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Hospital-Acquired Infection Outcomes Under a Patient-Centered Hand Hygiene Initiative

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HOSPITAL-ACQUIRED INFECTION OUTCOMES UNDER A PATIENT-CENTERED HAND HYGIENE INITIATIVE

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Abstract

Hospital-acquired infections are common and represent the most frequent adverse event in healthcare delivery. Hand hygiene has been identified as the most effective intervention to prevent the spread of hospital-acquired infections. Although patients have been identified as vectors, the role of increased patient hand hygiene in the reduction of hospital-acquired infections has not been determined. We propose that the addition of a patient-centered hand hygiene intervention among hospitalized adult patients on general medicine floors will result in a 30% reduction in acquisition of hospital-acquired infections over the time period of 18-months in comparison to the standard of care focused on clinician hand hygiene only. We will complete a single-blinded cluster randomized control trial to evaluate the effect of a patient hand hygiene intervention on rates of hospital-acquired infections. The results of this trial could play a role in the development of new hospital initiatives focused on increasing patient hand hygiene.

Chapter 1: Introduction

1.1 Background

Hospital-acquired infections (HAIs) are common, affecting more than 1.4 million patients at any point in time, and represent the most frequent adverse event in healthcare delivery worldwide.[1] According to the National Healthcare Safety Network (NHSN), a HAI is defined as any infection acquired greater than 48 hours after admission to an inpatient location, that was not present upon admission.[2] The most common types of HAIs include, but are not limited to, surgical site infections, central line-associated infections, healthcare-associated pneumonia, ventilator-associated pneumonia, skin and soft tissue infections, urinary tract infections, gastrointestinal infections, and device-associated infections.[2-6] HAIs develop secondary to a wide variety of pathogens, the most common being *Clostridiodes difficile* (C. *difficile*), *Staphylococcus aureus, Klebsiella pneumonia*, *Escherichia coli (E. coli)*, *Enterococcus* species, *Pseudomonas aeruginosa*, *Candida* species, *Streptococcus* species, *Acinetobacter Baumannii*, *Proteus mirabilis*, and include antibiotic-resistant pathogens such as methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus* (VRE), and other multi-drug resistant organisms (MDRO).[1,3-5,7] Although all patients admitted to the hospital are at risk for acquiring a HAI, advanced age, state of immunosuppression, extended hospital stays, admission to a large hospital, central catheter placement, mechanical ventilatory support, and admission to a critical care unit have been identified as factors that place patients at an increased risk.[4,5]

In the United States, the burden of HAIs is high, as current rates estimate that one out of every twenty-five hospitalized patients will develop a HAI during a hospital admission

and that more than 98,000 deaths annually can be attributed to HAIs.[4,8] Additionally, HAIs can lead to longer hospital stays, increased emergency department visits, and hospital re-admissions.[9] From an economic standpoint, the overall medical costs secondary to HAIs is between 9.8- 45 billion dollars annually in the United States.[3,10,11] Data demonstrates that up to 800,000 or 20% of cases of HAIs annually are preventable, yet rates remain high in the United States.[12,13]

The current standard of care in terms of infection prevention varies between hospital systems; however, despite numerous interventions targeting healthcare worker (HCW) hand hygiene, contact precautions, carrier identification, and decolonization, HAIs continue to pose a large threat to patients and hospital systems. Hand hygiene(HH) has been identified as the most effective intervention to prevent the spread of pathogens and HAIs.[14] Current interventions focus on HCWs as a point of transmission of pathogens; however, these interventions rarely incorporate patients as a reservoir for transmission despite the fact that the majority of HAIs are endogenous, meaning they develop due to organisms that were already colonizing the patient prior to the onset of infection.[15] A meta-analysis investigating pathogen transmission in the hospital setting, defined as the direct or indirect transfer of infectious agent from a reservoir to a susceptible host, reported the surface of origin of pathogens to be the patient or the environment in 94% of studies and identified patients as the primary source of environmental contamination.[16,17] Pitet et, al. identified the presence of pathogenic organisms on patients' skin or hands as the first step in cross-transmission of microbial pathogens to HCW, and subsequently to other patients.[18] Additionally, patient hand colonization with pathogenic organisms increases the risk of self-inoculation via wounds, devices, and ingestion of pathogens.[19]

Overall, patients have been identified as possible sources of transmission in four principal ways: pathogen transfer within the environment, direct transmission to other patients, cross-contamination through contact with HCWs, and as an endogenous source to themselves.[20] Focusing attention on eliminating pathogens from the hands of patients may have a direct and indirect reduction in HAIs.

Recent studies have highlighted the burden of patient hand contamination with microbial pathogens. Two prospective cohort studies have demonstrated that up to 25% of patients' hands were colonized with a MDRO upon discharge from an acute care hospital, a number that stayed consistent among different lengths of hospital stay.[21,22] Istenes et al. established that within 48 hours of admission to a medical/surgical floor, 39% of patients' hands were contaminated with a pathogenic organism.[23] Prevalence of *C. Difficile* hand colonization was also demonstrated to be high among hospitalized patients, with positive hand swabs seen in 32.1% of symptomatic patients and 37.5% of asymptomatic carriers.[24] A case-control study of 200 elderly persons demonstrated that 62% of patients admitted to a general medicine floor for at least seven days tested positive for hand colonization of *Enterococcus* species while the rate was only 10% in the control group ($p<0.001$).[25] This data demonstrates the high pathogen burden patients acquire while admitted to the hospital, thus justifying the need to target patients' hands as a potential etiology of HAIs.

Despite carrying a high burden of pathogens, patients report practicing HH four fewer instances per day while admitted to the hospital compared to their daily lives.[23] During 36-hours of direct observation within 27 wards across 9 hospitals, patients accounted for <1% of the use of alcohol-based hand sanitizer at the bedside.[26] A cross-sectional study

at a Veterans Affairs Medical Center investigating patient hand hygiene (PHH) rates highlighted the gap in practice as across 606 HH opportunities, patients performed HH 13% of the time before meals, 1% of the time upon room entry/exit, and only 8% of the time after toileting.[27] A separate cross-sectional study using electronic monitoring of PHH events on a multi-organ transplant unit found that PHH was associated with 29.7% of bathroom visits, 39.1% of mealtimes, 6.7% of room exits, and 2.9% of room entries.[28] Factors that contribute to low rates of PHH have been found to include lack of education, patient immobility, and lack of access to hand sanitizer or a sink.[29] This data demonstrates that patients are not practicing HH during the most crucial times while in the hospital, thus they continue to serve as a potential source of transmission of pathogens and there is significant room for improving PHH practices.

The importance of PHH in the prevention of transmission of pathogens is a concept that is understood by both patients and HCWs alike. At a large acute care teaching hospital, a cross-sectional survey determined that 99.8% of respondents (nursing staff) perceived PHH to be a crucial step in preventing HAI transmission.[30] Additionally, 100% of patients believed PHH to be an important part of infection prevention while in the hospital.[31] This data indicates that an intervention focused on PHH could be developed in a constructive environment if patients were given the resources necessary for completion. Additionally, interventions that involve both patients and HCWs as stakeholders in increasing PHH rates have the potential to be the most effective.

1.2 Statement of the Problem

Despite a plethora of information demonstrating that PHH plays a critical role in the transmission of multi-drug resistant organisms and potential development of HAIs, to

date, an adequately powered, randomized control trial has not been conducted to evaluate the effectiveness of a PHH intervention in reducing rates of HAIs. Given the fact that HH has been highlighted as the most effective way to reduce rates of HAIs and the evidence highlighting the fact that patients don't complete HH while in the hospital, an intervention focused on increasing PHH practices could have drastic effects on rates of HAIs. The results of the proposed research could aid in the reduction of HAI rates and subsequently improve health outcomes among patients. An intervention focusing on PHH presents a minimal risk, cost-effective, ethical means of reducing rates of HAIs and the burdens they place on the healthcare system.

1.3 Goals and Objectives

We aim to determine the efficacy of a patient-centered HH model on the reduction of HAI rates among patients on general medicine floors over an 18-month period compared to the current standard of care. Our objective is to present a standardized and controlled intervention among hospitalized patients to determine if increased PHH results in a subsequent change in rates of HAI or secondary outcomes. This will allow for the relationship between PHH and HAIs to be researched to a further extent than previous studies.

1.4 Hypothesis

We propose that the addition of a patient-centered hand hygiene intervention among hospitalized adult patients on general medicine floors will result in a 30% reduction in acquisition of hospital-acquired infections over the time period of 18-months in comparison to the standard of care focused on clinician hand hygiene only.

1.5 Definitions

Patient-Centered Hand Hygiene Intervention: The inclusion of patients in standard hand cleansing practices, defined as actively performing hand hygiene to remove dirt, organic material or microorganisms from hands via hand hygiene, as dictated by the experimental protocol.[32]

Hospital-Acquired Infection: An infection, defined by site-specific criterion, that occurs greater than 48 hours after admission to an inpatient location.[2] For the purposes of this proposal, this phrase is interchangeable with "healthcare-associated infection" and "nosocomial infection".

Standard of Care: The standard infection control guidelines employed by the hospital system.

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Chapter 2: Review of the Literature

2.1 Introduction

A comprehensive systematic literature search was conducted between July 2019 and March 2020 using PubMed, Cochrane, Scopus, Ovid, and MEDLINE. Assistance was provided by the Yale School of Medicine Librarians. The following combination of MeSH terms was used: “nosocomial infection”, “hospital-acquired infection”, “healthcare-associated infection”, “patient hand hygiene”, and “hand hygiene”. Due to the limited number of studies, we did not constrain data by year of publication, and we expanded our search by exploring the references listed in each study to identify additional relevant sources. We included qualitative studies, meta-analyses, quasi-experimental studies, and randomized controlled trials in our review. For our purposes, HAI and nosocomial infection are interchangeable throughout this review. PHH as a method of infection control is a strategy researchers have been investigating for many years. This literature review stands to explore the existing body of evidence while highlighting the limitations of the data, thus justifying the need for our proposed study.

2.2 Review of Empirical Studies Concerning Patient Hand Hygiene and Hospital-Acquired Infections

In 2003, Hilburn et al. conducted a quality improvement project investigating the effect of increased patient hand sanitizer allocation on rates of nosocomial infections in patients on a 498-bed orthopedic surgical unit. Investigators collected baseline infectious data on frequency of nosocomial infections in the six-month time period prior to implementation of the project. The intervention consisted of personal 4.25-ounce alcohol-based hand sanitizers given to all patients in the unit, along with educational materials on the importance of HH. Researchers collected infectious data during the 10-month

intervention period and for two months following completion of the study. Frequency of nosocomial infections was determined by comparing the prevalence and the infection rate per month within the unit in both the baseline and intervention period. Researchers used ANOVA to complete statistical analysis between the two time periods. Overall, a 36.1% decrease in infection rate over the 10-month intervention period was observed, though statistical significance was not mentioned.[1] The authors noted there were no other changes to the unit during the time period of the intervention, thus attributing the decrease in infection rate to the PHH initiative. Additionally, the authors completed a cost analysis based on the observed decrease in infection rate, in which the data was so convincing, hospital administrators adopted the PHH intervention as the standard of care for all units in the hospital. Although focused on a specific orthopedic surgical population and thus not broadly generalizable, the results of this study demonstrate that increased patient access to HH materials is associated with reduced rates of nosocomial infection in certain populations, and it serves as one of the earliest studies to investigate this relationship.

In 2005 Cheng, et al. demonstrated similar results with the application of a PHH intervention during outbreaks of nosocomial infections in a 610-bed inpatient psychiatric hospital in Hong Kong. Standard infection control measures during outbreaks included contact precautions, temporary ward closures, and environmental cleansing. Hospital epidemiologic data focused on the time period of outbreaks, the affected ward, causative organism, and attack rate (number of affected patients/staff) was collected for six months prior to, and twelve months following implementation of the intervention. Nasopharyngeal aspirate was collected and sent for viral analysis (influenza,

parainfluenza virus, respiratory syncytial virus [RSV], adenovirus, and human metapneumovirus) on any patient who was exhibiting respiratory symptoms during an outbreak. The intervention included the application of 3ml of regular alcohol-based hand rub to patients' hands at specified times during the day- 08:00, 12:00, 16:00, and 20:00. The material was dispensed by staff members who subsequently observed the patients rub their hands together for at least 15 seconds. Students t-test and chi-square analysis were used to analyze differences in number of affected patients and staff during nosocomial outbreaks that occurred before and after the experimental protocol.

The authors identified six nosocomial outbreaks that occurred during the six-month pre-intervention period, while four nosocomial outbreaks occurred in the twelve months after implementation of the intervention. Authors noted a decrease in the percentage of patients and staff involved in outbreaks from 12.5% to 6.6% ($p=0.004$), and a decrease in the percentage of just patients involved in outbreaks from 18.2% to 9.9% ($p=0.005$) after implementation of the patient-focused HH intervention.[2] The results of this study were analyzed by type of nosocomial infection, of which the greatest decrease was seen with respiratory viral infections with a decrease in total number of outbreaks secondary to a respiratory virus from four to one (no p-value reported) and a decrease in the percentage of patients and staff involved from 10.7% to 1.7% ($p <0.001$).

The results of this study highlight the potential effect that standardized inpatient HH completion can have on incidence of nosocomial infections and number of persons affected. One strength of this study included the direct observation of PHH, which ensured patient adherence to the intervention protocol. Additionally, all other infection precaution protocols stayed identical throughout the two periods of the study which

allowed the reported results to be attributed to the intervention itself. Although the results of this study are based on a specific population, authors noted that psychiatric patients oftentimes experience more difficulty with completing and adhering to a PHH initiative; thus, results can be extrapolated to a more general population that does not experience such barriers. Lastly, the pre/post intervention time periods were different lengths in time and occurred at different times during the year, which may have led to confounding in the type and total number of nosocomial infections that occurred. This study has highlighted the possible implications of increased PHH within a population at high risk for nosocomial infections.

In 2010, Gagne, Bedard, and Maziade proposed the critical role patients and visitors play in rates of nosocomial infections secondary to MRSA in a 250-bed community hospital in Canada. The authors conducted a hospital-wide intervention that consisted of disinfection of all patient and visitor hands with a gel rinse containing 70% ethyl alcohol and 0.5% chlorhexidine. A team of research staff visited each patient twice a day to provide information regarding the benefits of HH and to facilitate the use of the gel rinse. Patients underwent weekly nasal screening for MRSA colonization. The primary outcome reviewed by researchers included acquisition of a MRSA nosocomial infection more than 72 hours after admission as indicated in the medical chart, laboratory cultures, and antibiotic prescriptions. Data collected throughout the intervention was separated by subset of infection type and retrospectively compared to infectious data taken prior to the intervention. The authors determined that the ratio of MRSA nosocomial infections acquired, compared to the number of MRSA positive nasal swabs, decreased from 51% to 37% during the intervention period. The number of MRSA

nosocomial infections per 1000 admissions underwent a 51% decrease, including a 69% decrease in MRSA respiratory infections per 1000 admissions and a 44% decrease in MRSA bone and soft tissue infections per 1000 admissions.[3]

The raw data collected through this study indicates a relationship between PHH and MRSA nosocomial infection rates; however, the lack of statistical analysis is a large limitation. Apart from the inclusion of visitors in the HH initiative, authors also noted increased compliance with HH by HCWs, both of which may have contributed to decreased rates of MRSA nosocomial infections and therefore introduced positive confounding to the results. Additionally, this study solely focused on MRSA infections, thus limiting its generalizability to nosocomial infections as a whole. In spite of these limitations, the results from this study point towards a relationship between increased PHH and decreased MRSA infections, and warrant further investigation.

In 2014, Pokrywka et al. discussed the addition of PHH to a pre-existing bundle of infection precautions used when treating a patient with C. *difficile* at a 520-bed tertiary care hospital. Baseline data on the rates of nosocomial C. *difficile* infection in the year prior to the study were recorded. Cases were defined using the NHSN criteria of any patient with unexplained onset of diarrhea for at least 12 hours that occurred 48 hours after admission, as well as a positive C. *difficile* toxin test. Authors expanded the definition to include any patient with the above criteria who was re-admitted after being hospitalized in the previous three months. Patients who were asymptomatic colonizers of C. *difficile* were not included. The intervention consisted of brochures and signage on the importance of HH, and PHH assistance by staff members with soap and water or an alcohol wipe prior to meals. C. *difficile* infection rates of the year prior to the intervention

were compared to the year following the intervention using chi-square analysis. Authors discovered a decrease in C. *difficile* infection rate from 10.45 to 6.95 (p=0.0009) per 10,000 patient days after the addition of PHH to the infection prevention bundle.[4]

This study exemplifies the drastic effect the addition of PHH to patient care routines can have on rates of certain nosocomial infections, such as C. *difficile*. Although authors did not measure adherence to the intervention protocol, they involved multiple members of the care team which in theory allowed the patients multiple opportunities to perform HH. The addition of the PHH initiative as part of a bundle approach may introduce bias to the results reported by authors as the decrease in C. *difficile* infections may be attributable to another aspect of the bundle. However, authors highlighted the fact that the other parts of the infection bundle had been present for over a year prior to the implementation of the study, making PHH the only change to infection procedures during the time period of the intervention. The focus of this intervention on C. *difficile* infections specifically limits its generalizability to all nosocomial infections; however, this organism is one of few which requires soap and water for effective removal of pathogens,[5] and thus the data suggests a similar intervention would demonstrate similar or improved results for other pathogens known for causing nosocomial infections.

The authors hoped to further investigate the above results with a quasi-experimental study at a 495-bed medical center in 2017. The intervention consisted of a hospital-wide, patient-centered HH initiative which involved educational presentations to all staff and admitted patients regarding patients' attitudes towards, and the importance of HH, along with information about nosocomial infections. Patient rooms were fitted with additional alcohol wipes and posters encouraging HH. Staff were instructed to assist

patients with bedside HH and to aid in the use of soap and water handwashing, when appropriate. Staff members received reminders via signage in staff areas and screensavers on communal computers. The authors compared the NHSN Standardized Infection Ratios (SIRs) between the time period prior to implementation and the time period after implementation. In the first two quarters following the intervention, SIRs of C. *difficile* decreased in a statistically significant manner from previous quarter values of 0.84 to 0.572 (p=0.0157, 0.338- 0.909) and 0.497 (p=0.0103, 0.261-0.863).[6] Analysis of the subsequent quarter demonstrated a non-statistically significant decrease from baseline in the SIRs to 0.813 (p=0.3844, 0.497-1.259). Authors noted that their initiative was the only change in the infectious disease management of cases of C. *difficile* during the intervention time period.

The results from this study illustrate the potential immediate effect of increased PHH on C. *difficile* SIRs. Although there was an increase in C. *difficile* in the third quarter, the ratio still remained below the baseline from prior to the intervention. The data analysis included only three quarters following implementation, which could have limited the ability to account for seasonal variability of C. *difficile* infections, the amount of data collected, and the statistical analysis that was performed. The limitations in the study design include the fact that the authors completed a hospital-wide implementation of the HH initiative, which restricted their ability to assess adherence or problem-solve issues that may have arose as they were dealing with a large patient population and many staff members. Additionally, by incorporating all patient populations, including those who may have limited mobility or functional status, the authors may have introduced selection bias, as those patients are less likely to be able to complete HH with soap and water,

which is what is recommended to remove C. *difficile* spores from patient hands.[5] These two studies by Porkrywka et al. demonstrate the potential effect of increased PHH on rates of C. *difficile* at two large medical centers and warrant further investigation.

Cheng et al. conducted a prospective observational study looking at the effect of system-wide directly observed PHH on rates of VRE. Authors implemented this intervention in 42 public hospitals throughout Hong Kong during a prolonged outbreak of VRE from 2013-2015. All conscious patients were directly observed practicing HH with alcohol-based hand rub before meals and medications by hospital staff members. The intervention also included eye-level posters reminding patients to complete HH. Standard hospital system precautions such as single room isolation for confirmed cases of VRE and active surveillance culturing were continued as usual throughout the intervention. The number of new VRE cases was uploaded to the public domain and segmented Poisson regression was used to analyze the changes in monthly VRE incidence rates between the time period before the intervention and the time period after its implementation. The trend in outbreak rates (>3 patients in the same ward who acquired VRE within 48 hours) was analyzed in an identical manner. Authors reported a decrease in incidence rate of VRE by 9.8% ($p<0.001$) and a decrease in outbreak rate by 13.3% ($p<0.001$) after implementation of directly observed PHH.[7] The burden of VRE in the hospital system was reduced by 83% one year following the intervention. These numbers highlight the drastic reduction in both incidence and outbreak rates of VRE following a patient-centered HH initiative.

This study has high external validity via the inclusion of all conscious patients, regardless of functional status, and through the use of 42 different hospitals throughout

the Hong Kong area. Additionally, the study highlights the ease of introducing PHH initiatives, as this intervention was implemented in a large number of hospitals in a short period of time with a compliance rate of 97.3%. One major limitation of this study was the implementation of pan-screening for VRE colonization of all patients in one of the hospitals with the highest infection rates in the network during the last portion of the study period. Identification of asymptomatic carriers through this screening led to patients being put on contact precautions earlier thus reducing the likelihood of transmission, and this may have led to decreased infection rates that were falsely attributed to the HH intervention. However, as noted, this only occurred in one of the 42 hospitals that participated in the study which greatly lowers the impact it had on the statistical significance of the data as a whole. Although this study only focuses on VRE, the results could have wide-spread implications for the efficacy of PHH on rates of nosocomial infections during outbreaks.

In 2017, Haverstick et al. investigated the effects of the addition of a PHH initiative on rates of nosocomial infections in a 36-bed, adult, cardiothoracic surgical step-down unit in an academic medical center. The intervention consisted of a pre- and post-intervention questionnaire to all patients on the unit which assessed their attitudes and practices regarding HH. All patients then received a personal alcohol-based hand sanitizer, a brochure focused on the importance of HH, and daily reinforcements of proper technique from nurses and technicians. Patients with C. *difficile* were instructed to complete HH with soap and water only. Patient use of hand sanitizer was assessed during daily rounding, barriers to completion or replenishment of materials was addressed at this time as well. New cases of nosocomial infections, specifically MRSA, VRE, and C.

Difficile were noted in the infection prevention department monthly report. Total rates of nosocomial infections were compared during a 19-month period prior to the intervention and a 19-month period following the intervention using a Wilcoxon rank-sum test. Researchers noted a significant decrease in the median VRE infection rates from 1.6 to 0.50 (p=0.003) and the median MRSA infection rates from 0.82 to 0.50 (p=0.01) when comparing pre-intervention rates to post-intervention rates.[8] No significant difference was found in median infection rates C. *difficile* before and after the intervention. Responses from patient questionnaires imply that patients were not normally completing HH prior to the intervention and that rates of completion increased after implementation.

As noted by authors, a majority of the patients included in the intervention were not ambulatory, and thus had limited access to soap and water. This may have decreased patients' ability to complete HH and may have introduced selection bias into the study. Researchers did not assess adherence to the intervention, and they noted that staff members frequently reported not having the time to help patients complete HH, which limits the internal validity of the reported data. Authors noted a small sample size (n=76) and an underpowered study, which restricts the statistical significance of the results. Nonetheless, the decrease in VRE and MRSA infection rates reported by the authors highlight the implications of increased PHH on rates of nosocomial infections in post-surgical patients, especially those who are sedentary or with limited mobility.

In 2019 Rai et al. evaluated the impact of an educational PHH intervention on colonization with nosocomial pathogens and acquisition of a nosocomial infection. Authors conducted a 17-month, nonblinded, parallel randomized trial of the PHH intervention versus standard of care at a 210-bed acute care Veterans Affairs hospital.

Patients in four selected medical-surgical wards with an anticipated length of stay greater than two days were eligible to participate in the study. Those patients with dementia, inability to complete HH, or a known MRSA colonization were excluded. Patients were randomized to the control or intervention group. Patients in the control group received the standard of care which consisted of the standard single bottle of alcohol-based hand sanitizer provided to each patient in their toiletry kit. Patients in the intervention group received an experimental protocol which included educational posters and illustrations highlighting the efficacy of alcohol on removing MRSA particles from hands, and one additional bottle of alcohol-based hand sanitizer. Patients received daily follow-up visits from research personnel for five days, at which time personnel directly facilitated the completion of HH. Adherence to the intervention was measured using hand sanitizer usage via periodic weights.

Colonization status upon admission and discharge was assessed for patients in both the intervention and control group via perirectal swabs to assess for VRE, fluoroquinolone-resistant gram-negative bacilli, and *Candida* spp. The authors determined the primary outcome of the study to be new acquisition of colonization with at least one of the following pathogens: MRSA, VRE, fluoroquinolone-resistant gram-negative bacilli, and *Candida* spp. Secondary outcomes included newly acquired infection with any of the abovementioned pathogens. The primary and secondary outcomes were assessed via medical record review. Differences in the primary and secondary outcomes between the two groups was assessed using a Fisher exact test and the student paired t-test. The authors reported no significant differences in the percentage of patients acquiring colonization with at least one pathogen between the intervention and

control group ($p=1.0$), including when separated by pathogen ($p<0.49$).[9] Additionally, none of the patients in either group developed a nosocomial infection with any of the pathogens of interest.

The results of this randomized controlled trial are contradictory to previously mentioned results, as increased PHH was not demonstrated to have efficacy in reducing colonization with pathogens or acquisition of nosocomial infections. However, the study has some limitations. The baseline infectious data and nosocomial rates at this specific hospital were not discussed; thus, if baseline rates were low, it is possible that 17-months was not a long enough time period to see a significant difference in colonization or infection with nosocomial pathogens. Additionally, the study consisted of a small sample size ($n=82$) and was only powered at a level of 75% to detect a medium to large effect size which may not have been sufficient to see statistically significant results, if baseline colonization and infection rates were low. Researchers were interested in specific pathogens and thus only completed peri-rectal swabbing, which may have limited their results in terms of colonization. As this was a study focused on HH, it would have been more beneficial to complete swabbing on the hands of patients to assess for colonization as well.

Lastly, the study design allowed for the potential of cross-contamination between patients in the intervention group and control group as patients were randomized to different experimental groups. The possibility exists that patients from different experimental groups shared rooms or were on the same floor, in which case it is likely that patients in the control group observed or overheard the training given to those in the intervention group. This would introduce negative confounding, as those patients may

have subsequently increased their HH practices as well. Furthermore, if nurses or other staff members were aware of the intervention, they may have inadvertently encouraged HH to patients in the control group. Nonetheless, this study serves as one of few randomized trials looking at the relationship between patient HH and nosocomial infection rates. The results are not in agreement with the studies that were previously summarized, which sheds doubt on the true relationship between these two variables, and highlights the need for further research via a sufficiently-powered, randomized controlled trial.

2.3 Review of Studies to Identify Possible Confounding Variables

A major concern regarding PHH interventions is the difficulty of assessing levels of adherence to the intervention, thus limiting researchers' ability to correlate results with increased PHH behaviors. Researchers have attempted to quantify patient adherence through direct observation of HH; however, this practice is resource- and time-intensive, and it is subject to observer bias and to the Hawthorne effect, in which the patient is aware they are being observed and subsequently performs HH more frequently.[10] These limitations heavily restrict the generalizability of results of adherence through direct observation. Savage et al. discussed the use of procurement data, or volume measurement of HH products, as an opportunity to overcome some of the obstacles faced with direct observation, presenting an objective measurement of patient adherence.[10] Ellingson et al. discusses the limitations of procurement data, including inability to distinguish between users (patients versus visitors), and to assess fidelity to intervention technique.[11]

Another possible confounding variable in PHH initiatives is the indirect increase in provider HH practices. Gagne et al, demonstrated an increase in HCW HH during

times of patient-centered interventions.[3] This increase in provider HH could positively skew the results of the intervention away from the null hypothesis and correlate decreases in nosocomial infections to PHH, when in reality the results could be associated with the increase in provider HH as well.

Patient colonization with pathogenic organisms has been linked to environmental contamination, and patients admitted to a room previously occupied by a patient with a nosocomial infection are more likely to acquire said pathogen.[12] Inability to control for environmental contamination that may increase a patients baseline risk of acquiring a nosocomial infection introduces a possible confounding variable when assessing the results of studies focused on the acquisition of nosocomial infections, regardless of the proposed intervention. The possible confounding variables mentioned in this section will be taken into consideration throughout the development of our proposed study.

2.4 Review of Relevant Methodology

This section serves to review literature relevant to the methodology section. Please see Chapter 3 for a more detailed description of the proposed study methods.

2.4.1 Study Design

Randomized control trials (RCTs) are the gold standard in clinical research, as they provide a set structure in which correlation between intervention and outcome can be measured in an organized fashion. Cluster randomized trials, a subset of RCTs in which larger groups such as units or hospitals are randomized, are common in studies focused on healthcare outcomes and infection control, such as HAIs.[13] The use of this type of study allows for the assumption that contamination of information between the intervention group and the control group would occur if patient-level randomization were

to be utilized; thus, the cluster-level randomization is helpful to reduce this "cross-contamination".[14] Intervention cross-contamination occurs when patients in the control group are exposed to a portion of the intervention either directly between patients or indirectly by various stakeholders in the intervention. Cluster randomized trials have advantages compared with clinical trials that are randomized at the individual level. Such advantages include increased feasibility of cluster-wide application of the intervention, improvement in patient compliance, and increased productivity of staff training.[15,16]

Randomization at the cluster-level that includes all patients in a specific unit or hospital increases the external validity of a study, making the results more relevant to the general public.[13] Statistically, the utilization of cluster randomized trials is more complicated, requiring the use of intra-cluster correlation (ICC) when calculating sample size. The ICC accounts for variation at baseline between individuals within a cluster, and its use often times increases the required sample size to ensure an adequately powered study.[16,17] Overall, a cluster-randomized trial is the most appropriate choice of study design when investigating epidemiologic outcomes such as HAIs. In comparison with many quality improvement studies, a cluster-randomized trial will allow for direct comparison of HAIs in clusters following a PHH initiative. Due to the nature of the intervention, patients and clinicians will not be blinded to the experimental group assignment; however, researchers assessing the outcome will be blinded.

2.4.2 Primary and Secondary Outcomes

Previous studies have found statistically significant differences in various pathogen-specific nosocomial infections following implementation of PHH interventions,[2-4,6,8]. The results of these studies justify the need to investigate the effect of

similar interventions on nosocomial infections as a whole. The use of acquisition of a HAI as a composite measure is a more feasible choice of primary outcome when compared to pathogen- or site-specific infections due to the relatively high numbers needed for results to detect a statistically significant change.[13,18] The use of HAI as a composite primary outcome also allows researchers to study the effect of the proposed intervention on the greater category of HAIs, making the results of the study more generalizable to diverse populations and hospital systems. Acquisition per patient days at risk allows for a standardized comparison between the intervention and control group, regardless of number of admissions or individual length of stay.[4,18-21]

Colonization with various healthcare-associated pathogens is a known risk factor for acquiring a nosocomial infection via direct and indirect transmission.[22] It is recognized that patients' hands are commonly colonized with said pathogens upon admission to the hospital, or they become colonized throughout their hospitalization.[23-27] Implementation of PHH has been shown to decrease colonization with nosocomial pathogens including MRSA, and VRE.[22,28,29] This information justifies the inclusion of pathogen colonization upon discharge as a secondary outcome of interest, to assess the effect of PHH on this variable. Nosocomial infections are known to increase length of hospital stay, mortality rates, emergency department visits, and re-admission rates thus making these variables important secondary outcomes in a study looking at the efficacy of an intervention in reducing nosocomial infections.[24,30]

2.4.3 Study Population and Recruitment Approaches

Acute-care hospitals have the highest rates of nosocomial infections, which classify them as the ideal location for the completion of an intervention targeted at

lowering infection rates.[31] General medicine floors provide a varied patient population with a wide range of admission diagnoses, comorbidities, and indwelling device presence. Patients on general medicine floors are less likely to be intubated, heavily sedated, or experiencing sickness that would prohibit them from participating in a HH intervention when compared to intensive care units. The use of a cluster randomized design will allow for the inclusion of all patients admitted to participating wards in the intervention, granted they meet inclusion and exclusion criteria, and that will increase overall external validity of the results. Patients admitted within the prior 48 hours to participating general medicine floors will be eligible for the study if they are greater than 18 years old. Based on the NHSN definition of a hospital-acquired infection, known hand contamination after 48 hours in the hospital, and baseline rates of hand colonization in long-term care facility residents, patients who have been admitted to the hospital for greater than 48 hours, transferred from another facility, or admitted from a nursing home or long-term care facility will be excluded from the study.[24,32]

A patient-participation centered intervention relies on the fact that patients are able to complete the proposed intervention. For our purposes, all patients who are functionally able to complete the HH protocol will be included in the study. Previous studies have attempted to address concerns regarding patients' mental capacity to adhere to HH interventions by excluding all patients with a psychiatric illness [24,33]. However, this exclusion limits the generalizability of the results of those interventions. The Mini-Mental State Exam (MMSE) is the most widely used and generalizable means of assessing cognitive function. [34] Therefore, we have chosen an MMSE score of less than 12 as a measure of a mental status incompatible with our proposed intervention and will

use this as an exclusion criterion during recruitment. Although most RCTs require written consent from each individual patient, a waiver of informed consent is appropriate in the setting of a minimal risk intervention, such as an intervention focused on HH.[13] For more detailed information on the proposed study population, recruitment process, and inclusion/exclusion criteria please see Chapter 3.

2.4.4 Intervention

Patient-centered interventions rely on patient participation and present a secure and applicable way for patients to play a larger role in their own healthcare. Historically, patients have been included in HH initiatives as monitors of the completion of HH by HCWs. In these situations, patients reported feeling apprehensive encouraging HCWs to complete HH, secondary to the power imbalance that exists in the clinician-patient relationship. [12] Patient-centered HH interventions eliminate this discomfort by allowing patients to take initiative of their own HH practices rather than monitoring that of HCWs. Their personal involvement can also act as a means of empowerment and motivation to HCWs to complete HH. As previously mentioned, studies have shown that an increase in PHH has shown to indirectly increase HCW HH as well, an additional benefit to including patients.[3] Additionally, patient-centered interventions develop a culture of accountability, shared responsibility, and ownership among patients.[35] In these systems, patients are able to play a greater part in their healthcare and to feel motivated to hold a larger stake in their overall health outcomes. Successful interventions focused on patient empowerment should include the following four essential aspects: patient participation, patient knowledge, patient skills, and a facilitating environment, all of which we aim to include in our proposed methodology. [35,36]

Previous studies have demonstrated that interventions focusing on PHH should address two main aspects: an educational model and an increase in access to HH materials. Educational initiatives pose a simple manner to increase patient education on certain topics and have been highlighted as a main contribution to improving patient health outcomes.[37] Patient-centered interventions can include a wide range of educational materials such as brochures, posters, presentations, live demonstrations, and access to infectious disease experts. Educational interventions have been utilized as an effective manner of improving PHH practices. An education-based implementation project established that patients' knowledge of HAIs and correct HH practices, assessed via correct survey responses, increased by 44.5% from baseline ($p<0.001$) following a short educational presentation upon admission to orthopedic wards in a tertiary hospital in Singapore.[38] Similar results were seen following a PHH educational intervention in a large academic medical center, where patient education regarding HH increased by 88.2% ($p< 0.001$), and opportunities for patients to complete HH increased by 43.3% ($p<0.001$) following the intervention.[6] There may be concerns that increased educational information does not get utilized by patients; however, through direct observation, McGuckin et al. reported that 80-90% of patients read the educational brochures focused on HAIs that were provided in several multicenter studies.[35] Hospital stays foster an environment that allows patients the time and interest in added reading or learning materials that prioritize their personal health.

In terms of HH, studies have shown that increased education translates into increased HH practices among patients. Rai et al. conducted a randomized trial at a Veterans Affairs Medical Center investigating the change in frequency of HH events

following an educational intervention versus standard of care of access to a personal alcohol-based hand gel. Patients received a poster and educational presentation on the importance of HH and key times for completion. The impact of the intervention was measured using weights of hand sanitizer bottles and direct observation of HH events. Patients in the intervention group used a mean of 3.6 grams of hand sanitizer daily, while the control group used 1.5 grams daily ($p<0.01$).[39] Authors also noted an increase in the percent of patients who completed HH upon entry of medical personnel from 15% in the control group to 40% in the intervention group ($p<0.01$). In another quasi-experimental study, PHH rates increased from 17.3% to 44.6% ($p=0.003$) following 30-minute educational presentations by investigators.[40] Hidden direct observation performed by Sunkesula et al. demonstrated an increase in patient HH events from 10% to 79% ($p<0.0001$) prior to mealtimes, and from 0% to 51% ($p<0.0001$) upon exit and entry of rooms following an education PHH intervention.[41] Multiple educational interventions have focused on highlighting key times for the completion of HH, resulting in 97% of participants to respond to feeling confident in their knowledge of the correct times to complete personal HH.[39,41] This data demonstrates that educational interventions are effective at increasing PHH practices and knowledge.

There is a wide variety of materials available to HCWs and patients to perform HH. However, not all are created equal in terms of their ability to kill pathogens responsible for nosocomial infections. Alcohol-based cleansers are more effective against most bacteria on hands than plain or microbial soaps.[11,42,43] Alcohol-based gel and hand wipes used prior to meals reduced the percentage of positive cultures of Enterobacteriaceae from 17% to 0.01% ($p<0.01$), and of Enterococci from 43% to 27%

(p=0.02) among the hands of patients at a rehabilitation clinic, though there was no significant difference in the number of samples with positive *Staphylococcus aureus* following application of alcohol-based gel or hand wipes.[28] In a study among known MRSA carriers, a single application of two mL of 70% alcohol-based gel reduced positive cultures taken from the hands of patients from 82% to 33% (p=0.001).[29] For those carriers whom a positive culture was still found following a single application, the number of MRSA colonies was reduced from 76 (+/-153) to 23 (+/-89) (p<0.001). Alcohol-based hand rub has also been shown to be more virucidal against various pathogens with the potential for causing nosocomial infections including rotavirus, rhinovirus, coronavirus, influenza A[25,44-46] The antimicrobial properties of alcohol stem from its ability to denature proteins of microbes,[47] and alcohol-based solutions containing 60-95% alcohol are most effective at killing pathogens.[5] This data indicates alcohol-based solutions as the correct choice of material when designing an intervention target at healthcare-associated pathogens.

The data supporting alcohol-based hand sanitizer is inconclusive with regards to spore-forming bacteria such as C. *difficile*. In pediatric and adult patients with a known C. *difficile* infection, pathogenic spores were recovered on the hands of 100% of patients who practiced HH with alcohol-based hand sanitizer versus 50% of those who utilized soap and water (p=0.182).[33] A statistically significant decrease in percent positive cultures from 48% to 10% (p=0.0005), and mean colony forming units (CFUs) of C. *difficile* from 13 CFUs to 1.7 CFUs (p=0.01) was demonstrated following 30 seconds of HH with soap and water in active and asymptomatic carriers of C. *difficile*.[48] In this same study, alcohol-based hand rub was not found to be effective in reducing percent positive

cultures, as results showed a decrease of only 53% to 48% (p=0.85) or mean CFUs, 11 CFUs to 10 CFUs (p=0.93). Additionally, it is thought that the use of soap and water in cases of C. *difficile* may aid in physically removing the spores from contaminated hands.[5] Worldwide, the WHO recommends the use of soap and water for completion of HHin cases of *C. difficile*, as in-vivo studies have demonstrated a degree of resistance of C. *difficile* spores to alcohol-based hand sanitizer, and soap and water have been shown to be more effective in removing C. *difficile* spores from hands of volunteers.[49,50] Interventions with a combination of alcohol-based hand rub and soap and water showed the greatest decrease in the largest number of pathogens overall.[22,28] Due to the high burden of *C. difficile* infections among hospital systems, interventions targeting HAIs should include the use of both alcohol-based hand sanitizer and soap and water. Duration of use and proper technique vary based on the medium used to practice HH, thus such instructions should be available when implementing a proposed HH intervention.[36]

In addition to the material used to complete HH, a recent study completed by Knighton et, al. highlighted that the mode of delivery is another important aspect of the feasibility of HH interventions. In their mixed-methods descriptive study, patients at a Veterans Affairs Medical Center were assessed based on time for use of three separate hand sanitizer delivery methods; pushdown pump, pocket-sized re-capable bottle, and hand wipes. The time required to access the pushdown pump (0.45 seconds) was significantly less than the personal bottle (3.86 seconds) and the hand wipes (5.66 seconds) ($p<0.001$).[51] Additionally, 97% of the patients preferred the pushdown method compared to the other two options. A descriptive study based on patient interviews by Tanner et al. produced similar results, with pushdown alcohol foam being the preferred

method of hand sanitation among hospitalized patients.[52] These results are important when considering ease of intervention for patients along with patient adherence and efficacy of a HH intervention.

2.5 Conclusion

The studies reviewed in this review of the literature illustrate the potential effect of a PHH intervention on rates of different nosocomial pathogens in varied populations. Although the data from each study is variable, and oftentimes contradictory, the overall majority point towards a clear connection between increased PHH and nosocomial infections. The strengths and limitations of each studied mentioned will aid in the development of a sufficiently powered, cluster randomized control trial to evaluate the relationship between these two variables. Additionally, the literature of numerous studies has been reviewed to highlight the key portions of methodology necessary to conduct a standardized, controlled, and effective study while reducing bias and confounding where possible. The review of the existing body of evidence will allow us to best conduct our proposed study.

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Chapter 3: Study Methods

3.1 Study Design

We will perform a single-blinded, prospective, cluster randomized trial among hospitalized adult patients on four general medicine wards at the York Street Campus and four general medicine wards at the Saint Raphael Campus of Yale New Haven Hospital. At the start of the trial, one campus will be assigned the intervention arm and one campus will be assigned the control arm via a randomization computer software. Patients in the control arm will receive the standard of care which is consists of access to one alcohol-based hand sanitizer. Patients in the intervention arm will receive the standard of care in addition to an educational patient-centered HH intervention along with access to additional HH materials. We will compare rates of HAIs between the two study arms over an 18-month period. Researchers and participants will not be blinded to the assignment of the intervention; however, specified study personnel who will only be assessing the primary and secondary outcomes will be blinded to the intervention assignment.

3.2 Study Population and Sampling

Our source population will be comprised of hospitalized medical patients ages 18 and older with an expected length of stay greater than two days who are admitted to general medicine floors at the York Street Campus and the Saint Raphael Campus of Yale New Haven Hospital, within an 18-month time period starting May 1st, 2020. The four eligible patient wards at each campus include**:** Fitkin 5-5, Fitkin 5-6, Generalist 9-7, and Generalist 9-8 at the York Street Campus, and Celentano-3, Celentano-4, Sr. Louise Anthony-4, and Sr. Louise Anthony-5 at the Saint Raphael Campus. We will utilize

uniform surveillance to identify hospitalized patients who fulfill the set inclusion criteria until we achieve our goal sample size of 668 patients.

Enrollment will be conducted on a daily basis to approach all newly admitted patients as identified via Epic Hyperspace. Inclusion criteria includes patients admitted to above-mentioned general medicine floors over the age of 18 years old. Exclusion criteria includes patients under observation status, patients transferred from an outside hospital, patients placed on contact precautions, long-term care facility residents, and patients previously enrolled in the study. Patients with poor functional status defined as the inability to rub hands together for 30 seconds will be excluded from the study due to the physical barriers leading to inability to follow study protocol accurately. All patients will undergo a Mini-Mental Status Examination (MMSE) to evaluate cognitive functional status. Any patient who scores less than 12 on the above-mentioned exam will be excluded from the study.

3.3 Subject Protection and Confidentiality

The protocol for the proposed randomized cluster trial will be submitted and reviewed by the Yale University Human Investigation Committee for authorization to be completed at York Street Campus and St. Raphael Campus of Yale New Haven Hospital. The study will be compliant with any additional requirements set forth by the committee. All study personnel will have documentation of training in the Health Insurance Portability and Accountability Act of 1996 (HIPPA) Privacy Training.

Study personnel will maintain patient privacy throughout the study. Informed consent to review medical records, and collect samples will be collected verbally from each patient. Patient information will be de-identified as each patient will receive a

unique study code that will be applied to all medical records and samples collected from the patient and their room. Patient data will be accessed solely on secure servers. Patients will retain the right to withdraw from the study at any time they deem necessary.

3.4 Recruitment

All newly admitted patients on the eight participating wards will be screened to participate in the study. Study personnel will perform screening on Epic Hyperspace to be made aware of new admissions on each floor. A HIPAA waiver will be obtained to allow for medical record review to assess for eligibility. Researchers will be assigned to specific floors based on the medical teams admitting day.

Study personnel will perform a chart review to ensure patients meet the predetermined inclusion/exclusion criteria. Once a patient has been deemed eligible to participate in the study they will receive information regarding study guidelines, including potential risks and benefits. Recruiters will explain the clinical intervention to the patient, and explain that the intervention will occur at no additional cost to the patient. If a patient is interested in enrolling, study personnel will evaluate the patient to ensure they are able to complete basic HH and properly follow the study protocol. Study personnel will model a HH procedure using alcohol-based gel, and ask the patient to complete the procedure as well. If a patient is unable to follow a simple HH procedure exampled by study personnel, they will be excluded from the study. Recruiters will obtain verbal consent from all patients who are eligible and interested in participating in the study. Additionally, recruiters will receive approval from the primary medical provider for patient participation in the study. Due to the time-sensitive nature of the

outcome, we will aim to complete recruitment as close to admission as possible, including while patients are in the emergency department waiting for a bed.

3.5 Study Variables and Measures

The independent variable in this study will be the application of a patient-centered educational intervention encouraging HH along with the allocation of two additional HH materials to the patient. The control group will receive the current standard of care which consists of a personal bottle of 8oz Purell alcohol-based gel hand sanitizer.

The primary dependent variable in this study will be the acquisition of a HAI per 1000 patient days at risk presented as an incidence rate ratio. The definition of HAI will be based on the NHSN guidelines and will be defined as an infection acquired at any point greater than 48 hours after admission, that was not present on admission. The presence of infection will be defined by clinician documentation in the patient medical record and will include the standardized NHSN infections of central-associated bloodstream infection (CLABSI), non-central line-associated bloodstream infection (BSI), ventilator-associated pneumonia (VAP), healthcare-associated pneumonia (HCAP), catheter-associated urinary tract infection (CAUTI), non-catheter-associated urinary tract infection (UTI), other urinary system infection (USI), surgical site infection (SSI), ventilator-associated event (VAE), multidrug-resistant organism (MDRO), and *Clostridium difficile* infection (CDI). We will also conduct subgroup analysis on the primary outcome to stratify data based on common causative organisms (MRSA, VRE, *Pseudomonas*, *Klebsiella*, *C. difficile*, *Candida, E. coli*, other).

The secondary dependent variables in this study include length of hospital stay, 30-day Emergency Department visits, 30-day readmission rates, 30-day mortality rates,

pathogen colonization upon discharge, and number of antibiotic days of therapy. Potential confounding variables within our study include age, gender, duration of hospital stay, admission diagnosis, history of HAI/MDRO, patient comorbidity, level of dependency for Activities of Daily Living (ADLs), and previous room occupant history of HAI.

3.6 Methodology Considerations

Upon enrollment to the study, all patients will undergo baseline microbiological swabbing to determine pathogen colonization at the time of admission. Study personnel will swab both left and right hands identically, including the palms, fingers, and nail beds. Additionally, the interior of both nares of each patient will be swabbed to detect MRSA colonization. Study personnel will swab four high touch surfaces in all patient rooms upon admission including tray tables, sinks, doorknobs, and television remotes. All samples will be sent to the laboratory and assessed for the presence of colonization by pathogen of interest (MRSA, VRE, MDR GNR [multidrug resistant gram-negative rods], *C. difficile*) following standard microbiology techniques. All patients and high touch surfaces will be swabbed in identical fashion upon discharge from the hospital. Baseline characteristics of all patients will be recorded upon enrollment in the study. This data includes patient age, sex, Body Mass Index (BMI), race, admission diagnosis, Charlson comorbidity score, Katz Index of Independence ADLs, history of pathogenic MRSA/VRE swabs, history of pathogenic colonization in past 90 days, antibiotic use in last 90 days, presence of a urinary catheter, and presence of indwelling devices. Patients who are transferred to a non-participating floor, experience worsening functional status or

delirium, or are placed on contact precautions during their stay will withdraw from study participation.

3.61 Experimental Protocol

Upon enrollment in the study, patients in the intervention group will receive an educational intervention focused on the importance of HH, and basic information on HAIs. Patients in the intervention group will receive the standard 8oz bottle of Purell 70% alcohol-based hand sanitizing gel with a push-top mechanism that is provided to all patients at bedside, an additional 2oz Purell 70% alcohol-based hand sanitizing gel personal pump bottle in their toiletry supplies kit, and a packet of 36 count Purell 70% alcohol-based hand sanitizing wipes at their bedside. Study personnel will perform a real-time example of correct HH procedure with the three mediums that will be available to patients during the study. When using alcohol-based gel, patients will be instructed to use one pump on their hands, and rub hands together covering all surfaces until hands feel dry, a process that should take between 20-30 seconds. When using alcohol-based wipes, patients will be instructed to use one wipe to clean the entirety of both hands and allow moisture to dry. Study personnel will inform patients that hand sanitizing gel and wipes should not be used when hands are visibly soiled or after bathroom use, at which time patients should complete HH using anti-microbial soap and water when possible. When using antimicrobial soap and water, patients will be instructed to wet hands with warm water, use one pump of liquid soap, rub hands together until a lather forms and for 15 seconds thereafter, rinse hands under running warm water, and dry hands completely with a paper towel. Study personnel will ensure that patients understand and are able to

perform each process completely. They will also act as a resource for any questions or concerns patients may have regarding the correct procedures to completing HH.

Study personnel will present the patients with information regarding fundamental times to perform HH following the CDC Clean Hands Campaign model. Patients will be educated on the importance of completing HH before meals, before touching their eyes, nose, or mouth, before and after changing wound dressing and bandages, after using the restroom, after blowing their nose, coughing, or sneezing, and after touching hospital surfaces such as bed rails, bedside tables, doorknobs, remote controls, or the phone. Patients will be instructed to practice HH before leaving their rooms, after returning to their rooms, and before coming into contact with HCWs.

Patients in the intervention arm of the study will receive educational materials to serve as a more in-depth explanation of the importance of HH and HAIs as an adverse health outcome, and as a reminder to practice HH. These educational materials include a "Four moments for hand hygiene" flyer, CDC patient hand hygiene factsheet, and an educational brochure documenting HAI rates and risks (Appendices B-D***).*** There will be reminders to perform HH, in the form of flyers stating "Did you wash your hands today?", posted on the wall in front of the patient, the doorway of the exit of the patients' room, and the bathroom mirror. Study personnel will visit each patient in the intervention group daily to remind them of the importance of HH and serve as a resource for any difficulties in completing HH the patients may be facing. If indicated by medical record review or study personnel impression, the MMSE may be repeated throughout the study time period to assess for change in cognition or development of delirium.

In addition to the key role played by study personnel, we will involve multiple stakeholders in this study who will act as an encouragement to patients to practice proper HH. Once randomization has occurred, nurses on the participating floors of the campus chosen for the intervention group will receive a short presentation regarding patient HH and the intervention procedures. They will be encouraged to remind patients to complete HH during their daily rounds and interactions with patients. Foodservice members at the intervention hospital will also receive similar training as the nurses and will be instructed to remind patients on participating floors to use the standard single-use sanitization wipe provided with each meal before eating as opposed to after completing their meal.

The control group will receive the standard of care which includes access to one dispenser of 70% alcohol-based hand sanitizer, and a single-use hand sanitizing wipe provided with meals. All hospitalized patients on general medicine floors at both York Street Campus and St. Raphael Campus currently receive this standard of care. Nurses and foodservice members at the control hospital will receive no additional training on patient HH. Nurses and foodservice workers on selected general medicine floors work exclusively York Street Campus or St. Raphael Campus, so there is little concern for contamination between the intervention arm and the control arm regarding their involvement.

3.62 Blinding of Intervention

Due to the patient-centered nature of the study, it is not possible for the intervention to be blinded. Patients who are receiving the intervention will be aware of such, as they are required to be an active participant in the study for its completion to be

successful. Additionally, study personnel who are providing the intervention to the patients will also be aware of the assignment of the intervention.

3.63 Blinding of Outcome

The primary outcome, acquisition of a HAI per 1000 patient days at risk, will be determined through chart review. The study personnel selected to complete this chart review will be blinded to the assignment of the patients in either the intervention or control group.

3.64 Assignment of Intervention

Assignment of either the York Street Campus or the St. Raphael Campus to the intervention arm will be done by a randomization software. The participating wards at each hospital will then be assigned to the intervention or control arm accordingly. Patients will be admitted to the participating wards in normal fashion.

3.65 Adherence

We hypothesize that each patient should practice HH at least five times per day. Based on this anticipated use, we will be able to measure adherence to the study protocol. This calculation is based on the "Four times for patient hand hygiene" model (Appendix D) and includes three daily meals, and daily rounding by various practitioners. We anticipate the number of HH events daily to differ greatly between patients, thus this number is the minimum to be considered adherent to the intervention protocol. We assume that patients who are able to mobilize to the bathroom will use water and soap for HH purposes after they use the restroom, and thus we will not be able to quantify adherence to those episodes.

In order to assess adherence, alcohol-based gel will be weighed and wipes will be counted upon admission, weekly thereafter, and upon discharge. Patients are instructed to use one pump of alcohol-based hand sanitizer which distributes one milliliter of gel or one alcohol-based hand wipe per HH event, thus patients will be expected to use five milliliters of alcohol-based gel or five alcohol-based hand wipes daily. Additionally, study personnel will be alerted by nursing staff on each floor if a patient needs a new bottle of alcohol-based gel or packet of alcohol-based wipes. This will allow researchers to assess adherence outside of the set times. We will consider patients to be fully adherent to the intervention if they are found to be adherent greater than 80% of the times they are assessed.

3.66 Monitoring of Adverse Events

Patients will be monitored for adverse events during the daily visits by study personnel. Although the intervention is overall low-risk patients will be assessed for skin irritation, skin dryness, hypersensitivity, contact dermatitis, eye irritation, or complaints of irritation at the site of open cuts on hands. Patients will be educated on the adverse effects of ingestion of alcohol-based hand sanitizer. If any patient undergoes an adverse event that is not relieved by the administration of an emollient, they will be withdrawn from the study.

3.7 Data Collection

Study personnel will conduct medical chart review daily to assess for both primary and secondary outcomes. The primary outcome, acquisition of HAI, will be defined by the NHSN guidelines and be identified in patients' charts as the presence of infection by the clinician. Secondary outcomes will be obtained through medical chart

review. This chart review will continue daily until discharge, at which point patients' charts will be followed and assessed for either primary or secondary outcomes for a total of 30 days.

3.8 Sample Size Calculation

The sample size was calculated using the 10% baseline incidence data for HAIs in acute care hospitals, and we estimated a 30% reduction in rates of HAI over the study period to be a meaningful clinical effect, giving a Cohens effect size (d) of 0.8.[1] Based on results of similar studies, an intra-cluster correlation coefficient of 0.05 was applied to the calculation.[2-8] We determined 400 patients in each group would be needed to detect a clinically significant difference between the intervention and control group, and account for loss to follow-up throughout the study period. We anticipated a power of 96% with a two-tailed hypothesis and an alpha of 0.05.

3.9 Analysis

The primary outcome, acquisition of HAI per 1000 patient days at risk will be assessed as an incidence rate ratio at the cluster level and will be manipulated using a Poisson regression model analysis to determine statistical significance between the intervention group and the control group. Exploratory subgroup analysis will be performed classifying the primary outcome by site of infection and causative pathogen, this data will also be manipulated using a Poisson regression model. Secondary outcomes in this study are continuous variables and thus will be analyzed using multivariate linear regression.

3.10 Timeline and Resources

The planned start day of the proposed study is May 01, 2020. There will be a month-long period of training for all study personnel, participating floor nurses, and foodservice personnel. After the training period, patients will be enrolled in the study on a rolling basis over the time period of 18 months. Data collection will continue for 30-days following the discharge of the last patient. Three months' time will be allotted for statistical analysis. The proposed study requires 8 research personnel dedicated to recruiting patients and performing daily visits. An additional 4 personnel will be needed to perform daily chart review assessing for primary and secondary outcomes.

3.11 References

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Chapter 4: Conclusion

4.1 Study Advantages and Disadvantages

The proposed study has many strengths. First, our intended study population are patients admitted to general medicine floors and present with a wide variety of admission diagnoses, medical comorbidities, functional status, and secondary characteristics. Our use of a comprehensive population will increase the external validity of the study results and make them more generalizable to a larger subset of the population and the overall users of the hospital system. The use of this diverse population will allow the results of the study to illustrate the relationship between the independent variable and the primary and secondary outcomes in a stratified manner, which may increase our knowledge of the specific relationship between HH and HAIs. Additionally, previous studies have excluded patients with any psychiatric illness, whereas our proposed study will use the MMSE as a screening tool for mental cognition and ability to adhere to the intervention, thus allowing for the inclusion of a greater subset of populations.

As patient health status can be fluid and change quickly throughout a hospital admission, daily check-ins with research staff allow for repeated evaluation of the patient and their ability to continue in the HH intervention. During these visits, patients will have the opportunity to ask questions and seek assistance in their completion of the intervention which increases the likelihood that patients will be adherent to the intervention and will be completing HH practices in the correct manner. Lastly, our study proposes a low-cost, low-expenditure, low-risk, ethical intervention following guidelines set by national and international healthcare agencies to encourage basic hygiene practices. By utilizing multiple vehicles to encourage HH, our proposed study includes

many informative ways to highlight the key aspects and importance of HH that are translatable across differing levels of health literacy and ultimately aim to promote patient empowerment in healthcare.

Despite extensive research to ensure a quality experimental protocol, our proposed study has some limitations. Due to inherent bias introduced through the recruitment and consent process, we predict that rates of PHH will increase in both arms of the study. However, we predict this increased rate will be greater in the intervention group due to increased exposure to the intervention, thus we do not expect the increase seen in both groups to change the statistical significance of the data. Secondary to the nature of the protocol, patients with decreased physical or mental functional status, including those who are sedated, or intubated, will be excluded from the intervention. This exclusion limits a large number of patients who are in intensive care units, a group that has been noted to be at the highest risk of acquiring HAI. By excluding this group in our analysis, the generalizability of our results to these populations may be limited.

The proposed intervention requires a significant amount of follow-up by researchers in terms of completing daily visits and personalized instruction to all patients. The allocation of a specific healthcare team member responsible for this task is not feasible in most hospital systems; however, if the standard of care in infection control shifted to include patients, multiple team members could carry this responsibility thus making it a smaller burden to all. Lastly, the utilization of two different hospital campuses may act as a confounding variable to the results of the study, as there may be inherent differences between them; however, the use of general medicine floors will ensure similar patient populations. Additionally, the two campuses we plan to utilize for

our proposed study are part of the same hospital system, serve the same patient population, follow identical administrative guidelines, and have similar baseline epidemiologic profiles therefor inherent differences should be minimal.

4.2 Clinical and Public Health Significance

As HAIs continue to pose a major threat to patients worldwide, our proposed study has the potential to introduce a new means of combating these costly and deadly adverse events in healthcare. In an ideal world, patients should be admitted to the hospital under one diagnosis and not be discharged with another one that was imposed by the system itself. Patient safety in the hospital is a major concern, and the results of our study could serve to alter the standard of care in terms of PHH to a manner that is doing more to protect patients. If a reduction in HAIs is seen through our proposed intervention, the consequences could be significant in the direct decrease of complications of such infections, but also indirectly with a decrease in associated healthcare costs and antibiotic utilization. In the era of increased antibiotic resistance, decreasing HAI rates is crucial to combatting resistant organisms and improving patient care. The results of our proposed study, including primary and secondary outcomes, can serve to lead future research focused on further investigation of rates of HAI, environmental contamination, and patient empowerment. As healthcare providers, we would be doing a disservice to our patients to not provide them with the tools necessary to complete basic HH, especially with the data demonstrating the potential they hold to transmit HAIs and the subsequent effects on patient health outcomes.

Appendix A: Verbal Consent Form

APPENDIX A: Information Sheet Verbal Consent for Participation in a Research Study

YALE UNIVERSITY

YALE UNIVERSITY SCHOOL OF MEDICINE – YALE-NEW HAVEN HOSPITAL

YALE UNIVERSITY SCHOOL OF MEDICINE – YALE-NEW HAVEN HOSPITAL: SAINT RAPHAEL CAMPUS

200 FR 9 (2017-2)

Study Title: Hospital-acquired Infection Outcomes Under a Patient-Centered Hand Hygiene Initiative

Principal Investigator(s): Manisha Juthani, MD and Nina Fiellin, PA-SII

Introduction

You are being asked to join a research study. The following information will explain the purpose of the study, what you will be asked to do, and the potential risks and benefits. You should ask questions before deciding whether you wish to participate, or at any time during the course of the study.

Purpose

The purpose of this study is to determine if there is a decrease in rates of hospital-acquired infections in general medicine patients receiving a hand hygiene intervention. You are being asked to participate because you have been identified as someone who is admitted to the general medicine floors that are participating in the study and you are over the age of 18 years old.

Procedures

If you choose to participate in the study personnel will swab your hands, nares, and selected areas of your room. This swabbing will be repeated on the day you are discharged from the hospital. You will then be randomized to either the intervention or control group. Patients who are in the intervention group will receive an educational presentation from study personnel regarding correct hand hygiene practices. Following the presentation, you will receive additional hand hygiene supplies to aid you in the completion of hand hygiene at specified times throughout the day. You will receive a follow-up visit from study personnel daily to answer any questions you may have about the intervention and to ensure you are completing it properly. Nursing staff and food service workers will periodically remind you to complete hand hygiene. Patients randomized to the control group will have access to the normal amount of hand hygiene

materials that all hospitalized patients are granted and will not additional educational presentation or visits from study personnel.

Possible Benefits

This research may or may not benefit you as a patient directly if increased patient hand hygiene is found to decrease hospital-acquired infections. However, knowledge gained from the results may help us to better understand the relationship between patient hand hygiene and hospital-acquired infections.

Possible Risks

Your part in this research study consists solely of completing hand hygiene practices that are standard of care and most likely part of your daily routine. This study does not require you to have procedures or treatments. Therefore, being in this study does not involve any physical risks to you. However, there is a slight risk regarding the confidentiality of your participation in this study, if information about you becomes known to persons outside this study. The researchers are required to keep your study information confidential, however, so the risk of breach of confidentiality is very low.

Alternatives to Participation

The only alternative to participation is to decline participation in the study.

Privacy / Confidentiality

To protect your confidentiality, your name and other identifying information will not be recorded on any study documents. You will be assigned a study number and the code linking your number with your name will be stored in a separate locked file cabinet. We will only collect information that is needed for research. Only the researchers involved in this study and those responsible for research oversight will have access to the information you provide. Examples of information that we are legally required to disclose include certain reportable diseases.

Research Authorization: Except as permitted by law, your health information will not be released in an identifiable form outside of the Yale University research team. Examples of information that we are legally required to disclose include abuse of a child or elderly person, or certain reportable diseases. Note, however, that your records may be reviewed by those responsible for the proper conduct of research such as the Yale University Human Research Protection Program, Yale University Human Subjects Committee. The information about your health that will be collected in this study includes: age, gender, weight, height, race, admission diagnosis, medical comorbidities, length of hospital stay, infectious disease history, antibiotic use history and presence of indwelling devices. Information may be re-disclosed if the recipients are not required by law to protect the privacy of the information. At the conclusion of this study, any identifying information related to your research participation will be destroyed. By agreeing to participate in this study, you authorize the use and/or disclosure of the information described above for this research study. The purpose for the uses and disclosures you are authorizing is to ensure that the

information relating to this research is available to all parties who may need it for research purposes.

This authorization to use and disclose your health information collected during your participation in this study will never expire.

Voluntary Participation

Participation in this study is completely voluntary. You are free to decline to participate, to end participation at any time for any reason, or to refuse to answer any individual question at any time. Refusing to participate will involve no penalty or loss of benefits to which you are otherwise entitled (such as your health care outside the study, the payment for your health care, and your health care benefits). By providing verbal consent, you have not given up any of your legal rights.

Questions

You have heard the above description of the research study. You have been told of the risks and benefits involved and, at this point, all of your questions regarding the study have been answered.

If you have any further questions about this study, you may contact the principal investigator, Dr. Manisha Juthani (203) 785-4140 or co-investigator Nina Fiellin, PA-SII. If you would like to talk with someone other than the researchers to discuss problems, concerns, and questions you may have concerning this research, or to discuss your rights as a research subject, you may contact the Yale Human Investigation Committee at (203) 785-4688.

Appendix B: CDC Clean Hands Campaign

PATIENTS AND VISITORS

CLEAN HANDS COUNT

KNOW THE TRUTH TO PROTECT YOURSELF FROM SERIOUS INFECTIONS

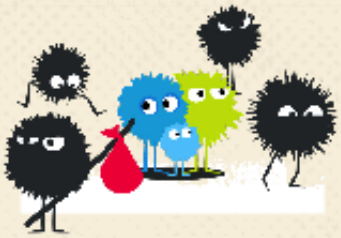
TRUTH
On average, healthcare providers clean their hands less than half of the times they should.

THE NITTY GRITTY:
This can put you at risk for a serious infection. It's OK to ask your care team questions like, "Before you start the exam, would you mind cleaning your hands again?" Another way to bring it up is to thank them for cleaning their hands if you are uncomfortable asking.

TRUTH
Alcohol-based hand sanitizer does not create antibiotic-resistant superbugs.

THE NITTY GRITTY:
Alcohol-based hand sanitizers kill germs quickly and in a different way than antibiotics. Using alcohol-based hand sanitizers to clean your hands does not cause antibiotic resistance.

TRUTH
Alcohol-based hand sanitizer kills most of the bad germs that make you sick.

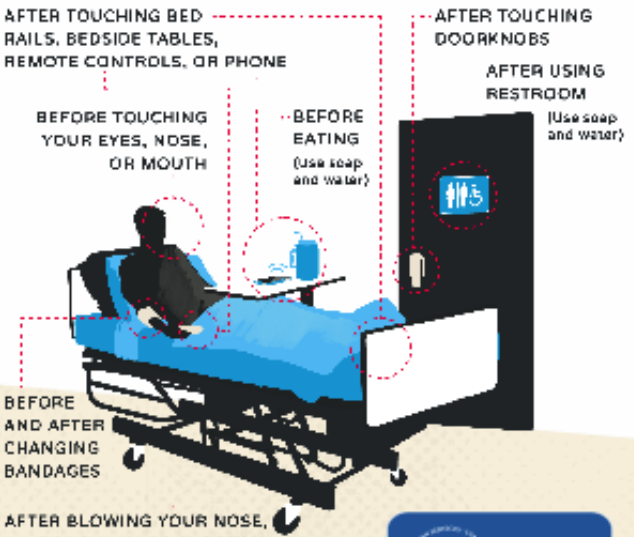


THE NITTY GRITTY:
Your hands have good germs on them that your body needs to stay healthy. Your hands can also have bad germs on them that make you sick. Alcohol-based hand sanitizers kill the good and bad germs, but the good germs quickly come back on your hands.

ALCOHOL-BASED HAND SANITIZER
is a product that contains at least 60% alcohol to kill germs on the hands.

TRUTH
Your hands can spread germs.

THE NITTY GRITTY:
Make sure you and your visitors are cleaning your hands at these important times:



TRUTH
Alcohol-based hand sanitizer does not kill *C. difficile*.

THE NITTY GRITTY:
If you have a *C. difficile* infection, make sure your healthcare providers wear gloves to examine you. You and your loved ones should wash your hands with soap and water to prevent the spread of *C. difficile*.

WHAT IS *C. DIFFICILE*?
C. difficile or "*C. diff*" is a common healthcare-associated infection that causes severe diarrhea.

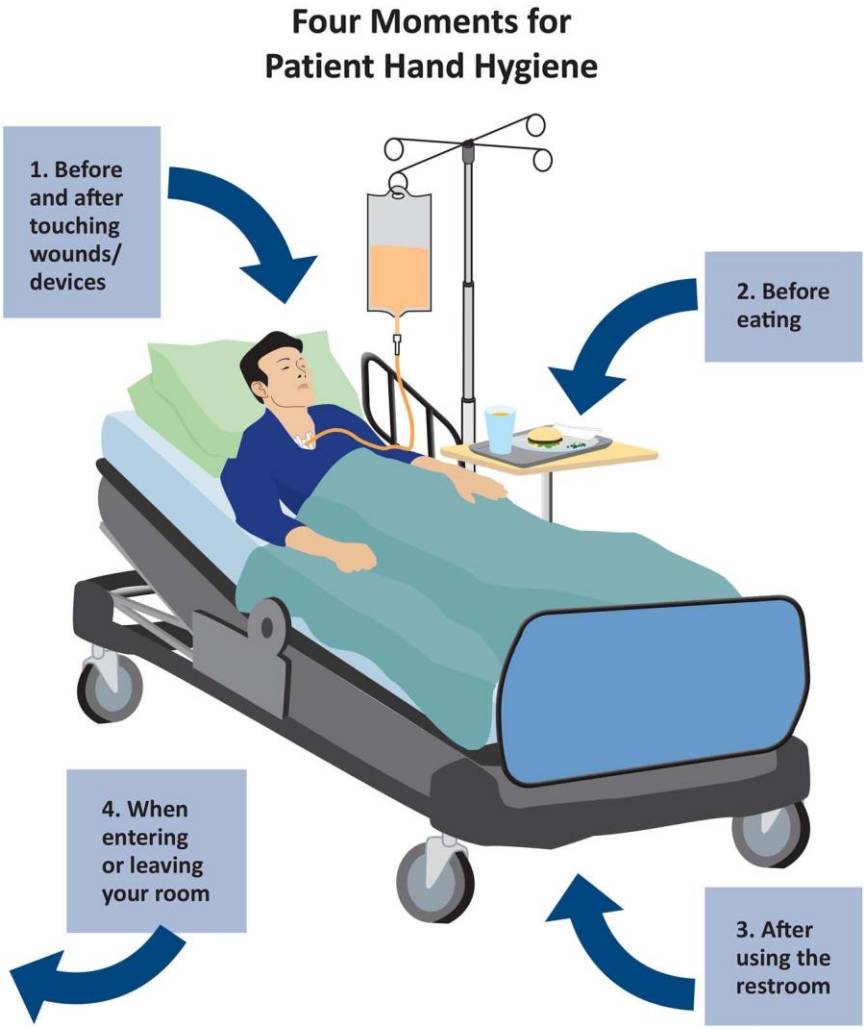
www.cdc.gov/HandHygiene

This material was developed by CDC. The Clean Hands Count Campaign is made possible by a partnership between the CDC Foundation and GOJO.

CDC

Appendix C: Patient Educational Brochure

Appendix D: "Four Moments for Hand Hygiene"



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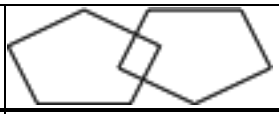
Appendix E: Mini Mental State Exam (MMSE)

Mini-Mental State Examination (MMSE)

Patient's Name: Date:

Instructions: Ask the questions in the order listed. Score one point for each correct response within each question or activity.

Maximum Score	Patient's Score	Questions
5		"What is the year? Season? Date? Day of the week? Month?"
5		"Where are we now: State? County? Town/city? Hospital? Floor?"
3		The examiner names three unrelated objects clearly and slowly, then asks the patient to name all three of them. The patient's response is used for scoring. The examiner repeats them until patient learns all of them, if possible. Number of trials: _____
5		"I would like you to count backward from 100 by sevens." (93, 86, 79, 72, 65, ...) Stop after five answers. Alternative: "Spell WORLD backwards." (D-L-R-O-W)
3		"Earlier I told you the names of three things. Can you tell me what those were?"
2		Show the patient two simple objects, such as a wristwatch and a pencil, and ask the patient to name them.
1		"Repeat the phrase: 'No ifs, ands, or buts.'"
3		"Take the paper in your right hand, fold it in half, and put it on the floor." (The examiner gives the patient a piece of blank paper.)
1		"Please read this and do what it says." (Written instruction is "Close your eyes.")
1		"Make up and write a sentence about anything." (This sentence must contain a noun and a verb.)
1		"Please copy this picture." (The examiner gives the patient a blank piece of paper and asks him/her to draw the symbol below. All 10 angles must be present and two must intersect.)

		
30		TOTAL

Instructions for administration and scoring of the MMSE

Orientation (10 points):

- Ask for the date. Then specifically ask for parts omitted (e.g., "Can you also tell me what season it is?"). One point for each correct answer.
- Ask in turn, "Can you tell me the name of this hospital (town, county, etc.)?" One point for each correct answer.

Registration (3 points):

- Say the names of three unrelated objects clearly and slowly, allowing approximately one second for each. After you have said all three, ask the patient to repeat them. The number of objects the patient names correctly upon the first repetition determines the score (0-3). If the patient does not repeat all three objects the first time, continue saying the names until the patient is able to repeat all three items, up to six trials. Record the number of trials it takes for the patient to learn the words. If the patient does not eventually learn all three, recall cannot be meaningfully tested.
- After completing this task, tell the patient, "Try to remember the words, as I will ask for them in a little while."

Attention and Calculation (5 points):

- Ask the patient to begin with 100 and count backward by sevens. Stop after five subtractions (93, 86, 79, 72, 65). Score the total number of correct answers.
- If the patient cannot or will not perform the subtraction task, ask the patient to spell the word "world" backwards. The score is the number of letters in correct order (e.g., dlrow=5, dlorw=3).

Recall (3 points):

• Ask the patient if he or she can recall the three words you previously asked him or her to remember. Score the total number of correct answers (0-3).

Language and Praxis (9 points):

- Naming: Show the patient a wrist watch and ask the patient what it is. Repeat with a pencil. Score one point for each correct naming (0-2).
- Repetition: Ask the patient to repeat the sentence after you ("No ifs, ands, or buts."). Allow only one trial. Score 0 or 1.
- 3-Stage Command: Give the patient a piece of blank paper and say, "Take this paper in your right hand, fold it in half, and put it on the floor." Score one point for each part of the command correctly executed.
- Reading: On a blank piece of paper print the sentence, "Close your eyes," in letters large enough for the patient to see clearly. Ask the patient to read the sentence and do what it says. Score one point only if the patient actually closes his or her eyes. This is not a test of memory, so you may prompt the patient to "do what it says" after the patient reads the sentence.
- Writing: Give the patient a blank piece of paper and ask him or her to write a sentence for you. Do not dictate a sentence; it should be written spontaneously. The sentence must contain a subject and a verb and make sense. Correct grammar and punctuation are not necessary.
- Copying: Show the patient the picture of two intersecting pentagons and ask the patient to copy the figure exactly as it is. All ten angles must be present and two must intersect to score one point. Ignore tremor and rotation.

  (Folstein, Folstein & McHugh, 1975)

Interpretation of the MMSE

Method	**Score**	**Interpretation**
Single Cutoff	<24	Abnormal
Range	<21 >25	Increased odds of dementia Decreased odds of dementia
Education	21 <23 <24	Abnormal for 8th grade education Abnormal for high school education Abnormal for college education
Severity	24-30 18-23 0-17	No cognitive impairment Mild cognitive impairment Severe cognitive impairment

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Source: www.medicine.uiowa.edu/igec/tools/cognitive/MMSE.pdf Provided by NHCQF, 0106-410

Appendix F: Sample Size Calculation

Alpha	0.05
Number of Tails	2
Power	0.96
Intervention Mean	0.10
Control Mean	0.7
Standard Deviation	0.375
Estimated Effect Size	0.8
Intra-Class Correlation Coefficient	0.05
Number of clusters	8
Participants per cluster	100

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