interventions that mitigate their effects. For each site, at least 2 human factors experts reviewed each simulation to identify FMs in the major doffing steps; judges considered elements such as knowledge of a site's doffing protocol, the PPE likely to be contaminated, as well as evident human factors missteps (eg, errors of execution). Two human factors experts independently identified similar FMs that occurred at either most or all of the sites (ie, common FMs); reliability was assessed with percentage agreement.

For each site, 2 raters independently tallied the frequency at which each FM occurred in the simulations using the Observer XT version 12.5 (Noldus Information Technology, Leesburg, VA). Raw frequencies were transformed into a 5-point frequency scale. At each site, human factors and subject matter experts (eg, infectious disease physicians and nurses experienced in donning and doffing) independently rated the severity of the effect(s) of each FM using a 5-point scale that ranged from 1 (negligible) to 5 (catastrophic). For each FM at a site, we then calculated a risk index by multiplying the average severity rating for that FM by its transformed frequency value. We assessed the reliability of coding the frequency and sequence of FMs with Cohen's kappa and the reliability of the average severity rating of FMs with an average measures intraclass correlation. Immediately after doffing, half of the HCWs at each site (n = 5) completed the NASA Task Load Index (NASA-TLX) for the major doffing steps at their facility. The NASA-TLX comprises 6 subscales of workload (mental demand, physical demand, temporal demand, performance, effort, and frustration) that are each rated on a 100-point scale, with larger values corresponding to greater amounts of perceived workload.

Aim 3b: Changes in risk resulting from the adoption of alternative practices for wearing and removing PPE

Our evaluation of changes in risk from alternative practices encompassed key themes: changes in the doffing process, changes in the physical environment, and changes in the use of the powered air purifying respirator (PAPR) component of the PPE.

Iterative simulations

In collaboration with Emory scientists and scientists at the Georgia Institute of Technology, we used an iterative simulation approach to test possible risk mitigation measures incorporated into PPE protocols and into the patient care environment. Through a stepwise approach, in three phases we assessed how the physical environment can support the high-risk step of removing shoe covers, specifically evaluating four different stability aids (L-shaped stool, chair, horizontal bar, and vertical grab bar). Our objective was to assess the effectiveness of design improvements of the doffing area by comparing the results of Phase I (original layout) and Phase III (redesigned layout) on HCW performance, physical load and cognitive load. In the first phase, we analyzed the layouts of the biocontainment units at the four state-designated Ebola treatment centers in Georgia and observed a series of simulations in all four BCUs. We conducted some of the simulations in one replicated high-fidelity BCU mockup that included walls, doors, windows, a bed and other realistic features built in the SimTigrate Design Lab at the Georgia Institute of Technology. This phase included 41 doffing HCWs (including nurses and physicians) and 15 trained observers (TOs), all of whom were trained on using Ebola-level PPE. Participants were asked to don the PPE, perform a simulated patient care task and then doff the PPE following the step-by-step protocol adopted by their hospital while the TO guided the HCWs through the doffing process.

In the second phase, we tested different balance aids (stool, L-shaped step stool, vertical grab bar and horizontal grab bar) and different levels of space flexibility with 31 undergraduate students with no PPE training (Phase IIA). Based on the framework from Phase I and our findings from Phase IIA, we designed two optimized layouts that we hypothesized would reduce physical and cognitive load and reduce the occurrence and number of observed risky behaviors. We built these layouts in the SimTigrate Design Lab's high-fidelity BCU mockup and tested with an additional nine students (Phase IIB). Using the input from the questionnaire administered to students, and results for performance, physical and cognitive load we selected one final layout (Figure 1). In the third phase, we tested the redesigned doffing area layout from Phase II in simulations with 10 trained HCWs and one TO.

Simulations were recorded using between two and five stationary cameras and an additional handheld camera for Phase I and III. We coded each video to identify the number of risky behaviors a HCW performed and tested for and achieved interrater reliability using Pearson 2-tailed correlation (0.89, p = 0.001). We define risky behaviors as

actions that could increase the risk of self- and cross-contamination or occupational injury [5,6]. Based on our previous work, we identified 11 risky behaviors that are impacted by the built environment and defined their risk domain. We measured physical load at the moment of removing the disposable shoe covers, using the Rapid Entire Body Assessment (REBA) when participants were standing, and the Rapid Upper Limb Assessment (RULA) when participants were sitting. REBA (score range: 1-15) and RULA (score range: 1-13) are assessment tools that measure the physical load of a task and the risk of occupational injury by evaluating posture, with higher scores indicating higher physical load. The score quantifies the position, angle, and twist of upper and lower limbs, the neck and the trunk with regards to other body parts. We used the NASA Task Load Index (TLX), a questionnaire tool, to measure the perceived workload of a task on six different subscales (Mental Demand, Physical Demand, Temporal Demand, Frustration, Effort and Performance). The TLX scores for perceived workload range between 0 and 100, for all six subscales. Higher scores indicate higher perceived workload. Some participants in Phase I (N = 19) and all in Phase III provided their workload rating on each subscale and after each major task. We analyzed REBA/RULA scores by one-way ANOVA to determine if there were differences in physical load when participants used different balance aids. We compared the number of risky behaviors between Phase I and Phase III using the Mann U Whitney test; we determined the change in occurrence of specific behaviors by calculating the percentage change and tested for association between phase and the risky behaviors using Fischer's exact test. For Phase I, we excluded incomplete data from the analysis and data for three HCWs because the TO removed the shoe covers for those HCWs; in Phase II data was incomplete for seven participants; in Phase III data was excluded for one of the participants who did not use the balance aid.

Simulations focusing on PAPR use

A trained observer (TO) verbally guided participants through donning and doffing of high-level PPE in a biocontainment unit. PPE donned and doffed by participants consisted of a Tyvek suit, a fluid-resistant apron, one pair of short inner gloves, one pair of long outer gloves, a PAPR, a PAPR hood, and fluid-resistant shoe covers. Following donning, 5 µL of a mixture of candidate Ebola surrogate viruses (Φ6 an enveloped bacteriophage and MS2 a non-enveloped bacteriophage) suspended in phosphate-buffered saline (PBS) containing a fluorescent tracer (GloGerm, Moab, Utah) was applied to the top side of the PAPR hood opposite the dominant hand. To simulate actual task done during patient care, participants proceeded into the patient area in the biocontainment unit and turned on the television facing the patient bed using a remote control placed on a bedside table in the patient area. Following the task, participants were guided through doffing using a structured doffing protocol as described by Casanova et al. (2018). Each participant performed two simulations on two separate visits to the biocontainment unit. The first simulation used a one-layer hood comprising one shroud laid over the Tyvek suit. The second simulation used a two-layer hood comprising two shrouds. The top shroud laid over the Tyvek suit while the bottom shroud was tucked into the suit. The TO guided each participant through doffing all PPE items. Steps in the doffing protocols used for each hood were identical except for the steps for doffing the hood (table 1).

During the doffing of PPE, inner gloves were collected for virus assay. After doffing, participants' face and hands were sampled, and scrubs were collected for virus assay. After collection, samples were placed on ice and immediately transported back to the laboratory for analysis. All samples were assayed for Φ6 and MS2 using the single agar layer assay. Virus recovered from each site was expressed as plaque-forming units (PFU). A McNemar's test was used to compare the proportion of participants with contamination on any site using the one-layer versus the two-layer hood. A Wilcoxon rank sum test was applied to compare the difference in the number of viruses recovered from inner gloves of participants using the one-layer versus the two-layer hood. All statistical analyses were performed using SAS 9.4 (Cary, NC).

All simulations were video recorded from different angles using four stationary cameras and one hand-held camera. A failure modes effect analysis (FMEA) was performed as described by Mumma et al. (2018). Briefly, video recordings of simulations were reviewed by X human factors experts to identify failure modes (FMs). Raw frequencies of each FM identified were obtained by summing their occurrence(s) in each simulation video recording. Severity of FMs was independently rated using a 5-point scale by nurses experienced in doffing high-level PPE. A risk index (RI) was calculated by transforming raw frequencies of each FM to quintiles and multiplying the resulting quintile frequency score for each FM by the average severity rating for that FM.

Table 2. Doffing Protocol for One-Layer and Two-Layer Hood

Step	One-layer Hood	Two-layer Hood
1.	Untie hood ties completely.	Rip and create an 8-inch piece of tape.
2.	Grasp side of face shield and pull out snaps.	Untie top tie and tie again loosely distally
3.	Push face shield forward and release helmet pin.	Untie torso hood tie. Grab tie from each side around torso. Do not let go.
4.	Grab top of hood. Pull back and then pull forward to remove PAPR hood.	Bring tie backwards and halfway over PAPR helmet.
5.	Sanitize gloves.	Sanitize gloves.
6.	n/a	Grab outer PAPR shroud at shoulders roll inward toward neck neatly. Continue to roll front anterior portion into neat roll.
7.	n/a	Grab prepared tape and tape shroud roll to visor on PAPR bottom.
8.	n/a	Sanitize gloves.
9.	n/a	Lift and flip inner shroud over PAPR helmet
10.	n/a	Starting from rear of PAPR, peel shroud off of PAPR helmet.
11.	n/a	Peel and unsnap visor off of PAPR hood
12.	n/a	Sanitize gloves

Results, Discussion, and Conclusions.

Specific Aim 1: Results

The conceptual model includes parameters I identified in exploration of the literature as necessary to define the exposure to virus in this scenario. Parameters that can be defined using data from human volunteer simulations are in bold. I designed compartmental models of transmission from patient to HCP during a patient care encounter. In this model, the compartments represent the number of viruses in different locations in the patient care environment, including on the HCP's face, hands, and N95 respirator. Viruses flow from compartment to compartment (for example, from hands to face when the HCP touches their face). The flow between compartments has probabilities attached. The numbers of viruses in the compartments and the rates of flow between compartments are the parameters of the exposure model. At the start, these values are undefined. I identified the parameters that must be defined to transform a conceptual model into a quantitative model of exposure. The main model used for simulation design is shown in Figure 1.

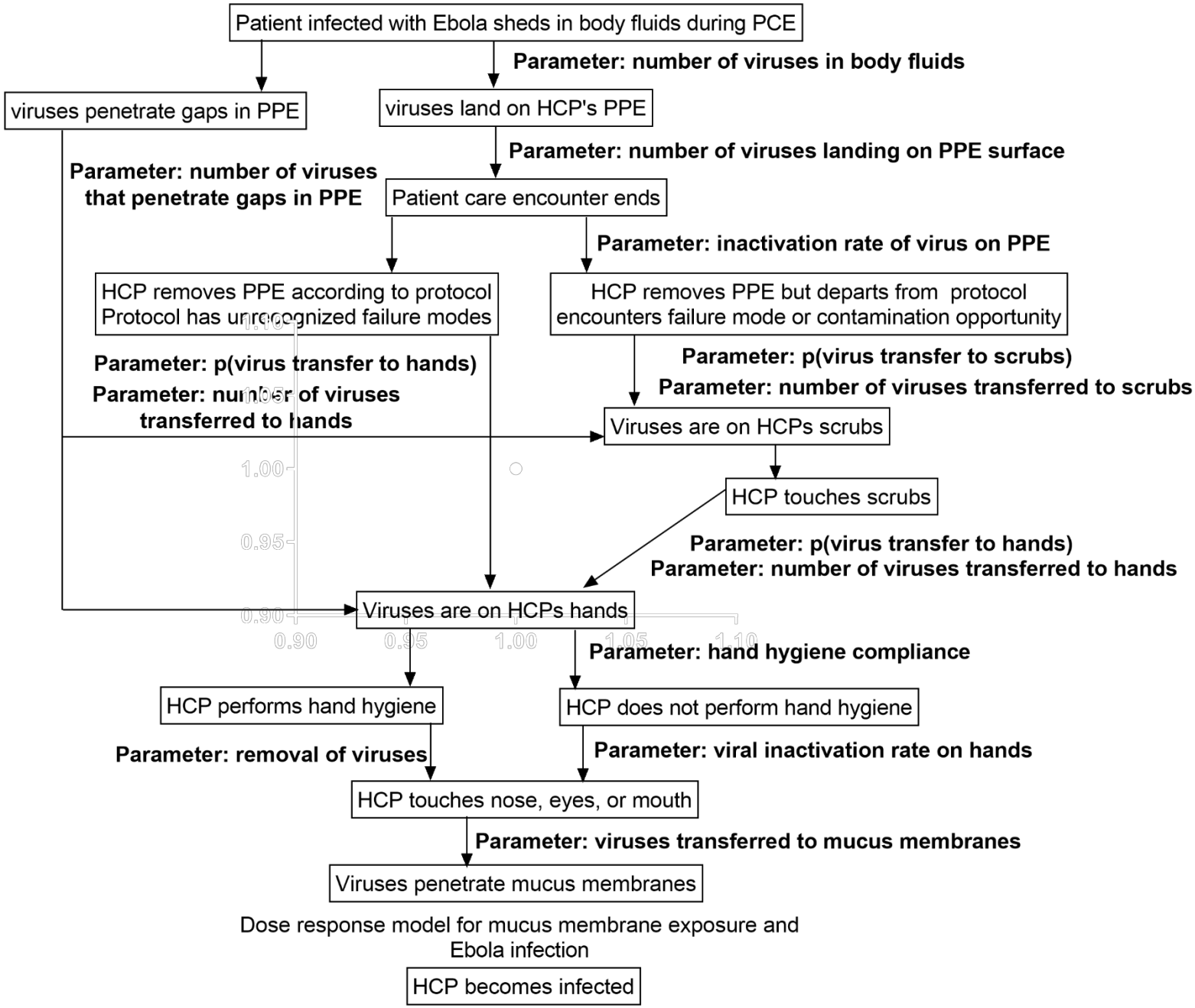

Figure 1. Risk model of possible exposure while wearing and doffing complex Ebola PPE

Specific Aim 2: Results

Simulate and measure how HCPs become contaminated with viruses using realistic experimental laboratory simulations of patient care with human volunteers.

Aim 2a. Develop and test a precision aerosol delivery system that simulates the spread of respiratory viruses by coughing, sneezing, and medical procedures, such as intubation and suctioning.

This aim ended up being exceptionally difficult. Building a system in my laboratory was more challenging than anticipated and was not finished during the grant. I have now obtained a human breathing and cough simulator custom built by a NIOSH engineer, and am collaborating with colleagues on methods to protect HCP from respiratory exposures. The system is much more sophisticated than I originally envisioned and can be used in my laboratory and a patient care simulation facility at Emory. This has allowed me to move forward with projects that are related to the original aims of this grant. Given these obstacles and the new opportunities and direction provided by my collaborations, I decided to pivot the simulations to focus on the use of complex Ebola PPE.

Aim 2b. Integrate this aerosol delivery system into simulations of HCPs using PPE. Using a non-pathogenic virus (bacteriophage Φ6) that simulates the behavior of human respiratory viruses, simulate replicable dispersion patterns and doses of virus. The result will be an exposure assessment system where contamination can be measured during simulated patient care.

A total of 10 HCW participated in the initial round of 10 simulations (9 RNs and 1 MD). Participants were 60% female, with a at least 3 years of healthcare experience (range: 3->25 years); most (9) had donned and doffed EVD PPE during care of a confirmed EVD patient. All had >1 year of training with EVD PPE, and 9/10 had trained within the last four months prior to participation. Seven HCWs reported receiving training within 2 months prior to participating, 3 HCWs within 3-4 months, and 1 HCW more than a year prior. The median number times doffing during training and patient care were 11 (range: 3 – 101) and 21 (range: 0 – 144), respectively. Ten HCWs reported having cared for a patient with confirmed EVD.

The four Georgia hospitals designated by the state as Ebola treatment centers allowed us to observe HCWs trained to care for patients with serious communicable diseases don and doff PPE in their physical setting using a standardized simulated situation. There were 10 simulations at each of the four hospitals (with an additional simulation at one hospital). For our simulations, a different individual preformed the role of HCW each time. All simulations involved a trained observer (TO) and at two sites, one person served as TO for either all or nearly all (9/10) of the simulations.

Based on results from these previous simulations, we designed an optimized doffing area by marking the doffing spot that indicates the location to stand during doffing; providing a built-in balance aid within reach of the defined doffing spot; and locating a mirror directly in front of the HCW for self-monitoring and self-inspection. We restricted the location of where the HCW stands and added colored demarcation on the floor to signify the zones and different level of contamination risk: red (contaminated), yellow (likely contaminated) and green (clean), similar to the designations of “hot, warm, and cold” zones. The doffing area has a unidirectional flow from contaminated to cleaner areas, to the outside of the patient room in a continuous forward motion. The two windows located parallel to the doffing area allow a trained observer to directly visualize the HCW doffing at all times.

Aim 2c. Using this experimental exposure assessment system, determine the values of undefined parameters in the mathematical risk models. Specifically, we will estimate the transfer efficiency of virus from a patient to the HCP’s hands, face, and clothing, as well as viral die-off rates on a HCP’s hands, face, and clothing during and after patient care.

No detectable transfer of enveloped bacteriophage Φ6 to inner gloves, hands or face for any participants was observed. There was transfer of Φ6 to scrubs for one participant (~ 140 PFU, 0.002% of original inoculum). Detectable transfer of non-enveloped bacteriophage MS2 (Table 3) was observed in 7/10 HCWs. Sites of contamination with MS2 included scrubs, hands, and inner gloves, but not face. MS2 was detected on the inner gloves for most participants (7/10, mean 8.8×10^5 PFU, 7% of original inoculum), and on scrubs (2/10, mean 1.5×10^3 PFU, 0.004% of original inoculum) and hands (1/10, ~100 PFU, <0.00003% of the original inoculum) for the minority of participants. Most (8) had detection of MS2 at only 1 site, while 2 had virus at 2 sites (inner gloves and either scrubs or hands). Fluorescent tracer was not detected on PPE, skin, or scrubs under UV light. A total of 21 surface sites were sampled because fluorescent tracer was visible by examination under UV light, including door handles, toilet handles, and bed rails. No bacteriophage was detected on any of these sites.

Table 3. Detection of non-enveloped bacteriophage MS2 after doffing Ebola-level personal protective equipment in 10 simulation studies*

HCW	Non-dominant hand (PFU)	Dominant hand (PFU)	Gloves (PFU)	Face	Scrubs (PFU)
1	ND	ND	ND	ND	ND
2	ND	ND	2.50×10^{1}	ND	ND
3	ND	ND	3.42×10^{4}	ND	1.33×10^{4}
4	ND	ND	1.44×10^{3}	ND	ND
5	ND	ND	ND	ND	ND
6	144	96	8.64×10^{6}	ND	ND
7	ND	ND	1.30×10^{5}	ND	ND
8	ND	ND	ND	ND	1.27×10^{3}
9	ND	ND	4.60×10^{4}	ND	ND
10	ND	ND	3.00×10^{2}	ND	ND
Arithmetic Mean	144	96	8.82×10^{5}	--	1.46×10^{3}
St. dev	--	--	2.72×10^{6}	--	4.18×10^{3}

*(ND=not detected; PFU=plaque forming units; st dev= standard deviation)

Ten HCWs contributed behavioral and contamination data for the FTAs; contamination data were unavailable for 1 HCW. ϕ6 was detected on 10% of HCW's scrubs. The fault tree predicted a 10.4% contamination rate for scrubs ($p = 0.96$), which most likely occurred when the PAPR hood inadvertently contacted scrubs during removal or, less likely, during coverall removal, when contaminated inner gloves contacted the inside of the PAPR hood shroud, which later rest against the scrubs. ϕ6 was not detected on bare hands (predicted rate = 0.15%, $p = 0.87$). The model predicted some inner glove contamination (predicted rate = 10.3%, $p = 0.14$), but none was observed. Although the failure modes used in our definition of inadequate hand hygiene were among the riskiest in the FMEA, the FTAs show that the conjunction of these behaviors was unlikely (0.14). This suggests that, overall, hand hygiene was not as poor as the FMEA indicates, corroborating the low ϕ6 contamination rates.

MS2 was detected more frequently than ϕ6 (20% of scrubs, 70% of inner gloves, and 10% of hands). The predicted contamination rates for scrubs, inner gloves, and hands, were 19.38% ($p = 0.96$), 73.40% ($p = 0.81$), and 7.34% ($p = 0.76$), respectively. FTAs for MS2 suggest that the route of scrub contamination was similar to that for ϕ6 (Figure 6). The most likely source of inner glove contamination was touching the PAPR hood face shield during PAPR hood removal, although other routes, such as the ABHR dispenser, were also possible. Moreover, hand contamination of the one HCW was likely due to snapping during the removal of inner gloves, for which the probability of being contaminated was high (0.73).

We also analyzed the data from all 41 simulations as a whole. Virus results are shown in Table 4Table 4.

Table 4. Results across all 41 simulations and 4 sites

Φ6					MS2			
HCW	Non-dom	Dom	Gloves	Scrubs	Non-dom	Dom	Gloves	Scrubs
1	ND	ND	ND	ND	144	96	8.64×10^{6}	ND
2	ND	ND	ND	ND	ND	ND	ND	1.27×10^{3}
3	ND	ND	ND	ND	ND	ND	3.00×10^{2}	ND
4	ND	ND	ND	ND	ND	ND	ND	ND
5	ND	ND	ND	ND	ND	ND	2.50×10	ND
6	ND	ND	ND	ND	ND	ND	4.60×10^{4}	ND
7	ND	ND	ND	ND	ND	ND	1.44×10^{3}	ND
8	ND	ND	ND	ND	ND	ND	ND	ND
9	ND	ND	ND	ND	ND	ND	1.03×10^{5}	ND
10	ND	ND	ND	140	ND	ND	3.42×10^{4}	1.33×10^{4}
1	ND	ND	ND	ND	108	ND	ND	ND
2	ND	ND	ND	ND	ND	ND	ND	ND
3	20	4	ND	ND	ND	ND	ND	ND
4	ND	ND	ND	ND	ND	ND	ND	ND
5	ND	ND	ND	ND	ND	ND	ND	40
6	ND	ND	ND	ND	ND	ND	ND	ND
7	ND	ND	ND	ND	ND	ND	5	10
8	ND	ND	ND	ND	ND	ND	ND	ND
9	196	64	ND	ND	64	44	10	20
10	ND	ND	ND	ND	ND	ND	ND	ND
1	ND	ND	ND	ND	ND	ND	ND	ND
2	ND	ND	ND	ND	ND	ND	2.25×10^{5}	1.00×10^{1}
3	20	4	ND	ND	ND	ND	5.00×10^{1}	ND
4	ND	ND	ND	ND	ND	ND	1.00×10^{1}	ND
5	ND	ND	ND	ND	ND	ND	1.66×10^{4}	ND
6	ND	ND	ND	ND	ND	ND	1.81×10^{4}	ND
7	ND	ND	ND	ND	ND	ND	ND	ND
8	ND	ND	ND	ND	ND	ND	2.00×10^{1}	ND
9	196	64	ND	ND	ND	ND	8.76×10^{3}	ND
10	ND	ND	ND	ND	ND	4	9.43×10^{3}	1.10×10^{2}
1	ND	ND	ND	ND	ND	ND	ND	ND
2	ND	ND	ND	ND	ND	ND	ND	2.55×10^{3}
3	ND	ND	ND	ND	ND	ND	ND	1.30×10^{2}
4	ND	ND	ND	ND	ND	ND	2.50×10	ND
5	ND	ND	ND	ND	ND	ND	ND	5.90×10^{2}
6	ND	ND	ND	ND	ND	ND	9.20×10^{2}	ND
7	ND	ND	ND	ND	ND	ND	2.50×10^{2}	ND
8	ND	ND	ND	ND	ND	ND	1.70×10^{2}	6.10×10^{2}
9	ND	ND	ND	ND	ND	ND	ND	ND
10	ND	ND	ND	ND	ND	ND	8.17×10^{3}	2.00×10

Specific Aim 3: Results

Define the parameters of mathematical models (developed in Aim 1) with data from Aim 2 to predict infection risks to HCPs using PPE. Specifically, we will examine:

Aim 3a. Risk of infection from current PPE use practices.

No detectable transfer of enveloped bacteriophage Φ6 to inner gloves, hands or face for any participants was observed. There was transfer of Φ6 to scrubs for one participant (~ 140 PFU, 0.002% of original inoculum). Detectable transfer of non-enveloped bacteriophage MS2 (Table 2) was observed in 7/10 HCWs. Sites of contamination with MS2 included scrubs, hands, and inner gloves, but not face. MS2 was detected on the inner gloves for most participants (7/10, mean 8.8×10^5 PFU, 7% of original inoculum), and on scrubs (2/10, mean 1.5×10^3 PFU, 0.004% of original inoculum) and hands (1/10, ~100 PFU, <0.00003% of the original inoculum) for the minority of participants. Most (8) had detection of MS2 at only 1 site, while 2 had virus at 2 sites (inner gloves and either scrubs or hands). This suggests current complex Ebola PPE use practices pose a measurable risk of viral contamination of hands and underlying clothing. Modeling approaches taken from HFE can give us insight into why.

In the FMEA (Table 5), 51 failure modes were identified and grouped by major doffing step, as defined by the protocol. Steps varied in the number of failure modes (median: 6, range: 1 to 13) and the risk index (RI) associated with their failure modes (median: 7, range: 2 to 18). Hand hygiene (ΣRIs = 111) and removing the PAPR hood (ΣRIs = 70) had the greatest summative RIs owing, in part, to the number of different ways failure occurred (n = 9 and 13, respectively). The summative RIs were moderately high for removing coveralls (60), booties (40), tape (39), and apron (37). The summative RIs for removing gloves (20), engage the TO's attention to begin doffing (12), and removing the PAPR helmet (4) were lower. Many failure modes were thought to potentially spread contamination, either to a HCW's PPE (n = 31, 60%), skin (n = 2, 4%), or the environment, (n = 14, 27%), followed by delaying or disrupting the process (n = 11, 21%), compromising PPE (n = 4, 8%), occupational injury (n = 3, 6%), or reusable equipment damage (n = 1, 2%). Some failure modes, such as not rubbing hands until dry, had more than one effect (i.e., spreading contamination and delaying later processes).

Table 5. Failure Modes and Effects Analysis

Doffing Step	Failure Mode	Effect(s)	Severity Score	Frequency	Risk Index
Engage TO	TO does not inspect HCW for visible contamination	Disrupt process sequence/Delays process	3.00	4	12
Hand Hygiene	Does not disinfect alcohol pump after using	Spread contamination to Environment	3.17	5	16
Hand Hygiene	Does not disinfect between fingers	Spread contamination to PPE and Environment	3.17	5	16
Hand Hygiene	Does not disinfect wrists	Spread contamination to PPE and Environment	3.50	5	18
Hand Hygiene	Does not disinfect thumbs	Spread contamination to PPE and Environment	3.67	4	15
Hand Hygiene	Does not rub hands until dry	Spread contamination to PPE and Environment, Disrupt process sequence/Delays process	3.33	5	17
Hand Hygiene	Hand hygiene appeared to have been cut short by TO giving instructions	Disrupt process sequence/Delays process, spread contamination to PPE and Environment	2.83	4	11
Hand Hygiene	Shaking hands to dry	Spread contamination to Environment and PPE	2.83	4	11
Hand Hygiene	Stretching to reach alcohol pump	Occupational injury	1.50	3	5
Hand Hygiene	Steps back onto coverall/mat after stepping off to reach alcohol pump	Spread contamination to PPE	2.33	1	2

Remove Apron	Grabs front of apron	Spread contamination to PPE	2.50	4	10
Remove Apron	Touching coverall sleeves to front of apron	Spread contamination to PPE	2.67	3	8
Remove Apron	Touches apron excessively	Spread contamination to PPE	2.50	3	8
Remove Apron	Snaps apron roughly	Spread contamination to PPE and Environment	3.17	2	6
Remove Apron	Apron touches wall when removing	Spread contamination to Environment	3.00	1	3
Remove Apron	Outer gloves touch front of coverall when rolling apron up	Spread contamination to PPE	1.67	1	2
Remove Booties	Crosses leg in front of self	Spread contamination to PPE	2.17	5	11
Remove Booties	Touches bootie excessively	Spread contamination to PPE	2.33	3	7
Remove Booties	Touches back of bootie to front of coverall leg	Spread contamination to PPE	2.17	3	7
Remove Booties	Unstable posture (loss of balance)	Occupational injury	2.33	3	7
Remove Booties	Swings legs excessively while removing booties	Spread contamination to PPE	1.83	2	4
Remove Booties	Touches same bootie with more than one hand	Spread contamination to PPE	2.17	1	2
Remove Booties	Touches stool with each hand	Spread contamination to Environment	2.67	1	3
Remove Tape	Wrist exposed after removing tape	PPE compromised	3.17	4	13
Remove Tape	Roughly removes tape	Spread contamination to PPE and Environment	3.00	4	12
Remove Tape	Coverall sleeves tear	PPE compromised	2.83	5	14
Remove Gloves	Difficulty pinching cuff with beaked hand (requires multiple attempts)	Disrupt process sequence/Delays process	2.17	5	11
Remove Gloves	Glove snaps when removing glove	Spread contamination to PPE and Environment	2.50	3	8
Remove Coveralls	Inner gloves coming off when removing coverall sleeves	PPE compromised	3.67	5	18
Remove Coveralls	Touches outside of coverall sleeve with inner gloves	Spread contamination to PPE	2.83	3	9
Remove Coveralls	Lower back is exposed after removing coverall	PPE compromised	2.17	3	7
Remove Coveralls	Coverall is off of mat	Spread contamination to PPE	2.33	3	7
Remove Coveralls	Pushes coverall down legs with inner gloves	Spread contamination to PPE	2.83	2	6
Remove Coveralls	Stepped off mat into red zone, then entered anteroom	Spread contamination to Environment	3.17	1	3
Remove Coveralls	Unstable posture (loss of balance)	Occupational injury	2.50	2	5
Remove Coveralls	Touches front outside of coverall with inner gloves	Spread contamination to PPE	3.33	1	3

Remove Coveralls	HCW grabbed hood ties	Disrupt process sequence/Delays process	2.83	1	3
Remove PAPR Hood	PAPR hood contacts exposed arms	Spread contamination to HCW	3.33	4	13
Remove PAPR Hood	Touches ties excessively	Spread contamination to PPE	2.50	4	10
Remove PAPR Hood	Squeezes front of face shield to remove from peg	Spread contamination to PPE	2.33	4	9
Remove PAPR Hood	Pulls PAPR hood off by grabbing near front rather than the back	Spread contamination to PPE, Disrupt process sequence/Delays process	2.33	3	7
Remove PAPR Hood	Touches face shield excessively	Spread contamination to PPE	2.33	3	7
Remove PAPR Hood	HCW almost handed PAPR hood to TO	Spread contamination to PPE (TO), Disrupt process sequence/Delays process	3.50	1	4
Remove PAPR Hood	Touches PAPR hood excessively when removing it with both hands	Spread contamination to PPE	2.83	1	3
Remove PAPR Hood	Bumps into door (e.g., with PAPR hood, scrub shoulder)	Spread contamination to Environment	2.83	2	6
Remove PAPR Hood	TO's arm contacts with PAPR battery cord	Spread contamination to PPE (TO)	1.83	2	4
Remove PAPR Hood	Drops PAPR unit	Equipment damage	2.00	1	2
Remove PAPR Hood	Grabs PAPR hood too far back	Disrupt process sequence/Delays process	2.33	1	2
Remove PAPR Hood	TO says "unsnap PAPR hood" before "untie PAPR hood"	Disrupt process sequence/Delays process	1.83	1	2
Remove PAPR Hood	Unsnaps hood before untying ties	Disrupt process sequence/Delays process	1.67	1	2
Remove PAPR Helmet	Wipe face with scrub shoulder	Spread contamination to HCW	3.83	1	4

The raters showed substantial agreement for coding doffing steps, sub-steps, and the frequencies of failure modes (mean $\kappa = 0.77$). Box plots showed variation in the duration of each doffing step (Figure 1), with complete doffing requiring a median of 5.7 minutes (range: 3.7 to 9.9 minutes). Removing coveralls was the most time-consuming step (median: 83.4 seconds, range: 41.7 – 116.5 seconds). Moreover, coverall and outer glove removal had the largest interquartile ranges (IQR = 46.7 and 39.4, respectively), suggesting that these steps have the greatest need for reduced process variability. Contributors to variability in glove removal and their relation to contamination are discussed in the following sections. HCWs performed hand hygiene with ABHR for a median duration of 7.3 seconds (range: 0.7 - 39.2 seconds), with higher median durations occurring after apron removal (median: 14.1 seconds, range: 3.2 – 21.9 seconds) and inner glove removal using soap and water (median: 25.6 seconds, range: 14.5 – 31.8 seconds; Figure 2).

Among the failure modes (FMs) with the highest RI were several related to hand hygiene (RIs > 73% - 94% of all FMs). These were not disinfecting ABHR dispenser after use (64% of hand hygiene instances), not rubbing hands until dry (36%), not cleaning wrists (30%), between fingers (15%), or thumbs (5%), hand hygiene truncated by TO moving to next step (11%), and shaking hands to dry (4%). An insufficient duration of hand hygiene (until gloves were dry) appeared to be causally related to FMs during glove removal. Specifically, if gloves were slick from hand sanitizer, firmly gripping one glove with the other gloved hand became challenging, particularly with the reduced dexterity from double gloving. Across the 11 HCWs, there was a total of 111 attempts at pinching the cuff of one glove with the “beaked” glove (5 times more than what should be necessary), 71% of which occurred during outer glove removal. Removal of the outer gloves (median = 21.5 seconds, range: 7.4 – 70.1 seconds) took statistically

longer than inner gloves (median = 11.3 seconds, range: 6.8 – 64.7; p = 0.02). Moreover, poor grip can lead to glove-snapping and, although rare, snapping the inner gloves during removal emerged as part of a critical pathway for hand contamination in the FTAs (see below).

Another family of FMs concerned compromised PPE (RIs > 62% - 96% of all FMs), particularly of the wrists and hands during tape and coverall removal. One of these FMs appeared to be related causally to another; coverall sleeves are tucked into the inner gloves, which can pull the gloves off when HCWs remove their hands from their sleeves. Some HCWs anticipated this problem and loosened their sleeves with their inner gloves before removing their coveralls. A final family of FMs emerged that can be characterized, generally, as “mishandling PPE” comprising grabbing the front of the apron (36% of HCWs) and several FMs specific to PAPR hood removal (RIs > 63% - 83% of all FMs): squeezing front of face shield (45% of HCWs), fumbling with PAPR hood ties (36%), and PAPR hood shroud contacting exposed arms (36%).

Ten HCWs contributed behavioral and contamination data for the FTAs. ϕ6 was detected on 10% of HCW’s scrubs. The fault tree predicted a 10.4% contamination rate for scrubs (p = 0.96), which most likely occurred when the PAPR hood inadvertently contacted scrubs during removal or, less likely, during coverall removal, when contaminated inner gloves contacted the inside of the PAPR hood shroud, which later rest against the scrubs. ϕ6 was not detected on bare hands (predicted rate = 0.15%, p = 0.87). The model predicted some inner glove contamination (predicted rate = 10.3%, p = 0.14), but none was observed. Although the failure modes used in our definition of inadequate hand hygiene were among the riskiest in the FMEA, the FTAs show that the conjunction of these behaviors was unlikely (0.14; Figure 2, Figure 3. Fault tree analysis of scrub contamination, Figure 4). This suggests that, overall, hand hygiene was not as poor as the FMEA indicates, corroborating the low ϕ6 contamination rates.

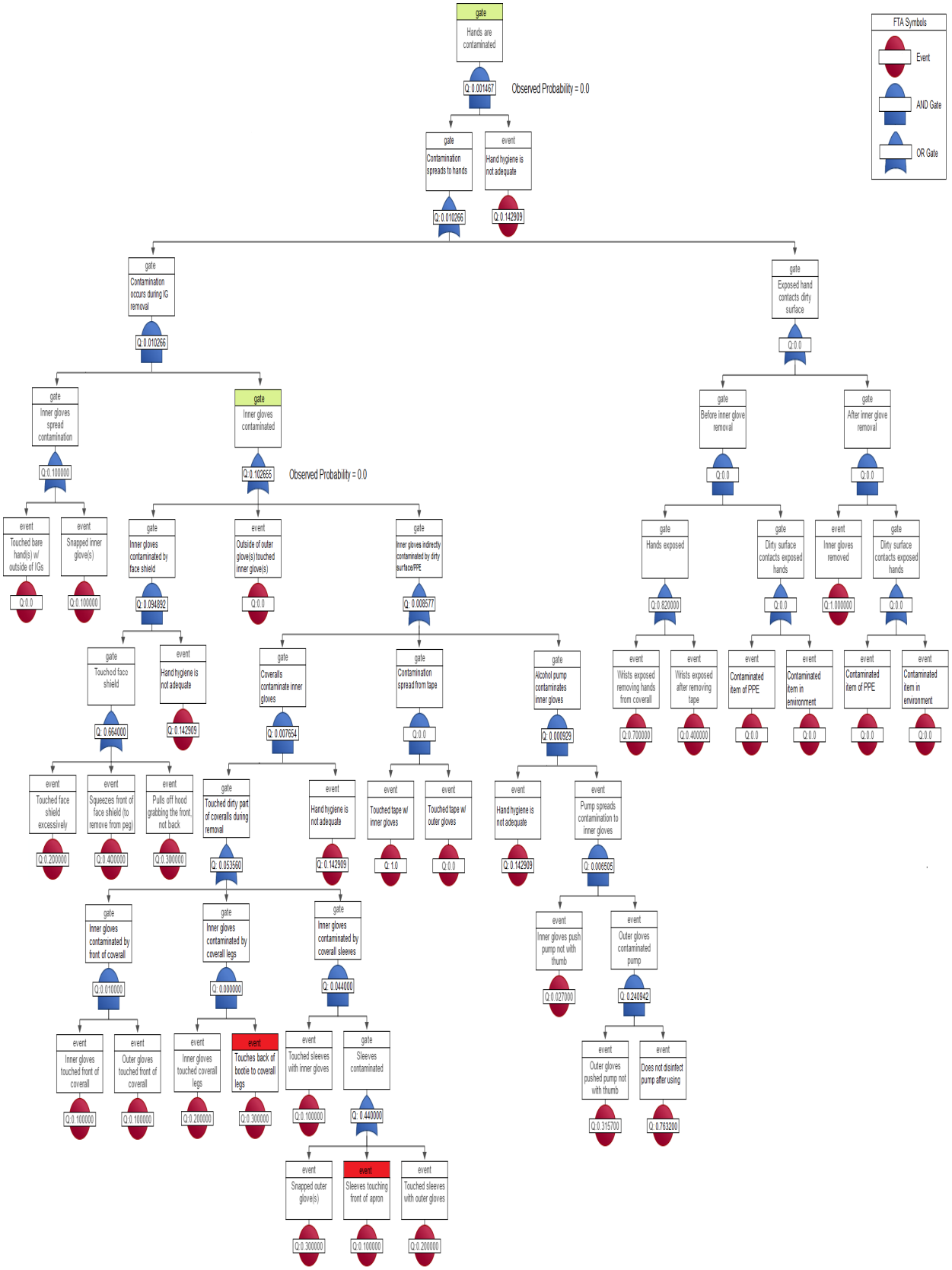

Figure 2. Fault tree analysis of hand contamination

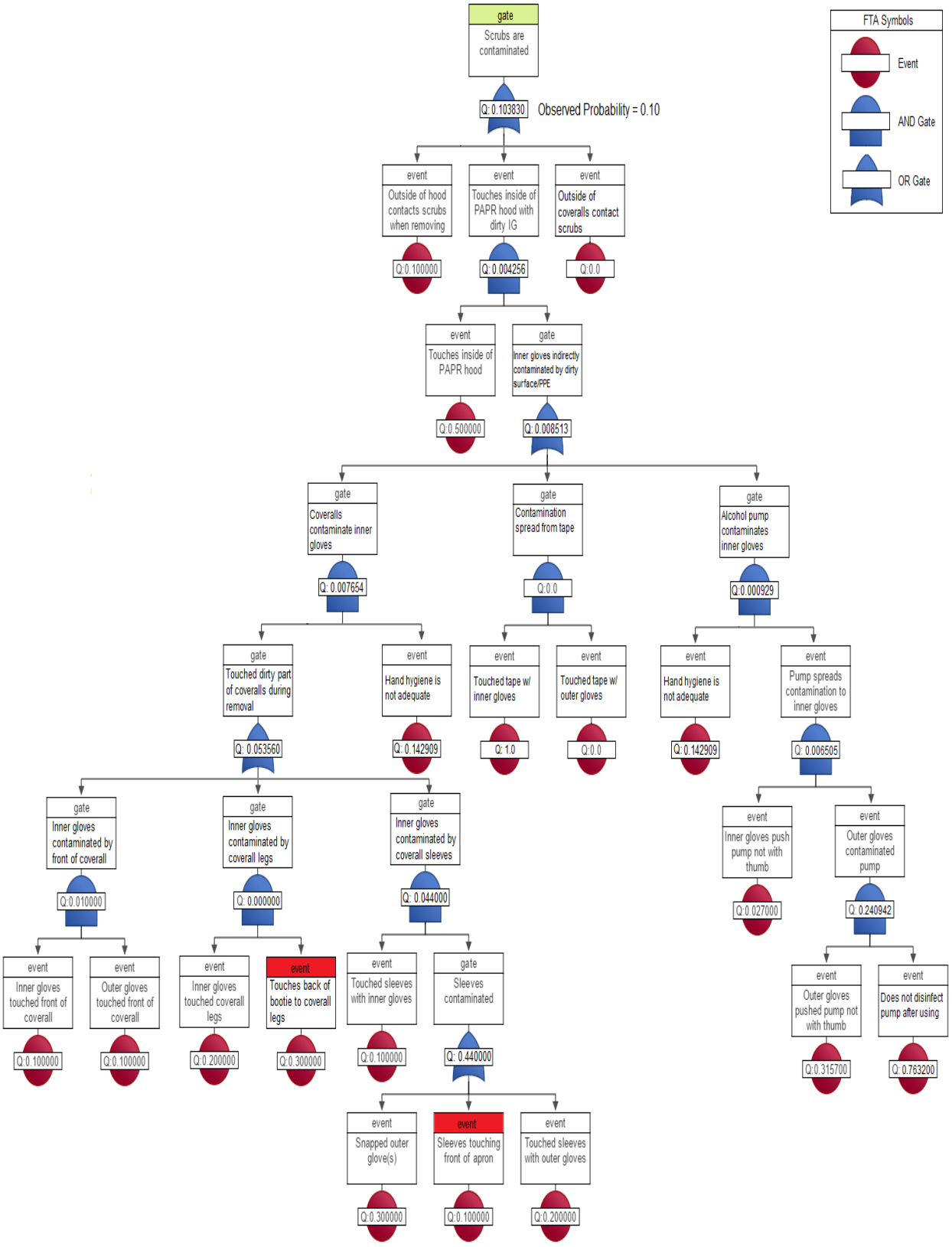

Figure 3. Fault tree analysis of scrub contamination

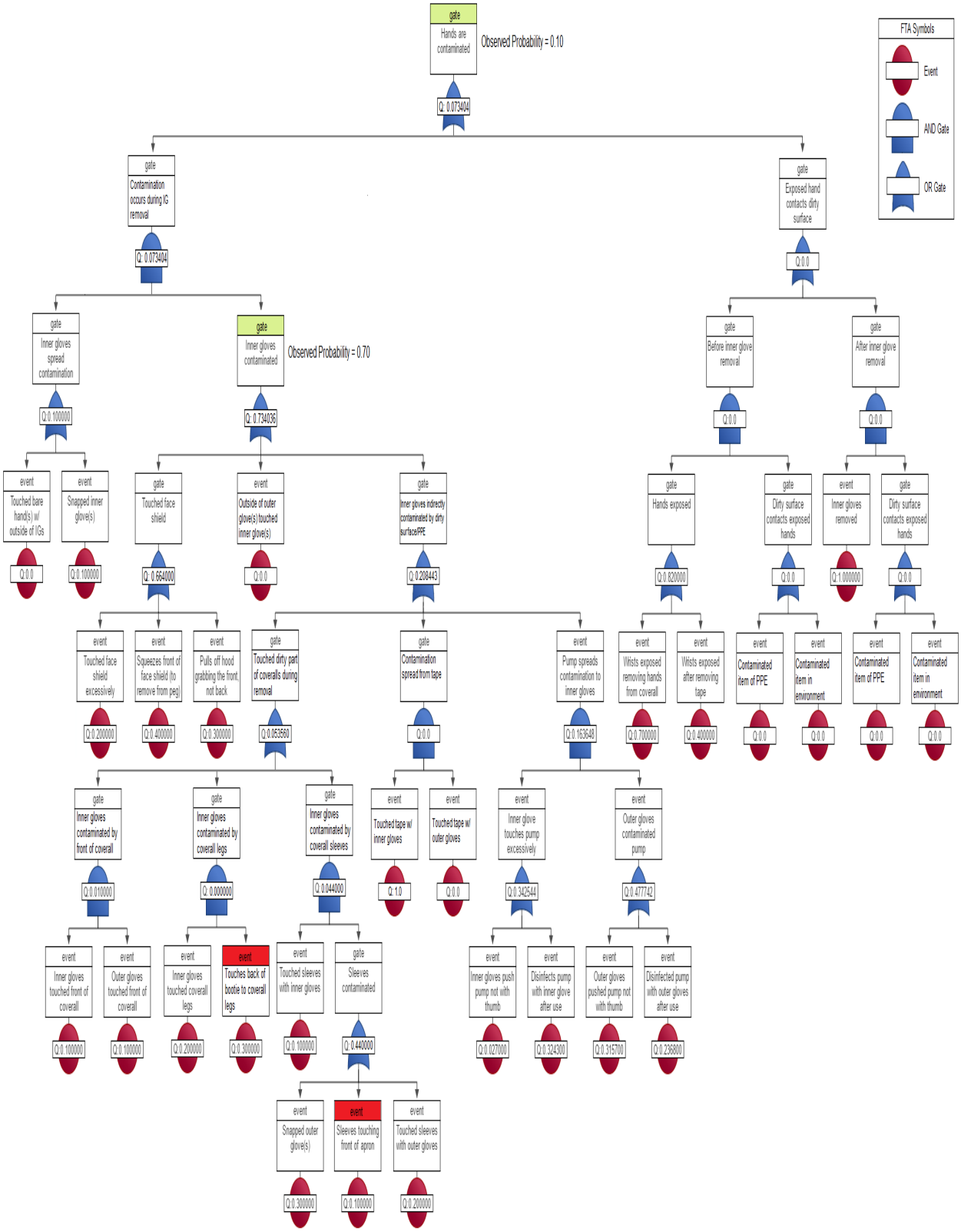

Figure 4. Fault tree analysis of hand and inner glove contamination

MS2 was detected more frequently than ϕ6 (20% of scrubs, 70% of inner gloves, and 10% of hands). The predicted contamination rates for scrubs, inner gloves, and hands, were 19.38% (p = 0.96), 73.40% (p = 0.81), and 7.34% (p = 0.76), respectively. FTAs for MS2 suggest that the route of scrub contamination was similar to that for ϕ6 (Figure 5). The most likely source of inner glove contamination was touching the PAPR hood face shield during PAPR hood removal, although other routes, such as the ABHR dispenser, were also possible. Moreover, hand contamination of the one HCW was likely due to snapping during the removal of inner gloves, for which the probability of being contaminated was high (0.73).

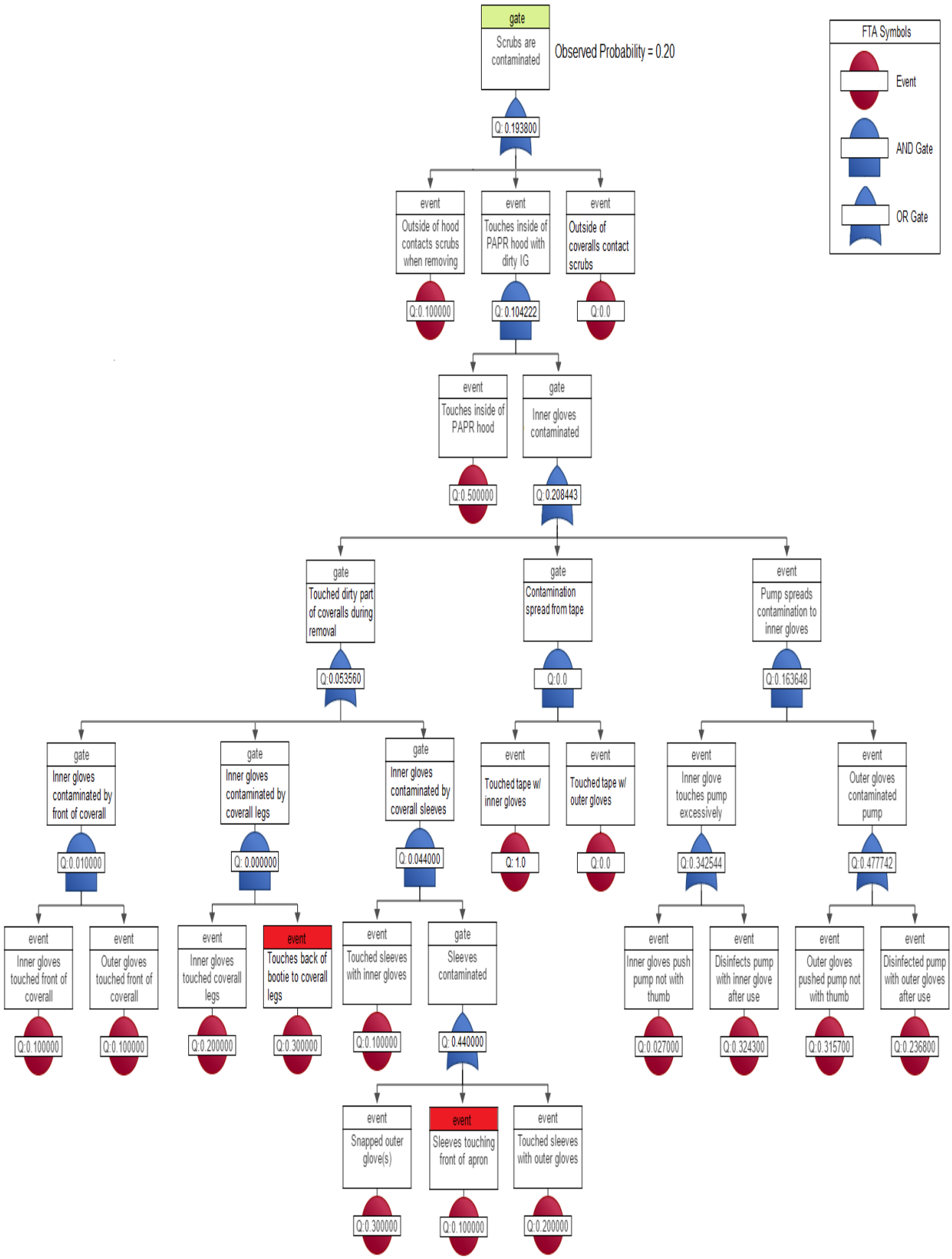

Figure 5 Fault tree analysis for a non-enveloped virus (MS2)

For all 41 simulations across 4 sites, virus results show that there is a low, but real, risk of contaminating hands with very small quantities of virus. This may be related to the high probability of contamination on gloves, which maybe transfer when removed. There is also a low risk of contaminating scrubs during removal. Overall, these results suggest that there is a quantifiable risk of transferring measurable amounts of virus to hands and clothing from contaminated PPE. Again, HFE related modeling can give insight into what routes of transmission are operating to produce this risk.

All protocols involved doffing of the boot covers, gloves (i.e., outer and inner pairs), outermost garment (i.e., coveralls or a surgical gown), PAPR hood, PAPR helmet/battery/belt, as well as repeated hand hygiene (with alcohol-based hand rub or disinfecting wipes) and lastly, washing hands with soap and water as one of the final doffing steps. Across the hospitals, there were many commonalities. For example, the order of steps followed a prototypical sequence of: boot cover removal before outer gloves (bar Site C) < outermost garment before PAPR hood (bar Site C) < inner gloves before the PAPR helmet, with hand hygiene following each step. For three of the hospitals, doffing began in the patient room and continued into an anteroom. Site C, however, began doffing in a clean room between the patient and anteroom, then finished in the anteroom. Lastly, only Site A removed the PAPR hood in the anteroom.

The role of TO also showed a typical structure consisting of observing and verbally guiding the HCW with a written doffing checklist. However, Site C divided observation of the HCW and reading the checklist between two observers. At Site D, the TO physically helped remove the HCW's PPE (e.g., coveralls). At Site D, the HCW and TO wore a headset underneath their PAPR hood.Across the four hospitals, there was notable site-specific variation in PPE items and how those items were removed. Site C was the only hospital to use surgical gowns (rather than coveralls) and to give the doffer the option to sit on a chair during boot cover removal. Sites A and D removed their gloves using the "beaking method" (i.e., creating a "beak" by pulling the inside surface of a glove over all 5 fingers) whereas Sites B and C used the CDC's recommended, "glove-in-glove" method[13]. Typically, sites used alcohol-based hand rub (ABHR) for hand hygiene instances, however, Site C used disinfecting wipes predominantly (except for bare hands). Site D was the only site to use automated ABHR dispensers and to have the HCW and the TO sing "Happy Birthday" aloud during each hand hygiene instance and six times during final hand washing to regulate the length of time.

Across hospitals, the mean reliability of coding the frequencies and sequence of behaviors was .71 (Range = .61 - .79), which corresponds to substantial agreement. Across hospitals, the mean duration of doffing was 9.5 minutes (*SE* = 2), excluding the duration of hand hygiene and final hand washing. Doffing steps varied in duration (Figure 1), with the following ordering of durations holding generally for each hospital: the outermost garment took substantially longer to remove than outer gloves, followed by boot covers, and lastly, the PAPR helmet/battery/belt. Removing the outermost garment tended to take at least a minute (Mean = 112 s, *SE* = 34) at each of the hospitals and as much as 225 seconds for Site D, where the TO helps remove the outermost garment. Usually, outer gloves took longer to remove than inner gloves (Bar Site D): On average, outer gloves (Mean = 31 s, *SE* = 4) required more time to remove than did inner gloves (Mean = 22 s, *SE* = 4). It is also worth noting that there was no difference in mean durations between hospitals that used the "beaking" method of glove removal (Mean = 26 s, *SE* = 6; Sites A and D) and hospitals using the CDC's recommended method of glove removal (Mean = 27 s, *SE* = 5; Sites B and C). Finally, it is noteworthy that only 44% of the 354 hand hygiene instances observed across the four hospitals (16%, 18%, 66%, 75%, for Sites A, B, C, D, respectively) met the World Health Organization's (WHO) recommended duration of at least 20 to 30 seconds. Across hospitals, the mean duration of hand hygiene between doffing steps was 17 seconds (*SE* = 5).

The total number of FMs varied between hospitals: 51, 85, 73, and 92, for Sites A, B, C, D, respectively. Summing across the common doffing steps at each hospital yielded a total of 256 FMs (or 85% of the total number of failure modes across hospitals). Individual doffing steps also varied in the total number of FMs with some steps failing in a limited number of ways whereas others failing in a variety of ways. Regarding the total number of failure modes, hand hygiene and outermost garment removal were always in the top three at every hospital along with PAPR hood removal at all but one hospital. On the other hand, PAPR helmet/battery/belt removal was always in the bottom two at every hospital (Table 6).

Of the 256 FMs pertaining to the common doffing steps, two raters independently identified FMs that occurred at most or all of the hospitals. Agreement on these common FMs was 84%. Differences were resolved via discussion. Of the 256 FMs, 61 were judged to be occurrences of 19 common FMs, which were observed at least once at either most or all of the hospitals. As the majority of these common FMs had risk indices that were above average, common FMs tended to be risky FMs. Moreover, multiple hospitals had FMs for both gloves and hand hygiene with risk indices

that were over one standard deviation above the hospital's mean risk index. Hand hygiene risk was especially egregious with each hospital having at least two, sometimes as many as four, common FMs that, on occasion, ranged above two standard deviations.

Table 6. Risk indices for common failure modes standardized within each hospital site

		Hospital Site			
Common Doffing Step	Common Failure Mode	A	B	C	D
Hand Hygiene	Does not disinfect wrist	2.08	1.20	--	1.21
	Does not rub gloves until dry	1.90	0.87	0.46	-0.66
	Does not disinfect thumb	1.48	1.53	2.58	1.21
	Does not disinfect between fingers	1.73	1.53	2.35	-0.04
	Gloves touch PAPR hood shroud	--	1.53	0.55	-0.58
	Shaking hands to dry	0.78	-1.13	--	0.09
Remove Boot Covers	Touches boot covers more than necessary	-0.14	-0.08	-1.29	0.59
	Crosses leg in front of self	0.67	--	0.60	-0.66
	Whips boot cover off	--	0.71	0.19	2.26
Remove Gloves	Snaps glove	-0.03	1.36	--	-0.41
	Whips glove off when removing	--	-0.54	1.66	1.09
	Difficulty pinching	0.67	-0.15	-0.23	--
	Inner gloves touch outside of outer gloves	--	-0.34	-0.46	0.34
Remove Outermost Garment	Coverall is off the mat	-0.14	0.45	--	0.42
	Lower back is exposed	-0.24	1.04	--	0.09
Remove PAPR Hood	Difficulty unsnapping PAPR hood	--	-1.33	-0.23	0.09
	Touches PAPR hood excessively	-1.01	0.18	-0.09	--
	Removes PAPR hood by pulling from front, not back	-0.14	1.23	0.19	--
	Inner gloves touch face shield	0.65	1.69	-1.42	--

The overall "riskiness" of a doffing step depends on a) how many FMs are associated with that step, b) how frequently each FM occurs, and c) how severe the consequences of those FM are (e.g., spreading contamination or disrupting the doffing process). Consequently, the overall riskiness of a doffing step is indicated by the sum of the risk indices (ΣRIs) of all FMs associated with that step. Across hospitals, the mean reliability of the severity ratings of FMs was .56 (Range = .43 - .76), which range from fair to excellent.

At all hospitals, hand hygiene, removing the outermost garment, and boot covers had above average ΣRIs. At most hospitals (Bar Site D), this was also true for PAPR hood removal. It is of interest that hand hygiene had ΣRIs that were nearly two standard deviations above the mean ΣRIs at each hospital. Considering the risk indices of the common FMs of hand hygiene (e.g., "Does not disinfect thumb"), eliminating these behaviors would reduce the overall riskiness of hand hygiene at a hospital by 47%, on average. At all hospitals, removing inner gloves, the PAPR helmet/battery/belt, and washing hands had below average ΣRIs and at most hospitals (Bar Site D), the removal of outer gloves was also below average.

Aim 3b. Changes in risk resulting from the adoption of alternative practices for wearing and removing PPE

Using the FMEA and fault tree analysis, we identified contact with the PAPR as a risk point during PPE use and doffing. Based on this finding, we conducted a further series of simulations to optimize the use of the PAPR, with virus transfer and human factors analysis. Eight participants (7 nurses and one physician) completed 16 simulations. Transfer of Φ6 or MS2 to face was not observed for any participants. Using the one-layer hood, Φ6 transfer to both hands, inner gloves and scrubs were observed for 1 participant. Using the two-layer hood, Φ6 transfer to scrubs was observed for 1 participant. Table 2 presents results for MS2 transfer for both the one-layer and two-layer PAPR

hoods. Overall, MS2 was detected on 10/36 sites and 5/36 sites sampled for the one-layer and two-layer hood respectively. Contamination of hands was observed for two participants using the one-layer hood. None of the participants contaminated hands during use of the two-layer hood. Using the one-layer hood, inner glove contamination was observed for six participants compared to two participants using the two-layer hood. Contamination of scrubs was slightly higher when using the two-layer (3/8 participants) compared to the one-layer hood (1/8 participants).Results from the McNemar's test revealed no statistically significant difference in the proportion of participants with contamination on at least one of the four sites sampled following each simulation (difference in proportion= 0.33, p=0.56). However, a statistically significant difference was observed in the number of MS2 virus particles recovered on inner gloves of participants using the one-layer versus the two-layer hood (median difference= 2.27×10^4, p=0.03).

Table 7. MS2 Virus Recovery Using One-Layer and Two-Layer PAPR Hood

Participant	One-layer Hood				Two-layer Hood			
ID	DH	Non-DH	Gloves	Scrubs	DH	Non-DH	Gloves	Scrubs
1	4	4	8.98×10^4	10	ND	ND	1.40×10^3	ND
2	ND	4	6.66×10^4	ND	ND	ND	ND	ND
3	ND	ND	6.80×10^3	ND	ND	ND	ND	ND
4	ND	ND	3.87×10^3	ND	ND	ND	ND	6.60×10^2
5	ND	ND	4.17×10^4	ND	ND	ND	ND	3.00×10
6	ND	ND	3.86×10^4	ND	ND	ND	45	ND
7	ND	ND	ND	ND	ND	ND	ND	1.10×10^3
8	ND	ND	ND	ND	ND	ND	ND	ND

FMEA results are presented in

Table 8. During use of the one-layer hood 32 failure modes were identified and grouped into categories based on major components of the PAPR hood doffing steps. Overall, median RI for all FMs was 5 (range, 1 – 20). Tie (ΣRI =76) and roll (ΣRI=63) related FM categories had the highest summative RIs. The most frequently occurring categories of all FMs were tie (n=14, 43.75%), roll (5, 15.625%), and touch (5, 15.625%) related. The riskiest (top 25%) FMs were tie (4, 50%), roll (3, 37.5%), and snap (1, 12.5%) related. Using the two-layer hood, 75% (24 of 32) of the total FMs were eliminated including seven of the top 8 (87.5%) riskiest FMs. These included all tie-related (previously 50%) and all roll-related (previously 37.5%) FMs.

Table 8. Failure Modes Effect Analysis

Category	Failure Mode	Severity	Frequency	Risk Index
Roll*	Does not properly roll up outer shroud	4	5	20
Roll*	Rolled up shroud unravels/requires multiple attempts	4	4	16
Roll*	Back of outer shroud falls down	4	4	15
Ties*	Unnecessarily touching ties with inner gloves	3	4	13
Ties*	Ties touch exposed arm	4	3	13
Snaps	Grabs sides snaps outside of PAPR Hood when unsnapping	3	4	12
Ties*	Grabbing tie requires multiple attempts	2	5	12
Ties*	Ties touch coverall	2	5	12
Touches	Touches underneath of outer shroud with outer gloves	3	4	11
Touches	Sleeves touch outer shroud of PAPR hood	2	5	10
Tape*	Stick tape requires multiple attempts	2	4	9
Roll*	Starts to roll inner shroud instead of peeling	3	3	9
Touches	Touches outer shroud with gloves	2	5	8
Touches	Touches coverall with gloves	2	4	8
Ties*	Difficulty untying ties	2	3	6
Tape*	Grabbing tape requires multiple attempts	2	3	5
Snaps	Hands go inside helmet	5	1	5
Coordination*	HCW hands PAPR hood to TO to dispose	4	1	4
Roll*	Peels by grabbing top of inner shroud instead of going underneath	3	1	3
Touches	Touches inner shroud with outer gloves	3	1	3
Snaps	Unsnaps before peeling	3	1	3
Ties*	Ties touch inner shroud	3	1	3
Ties*	Ties touch face shield	3	1	3
Tape*	Tape sticks to coveralls	3	1	3
Ties*	Drops outer shroud side tie	3	1	3
Ties*	Ties touch ground in patient room	3	1	3
Ties*	PPE not properly disposed	3	1	3
Tape*	Touches face shield with gloves	2	1	2
Ties*	Re-tying shroud tie requires multiple attempts	2	1	2
Ties*	Ties touch face shield	2	1	2
Ties*	Started to untie torso tie before top tie was complete	1	1	1
Ties*	Ties touch outer gloves	1	1	1

Based our results, we conducted simulations experimenting with altering aspects of the built patient care environment to reduce risk of exposure. We designed an optimized doffing area by marking the doffing spot that indicates the location to stand during doffing; providing a built-in balance aid within reach of the defined doffing spot; and locating a mirror directly in front of the HCW for self-monitoring and self-inspection. We restricted the location of where the HCW stands and added colored demarcation on the floor to signify the zones and different level of contamination risk: red (contaminated), yellow (likely contaminated) and green (clean), similar to the designations of "hot, warm, and cold" zones [7,8]. The doffing area has a unidirectional flow from contaminated to cleaner areas, to the

outside of the patient room in a continuous forward motion. The two windows located parallel to the doffing area allow the TO to directly visualize the HCW doffing at all times.

The floor demarcation also indicates the location of key items, such as the trash can and chemical mat, as well as proper location and orientation for the HCW when doffing. We introduced these changes to help reduce the cognitive load of HCWs and prevent items from being moved and placed at inconsistent locations. The zones have various thresholds (indicated by color gradients, Figure 1.10) to accommodate HCWs of different body dimensions with the purpose of reducing the physical load of HCW and preventing risky behaviors such as bumping with the environment or reaching to the trash can. The size of the doffing area ensures that all the items are always within arm's reach of the HCW (the horizontal grab bar used as balance aid, primary and backup hand hygiene and wipes). The trash can and balance aid are located on opposite sides of the chemical mat to encourage using one hand to hold on to the bar and the other hand to remove the shoe covers, with the intention of reducing the risk of spreading contamination to the environment. To assist during shoe cover removal, improve posture and enable self-inspection we placed a mirror directly in front of the HCW.

Participants used either a chair (N=10), horizontal grab bar (N=9), vertical grab bar (N=8), L-shaped step stool (N=17) or no tool at all, "no aid" (N=3), while removing their disposable shoe covers. Participants had the highest physical load when attempting to remove shoe covers with "no aid", while the use of a chair required lowest physical effort from a HCW. Except for the L-shaped step stool, the physical load was lower when participants used the chair, the horizontal grab bar, and the vertical grab bar, compared to the physical load when they were not using any balance aid at all.

The overall number of HCW risky behaviors observed significantly decreased in Phase III (median = 1.0) as compared to Phase I (median = 2.0, $p = 0.004$). In Phase III, we also detected an increase in the percent of HCWs who performed two specific risky behaviors: when the participant would use hands to push body to stand up or touch the balance aid with both hands; and touching the removed shoe cover with both hands. Five of the other risky behaviors not only decreased, but were eliminated in Phase III: sitting while removing shoe covers; bumping with the environment; missing the opening of the trash can when disposing of items; tossing waste to trash can/reaching to trash can; and, moving (mobile) balance aid in the middle of the task or scooting. There was a significant association between Phase and the observation of HCWs tossing waste to the trash can or reaching to the trash can ($p = 0.003$). Two of the listed behaviors were not observed in either phase: participants were never seen stretching to reach aid nor failing to step on the chemical mat.

To assess the effectiveness of design improvements on reducing HCW physical load during shoe cover removal, we compared the REBA/RULA scores from Phase I (N = 38) and Phase III (N = 9 – while 10 subjects completed Phase III, one of those did not use the balance aid, therefore, we only report results of 9 subjects for this comparison). REBA/RULA scores for Phase I (median = 5.5, IQR = 1.5) were significantly higher than those in Phase III (median = 4.5, IQR = 1.0, $p = 0.04$). To assess changes in HCW cognitive load, we compared the TLX scores from Phase I (N = 19) and Phase III (N = 9) for shoe cover removal. TLX scores remained similar in Phase III (median =25.0, IQR = 7.5, $p=0.43$) as in Phase I (median = 27.5, IQR = 19.2). We also compared the task load by subscale using a spider plot (Figure 3) and found no significant differences between scores for Phase I and III, though when inspected visually the scores were lower on some of the subscales.

Discussion and conclusions

The research product from this aim is a dynamic, flexible, adaptable transmission model where virus is continuously shed by an infected patient in body fluids and is spread to the HCP through 1) skin contact with viruses that penetrate gaps in PPE 2) skin contact that occurs during unrecognized failure modes while doffing contaminated PPE, 3) skin contact that occurs during errors and departures from protocol while doffing contaminated PPE, and 4) the HCP's hands acting as vectors for self-inoculation after contact with contaminated PPE, contaminated scrubs, and contaminated fomites. I identified parameters that contribute significantly to 1) total exposure and 2) variability and uncertainty of exposure estimates. Parameters that contribute significantly to the total uncertainty and variability in the exposure model were used to design simulations of PPE donning, use and doffing using surrogate viruses and HFE analysis.

Our studies are the first to experimentally evaluate viral self-contamination during EVD PPE doffing under controlled conditions in HCWs who have cared for patients with EVD. Although the integrity and effectiveness of PPE during patient care is crucial for HCW protection from contamination, doffing is a critical point for assessing contamination risk, due to the necessity of touching and handling contaminated PPE at multiple points in the process. Previous simulation research has shown that hand contamination with a non-enveloped virus is common with standard contact isolation PPE,[9] where doffing is often not structured. Using a structured, observed EVD PPE doffing protocol in a population of providers who were trained but had no direct EVD patient care experience, prior simulations studies found no transfer of an enveloped surrogate for Ebola virus to hands, face, or inner gloves.[10] The results of this study suggest that current structured, observed doffing protocols, including the use of alcohol based hand rub for sanitizing gloves, are protective against hand contamination with an enveloped virus when used by HCWs with differing levels of training and experience.

However, other simulations of structured observed doffing have found transfer of non-enveloped virus to inner gloves, scrubs, and hands. In this study, there was low but detectable transfer of non-enveloped MS2 to hands (one participant) and scrubs. The fact that most participants had detectable MS2 on their inner gloves but not on their hands suggests that inner gloves are playing a vital role in protection against direct hand contamination. Because gloves are repeatedly touching PPE during the doffing process, even use of ABHR on the outside of gloves between doffing steps may not completely prevent inner glove contamination with a non-enveloped virus. Human factors analyses suggest that the mishandling of certain items of PPE during doffing contributes considerably to the probability that a HCW's gloves, scrubs, and hands become contaminated. For example, when ABHR does not have adequate time to dry after application, it may make gloves slippery and harder to manipulate. This in turn may contribute to accidental glove "snapping" due to loss of grip on the glove during removal, potentially leading to hand contamination.

If contamination occurs, hand hygiene plays a vital role; human factors analysis suggests that the hand hygiene steps present multiple opportunities for error during the doffing process. Human factors analyses suggest room for improvement in hand hygiene technique with alcohol based hand rub, including taking adequate time that allows for coverage of all hand surfaces as well as adequate drying (and associated killing action) before proceeding to the next step. Hand hygiene agents may play an important role in the differences in how lipid-enveloped and non-enveloped viruses survive during PPE doffing. Enveloped Φ6 was not detected on inner gloves, but MS2 was. This is an expected result, as evidence supports that alcohol based hand rub is more effective against enveloped viruses such as Ebola than against non-enveloped viruses.[11-14] To minimize viral load on inner gloves, both careful doffing and control measures such as stronger glove sanitizing agents (such as hypochlorite or povidone-iodine) may be needed, particularly if non-enveloped viruses emerge as high-risk pathogens. However, whether units use ABHR or other hand sanitizers with demonstrated in vitro effectiveness against viruses, contact time and technique are still important.[15] These results highlight the fact that even when wearing PPE that provides whole body coverage, hand hygiene after doffing is still critical, with hand hygiene agents that are effective against a range of organisms. Defects in hand hygiene maybe an important risk factor for HCWs to acquire EVD.[16] While the CDC guidelines do not specify the hand hygiene product, the World Health Organization and Médecins Sans Frontières recommend use of 0.5% chlorine for all hand hygiene events, which has been supported by some data using Φ6.[17]

Opportunities for unintentional contact with PPE with hands, wrists, neck, and scrubs underscores the need for close observation during the complex doffing process. Post-simulation viewing of video recording suggested that there may be contact and contamination events that are not recognized by the doffer or the TO during the process. In this and other doffing protocols, scrubs are touched with bare hands, and may be removed and handled after exiting the patient care area. The detection of virus on scrubs suggests that disposable scrubs that are carefully

handled and disposed of after doffing may be safest. Improved PPE designs that allow for easier removal without touching the outside of PPE items may also mitigate this risk, as well as reduce the risk of virus transfer to the TO by eliminating any need for them to physically assist with doffing.

These simulations of PPE doffing have applications for biocontainment units beyond Ebola. Enveloped bacteriophage Φ6 was chosen as a surrogate because it serves as a model not only for Ebola, but other high consequence pathogens, such as Lassa, Marburg, and smallpox. Imported cases of Lassa fever are an emerging problem;[18] biocontainment units in the U.S. and elsewhere have also cared for suspected and actual cases of Lassa infection.[19,20] The findings of this research are applicable to preparedness for this threat as well. Recent high consequence emerging pathogens such as SARS, MERS, and Ebola are enveloped viruses, but the possibility of emerging non-enveloped pathogens exists as well. The use of MS2 not only provides a model for possible non-enveloped viral threats, but serves as a very conservative surrogate for measuring the effectiveness of disinfection and hand hygiene steps in PPE doffing.

Our findings with complex PPE may be directly applicable to HCWs outside biocontainment units. All US acute care hospitals are required to be prepared to triage a patient with potential or suspected Ebola and may encounter an unknown or emerging pathogen. "Rule out" scenarios are much more common than care for a patient with known infection, but both require the appropriate and safe use of PPE to protect HCWs. Further, the more typical PPE used by HCWs in other clinical settings may be contaminated in a similar method, though more studies are needed with these types of PPE and markers that mimic bacterial pathogens that remain significant public health concerns, including those that are multidrug resistant.

Previous studies of complex PPE doffing using fluorescent tracers as markers of contamination found contamination of hands after PPE removal.[21-23] PPE removal studies using both fluorescent markers and infectious viruses simultaneously have been done with MS2; in one study rates of self-contamination with fluorescent tracer and MS2 were similar,[9] in others they were not.[22,24] These types of studies have not yet been done using enveloped viruses, and our findings suggest that fluorescent tracers alone may not be a reliable indicator of self-contamination with infectious viruses since none were found despite clear evidence of virologic transfer. Variation in the type and use of these markers may explain some of these observed differences, and standardization of these approaches is needed.

A structured doffing protocol using a trained observer, double gloves, and multiple glove sanitizing steps appears to protect against self-contamination with enveloped viruses. There was a low risk of self-contamination with a non-enveloped virus, possibly due to their higher resistance to agents used to sanitize gloves. Improved doffing protocols that are highly protective against all types of viruses may need to incorporate changes in the removal process, reinforcement of hand hygiene, careful handling of scrubs, and highly effective glove sanitizing and hand hygiene agents.

We also demonstrated that the built environment has a measurable impact on HCW contamination risk while doffing PPE after simulating activities associated with the care of patients with a high consequence pathogen. Through optimizing the design and layout of the doffing space we were able to make improvements in the performance and reduced both the physical and cognitive load of HCWs, thus reducing their risk for self-contamination. The HCWs' physical load decreased in the optimized doffing environment (Phase III) when compared to HCW performance in the initial settings (Phase I). The average number of risky behaviors observed per doffing session was reduced, and some risky behaviors were completely eliminated in the optimized doffing setting. While the cognitive load measured by the NASA-TLX for the shoe cover removal was not significantly lower, this may be due to the small sample size in the Phase III. Regardless, the decrease in risky behaviors suggests the importance of design in improving HCW safety in this high-risk environment. Our redesign employed several strategies including demarcation of the doffing zone to define the location to stand during doffing; providing a built-in balance aid within reach of the defined doffing spot; and locating a mirror directly in front of the HCW for self-monitoring and self-inspection. Several of these strategies have already been implemented in the study sites.

We provided markings on the floor to guide HCW placement during doffing, their orientation and the location of the chemical mat. By indicating the location of the HCW at every doffing step, we were able to arrange the critical infrastructure (trash can, balance aid, hand hygiene dispenser, wipes) at a more ergonomic position for the HCW to minimize physical effort and reach. Our findings confirm previous research on the usefulness of color-coded zones with clear demarcation and a restricted doffing area. Using high-contrast coloring in the areas in the optimized doffing layout made it easier for participants to move following a unidirectional flow within the doffing area without having to frequently look at the floor. Providing flexibility--in the form of thresholds for the location of the mat--allows the HCW to set up the doffing area so that it is most comfortable and safe for them. Because of the defined space, we

eliminated risky behaviors associated with inadequate posture, such as reaching for the trash can, and another based on proximity (tossing waste into the trash can or missing the opening of the trash can). This also likely reduced the cognitive load for the HCW who no longer had to decide where to situate themselves for doffing. We suggest that the balance aid be located to one side of the HCW, the trash can to the other, to discourage risky behaviors such as touching the balance aid or the shoe covers with both hands. We recommend that the TO also verbally indicates through the doffing protocol which hand to use for each task, and which shoe cover to remove first to further eliminate the need for the HCW to make decisions during this step; this can be decided during training, for each particular doffing area and protocol.

We tested four different balance aids and found that there was a significant difference in the physical load associated with their use. Participants who opted to remove their shoe covers without using any balance aid had the highest physical load, followed by those using the step stool. Providing a balance aid is critical to increasing HCW safety during doffing, particularly during shoe cover removal. We suggest using mobile balance aids (such as the L-shaped step stool) only as a last resort for two reasons: they will be moved and placed in inconsistent locations, resulting in opportunities for risky behaviors like stretching to reach the trash can or not stepping on the chemical mat after removing shoe covers; and they are not as stable and sturdy as their built-in counterparts, resulting in physical instability. Corroborating previously reported findings the lowest physical load was seen for participants using the chair/stool and vertical grab bar or horizontal grab bar. However, given that sitting increases the risk of spreading contamination to other parts of the PPE, we suggest installing built-in grab bars.

In the final design, we provided a fixed horizontal grab bar for balance support, saw a much lower rate of unstable postures, and eliminated the risky behavior of moving the balance aid in the midst of doffing. Grab bars should be placed in a convenient spot because previous studies found that if done improperly, use of a balance aid may increase the contamination risk during shoe cover removal (switching hands or removing shoe covers in the incorrect order).

The design of our optimized doffing space included a mirror placed directly in front of the HCW. Importance of having a mirror for self-inspection was previously reported. While many of the doffing zones included mirrors, they were sometimes placed to the side or back of the HCW, or not at eye level. This small adjustment of making the mirror easily visible to the HCW seemed to make a big difference, allowing the HCW to inspect their PPE without having to turn or bend. This is particularly important when the HCW removes the shoe covers, given that the PAPR hood limits their ability to see their feet. Overall, our findings underscore the importance of the design and layout of the doffing space as a strategy for enhancing healthcare worker safety. When the space and protocol work together, HCW performance can be highly reliable and errors will be rare.

With our unique integrated approach we found that human factors methodologies can provide insight and solutions for optimizing PPE doffing and resources exist to help medical professionals utilize them. To ensure the safety of HCWs, these tools should be integrated and individualized to different settings, ideally before providing direct patient care. The FTAs suggest that touching the PAPR hood's face shield, if contaminated, can be a critical route for contaminating the inner gloves. While failure modes related to this behavior in the FMEA are not particularly risky in themselves, the FTA implicates them as a major cause of self-contamination that would have otherwise been underestimated by the FMEA alone. The FTA also suggests that while inner gloves protect the HCW from hand contamination, they may inadvertently contaminate clean items of PPE, such as scrubs. Lastly, the FTA reveals a "near-miss" in the doffing protocol with potentially serious consequences; the probability that some part of HCW's hands are exposed in the steps before inner glove removal is 0.82. Fortunately, these events did not propagate any further up the tree because a contaminated object never happened to touch exposed hands.

We observed a range of errors with varying degrees of risk among experienced and highly practiced HCWs doffing Ebola-level PPE with a trained observer. Among the highest risk errors identified by the FMEA were those related to hand hygiene, compromised PPE (exposed hands and wrists), and mishandling PPE, particularly the face shield of the PAPR hood. The extent to which these errors may have contributed to self-contamination was characterized by the FTAs. Despite observing deficiencies in hand hygiene technique, the probability of committing those errors together was fortunately rather small, which agrees with the low self-contamination rates with the enveloped virus. Still, deficiencies in hand hygiene technique are concerning since non-enveloped viruses may be more resistant to ABHR and consequently, result in higher contamination. Compromised PPE led to a near miss while mishandling PPE emerged as a major source of contamination of the inner gloves.

PPE can both protect and endanger HCWs throughout the doffing process. For example, inner gloves were largely effective at protecting HCW's hands, but may have spread contamination to clean items of PPE (e.g., when unzipping coveralls). Thus, opportunities for incidental contact during doffing should be minimized. Our findings also suggest

that some protections may be conditional. For example, the "beaking" method minimizes contact with the contaminated outer surface of the glove. If gloves are slick from ABHR, however, HCWs may put themselves at risk for self-contamination via glove-snapping. Thus, "beaking" may be most effective only when HCWs have allowed the ABHR to dry completely.

Our findings also highlight the importance of considering self-contamination during doffing as a probabilistic event. Although only 2 out of all the HCWs who treated EVD patients in the United States contracted the disease, this achievement may have involved a certain amount of luck as our simulation approach revealed that a confluence of random events is often necessary for self-contamination to occur. Existing protocols include redundancies, such as frequent hand hygiene, to reduce the chances that an error will propagate contamination forward. However, our results suggest that these steps may be abbreviated in practice and, when combined with other errors, may result in pathogen transmission. Despite our sample's extensive training and experience with PPE, many of our findings related to hand hygiene and glove removal, which are performed routinely by HCWs in any clinical setting. Many HCWs, however, receive PPE training on the job rather than from a standardized, rigorous process. Moreover, PPE elements vary across facilities, which may result in suboptimal use of PPE when combined with the mobility of HCWs and lack of standardized training. The optimal type and frequency of training for PPE remains unclear, although education and practice appears to decrease self-contamination when doffing routine PPE, such as gowns and gloves.

When selecting PPE and designing a doffing protocol, stakeholders should not only test the usability of various ensembles, but also combine these assessments with a formal risk analysis to identify specific objectives for testing. Beginning with the riskiest behaviors, stakeholders should develop remediation strategies and then test the effectiveness of those solutions. For example, the problems of coverall sleeves pulling off inner gloves and snapping gloves during removal may be remediated by using extended-cuff inner gloves and a different glove removal technique, respectively. Afterwards, the change in severity, frequency, or probabilities of these failure modes and top events should be reassessed iteratively until effective control measures have been established.

Expanding across multiple sites, Human factors methodologies revealed differences as well as similarities in doffing across four state-designated Ebola treatment centers. Although hospitals used PPE that differed in their details and protocols that varied from site to site, the resemblance that emerges across these technologies and behaviors points to common problems and common solutions.

Only 44% of all hand hygiene instances met WHO duration standards of at least 20 seconds. Of the three hospitals that primarily used ABHR for hand hygiene (Sites A, B, and D), however, Site D was the only hospital to enforce the duration of hand hygiene (by singing "Happy Birthday" aloud) and had a substantially larger percentage of hand hygiene instances lasting at least 20 seconds than did Sites A and B (75% versus 16% and 18%, respectively). Nonetheless, there were clear opportunities for improving hand hygiene at most, if not all, hospitals. All hospitals failed to ensure that hands were rubbed thoroughly (i.e., thumbs and between fingers) and until they were dry; they also had instances of incidental contact (e.g., with potentially contaminated PPE, such as the PAPR hood shroud). Most hospitals—with the exception of the one hospital that predominantly used disinfecting wipes (Site C) instead of ABHR—also shook hands in order to dry them and did not consistently disinfect their wrists.

Removing the outermost garment (i.e., coveralls or surgical gown) was always among the top three riskiest doffing steps at each hospital. It required, by far, the greatest amount of time of the common doffing steps. Likewise, HCWs perceived outermost garment removal as one of the most effortful steps. The primary task demand tended to be physical, rather than mental or temporal, particularly for coveralls. For sites using coveralls, there were instances where the HCW's lower back became exposed, but this did not manifest with the surgical gown at Site C. Moreover, Site C doffed in a clean room, obviating the need for a disinfecting mat, on which the other hospitals struggled to contain their coveralls.

Outer gloves tended to take longer to remove than inner gloves (Bar Site D) and was viewed as the most effortful doffing step (Bar Site B). Furthermore, each hospital viewed outer glove removal as more mentally demanding than physically or temporally demanding. Each site had a high-risk failure mode associated with their glove removal protocol (e.g., whipping glove off when removing), but a high-risk factor at one hospital might be low risk or even absent at another hospital. Speculation that this was due to using "beaking" (Sites A and D) versus glove-in-glove (Sites B and C) techniques cannot account for the FM pattern. Furthermore, the CDC's glove-in-glove method and "beaking" took a comparable amount of time, and there were no clear differences in either the workload analysis or the risk analysis.

Removing the boot covers was a moderately risky doffing step at each hospital and HCWs clearly struggled during this step. In fact, removing the boot covers was typically the most physically demanding (Bar Site C) doffing step,

with each hospital having instances of touching the boot covers excessively during removal as well as other common FMs (e.g., whipping boot covers off).

Finally, these common problems may also benefit from common interventions not observed at any of the hospitals. For example, having the TO ask, "Are your hands dry?" at the end of each hand hygiene instance could address a common high-risk component of doffing, and one that has ramifications for subsequent steps since the "snapping of gloves" is due, in part, to removing gloves while they are still wet from ABHR[7]. Other interventions are also suggested (e.g., installing a mirror) to further mitigate excessively touching PPE (e.g., the PAPR hood). Finally, points in the protocol that can be improved with training are also immediately identifiable, such as sanitizing hands more thoroughly (e.g., in between fingers, wrists, and thumbs).

PAPR hood removal tended to be a risky endeavor at most hospitals. Self-removal of the PAPR hood led HCWs to touch their hood excessively, remove the hood by pulling from the front (rather than the back), and touching the face shield with their inner gloves. Having the TO remove the PAPR hood (Site D) appeared to mitigate excessive touching and improper removal. In addition, Site D was the only site that used their outer gloves to disconnect the hood from the helmet, eliminating inner gloves touching the face shield, which is likely to become contaminated during patient care. Our resulting subsequent PAPR simulation study showed that the number of participants for which self-contamination was observed for at least one site was lower when using the two-level hood compared to the one-level hood, although the difference was not statistically significant. A statistically significant difference was found in the number of participants with self-contaminated gloves and the number of viral particles recovered from gloves during use of the one-layer vs. the two-layer hood. This suggests that although doffing the two-layer hood had a higher complexity, the extra layer, the shroud tucked into the Tyvek suit, may have protected the contaminated outer portion of the hood limiting contamination of the inner gloves and subsequently hands. Scrub contamination was observed for a slightly higher number of participants using the two-layer compared to the one-layer hood. However, the level/degree of contamination was similar. The two-layer hood has a larger surface area due to the additional shroud which could have increased the likelihood of scrubs getting contaminated during removal. This observation may require the TO to remind the HCW to avoid contact between the hood and scrubs when removing the hood from the PAPR helmet. As a result of these findings, Emory University has changed their PAPR use methods to incorporate risk mitigation strategies based on our suggestions.

Our work has targeted the Healthcare and Social Assistance Sector, and two cross-sectors: Exposure Assessment and Respiratory Diseases. We directly addressed NIOSH Priority Goal for Research 5: STOP transmission of infectious diseases in HCSA settings among workers, patients and visitors. Preventing occupational infection among HCPs protects them, their families, and the patients they care for. The models resulting from this study improve our understanding of mechanisms and determinants of the linked routes (fomites, hands, air) by which infectious diseases are transmitted in the HCSA setting (Goal 5.1). A significant challenge in identifying and applying effective prevention measures for occupational infectious disease is that we lack understanding of the roles played by different transmission routes. Even when there are guidelines in place for preventing occupational respiratory transmission that appear to be reducing infections, it can be difficult to know which preventive measures are actually having the most impact; there can be knowledge gaps regarding which transmission routes are the most important. Our integrated experimental laboratory simulation, human factors analysis, and modeling approach makes it possible to *identify individual pathways* of transmission (e.g., direct exposure to virus, touching contaminated objects, touching face and eyes) and define the important parameters associated with these pathways. The modeling tools can use the resulting data to determine which exposure pathways are most important for disease transmission. The development of these simulation and modeling tools addresses the Cross Sector Program *Exposure Assessment*, specifically this cross sector's Strategic Goal 2: *Develop or improve specific methods and tools to assess worker exposures to critical occupational agents and stressors*. We can now model how transmission pathways interact, and which parameters that define transmission are most important for predicting the risk of infection. This approach can be used to assess the risks from multiple exposure pathways, determine which pathways are most important, and predict both the risk of infection and the effectiveness of strategies to reduce risk. The development of these modeling tools already informs practice toward fulfilling the goals of Cross Sector Program *Respiratory Diseases*, specifically the Strategic Goal *Prevent and reduce work-related respiratory infectious diseases*.

Career Development

I received training in occupational health, responsible conduct of research, clinical research, and grant writing. I have completed didactic coursework in clinical research design and the responsible conduct of research. I have completed a semester long clinical research design and fundamentals course offered online through the National Institutes of Health and completed the NIH Bioethics in research course. Although I originally planned to take an occupational health course through the University of Georgia, I instead took an intensive weeklong occupational health/industrial hygiene course through the University of North Carolina Chapel Hill. This was an opportunity to learn occupational health from a senior industrial hygienist with extensive applied experience in the field, with classmates who worked in professional industrial hygiene positions. I received one-on one individualized training and mentoring in grant writing from a professional consultant who provided feedback on my work.

One of my most important current projects is a collaboration with Emory University on a NIOSH contract to evaluate the rollout and use of elastomeric half-face respirators (EHFR) to protect HCP from respiratory pathogens if supplies of disposable filtering facepiece respirators such as N95s have shortages. I am a co-investigator on this grant. My role is to evaluate the efficacy of different disinfection practices to be used on EHFR by HCP between patients and between shifts. After identifying optimal disinfection methods, we will conduct laboratory simulations using HCP volunteers to test the efficacy and usability of disinfection under realistic use conditions.

As a result of my previous work with enveloped viruses and the use of simulations to understand PPE use, I was approached by a team of multiple research collaborators to study healthcare worker PPE to protect against Ebola. This included physician-scientists and nurses from Emory Healthcare, human factors engineers from the Georgia Institute of Technology, and healthcare built environment design experts from Georgia Tech. They invited me to become a co-investigator for an application for a CDC-funded Healthcare Infection Prevention Epicenter focused on Ebola protection and PPE. I wrote and was PI of an R01 level project within this center grant, which encompassed the aims I have described in this report. With my center collaborators, I wrote a subsequent epicenter grant in response to a new RFA, focused on the effect of PPE and the environment on transmission of infections from HCP to patients in long term care. Again, I wrote and am PI on an R01 equivalent project in this application, which received an overall score of 20 but has not had a funding decision made. Our original epicenter grant has subsequently been supplemented with bridge funding in possible anticipation of this new award. Our bridge funding supported a recently completed project in which we used realistic simulations and HFE to measure transmission of bacteria during wound care. Our current bridge funding is for an ongoing project where we will use our aerosol system to evaluate the effectiveness of currently used PPE for protecting HCP from SARS-CoV-2 during patient care.

I have also been a co-investigator on two CDC Broad Agency Announcement grants. One is with the University of Arizona, evaluating cleaning practices in hospital rooms and their effect on pathogens on surfaces. This will result in risk models of healthcare acquired infections using surface contamination data. The second will use the breathing/cough simulator to evaluate different mask materials and designs for reducing transmission of SARS-CoV-2. As described in the original grant, with support from my mentoring team I compiled and submitted my file for promotion and tenure at Georgia State. I was promoted to associate professor with tenure in spring 2017. I am on track for promotion to full professor, which I will apply for at my first eligible point, after 5 years at the rank of associate professor. I have a close network of healthcare and human factors collaborators with whom I continue to write grants and conduct research. As set out in this career development award, I have progressed to being a successful, externally funded investigator with a national reputation in the areas of healthcare PPE, HCP occupational infection prevention, and healthcare-associated infection prevention more broadly.

Publications

Most recent competitive period, 9-1-2017 to 9-1-2018

1. Zimring CM, Matić Z, Wong Sala M., Mumma, JM, Kraft CS, Casanova LM, Erukunuakpor K, Durso FT, Walsh VL, Shah P, Jacob JT, DuBose JR for the CDC Prevention Epicenters Program: [2018] Making the invisible visible: Why does design matter for safe doffing of personal protection equipment? Infection Control and Hospital Epidemiology 39:11.
2. DuBose JR, Matić Z, Wong Sala M., Mumma, JM, Kraft CS, Casanova LM, Erukunuakpor K, Durso FT, Walsh VL, Shah P, Jacob JT for the CDC Prevention Epicenters Program: [2018] Design Strategies to Improve Healthcare Worker Safety in Biocontainment Units: Learning from Ebola Preparedness. Infection Control and Hospital Epidemiology 39:961-7.
3. Casanova LM, Erukunuakpor K, Kraft CS, Mumma, JM, Durso FT, Ferguson AM, Gipson CL, Walsh VL, Zimring CM, DuBose JR, Jacob JT: [2018] Assessing viral transfer during doffing of Ebola-level personal protective equipment in a biocontainment unit. Clinical Infectious Diseases, 66:945-949.
4. Mumma, JM, Durso FT, Ferguson AM, Gipson CL, Casanova LM, Erukunuakpor K, Kraft CS, Zimring CM, DuBose JR, Jacob JT: [2018]. Human factors Risk Analyses of a Doffing Protocol for Ebola-level Personal Protective Equipment: Mapping Errors to Contamination. Clinical Infectious Diseases, 66:950-58.
5. Mumma, JM, Durso FT, Ferguson AM, Gipson CL, Casanova LM, Erukunuakpor K, Kraft CS, Ray SM, Shane AL, Shah P, Zimring CM, DuBose JR, Jacob JT: [2018]. Common Behaviors and Faults When Doffing Personal Protective Equipment for Patients With Serious Communicable Diseases

Materials available for other investigators

Our simulation and human factors protocols are now available in the peer-reviewed literature for other investigators to apply. There has been a great deal of interest in the use of the enveloped bacteriophage Φ6 as a surrogate for viruses like Ebola and now SARS-CoV-2, and this has previously not been a widely used surrogate. I have made stocks of the bacteriophage host, the virus, and the propagation and assay protocols available to other investigators who request them.

References

1.Kreuels B, *et al.* A case of severe Ebola virus infection complicated by gram-negative septicemia. *N. Engl. J. Med.* 2014; **371**(25): 2394.

2.Schieffelin JS, *et al.* Clinical illness and outcomes in patients with Ebola in Sierra Leone. *N. Engl. J. Med.* 2014; **371**(22): 2092.

3.Wolf T, *et al.* Severe Ebola virus disease with vascular leakage and multiorgan failure: treatment of a patient in intensive care. *Lancet* 2014.

4.Casanova L, *et al.* Methods for the recovery of a model virus from healthcare personal protective equipment. *J. Appl. Microbiol.* 2009; **106**(4): 1244.

5.DuBose JR, *et al.* Design strategies to improve healthcare worker safety in biocontainment units: learning from Ebola preparedness. *Infection Control & Hospital Epidemiology* 2018; **39**(8): 961.

6.Zimring CM, *et al.* Making the invisible visible: Why does design matter for safe doffing of personal protection equipment? *Infection Control & Hospital Epidemiology* 2018; **39**(11): 1375.

7.Guttman O, *et al.* Personal protective equipment and simulation: use of chemiluminescent glow sticks as a game changer? *Joint Commission journal on quality and patient safety* 2015; **41**(5): AP1.

8.Herlihey TA, *et al.* The Impact of Environmental Design on Doffing Personal Protective Equipment in a Healthcare Environment: A Formative Human Factors Trial. *Infect Control Hosp Epidemiol* 2017: 1.

9.Tomas ME, *et al.* Contamination of Health Care Personnel During Removal of Personal Protective Equipment. *JAMA internal medicine* 2015; **175**(12): 1904.

10.Casanova LM, *et al.* Assessment of Self-Contamination During Removal of Personal Protective Equipment for Ebola Patient Care. *Infect. Control Hosp. Epidemiol.* 2016: 1.

11.Grayson ML, *et al.* Efficacy of soap and water and alcohol-based hand-rub preparations against live H1N1 influenza virus on the hands of human volunteers. *Clin. Infect. Dis.* 2009; **48**(3): 285.

12.Kampf G, *et al.* Efficacy of three ethanol-based hand rubs against feline calicivirus, a surrogate virus for norovirus. *J. Hosp. Infect.* 2005; **60**(2): 144.

13.Larson EL, *et al.* Analysis of alcohol-based hand sanitizer delivery systems: efficacy of foam, gel, and wipes against influenza A (H1N1) virus on hands. *Am. J. Infect. Control* 2012; **40**(9): 806.

14.Sickbert-Bennett EE, *et al.* Comparative efficacy of hand hygiene agents in the reduction of bacteria and viruses. *Am. J. Infect. Control* 2005; **33**(2): 67.

15.Eggers M, *et al.* Povidone-iodine hand wash and hand rub products demonstrated excellent in vitro virucidal efficacy against Ebola virus and modified vaccinia virus Ankara, the new European test virus for enveloped viruses. *BMC Infect. Dis.* 2015; **15**(1): 375.

16.Olu O, *et al.* Epidemiology of Ebola virus disease transmission among health care workers in Sierra Leone, May to December 2014: a retrospective descriptive study. *BMC Infect. Dis.* 2015; **15**(1): 416.

17.Wolfe MK, *et al.* Handwashing and Ebola virus disease outbreaks: A randomized comparison of soap, hand sanitizer, and 0.05% chlorine solutions on the inactivation and removal of model organisms Phi6 and E. coli from hands and persistence in rinse water. *PLoS One* 2017; **12**(2): e0172734.

18.Macher AM, *et al.* Historical Lassa fever reports and 30-year clinical update. *Emerg. Infect. Dis.* 2006; **12**(5): 835.

19.Fischer WA, *et al.* Moving Lassa Fever Research and Care Into the 21st Century. Oxford University Press US; 2017.

20.Raabe VN, *et al.* Favipiravir and Ribavirin Treatment of Epidemiologically Linked Cases of Lassa Fever. *Clin. Infect. Dis.* 2017; **65**(5): 855.

21.Bell T, *et al.* Ebola virus disease: The use of fluorescents as markers of contamination for personal protective equipment. *IDCases* 2015; **2**(1): 27.

22.Kwon JH, *et al.* Healthcare Worker Self-Contamination During Standard and Ebola Virus Disease Personal Protective Equipment Doffing. Open Forum Infectious Diseases; 2016: Oxford University Press; 2016. p. 1387.

23.Zamora JE, *et al.* Contamination: A comparison of 2 personal protective systems. *Can. Med. Assoc. J.* 2006; **175**(3): 249.

24.Casanova L, *et al.* Virus transfer from personal protective equipment to healthcare employees' skin and clothing. *Emerg. Infect. Dis.* 2008; **14**(8): 1291.