An environmental cleaning bundle to reduce healthcare-associated infection rates in hospitals: a randomized clinical trial.

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Keywords (MeSH): cross infection, infection control, hospitals, health services, housekeeping, maintenance, translational research, environment

Word count: 4189

Summary

Background: We aimed to evaluate the effectiveness of an environmental cleaning bundle to reduce healthcare-associated infections in hospitals.

Methods: We undertook a pragmatic, multi-centre, randomized trial in 11 acute care Australian hospitals, between May 2016 and July 2017. The intervention was the introduction of the REACH cleaning bundle, a multi-modal intervention to improve routine and discharge hospital cleaning tailored to each hospital. The primary outcome measures were incidences of healthcare-associated *Staphylococcus aureus* bacteraemia, *Clostridium difficile* infection and infection with vancomycin-resistant enterococci (VRE). Our secondary outcome was the thoroughness of cleaning of frequent touch points, assessed by a Fluorescent Gel Marking Gel.

Findings: A reduction in VRE infections from 0.35 to 0.22 per 10,000 occupied bed days (RR 0.63, 95%CI 0.41–0.97, p=0.0340) was observed. There was no statistically significant change in *S. aureus* bacteraemia (0.97 to 0.80/10,000 occupied bed days; RR 0.82, 95% CI 0.60–1.12, p=0.2180) or *C. difficile* infections (2.34 to 2.52/10,000 occupied bed days; RR 1.07, 95%CI 0.88–1.30, p=0.4655). In the pre-intervention phase there were 230 cases of VRE infection, 362 of *S. aureus* bacteraemia and 968 *C. difficile* infections, for 3,534,439 occupied bed days. During intervention, there were 50 cases of VRE infection, 109 of *S. aureus* bacteraemia and 278 *C. difficile* infections, for 1,267,134 occupied bed days. The intervention greatly improved the percentage of frequent touch points cleaned in bathrooms from 55% to 76% (OR 2.07, 95% CI 1.83–2.34, p<0.0001) and bedrooms from 64% to 86% (OR 1.87, 95 %CI 1.68–2.09, p<0.0001).

Interpretation: Findings provide evidence that a clean hospital environment is important for the safety of patients. Our work will inform hospital cleaning policy and practice, demonstrating the value of investment in both routine and discharge cleaning practice.

Funding: National Health and Medical Research Council.

Research in context

Evidence before this study

The hospital environment is a reservoir for micro-organism transmission and infection. Some micro-organisms can survive in the hospital environment for several months posing an ongoing transmission risk. A systematic review undertaken by Mitchell and colleagues identified evidence that admission to a room previously occupied by carrier of observed bacteria is a risk factor for subsequent acquisition. The findings suggest that current hospital environmental cleaning practices fail to reduce the risk of acquisition. In addition, Han and colleagues performed a systematic review to explore the evidence of current methods of cleaning, disinfecting, and monitoring cleanliness of patient rooms, as well as contextual factors that may affect implementation and effectiveness, found there were no randomized multi-centred trials, exploring the efficacy of improved routine and discharge cleaning on infection. The authors concluded that future studies should be real-world interventions for reducing the risk of healthcare associated infections, and should assess the role of frequently touched objects and the impact of cleaning on patient-centred outcomes. A recent randomised control study undertaken by Anderson et al, demonstrated the value in ultraviolet light, with the focus on discharged cleaning only.

Added value of this study

To our knowledge, this is the first randomized multi-centre clinical trial to evaluate the effect of a cleaning bundle that focuses on both routine and discharge hospital cleaning on the incidence of healthcare-associated infections. The intervention does not require new technology, but prioritises evidence from previous studies based on feasibility and cost of implementation, using an implementation

science framework to guide application. As such, this bundle has the potential to be implemented into diverse existing hospital settings.

Implications of the all the available evidence

The findings from our real-world, pragmatic study suggest that improving hospital cleaning requires a multi-modal, tailored approach that considers the local setting. By using a bundle approach to improve routine and discharge cleaning, improved cleaning performance and a reduction of vancomycin resistant enterococci infections is possible. As vancomycin resistant enterococcus is a useful surrogate for other bacteria, there are potential benefits of a tailored cleaning bundle for other pathogens that survive in the environment. The effect of a cleaning bundle on *S.aureus* bacteraemia and *C.difficile* is less apparent.

Introduction

Healthcare-associated infections prolong lengths of stay in hospital, increase risk of mortality and pose a significant burden on healthcare services and populations.[1] Antimicrobial resistance is intensifying this problem and effective prevention programs are now even more important. Reducing the risk of healthcare-associated infection requires multifaceted, evidence-based approaches.[2]

The hospital environment is a reservoir for micro-organism transmission, that can lead to infection.[3] Some micro-organisms can survive in the hospital environment for several months posing an ongoing transmission risk, unless removed using a cleaning process.[3] Frequently touched hospital surfaces, such as bed rails and call bells act as reservoirs and present the largest risk of contamination, as pathogens can be spread via hands.[4] For this reason, previous studies have focused on improving cleaning of frequent touch points.[5] Evidence also suggests that patients admitted to a room previously occupied by another patient with a multi-drug resistant organism are at increased risk of subsequent colonization and infection with that organism.[6] This suggests that current cleaning practices fail to reduce the risk of acquisition and illustrates the critical role of hospital cleaning, also known as environmental hygiene, in infection prevention and control.

Studies to evaluate hospital cleaning and infection transmission have been largely quasi-experimental or single-centred,[7] with the exception of one trial that demonstrated a decrease in patient pathogen acquisition of vancomycin-resistant enterococci following enhanced terminal room cleaning and disinfection.[8] More studies on the impact of improved routine cleaning are needed. We used a rigorous and pragmatic approach for the Researching Effective Approaches to Cleaning in Hospitals (REACH) study,[9,10] that allowed evaluation of effectiveness of an environmental cleaning bundle in reducing healthcare-associated infections in hospitals.[11]

Methods

Study design and participants

The REACH Study was a multi-site, stepped-wedge, randomized trial of an environmental cleaning bundle implemented in 11 Australian hospitals from May 2016 to July 2017.

Large Australian hospitals were eligible for inclusion if they met the criteria detailed in the study protocol, which were focussed on identifying major hospitals treating large numbers of patients with high infection risk.[11] Inclusion criteria included: having an accredited intensive care unit; classification by the National Health Performance Authority as a major hospital (public hospital) or having over 200 in-patient beds (private hospital); and having an established healthcare associated infection surveillance programme. From May 2015, eligible hospitals were invited to participate. We purposively approached eligible hospitals to optimise the feasibility and practicality of completing the trial, and to ensure findings were generalizable by including a sample of public and privately funded hospitals, and at least four of the eight Australian states and territories. Additional information regarding recruitment is provided in the appendix (Figure S1). The stepped-wedge design meant cleaning bundle intervention periods varied in length from 20 weeks (Hospital F) to 50 weeks (Hospital G) (figure 1).

Our study was registered with the Australian and New Zealand Clinical Trial Registry (ACTRN12615000325505) on 09/04/2015. The study protocol has been published.[11] This project received human research ethics approval from the Uniting Care Health Human Research Ethics Committee (approval number 1413) and the Queensland University of Technology Human Research Ethics Committee (approval number 1400000828). Local ethics and site-specific governance approvals were obtained for all participating hospitals. Individual consent was not required for this study.

Randomization and masking

The stepped-wedge design minimises bias by randomly allocating the timing of the intervention, which means that hospitals also received varying intervention durations (from 20 to 50 weeks). Once all 11 hospitals were enrolled, the study statistician (AGB) used Microsoft Excel to randomly allocate hospitals to a starting time, corresponding to codes A to K (figure 1). Hospitals were informed of their start date and intervention timings eight weeks before the control phase. Site preparation and scheduling was conducted and context assessments commenced during the four-week establishment period. The cleaning bundle was a hospital wide intervention which included training, audit and feedback to staff. Therefore, blinding environmental cleaning staff to the intervention was not possible. The statisticians were aware of the timing of the intervention, for the purpose of analysis.

Procedures

The intervention was the introduction of the REACH Environmental Cleaning Bundle. To create the bundle there was: a review of peer reviewed publications and guidelines, prioritization of evidence by an expert panel (with a focus on easy to implement and low-cost interventions) and successful pilot-testing at a large Australian hospital.[11,12]

The REACH bundle makes recommendations on: optimal types of cleaning agents, frequency of cleaning, cleaning techniques and auditing strategies, environmental cleaning staff training and creating a hospital-wide commitment to improved cleaning (appendix). The cleaning bundle was implemented for routine

hospital ward cleaning across all wards in the participating hospitals. The bundle was not used for outbreak situations or periodic maintenance cleaning.

Training Cleaning Staff

The REACH training facilitator delivered training activities with environmental services staff with a role in ward cleaning in week one to two of the intervention phase. Core training content included cleaning roles and responsibilities, the cleaning bundle components and the impact of environmental cleaning on healthcare associated infections. The cleaning technique described to staff included a defined and consistent cleaning sequence, daily cleaning of the high-risk frequent-touch points, the use of sufficient pressure and movement, and adherence to manufactures' instructions for product use (i.e. dilutions, contact time). Tailored training activities and content reflected the trial site context, including existing cleaning products and schedules. Further detail regarding the extent of training and the changes in knowledge have been published.[13]

Communication

Communication was a key strategy to sustaining a hospital-wide commitment to improved cleaning and bundle components. Hospital-wide promotional activities to raise the profile and importance of cleaning in reducing infections was undertaken, to support a culture shift in the profile of environmental services staff. Daily contact between cleaning staff and ward leaders or managers was encouraged, with cleaning staff representation on relevant clinical governance committees.

Auditing

Trained site team members performed auditing of cleaning using DAZO UV fluorescent marker technology. This system uses gel dots applied to surfaces. The dots are invisible to the naked eye, resist dry abrasion, and removed completely by routine cleaning.[5] In each hospital, at least half of the wards and the intensive care unit were selected for data collection. Wards that presented the highest risk for infection transmission and where existing auditing processes such as hand hygiene compliance occurred, were selected for auditing by the hospital in collaboration with the study team. One participating hospital had more than one intensive care unit. In this instance, one unit was chosen for auditing. The study team trained a local site team in the sampling methodology and provided a hard copy randomized monthly schedule, generated using Microsoft Excel, of nominated patient cubicles/bathrooms in selected wards to be audited. Frequent touch points present the largest risk of contamination by pathogens and thus potential transmission.[14] Dots were applied by the site team to a number of nominated frequent touch points (range 9 to 16 points) in two bedrooms and bathrooms as per the schedule, consistent with the Centers for Disease Prevention and Control (CDC) Environmental Cleaning Checklist and previous literature.[5] Dots were applied in a manner that cleaning staff were not aware of their exact placement. Points cleaned only by clinical staff, predominantly equipment, were excluded, because clinical staff were not the focus of the cleaning bundle. Following cleaning, the sites were checked by the site team using the ultraviolet light torch to determine whether the dot had been completely removed. Audit results were fed back to individual staff at the time of audit and then hospital-level results fed back monthly to cleaning staff, with additional reports provided to clinical governance committees.

Monitoring the trial

We used several strategies to monitor cleaning bundle implementation, infection prevention and control program changes and outbreaks or other issues at each hospital during the trial period. The key strategy was regular email and telephone contact, at least monthly, between the study and site team. In addition, the study team requested a bi-monthly monitoring document be completed by the site team. This aimed to

systematically capture changes in any aspect of the infection prevention program, including screening and staffing changes, outbreaks and the fidelity of the bundle implementation. No site reported program changes or outbreaks that could have impacted the primary outcomes.

Outcomes

The primary outcomes, as identified in our study protocol,[11] were incidence rates of healthcare-associated infections: *Staphylococcus aureus* bacteraemia (methicillin resistant and sensitive), *Clostridium difficile* infection, and vancomycin-resistant enterococci infections (sterile sites only) at each hospital, per 10,000 occupied bed-days and the cost effectiveness of a decision to adopt the environmental cleaning bundle. The cost-effectiveness outcome will be reported in a separate paper. For calculation of healthcare associated infection rates, the pre-intervention data refers to the combined historical, establishment, control and first four weeks of implementation (figure 1). The post-intervention refers to the data collected from four weeks after the intervention commencement, to allow for a delay in the intervention effect. Standardized infection definitions were applied.[11]

Colonization with these organisms was not assessed; all outcomes were clinical infections. Subsequent infections in the same patient were excluded, consistent with national and international definitions.[15,16]Infections with multiple-resistant Gram-negative bacilli were not part of the primary outcomes; these organisms are not endemic in any Australian hospital.

The secondary outcome was thoroughness of hospital cleaning measured by the DAZO© Fluorescent Marking Gel and Ultraviolet Light System. Data collection of cleaning audits occurred during the control and intervention period (figure 1). The outcome was the probability that a dot was completely removed.

Other outcomes listed in our protocol were the bio-burden of frequent touch surfaces post cleaning, changes in staff knowledge and attitudes around environmental cleaning, changes in rates of screening and clinical isolates and changes in patients' perception of hospital cleanliness. These will reported in future studies, with the exception of changes in staff knowledge and attitude, which has been reported.[13]

Statistical analysis

Our power calculation used the stepped-wedge sample size formula from Hussey and Hughes,[17] informed by a dataset of over two million hospital admissions and infection data from nine Australian hospitals.[18] Due to conflicting evidence on the size of the effect expected from improving cleaning on different infection types, we decided to use a combined infection rate, rather than three separate power calculations for each infection type. We calculated that 11 hospitals with a pre-intervention infection rate (a combination of *S. aureus* bacteraemia, *C. difficile* infection, and vancomycin-resistant enterococci infection) of five per 10,000 patient days, gave 86% power to detect a 20% post-intervention reduction in infection risk. This was based on a 5% two-sided significance level, a within-hospital correlation in infection rates of 0·3, and pre-determined intervention timings as per figure 1.

We performed data analysis in R version 3·4·3, using package lme4, in line with the published protocol. Additional information is provided as an appendix. For both primary and secondary outcomes, model comparison was made using Akaike's Information Criterion.

For the primary outcome, Poisson generalized linear mixed models were fitted to weekly confirmed cases of *S. aureus* bacteraemia, *C. difficile* infection and vancomycin-resistant enterococcus infection. To

standardize rates, weekly numbers of occupied bed-days by hospital divided by 10,000 were included as a model offset. There is a standard method for collection of bed-day data in Australian hospitals. Models had a random intercept for each hospital to control for differences between hospitals; a linear fixed effect to control for unrelated changes over time; and a binary independent variable for the intervention that switched from 'no' to 'yes' four weeks after intervention commencement to allow for a delay in the intervention effect. To summarize overall effectiveness of the cleaning bundle, intervention effects on the three infections were combined, using meta-analysis to produce a combined estimate and corresponding 95% confidence interval.[11]

We used sensitivity analyses to: determine the possibility of a delayed intervention effect of longer than four weeks, the influence of each individual hospital, and the effect of the intervention on *S. aureus* bacteraemia classes (methicillin resistant and susceptible strains of *S. aureus*). The delayed intervention effect modelled was 8 weeks after each hospital's intervention start date. The influences of each hospital were examined using a leave-one-hospital-out analysis examining changes to the intervention effect and Cook's distances. We also examined models fitted to: i) methicillin resistant, and ii) methicillin susceptible *S. aureus* bacteraemia.

For the secondary outcome, data from monthly cleaning audits were analysed using a binomial generalized linear mixed model with a logit link function on the proportion of frequent touch points cleaned. A random intercept was included for each hospital and the room (bathroom, bedroom) was included as an independent variable. Three specifications of the intervention effect were tested: a binary intervention effect, to model an instant improvement in cleaning; a linear intervention effect, defined as weeks after each hospital's intervention start date, to model a more gradual improvement over time; and a combined binary-linear intervention effect. For each model specification, we further tested if the change

in cleaning performance was the same for bathroom versus bedroom frequent touch points. This was modelled by including two-way interaction terms between room and the binary and/or linear intervention effects.

Consistent with recent debate when discussing outcomes, our paper focuses on the effect of the intervention, plausibility of mechanism, study design, data quality and real-world benefits, rather than p-values in isolation.[19]

Role of the funding source

The funders had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Eleven hospitals participated, covering six of the eight States and Territories in Australia. Nine hospitals were public and two were private (figure 2). The median number of overnight beds was 500 (interquartile range 351 to 804). Higher baselines rates were observed for *C. difficile* infection (2.34, 95% CI 1.55 – 3.55) than for *S. aureus* bacteraemia (0.97, 95% CI 0.76 – 1.24) and vancomycin-resistant enterococcus infection (0.35, 95% CI 0.14 – 0.87), per 10,000 occupied bed days. Ward cleaning was performed by 1,729 different staff, across the 11 hospitals and involved 190 wards. Further analysis of variation of cleaning practices, governance and staff at baseline have been published.[20] Of the hospitals that were invited to participate, but did not take part, the reasons for exclusion are provided in figure 2. For excluded hospitals, we examined *S. aureus* bacteraemia rates, from eight hospitals whose data was

publically available for the years 2015-16. No difference in *S. aureus* bacteraemia rates were identified between these hospitals and the pre-intervention *S. aureus* bacteraemia rates for hospitals included in our study (appendix, figure S1 and Table S2). In previous work, we illustrated variation in cleaning practices in the participating hospitals.[20] We would expect variation in cleaning practices to also be present in hospitals excluded from our study.

For all infection types there was a reduction in unadjusted rates per 10,000 occupied bed-days during the intervention, compared with the pre-intervention phase (table 1, appendix table S2 and S3). Using the model with the best Akaike's Information Criterion, a binary switch with a 4-week intervention lag, we modelled the trend over time expected based on pre-intervention data. For *S. aureus* bacteraemia and vancomycin-resistant enterococcus infection, there was no pre-existing linear trend, however *C. difficile* infections were already decreasing prior to the intervention. We then modelled the additional effect of the intervention and observed a statistically significant 37% reduction in vancomycin-resistant enterococcus infections from 0.35 to 0.22 per 10,000 occupied bed days (RR 0·63, 95%CI 0·41–0·97, p=0·0340). Infection rates for *S. aureus* bacteraemia decreased from 0.97 to 0.80 (18% reduction, RR 0·82, 95% CI 0·60–1·12, p=0·2180) and *C. difficile* infections increased from 2.34 to 2.52 (7% increase, RR 1·07, 95%CI 0·88–1·30, p=0·4655) (table 2). Changes in *S. aureus* bacteraemia and *C. difficile* infection rates after the intervention were not statistically significant (figure 3).

The sensitivity analysis estimated a non-statistically significant 26% decrease in methicillin-susceptible *S. aureus* bacteraemia from 0.23 to 0.17 infections per 10,000 occupied bed days (RR 0·74, 95% CI 0·53–1·05, p-value=0·0828). For methicillin-resistant *S. aureus* bacteraemia, a 28% increase in rates from 0.07 to 0.09 per 10,000 occupied bed days (RR 1·28, 95% CI 0·62–2·67, p-value=0·5250) was associated with the intervention (appendix, table S7). The other sensitivity analyses are detailed in the appendix.

A meta-analysis estimate of the effect of the intervention on all three infections combined, estimated a non-statistically significant 6% reduction (RR 0·94, 95%CI 0·81–1·11, p=0·4246) in the combined incidence of these infections (figure 3 and appendix table S4).

Our secondary outcome was the thoroughness of cleaning. During the study, 25,443 individual frequent touch points (5134 control; 20,309 intervention) were audited (appendix table S8). The number of patient rooms audited over the whole trial was 11% of available beds every quarter (range 6%–16% between hospitals). There was a large increase in the proportion of frequent touch points cleaned in both the bathroom (OR 2·1, 95% CI 1·8–2·3, p<0·0001) and bedroom (OR 1·9, 95 % CI 1·7–2·1, p<0·0001) (appendix tables S8-S11). The percentages of frequent touch points cleaned before and after the intervention increased from 55% (95% PI 53%–57%) to 76% (95% PI 75%–78%) for the bedroom, and from 64% (95% PI 62%–66%I) to 86% (95% PI 84%–87%) for the bathroom (figure 4). No adverse effects or events associated with this study were reported.

Discussion

Using a robust pragmatic clinical trial we have demonstrated that a multi-faceted hospital cleaning bundle improved thoroughness of cleaning and led to an important reduction in vancomycin-resistant enterococcus infections. A non-statistically significant reduction in the incidence of *S. aureus* bacteraemia ad no significant changes in the incidence of *C. difficile* were associated with introduction of the cleaning bundle. A small, non-statistically significant reduction was identified in the combined infection rate. These findings support the theory that a clean hospital environment is important for the safety of admitted patients.

The reduction in the incidence of vancomycin-resistant enterococci in our study has been identified in other research, however, our study uniquely benefitted from the use of clinical infections as the primary outcome measure, rather than colonization.[21] The role of cleaning in reducing incidence of vancomycin-resistant enterococci is important when considering the increasing incidence of this healthcare-associated infection and the wider challenges of antimicrobial resistance. Reduction in vancomycin-resistant enterococci infection is not only important clinically, but has relevance for health services in the context of additional length of stay and anticipated costs of antimicrobial resistance in the future.[22,23] Vancomycin-resistant enterococcus is also a useful surrogate for other bacteria, given similarities of survival in the hospital environment and transmission pathways.[24] Therefore these identified reductions could extend to other pathogens that survive in the environment, such as *Acinetobacter* species.

Non-statistically significant reductions in the incidence of *S. aureus* bacteraemia were associated with introduction of the cleaning bundle. We are unaware of other research that has attempted to demonstrate the impact of hospital cleaning on *S. aureus* bacteraemia, with previous research predominantly focused on reducing environmental contamination. It is important to assess this finding in the context of *S. aureus* bacteraemia in Australia. National surveillance and targets of *S. aureus* bacteraemia, in addition to a national hand hygiene initiative, were embedded long before the commencement of our study.[25] Further, major reductions in *S. aureus* bacteraemia have already occurred.[26] It is possible that the transmitted proportion of *S. aureus* has already reduced by previous measures, with the residual now affected by the cleaning bundle. Therefore, the reduction we identified is likely to be clinically important in the context of already declining and relatively low incidences of these infections. Although there was an increase in methicillin-resistant *S. aureus* bacteraemia, baseline infection rates were very low (0.07, 95% CI 0.04 – 0.13) and the observed confidence interval was wide (RR 1·28, 95% CI 0·62–2·67) (appendix table S6).

We did not observe statistically significant changes in the incidence of *C. difficile* infection, after accounting for the already declining incidence. The incidence of *C. difficile* infection increased at the time of the intervention implementation, then decreased towards pre-intervention levels as the study progressed. It is unclear why this occurred, but there are several possible explanations for why a significant decrease in infection rates was not seen. First, there is evidence that in Australia there are now major reservoirs of *C. difficile* outside the hospital.[27] Second, genetically diverse strains of *C. difficile* from these reservoirs are being transmitted into hospitals and infecting patients.[28,29] In addition, not all hospitals used a sporicidal disinfectant for cleaning and hospital could choose which disinfectant they wished to used.[20] Six hospitals used a detergent for routine cleaning of a patients room, not under contact precautions. Thus, given these factors and improved understanding *of C.difficle* epidemiology and transmission pathways since the commencement of this study, it is not surprising that our cleaning bundle alone would be able to reduce the incidence of *C. difficile* in a hospital setting. All hospitals had an antimicrobial stewardship program in place throughout the study, and no major trends in antibiotic prescribing were observed (appendix).

The implementation of the REACH cleaning bundle resulted in improved thoroughness of cleaning that continued to improve over the intervention period (figure 4). The thoroughness of cleaning at baseline (control) was low. Our results are also consistent with previously published literature demonstrating the benefit of using a fluorescent gel to assess cleaning with provision of feedback to staff.[5] We examined the data to compare the thoroughness of cleaning between discharge and daily cleaning, with the same improvement identified as in our primary analysis. However, our intervention included other elements, such as a focus on cleaning technique, training, communication and correct product use. Using this bundled intervention, we identified changes in knowledge, practice and attitudes in environmental services staff, improvement in the thoroughness of cleaning and an overall reduction in healthcare associated infections.[13]

Our robust, yet pragmatic study design, assessed against the PRagmatic-Explanatory Continuum Indicator tool (appendix),[9] was implemented in hospitals with a wide variation of practices and staff knowledge levels at baseline.[20] We will report the degree of alignment with the five bundle components and homogeneity of the intervention in the context of primary and secondary outcomes observed in a separate paper.

Many previous studies of hospital cleaning have used a before and after design, or have occurred within outbreak settings, not controlling for pre-existing trends and erroneously claiming causality.[30] We modelled the impact of the intervention separately to infection trends observed over a long period and accounted for trends in our analysis. We collected data on potential confounders and no noticeable changes in hand hygiene compliance or antimicrobial use were identified during the trial period (appendix table S12, appendix figure S2-S3).

There were variations in screening intensity between hospitals, for methicillin resistant *Staphylococcus aureus* and vancomycin-resistant enterococcus observed at baseline. However monitoring confirmed that screening policies at hospitals did not change during the study. Several strategies were used to identify outbreaks or policy changes that could impact the trial outcomes (appendix). No such changes were reported by the participating hospitals. Clinical staffing levels and individual patient characteristics were not included in the statistical analysis because it was assumed that randomization and the stepped-wedge design (where hospitals act as their own controls) controlled for these factors.

Our study has some limitations. Due to the pragmatic approach taken we did not examine patient colonization, or undertake microbiological testing of the environment or whole genome sequencing to prove transmission pathways, due to financial constraints. Microbial testing of the environment also has limitations.[31] Staff undertaking gel dot auditing were trained and regular monitoring and feedback was given by the REACH Study team if anomalies were observed in data provided. However given the size of the study we did not have capacity to independently validate this data.

In contrast to previous research our bundle development process prioritized evidence-based strategies that were easier to implement and lower cost, over newer expensive technologies.[32] An economic evaluation of the REACH trial will now assess cost-effectiveness to inform a decision on whether to adopt the REACH bundle under conditions of scarce resources.

The bundle was very successful at improving cleaning thoroughness and showed great promise in reducing vancomycin resistant enterococci infections. The intervention is broadly applicable to cleaning in any hospital, throughout the continuum of care, as it does not solely focus on discharge cleaning. In addition, we have demonstrated the benefits of an approach to bundle implementation that accommodates the complexity of hospital environments and allows for better consideration of culture and context, and hopefully greater ownership by hospitals. As a result the findings of this study are relevant to hospitals internationally. This study therefore has clinical and policy implications. We recommend that health services and policymakers that are interested in reducing vancomycin resistant enterococci infections by improving hospital cleaning, should consider both this bundle and our implementation approach.

Role of funding source

The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Contributors

All authors contributed to the design of the study. The concept of this paper was developed by BM and LH. Initial drafting of the manuscript was undertaken by BM and LH. NW undertook the data analysis with input from AB. Critical review and input was undertaken by AF, AG, KH, KP, DP, TR, CG, AB and NG. All authors approved the final version of the article. NG is the Chief Investigator for this project.

Conflicts of interest

All authors report grants from National Health and Medical Research Council, non-financial support from Kimberly-Clark Professional, non-financial support from Ecolab Pty Ltd , non-financial support from Whiteley Corporation, during the conduct of the study.

Acknowledgements

The REACH study was a National Health and Medical Research Council (NHMRC)-funded 2014–2017 Partnership Project (GNT1076006), led by Queensland University of Technology in conjunction with Wesley Medical Research. Academic project partners at Avondale College of Higher Education, Australian Catholic University and The University of Western Australia provided in-kind contributions to the study design, conduct, data analysis and interpretation and the publication and dissemination of results. Industry partners Kimberly-Clark Professional, Ecolab Pty Ltd and Whiteley Corporation

provided financial and equipment (software and consumables) resources to support data collection but had no role in the study design, implementation or analysis. The contents of the published material are solely the responsibility of the administering institution, participating institutions and the individual authors; they do not reflect the views of the NHMRC.

The authors wish to thank the staff of the 11 study hospitals and the REACH study team members - Dr Michelle Allen, Carla Shield and Alexandra McGhie. Peer review prior to submission was undertaken by three experts - Professor Stephanie Dancer, Professor Allen Cheng and Martin Kiernan. The authors are grateful for their advice and feedback.

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Table 1. Crude and adjusted rates of healthcare associated infections

		Pre-Intervention	Intervention
Infection			
CDI			
	N	968	278
	Unadjusted rate	2.74 / 10,000 OBDs	2.19 / 10,000 OBDs
	SD	0.008	0.017
SAB – MSSA			
	N	296	87
	Unadjusted rate	0.84 / 10,000 OBDs	0.69 / 10,000 OBDs
	SD	0.002	0.005
SAB – MRSA			
	N	66	22
	Unadjusted rate	0.19 / 10,000 OBDs	0.17 / 10,000 OBDs
	SD	(0.0005)	(0.001)
VRE			
	N	230	50
	Unadjusted rate	0.65 / 10,000 OBDs	0.39 / 10,000 OBDs
	SD	(0.002)	(0.003)
Total occupied bed days		3,534,439	1,267,134

Note: Calculated using a linear trend (Model 1). Pre-intervention Includes historical, establishment, control phases and the first 4 weeks of intervention phase. Intervention= switch at 4 weeks from the start of the intervention phase. SAB = *Staphylococcus aureus* bacteraemia. VRE = vancomycin-resistant enterococcus clinical isolates. CDI = *Clostridium difficile* infections.

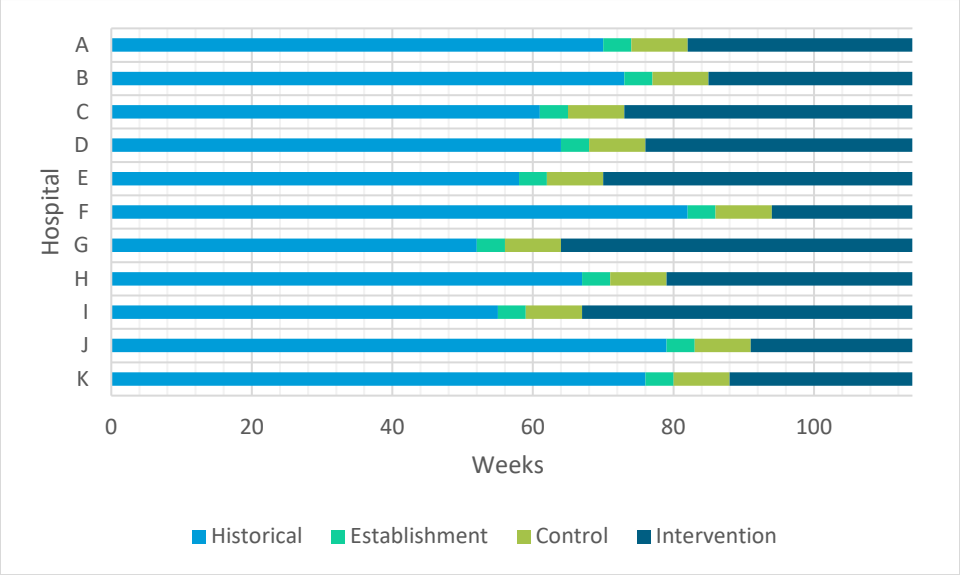


Figure 1. Study design.

Notes: There was a four week establishment period and an 8 week control period for baseline data collection of cleaning audits, context assessment and staff surveys.

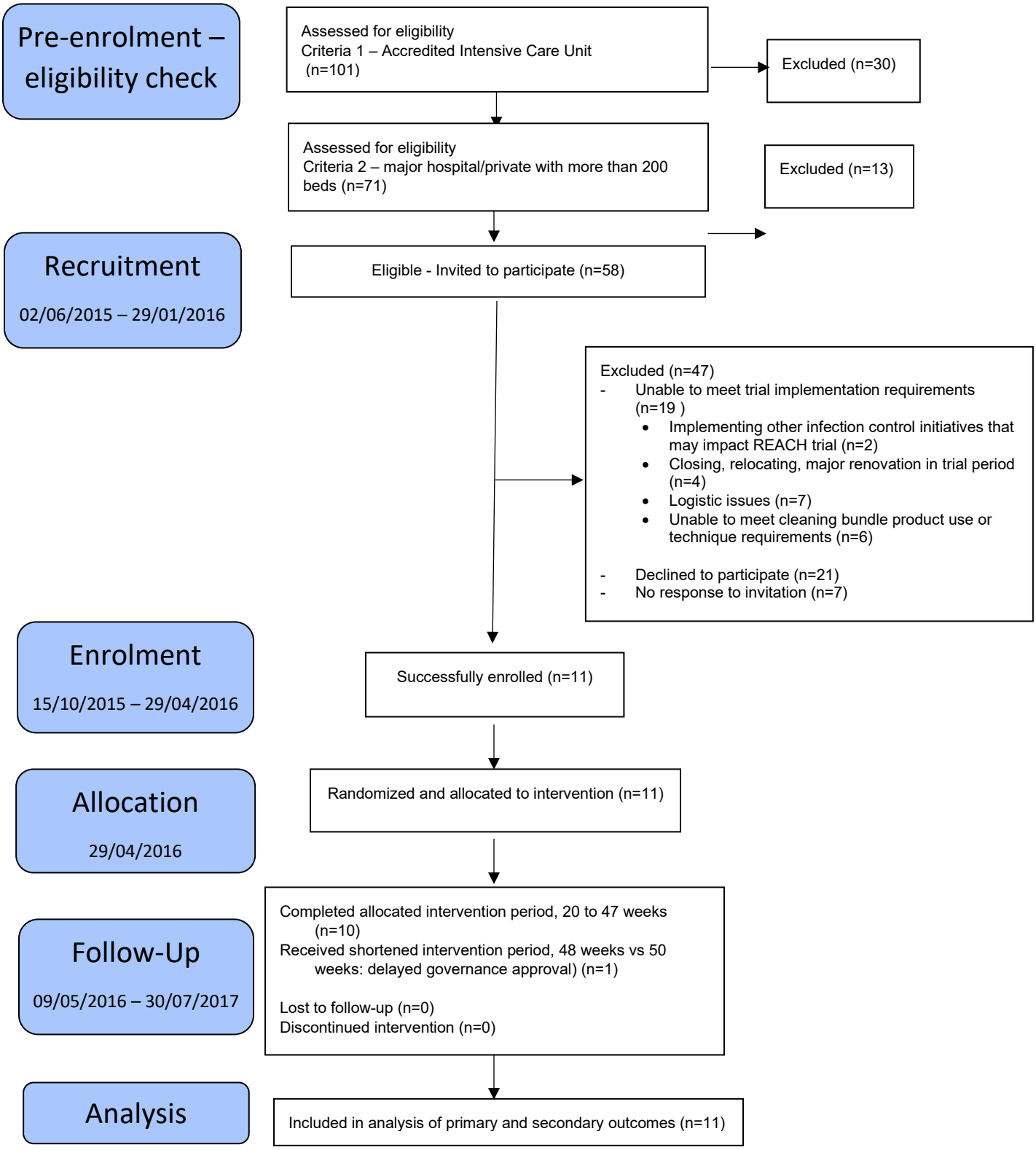
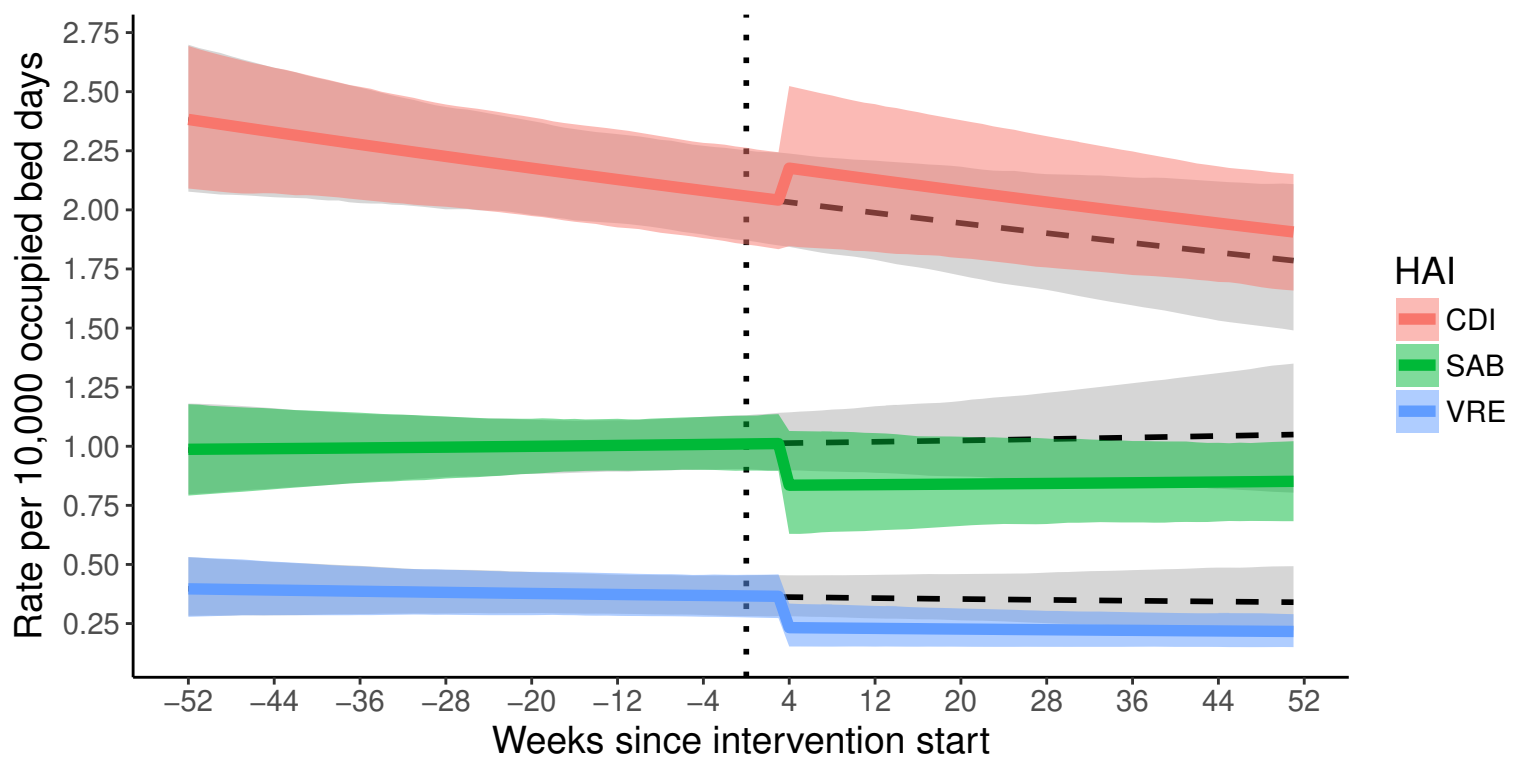
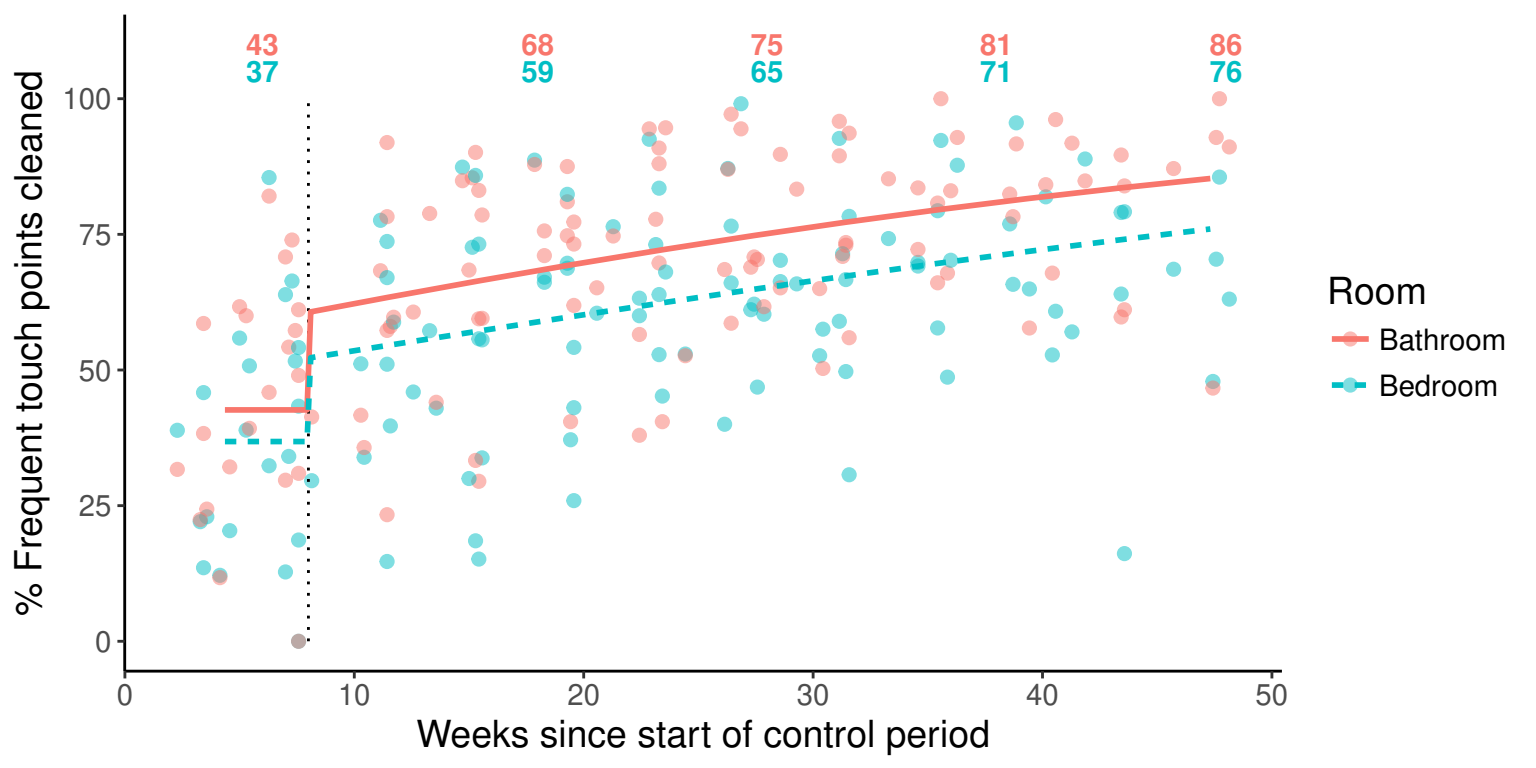


Figure 2. Flow chart of participation


Rate per 10,000 occupied bed days
2.75
2.50
2.25
2.00
1.75
1.50
1.25
1.00
0.75
0.50
0.25
−52
−44
−36
−28
−20
−12
−4
4
12
20
28
36
44
52
Weeks since intervention start
HAI
CDI
SAB
VRE


43
37
68
59
75
65
81
71
86
76
% Frequent touch points cleaned
100
75
50
25
0
0
10
20
30
40
50
Weeks since start of control period
Room
Bathroom
Bedroom

Supplementary Appendix

An environmental cleaning bundle to reduce healthcare-associated infection rates in hospitals: a randomized clinical trial.

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Contents

REACH Cleaning Bundle

The multimodal REACH cleaning bundle intervention had five interdependent components, which were ongoing across the intervention. The environmental cleaning bundle was delivered as a hospital wide intervention although only a percentage of wards were audited.

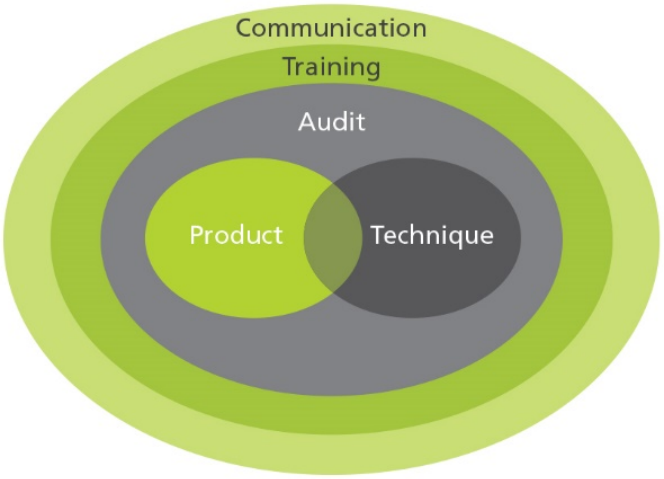
Summary of cleaning bundle components

Component	Key activities
Training	- tailored training activities with all environmental services staff with a role in ward cleaning in week 1-2 of the intervention phase, delivered by the REACH training facilitator - inclusion of REACH training content as part of induction for new cleaning staff, and as required throughout the intervention phase, delivered by site team using REACH training materials - training content that reflected the trial site context and included content on cleaning roles and responsibilities, the cleaning bundle and the impact of environmental cleaning on healthcare associated infections.
Technique	A sustained focus on cleaning technique, including: - a defined and consistent cleaning sequence - daily cleaning of the high risk frequent-touch points, as per the Centers for Disease Control checklist - the use of sufficient pressure and movement - adherence to manufactures' instructions for product use (i.e. dilutions, contact time).
Product	Use of products that: - ensured disinfectant minimally used for all discharge cleans and for daily cleans of high risk/precautions rooms. - ensured organic matter was removed effectively by using either a 2 in 1 detergent and disinfectant product or a 2-step process - minimally used detergent for routine cleans - used point of care wipes for medical equipment

	- were Therapeutic Goods Administration approved for that use and setting - adhered to manufacturers' instructions for use - were compatible with other product or application materials (e.g. microfiber cloths) in use
Audit	- monthly audit activities across the trial site using DAZO UV fluorescent marker technology, with markers applied and checked by trained site team members - site team auditor to provide regular and consistent audit feedback to cleaning staff - summarised audit results provided to staff and to clinical governance committees.
Communication	- promotion of a team approach and culture of hygiene through hospital wide promotional activities to raise the profile and importance of cleaning in reducing infections and support a culture shift in the perception of environmental services staff - maintaining a positive feedback loop to all staff about the audit results - daily contact between cleaning staff and ward leaders or managers - supporting cleaning staff representation on relevant clinical governance committees

The cleaning bundle was implemented for routine hospital ward cleaning. The bundle was not used for outbreak situations or periodic maintenance cleaning.

Components of the REACH cleaning bundle, for routine and discharge cleaning of clinical ward areas



Monitoring of site changes in infection prevention policies and practices, including screening

The study team used several strategies to monitor cleaning bundle implementation and to ensure they were informed of infection prevention program changes, outbreaks or other issues at each hospital during the trial period. The key strategy was regular email and telephone contact, at least monthly, between the study and site team. All emails and calls were documented, using Microsoft OneNote, and files reviewed at the end of the trial for relevant changes.

In addition, the study team requested a bi-monthly monitoring document be completed by the site team. This aimed to systematically capture changes in any aspect of the infection prevention program, including screening and staffing changes, outbreaks and the bundle implementation compliance. Thirty-nine monitoring episodes occurred, with 62% (n=24) records completed. No site reported program changes or outbreaks that could have impacted the HAI results.

Cleaning bundle timings

Bundle component timings in intervention phase

Bundle components	**Intervention weeks 1-20**										**Intervention weeks 21 - 50**																	
	1-2	3-4	5-6	7-8	9-10	11-12	13-14	15-16	17-18	19-20	21-22	23-24	25-26	27-28	29-30	31-32	33-34	35-36	37-38	39-40	41-42	43-44	45-46	47-48	49-50
Training																									
Technique																									
Product																									
Audit																									
Communication																									

Cleaning bundle - elements & specifications

Implementing the cleaning bundle

Each of the cleaning bundle components had essential (fixed) and flexible elements. This approach aimed to promote consistency across hospitals while allowing the bundle to be tailored and practical in the local context. Following review of each hospital's policies and procedures and analysis of staff survey data, a hospital specific bundle implementation plan was developed to inform and document the local delivery of the intervention.

Environmental cleaning bundle specifications – essential and flexible elements and degree of flexibility

Essential elements	***Flexible elements***	***Degree of flexibility (Extensive, partial, limited, none)***
COMPONENT 1: AUDIT		
UV audit of FTPs		**Partial flexibility**
At least 9 FTPs from CDC list, agreed with site in establishment phase, documented in data schedule, loaded into icombat.	Agreed number and type of FTPs to be audited Nurse cleaned FTPs may be audited as negotiated with the site - recorded / not recorded	Fixed - No variation once trial commences
Audit wards identified during establishment phase as per protocol and loaded into icombat Audit at least 2 x rooms and associated bathrooms in at least 50% of wards and ICU monthly throughout control and intervention phases, with one month between the audits on each ward	Exact number of wards - vary according to total number of wards at site Audit scheduling: may be spread over a whole month or part of a month to reflect auditor staffing	Fixed - No variation once trial commences
Completed by trained and designated site auditor/s or researcher/s	Individual trained auditor/s completing audit	Vary throughout trial - individual trained auditors only

Essential elements	*Flexible elements*	*Degree of flexibility (Extensive, partial, limited, none)*
Use iCombat software for all audit data collection, loaded with agreed FTPs and wards and range of bed numbers for each agreed ward		
Follow randomised schedule of actual cubicle numbers to be audited on each ward each month, as provided by the study team	Four randomised bed numbers provided each month to allow for a particular bed not being available on audit day Single room/shared room selection per ward – aim for one single room and one shared room per ward audit occasion, as per randomised schedule and availability	Fixed – follow schedule as provided
Follow study protocol and data schedule for: - process - choosing wards - timing - recording - use of icombat software		
Feedback/dissemination of UV audit results		**Limited flexibility**
Individual results fed back orally to each ESW for each audit occurrence	Timing of feedback to ESW - needs to fit with ESW availability and workload Nurse cleaned feedback to go to nurse managers as negotiated	Vary throughout trial: immediate or within 24 hours, depending on ESW and roster
Feedback occurrence and time taken recorded in icombat		
Feedback structured positively, follow consistent format		
Room feedback provided only to ESW involved and only about audit outcomes		
Ward level feedback provided to ES managers		
Aggregated feedback to nurse managers		
Site or study teams report aggregated scores to ESW team monthly	Format for reporting - meetings, notice boards, newsletters Frequency of reporting	Fixed - No variation once trial commences: minimum reporting frequency and format; may have additional activities

Essential elements	*Flexible elements*	*Degree of flexibility (Extensive, partial, limited, none)*
Site teams report aggregated scores to clinical governance at least second monthly	Site specific communication mechanisms and committees Frequency of reporting	Fixed - No variation once trial commences: minimum reporting frequency and key committees
ATP audit of FTP		**Limited flexibility**
Completed by REACH team member		
Audit wards identified during establishment phase as per protocol Audit at least 2 x rooms and associated bathrooms in at least 50% of wards and ICU once in control phase and second monthly throughout intervention phases	Exact number of wards - vary according to total number of wards at site	Fixed - No variation once trial commences
Follow agreed algorithm for swabbing process		
Follow study protocol and data schedule for: - choosing wards - timing - recording	Timing negotiated with hospital site	Fixed - No variation once trial commences
COMPONENT 2: PRODUCT		
Disinfectant		**Limited flexibility**
Disinfectant used for all FTP discharge cleans		
Disinfectant used for FTP daily clean in high risk/ infectious/precautions rooms	Site-specific agreed definition “high risk” rooms	Fixed - no variation once trial commences
Use defined concentration/ dilution for whole intervention period		
Use single product type/active ingredient for whole intervention period		
Detergent		**Limited flexibility**
Detergent used in routine cleans	Site-specific agreed definition routine cleans	Fixed - no variation once trial commences
Use defined concentration/ dilution for whole intervention period		

Essential elements	*Flexible elements*	*Degree of flexibility (Extensive, partial, limited, none)*
Use single product type/active ingredient for whole intervention period		
Point of care wipes		**Limited flexibility**
Point of care wipes for medical equipment (except CDI/Norovirus)	Site-specific agreed use as per hospital policy	Fixed - no variation once trial commences
Use similar product type for whole intervention period		
COMPONENT 3: TECHNIQUE		
Defined technique		**Limited flexibility**
Established and documented cleaning sequence/ process	Site specific process	Fixed - no variation once trial commences
Adherence to manufacturers' instructions, MSDS	Availability /access to manufacturers' instructions, MSDS	Fixed - no variation once trial commences
Use of sufficient pressure and movement		
Clearly defined 'who cleans what'	Site specific process	Fixed - no variation once trial commences
Focus on FTP		
COMPONENT 4: COMMUNICATION		
Daily communication ESW/ ward leader		**Limited flexibility**
Align with established process/practice	Extent and nature of established processes may differ between sites Ward leader/ manager role will differ between sites	Fixed - no variation once trial commences
Promote team approach		**Partial/extensive**
Planned series of activities promoting the team approach to cleaning	Type, timing, number of participants, and number of promotional tools/ activities will differ between sites. Hospital systems/ hierarchy/ stakeholders will be different per site	Flexible - to meet minimum expectations and reflect site requirements
Communication reflects project/trial key messages	Standard tools/templates will be modified to site-specific needs	Flexible - to meet site requirement; based on standardised tools, key messages
Representation		**Limited flexibility**

Essential elements	*Flexible elements*	*Degree of flexibility (Extensive, partial, limited, none)*
ESW participation in clinical governance activity	ESW representation level may differ between sites Committee type, structure and timing may differ per site	
COMPONENT 5: TRAINING		
Week 1- 2 of intervention		**Partial flexibility**
Minimal content: **- bundle components** **- impact of environmental hygiene on HAI** **- roles and responsibilities**	Product, technique, audit and communication content to reflect site context and outcomes of ESW surveys, including terminology, language requirements	Fixed for initial delivery, based on site specific requirements
Face - face session timing, structure and delivery to provide opportunity for all ESW staff to participate	Timing, number and type of participants, delivery style, learning activities and number of sessions	Fixed for initial delivery. Some flexibility - depending on participation levels and response, other activities at site
Core suite of training materials, include hands on, image and scenario based learning activities	Adapted to reflect site ESW learning styles and needs and site content requirements	Fixed for initial delivery. Some flexibility - depending on participation levels and response, other activities at site
Timing - week 1 or 2 of intervention phase	Timing, number of participants, and number of repeated sessions will be site specific	Fixed for initial delivery. Some flexibility - depending on participation levels and response, other activities at site
Delivered by REACH training facilitator or project manager		
At least 2 of the site team present		
New staff induction		**Partial flexibility**
Minimal content: **- bundle components** **- impact of environmental hygiene on HAI** **- roles and responsibilities**	Product, technique, audit and communication content to reflect site context and outcomes of ESW surveys, including terminology, language requirements	Fixed for induction session, based on site specific requirements
Adapted from core suite of training materials, include hands on, image and scenario based learning activities	Adapted to reflect site ESW learning styles and needs and site content requirements	Fixed for initial delivery. Some flexibility - depending on participation levels and response, other activities at site
Timing - as part of scheduled induction training		

Essential elements	*Flexible elements*	*Degree of flexibility (Extensive, partial, limited, none)*
Delivered by REACH training facilitator or project manager or trained site team member using REACH provided materials		
Updates		**Partial flexibility**
Content - aligned with minimal and site specific content only	Tailored to site progress/context	Flexible - based on site requirements
Timing - scheduled in response to specific needs identified at trial site and as part of providing feedback	Scheduled in response to identified training needs during trial (audit results, trial progress, other hospital changes)	Flexible - based on site requirements
Led by REACH training facilitator or project manager or site team member	Mode of delivery and linkage with other activities	Flexible - may be face-face, via written materials, at staff meetings

Notes: CDC – Communicable Diseases Centre; ESW- Environmental services worker; FTP – frequent touch point; MSDS – material safety data sheet

Table S1: Baseline infection rates, demographic and patient case mix of participating hospitals.

In Australia, public and private hospitals provide hospital services. Approximately 91% of hospital care in public hospitals is funded by government, 33% in private hospitals. Government funding is funding provided from both the state/territory government and the Commonwealth government. However, state and territory governments largely own and manage public hospitals. Private organisations (for-profit companies, or not-for-profit non-government organisations) mainly own and manage private hospitals.

Hospital	Selected overview of hospital services[+]
1	Acute renal dialysis unit, Alcohol and drug unit, Coronary care unit, Diabetes unit, Emergency department, Infectious diseases unit, Intensive care unit, Major plastic or reconstructive surgery unit, Obstetric services, Oncology unit, Paediatric service
2	Coronary care unit, Emergency services, Intensive care unit, Medical services, Surgical services.
3	Acute renal dialysis unit, AIDS unit, Alcohol and drug unit, Bone marrow transplantation unit, Burns unit, Cardiac surgery unit, Clinical genetics unit, Coronary care unit, Diabetes unit, Emergency department, Infectious diseases unit, Intensive care unit, Major plastic or reconstructive surgery unit, Neonatal intensive care unit, Neurosurgical unit, Obstetric services, Oncology unit,
4	Coronary care unit, Emergency services, Intensive care unit, Medical services, Surgical services.
5	Acute renal dialysis unit, AIDS unit, Cardiac surgery unit, Clinical genetics unit, Coronary care unit, Diabetes unit, Emergency department, Epilepsy centre, Geriatric assessment unit, In vitro fertilisation unit, Infectious diseases unit, Intensive care unit, Liver transplantation unit, Major plastic or reconstructive surgery unit, Neonatal intensive care unit, Neurosurgical unit, Obstetric services, Oncology unit, Paediatric service

6	Acute renal dialysis unit, Alcohol and drug unit, Bone marrow transplantation unit, Cardiac surgery unit, Clinical genetics unit, Coronary care unit, Diabetes unit, Emergency department, Epilepsy centre, Infectious diseases unit, Intensive care unit, Major plastic or reconstructive surgery unit, Obstetric services, Oncology unit, Paediatric service, Psychiatric unit.
7	Acute renal dialysis unit, Coronary care unit, Diabetes unit, Emergency department, Geriatric assessment unit, Intensive care unit, Obstetric services, Oncology unit, Paediatric service, Psychiatric unit, Rehabilitation unit.
8	Acute renal dialysis unit, AIDS unit, Alcohol and drug unit, Bone marrow transplantation unit, Cardiac surgery unit, Coronary care unit, Diabetes unit, Emergency department, Geriatric assessment unit, Infectious diseases unit, Intensive care unit, Neonatal intensive care unit, Neurosurgical unit, Obstetric services, Oncology unit, Paediatric service, Psychiatric unit, Rehabilitation unit, Renal transplantation unit.
9	Acute renal dialysis unit, Acute spinal cord injury unit, Alcohol and drug unit, Bone marrow transplantation unit, Cardiac surgery unit, Coronary care unit, Diabetes unit, Emergency department, Infectious diseases unit, Intensive care unit, Liver transplantation unit, Major plastic or reconstructive surgery unit, Neurosurgical unit, Oncology unit, Psychiatric unit, Rehabilitation unit, Renal transplantation unit.
10	Acute renal dialysis unit, Cardiac surgery unit, Coronary care unit, Diabetes unit, Domiciliary care unit, Emergency department, Geriatric assessment unit, Infectious diseases unit, Intensive care unit, Major plastic or reconstructive surgery unit, Obstetric services, Oncology unit, Paediatric service, Psychiatric unit.
11	Acute renal dialysis unit, Acute spinal cord injury unit, Alcohol and drug unit, Bone marrow transplantation unit, Burns unit, Cardiac surgery unit, Coronary care unit, Diabetes unit, Emergency department, Geriatric assessment unit, Heart transplantation unit, Infectious diseases unit, Intensive care unit, Maintenance renal dialysis unit, Major plastic or reconstructive surgery unit, Neonatal intensive care unit, Obstetric services, Oncology unit, Paediatric service, Psychiatric unit, Rehabilitation unit, Renal transplantation unit.

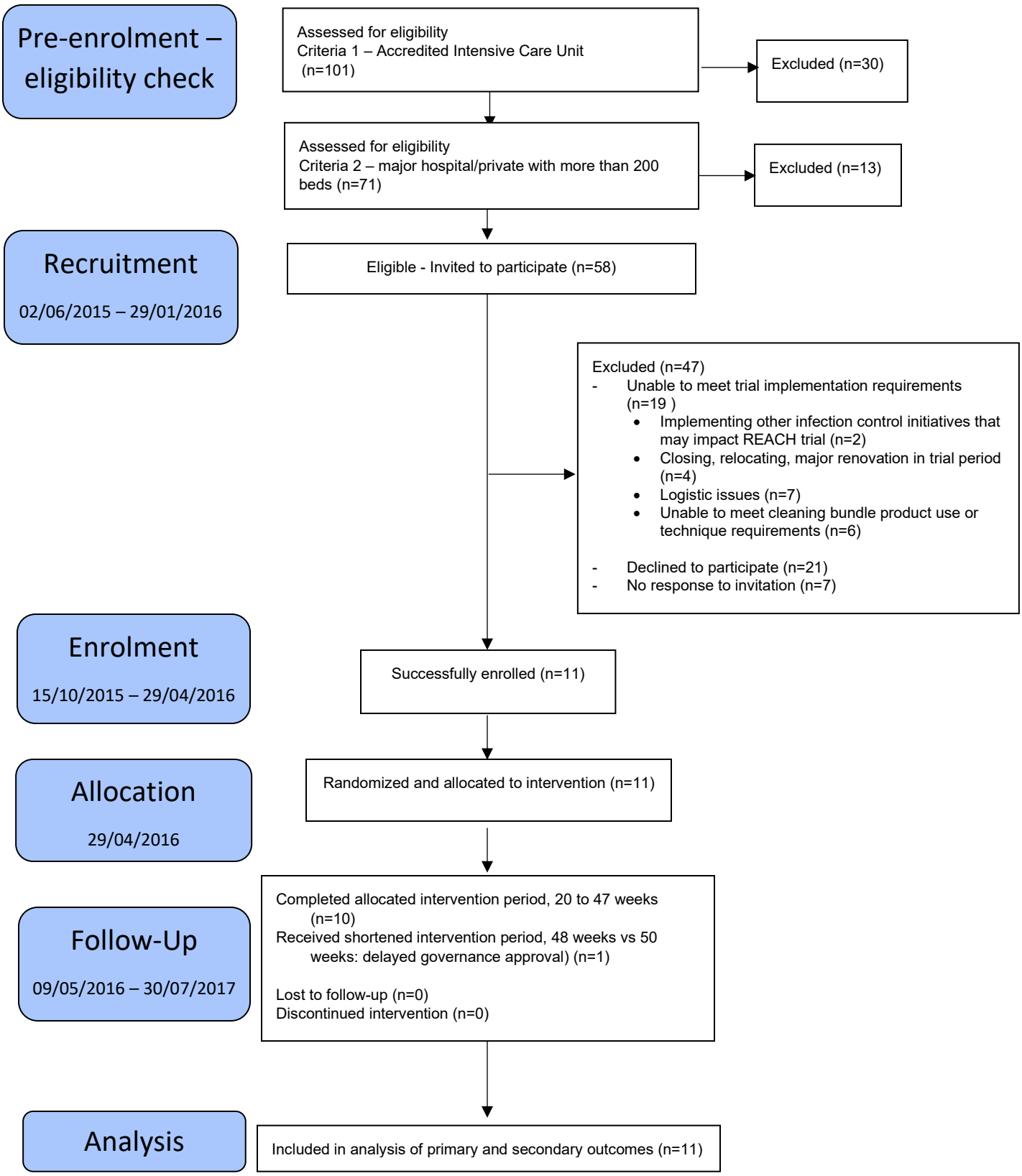
Notes: Data source was the Australian Institute of Health and Welfare, via the MyHospitals website. Participating hospitals (alphabetical order): Box Hill Hospital; Fiona Stanley Hospital; Flinders Medical Centre; Holy Spirit Northside Private Hospital; John Hunter Hospital; Launceston General Hospital; Northern Hospital; Princess Alexandra Hospital; Royal Brisbane and Women's Hospital; St Andrew's War Memorial Hospital; University Hospital, Geelong;

Baseline characteristics of participating hospitals at the start of the REACH Study.

Overnight beds^	**Patient admissions[+] (2015/6)**	**ED presentations[+] (2015/16)**	**Number of cleaners[%]**	**Healthcare associate infection rates per 10,000 occupied bed days (2015/16)**		
				VRE	SAB	CDI
600	65,027	60,642	115	2·89	1·57	2·01
227	N/A	N/A	40	0·24	1·69	0·00
930	112,569	77,323	220	1·62	0·88	0·44
252	N/A	N/A	45	0·59	0·23	0·00
500	71,665	82,756	320	2·37	1·05	0·55
394	73,533	67,505	198	3·16	0·89	0·42
350	44,300	43,788	141	1·21	0·98	1·21
921	79,063	76,474	168	2·29	1·36	2·02
825	104,238	60,430	230	1·44	0·75	0·06
351	58,847	85,007	102	5·64	0·51	0·67
783	102,038	103,234	150	6·80	1·13	0·27

Note: SAB = *Staphylococcus aureus* bacteraemia. VRE = vancomycin-resistant enterococcus clinical isolates. CDI = *Clostridium difficile* infections Notes: ^ Approximate number of overnight beds. ED = emergency department. + Data source was the Australian Institute of Health and Welfare, via the *MyHospitals* website. Most current available data used. N/A = Not available. [%] number of individual cleaners (not full time equivalent).

Figure S1. Flow chart of participation



Note: Eligible hospitals were contacted using a variety of methods including email and verbal discussions with infection control teams. We examined the unadjusted *S. aureus* bacteraemia rate for excluded hospitals. These data were publically available for eight hospitals, with a rate of 1.01 per 10,000 occupied bed days (95% CI 0.82-1.18). The unadjusted *S. aureus* bacteraemia was 1.02 per 10,000 occupied bed days in the hospitals included in our study, pre-intervention phase, see Table S2.

Table S2. Unadjusted infection rates by hospital, pre-intervention Vs intervention periods

	Pre-intervention							Intervention							
		CDI		SAB (MRSA)		VRE			CDI		SAB (MRSA)		VRE		
Hospital	**OBD**	**N**	**Rate**	**N**	**Rate**	**N**	**Rate**	**OBD**	**N**	**Rate**	**N**	**Rate**	**N**	**Rate**	**Weeks**
H18	519680	81	1·56	47 (11)	0·90	19	0·37	288317	50	1·73	24 (6)	0·83	5	0·17	44
H27	455979	113	2·48	61 (7)	1·34	78	1·71	130426	19	1·46	15 (3)	1·15	16	1·23	29
H33	224044	100	4·46	19 (5)	0·85	9	0·40	48313	11	2·28	7 (5)	1·45	0	0·00	23
H42	275016	99	3·60	28 (2)	1·02	17	0·62	105211	31	2·95	10 (0)	0·95	2	0·19	35
H45	597943	81	1·35	46 (6)	0·77	3	0·05	144828	16	1·10	8 (1)	0·55	0	0·00	26
H46	127476	8	0·63	2 (0)	0·16	0	0·00	58441	6	1·03	1 (1)	0·17	0	0·00	41
H51	218579	29	1·33	18 (5)	0·82	34	1·56	74167	14	1·89	7 (2)	0·94	14	1·89	32
H58	280066	63	2·25	33 (8)	1·18	15	0·54	117023	30	2·56	8 (2)	0·68	6	0·51	38
H70	115188	5	0·43	15 (2)	1·30	0	0·00	68338	5	0·73	6 (0)	0·88	0	0·00	47
H78	224067	67	2·99	30 (7)	1·34	40	1·79	144594	49	3·39	15 (1)	1·04	6	0·41	48
H91	496402	322	6·49	63 (13)	1·27	15	0·30	87477	47	5·37	8 (1)	0·91	1	0·11	20

Notes: Rate = number of infections per 10,000 occupied bed days. CDI = Hospital onset *Clostridium difficile* infection; SAB = Healthcare associated *Staphylococcus aureus* bacteraemia; VRE = Healthcare associated vancomycin resistant enterococcus infection; OBD = occupied bed days. Pre-intervention and Intervention period defined to be consistent with as per protocol analysis of HAI infection rates. Pre-intervention = Combined historical data, establishment period, eight week control period and first four weeks of implementation. Intervention = greater than first four weeks of implementation. For total reported SAB infections, the number of MRSA infections is listed in brackets. Hospital are numbered differently in this table, to avoid identification of hospitals.

Table S3. Unadjusted breakdown of vancomycin resistant enterococcus infection, by hospital, pre-intervention Vs intervention periods

	Pre-intervention				Intervention			
Hospital	**Blood**	**Urine**	**Bone**	**Sterile devices**	**Blood**	**Urine**	**Bone**	**Sterile devices**
H18	5	14	0	0	1	4	0	0
H27	7	70	0	1	4	11	0	1
H33	6	3	0	0	0	0	0	0
H42	7	8	1	1	0	2	0	0
H45	2	1	0	0	0	0	0	0
H46	0	0	0	0	0	0	0	0
H51	4	30	0	0	2	12	0	0
H58	11	4	0	0	5	1	0	0
H70	0	0	0	0	0	0	0	0
H78	23	16	1	0	3	3	0	0
H91	5	10	0	0	0	1	0	0
Overall	70	156	2	2	15	34	0	1

Note: Hospital are numbered differently in this table, to avoid identification of hospitals.

Table S4. Meta-analysis estimate of effect of intervention across infections

Model	Fixed effect (Intervention)			RR			% change			p-value
	Estimate	95% CI		Estimate	95% CI		Estimate	95% CI		
		Lower	Upper		Lower	Upper		Lower	Upper	
Model 1	-0·06	-0·22	0·09	0·94	0·80	1·09	-5·82	-19·75	9·42	0·4246
Model 2	0·05	-0·11	0·20	1·05	0·90	·122	5·13	-10·42	2·214	0·5593

Notes: Model 1= Linear calendar time and a binary switch to intervention 4 weeks after Intervention start date. Model 2: Linear calendar time and a binary switch to intervention, 8 weeks after Intervention start date (one month delay). Fixed effects meta-analysis was used to combine estimated intervention effect for all three infections, with the result in the form of a weighted average (Fixed effect: Estimate) and 95% confidence interval (Fixed effect, CI). This result was then transformed to produce a relative risk (RR) and percentage change compared to the pre-intervention phase (% change).

Sensitivity analysis

The introduction of a delayed intervention effect did not improve goodness of fit for *S. aureus* bacteraemia or vancomycin-resistant enterococcus infection, with a minor improvement for *C. difficile* infection (Table S5). The leave-one-out analysis did not identify any influential hospitals with respect to *C. difficile* infection or *S. aureus* bacteraemia (Table S6). Variation in calculated Cook's distances was observed for vancomycin-resistant enterococcus infection, but this this positively correlated with baseline incidence rates.

Table S5: Model comparison by AIC

Healthcare associated infection	**Model 1**	**Model 2**
Clostridium difficile infection	2988	2986
Staphylococcus aureus bacteraemia	1901	1902
Vancomycin-resistant enterococcus infection	1246	1248

Note: For *Clostridium difficile* infection, Model 2 has a marginally better fit relative to Model 1. However, given the small difference and for consistency, Model 1 was used in the analysis.

Table S6: Revised parameter estimates and standard errors for each hospital left out of the analysis

Model 1: Linear calendar time (week number scaled as 0:1) + binary switch to intervention 4 weeks after Intervention start date

Hospital excluded	CDI				SAB				VRE				Cooks distance by Site			Intervention time (weeks)
	Week no (scaled)		Intervention		Week no (scaled)		Intervention		Week no (scaled)		Intervention					
	Est.	SE	Est.	SE	Est.	SE	Est.	SE	Est.	SE	Est.	SE	CDI	SAB	VRE	
H18	-0·36	0·14	0·05	0·11	0·22	0·25	-0·30	0·17	0·06	0·31	-0·55	0·22	0·08	0·17	0·19	44
H27	-0·33	0·15	0·11	0·10	-0·03	0·26	-0·15	0·17	-0·23	0·38	-0·52	0·27	0·12	0·08	0·14	29
H33	-0·28	0·15	0·08	0·10	0·07	0·24	-0·25	0·16	-0·01	0·30	-0·52	0·22	0·17	0·04	0·10	23
H42	-0·32	0·15	0·08	0·10	0·01	0·24	-0·19	0·17	-0·20	0·31	-0·41	0·22	0·04	0·02	0·03	35
H45	-0·33	0·15	0·08	0·10	0·14	0·25	-0·23	0·17	-0·16	0·30	-0·46	0·22	0·02	0·10	0·13	26
H46	-0·37	0·14	0·08	0·10	0·03	0·23	-0·18	0·16	-0·17	0·31	-0·46	0·22	0·10	0·40	0·13	41
H51	-0·36	0·14	0·07	0·10	0·17	0·24	-0·27	0·16	-0·39	0·32	-0·54	0·25	0·04	0·09	0·58	32
H58	-0·33	0·14	0·04	0·10	-0·09	0·24	-0·09	0·17	-0·17	0·31	-0·51	0·23	0·04	0·15	0·05	38
H70	-0·32	0·14	0·06	0·10	0·09	0·24	-0·20	0·16	-0·18	0·30	-0·45	0·22	0·16	0·03	0·13	47
H78	-0·30	0·14	0·02	0·10	0·04	0·24	-0·18	0·17	-0·21	0·32	-0·25	0·23	0·11	0·04	0·49	48
H91	-0·44	0·18	0·15	0·12	-0·11	0·26	-0·09	0·17	-0·26	0·31	-0·40	0·22	0·26	0·17	0·03	20

Note: SAB = Healthcare associated *Staphylococcus aureus* bacteraemia; VRE = Healthcare associated vancomycin resistant enterococcus infection. Est.= estimate; SE = standard error. Hospital are numbered differently in this table, to avoid identification of hospitals.

Table S7: Sub-group analysis

Model 1: Linear calendar time (week number scaled as 0:1) + binary switch to intervention 4 weeks after Intervention start date

Infection	Parameter	Estimate	SE	z-value	p-value	RR			% change (100*(RR-1))		
						Estimate	95% CI (lower)	95% CI (upper)	Estimate	95% CI (lower)	95% CI (upper)
Methicillin sensitive SAB	Intercept	-0·31	0·14	-2·12	0·0340						
	Week no (scaled)	0·21	0·26	0·83	0·4083	1·23	0·74	2·05	23·37	-25·89	105·36
	Intervention	-0·30	0·18	-1·70	0·0891	0·74	0·52	1·05	-25·92	-47·94	5·42
Methicillin resistant SAB	Intercept	-1·47	0·24	-6·10	<0·0001						
	Week no (scaled)	-0·66	0·55	-1·20	0·2310	0·52	0·18	1·52	-48·31	-82·41	51·89
	Intervention	0·25	0·37	0·67	0·5020	1·28	0·62	2·65	28·40	-37·82	165·17

Note: Models fitted separately to MSSA, MRSA. SAB = Healthcare associated *Staphylococcus aureus* bacteraemia; VRE = Healthcare associated vancomycin resistant enterococcus (clinical isolates only)

Table S8: Florescent Gel Audits: Results by Hospital summarized by trial period (Control, Intervention)

Hospital	Control			Intervention			Rooms audited			Length of Intervention
	FTPs audited	Clean	%	FTPs audited	Clean	%	Number of bed audits	Total beds	%	Weeks
H18	479	94	19·62	2369	1227	51·79	380	930	40·86	44
H27	442	165	37·33	1784	1043	58·46	224	921	24·32	29
H33	416	318	76·44	1376	890	64·68	143	351	40·74	23
H42	481	186	38·67	1747	1105	63·25	178	394	45·18	35
H45	603	332	55·06	2077	1591	76·60	324	825	39·27	26
H46	222	134	60·36	1685	1384	82·14	135	252	53·57	41
H51	397	83	20·91	1490	944	63·36	277	350	79·14	32
H58	543	179	32·97	2708	1922	70·97	255	500	51·00	38
H70	241	26	10·79	1402	1015	72·40	127	227	55·95	47
H78	374	120	32·09	1303	586	44·97	144	600	24·00	48
H91	936	484	51·71	2368	1885	79·60	252	783	32·18	20
Total	5134	2121	41·31	20309	13592	66·90	2439	6133	39·77	

Notes: FTP = Frequent touch points. Analysis included monthly audit data up to 50 weeks since start of control period. Two sites (70,78) had an additional two audits past 50 weeks which were not included. Statistics include the number of gel dots audited and the number of clean sites (Clean) and corresponding percentages. Hospitals are numbered differently in this table, to avoid identification of hospitals.

Table S9: Florescent Gel Audits: Frequent touch points results by room

Hypothesis	Odds ratio	95% CI		p-value
	Estimate	(lower)	(upper)	
Bathroom: Intervention vs Control	2·07	1·83	2·34	<0·0001
Bedroom: Intervention vs Control	1·87	1·68	2·09	<0·0001
Bedroom vs Bathroom: Intervention vs Control	0·90	0·77	1·07	0·6367
Bathroom: Intervention Time	1·40	1·34	1·47	<0·0001
Bedroom: Intervention Time	1·31	1·26	1·36	<0·0001
Bedroom vs Bathroom: Intervention Time	0·51	0·88	0·99	0·1061

Table S10: Florescent Gel Audits: Model-based predictions over intervention period

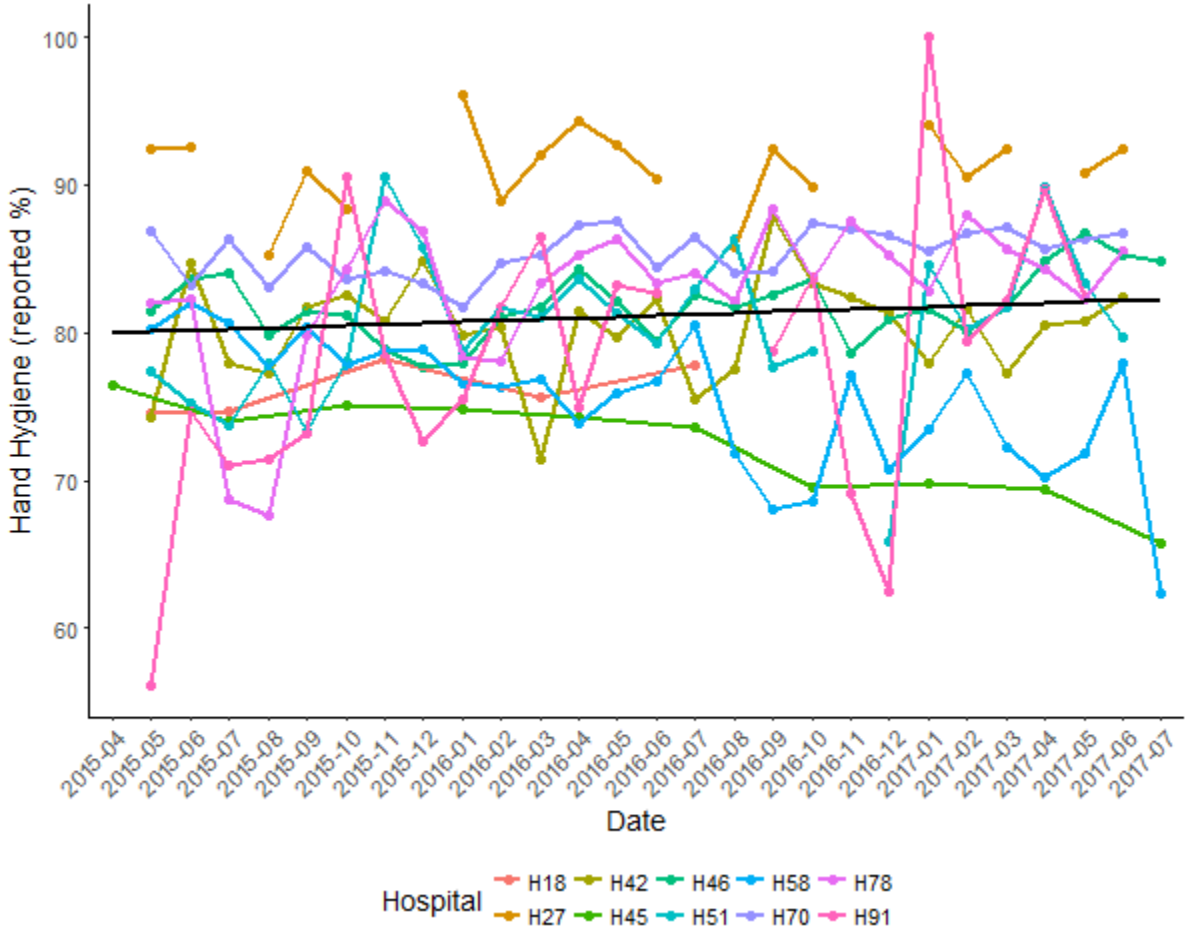
	% Frequent touch points cleaned					
Room	**Control Mean (95% PI)**	**Weeks since intervention start Mean (95% PI)**				
		0	**10**	**20**	**30**	**40**
Bathroom	42·6 (4·04, 44·7)	60·6 (58·5, 62·7)	68·3 (67·2, 69·5)	75·1 (74·2, 76·0)	80·9 (79·6, 82·0)	8·56 (84·0, 86·9)
Bedroom	36.8 (35·1, 38·7)	52·2 (50·2, 54·2)	58·9 (5·77, 6·00)	65·2 (64·3, 66·1)	71·1 (6·98, 7·23)	76.3 (74·6, 77·9)

Note: 95% bootstrapped prediction intervals are based on 1000 bootstrap replicates. PI: Prediction interval.

Table S11: Models used to evaluate the effect of the intervention on the proportion of frequent touch points deemed clean.

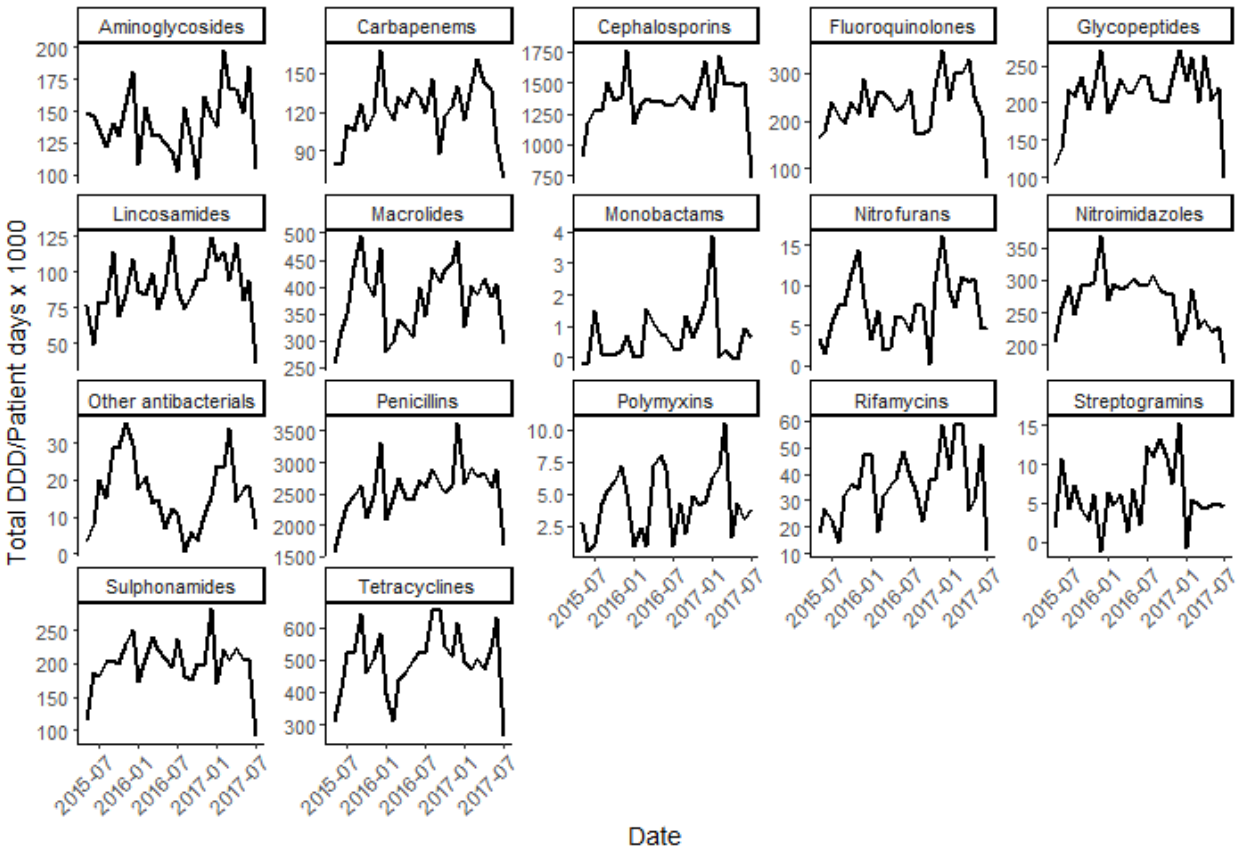
Model description	AIC
No intervention effect	5204
A simple binary intervention (yes/no)	3921
A linear intervention using the time since intervention (time scaled)	3789
Binary intervention + Linear trend	3529

Figure S2. Hand hygiene compliance



Note: Hand hygiene compliance was monitored in a standardized manner, according to the World Health Organisation's 5 moments of hand hygiene. Australia has a well-established hand hygiene program, audited in a consistent manner between hospitals.

Figure S3. Antimicrobial usage data.



Note: DDD = Daily defined dose. Data provided is aggregated data for nine of the 11 hospitals participating in the study. Data from two hospitals was not included as it was not available.

Table S12. Total monthly antimicrobial usage by hospital, pre-intervention Vs intervention periods

	Pre-intervention					Intervention				
Hospital	**Mean**	**Min**	**Max**	**25%**	**75%**	**Mean**	**Min**	**Max**	**25%**	**75%**
H18	522·0	46·8	776·5	532·9	647·7	558·1	519·8	657·1	532·2	565·3
H27	1046·0	858·1	202·03	954·5	1051·6	1495·2	973·4	2157·6	1089·7	2127·2
H33	1026·2	782·9	1220·5	100·47	1062·4	1057·2	994·8	1112·5	1029·6	1088·5
H42	448·5	340·6	726·4	374·5	462·5	682·1	628·1	764·7	650·7	702·6
H51	1178·3	854·6	1499·6	1066·8	1320·9	1159·3	940·8	1303·9	1124·5	1250·1
H58	897·7	750·4	1085·8	828·5	963·9	1115·7	925·0	2091·3	956·6	1006·0
H78	956·0	680·6	1238·3	817·6	1105·5	829·3	224·1	1015·2	826·0	965·6
H91	977·7	953·4	1001·9	965·6	989·8	1227·8	1227·8	1227·8	1227·8	1227·8
All hospitals combined	4613·9	46·8	785·83	3523·2	6181·8	3849·8	73·21	6765·1	2089·6	5957·3

Notes: Reported summary statistics are for monthly total daily defined dose (DDD) per 1,000 occupied bed days. The pre-intervention and intervention periods are defined as per the analysis of infection rates. Hospitals are numbered differently in this table, to avoid identification of hospitals. Antimicrobials included in this analysis are those listed in Figure S3. Min=Minimum. Max = Maximum. Distribution in the pre-intervention and intervention periods are similar.

Assessment of Pragmatism against the PRECIS-2 tool

An assessment of pragmatism for the REACH study was undertaken against the PRagmatic-Explanatory Continuum Indicator (PRECIS-2) tool. [1] Independent reviews were undertake by two members of the study team, one Chief Investigator (Professor Brett Mitchell) and the Project Manager (Alison Farrington). Where any discrepancies occurred, another Chief Investigator (A/Professor Lisa Hall) made the final decision. Each domain is scored using a 5-point Likert scale (1= very explanatory, 5 = very pragmatic). In pragmatic trials the comparator is usual care.[1]

Dimension	**Domain explanation**[1]	**Assessment evidence**	**Final score**
Eligibility	To what extent are the participants in the trial similar to those who would receive this intervention if it was part of usual care?	Hospital participants (score = 3) limited to: - only large hospitals, - those able to implement an intervention - able to be accessed by trial team already collecting HAI data Environmental services staff at each hospital: all environmental services staff with a role in ward cleaning (usual care) eligible (score = 5)	4
Recruitment	How much extra effort is made to recruit participants over and above what would be used in the usual care setting to engage with patients?	Hospitals: - some stratification applied to ensure multiple and varied hospitals: public/private, size range, location (11 hospitals in 6 states) Environmental services staff: - included those with a usual role in hospital ward cleaning, working day/evening/night - targeted invite and incentive for some activities, all within usual work requirements and setting, easily achievable.	4

		High potential for implementation in other hospitals as usual care (cleaning).	
Setting	How different are the settings of the trial from the usual care setting?	Identical setting to usual hospital cleaning environment/setting, and to where results are to be applied: - sample represented 11 major hospitals - a range of funding, locations and environmental services staff workforce structures and roles, and variation in cleaning practices and processes.[2,3] Not all types of hospital/patient case-mix included; could generalise results as used implementation science framework.	4
Organization	How different are the resources, provider expertise, and the organisation of care delivery in the intervention arm of the trial from those available in usual care?	The intervention was proactively aligned into usual organisation of care (hospital cleaning practice): - minimal additional resource implications in the setting - difference in some sites between usual and intervention practice as this was actually part of the intervention - the extent of practice change required was very pragmatic as reflected each site's context. In some sites used different resources to those usually available; in others only used resources currently available.	4
Flexibility in delivery	How different is the flexibility in how the intervention is delivered and the flexibility anticipated in usual care?	Flexibility similar to usual care (hospital cleaning) and consistent with that of introducing an intervention in hospital cleaning:	4

		- intervention included fixed and flexible elements. - delivery of interventions was tailored, based on a contextual assessment. included different numbers of staff at each hospital, with variation in experience and training - asked not to introduce other cleaning practice change; some requirements around timing	
Flexibility in adherence	How different is the flexibility in how participants are monitored and encouraged to adhere to the intervention from the flexibility anticipated in usual care?	Consistent with usual care (hospital cleaning): - no special measures to enforce engagement or compliance were included in the stud - no penalties for non-compliance compliance with elements of the cleaning bundle were assessed and feedback provided to staff (DAZO fluorescent marking gel and ultraviolet light assessment)	4
Follow-up	How different is the intensity of measurement and follow-up of participants in the trial from the typical follow-up in usual care?	No more follow-up than would be expected in usual care (hospital cleaning) for the majority of hospitals, except those non or partially compliant with evidence based practice: - Follow up responded to local issues and was within usual range for a cleaning practice change. - Reminders provided about audit timings. - Two monthly monitoring and general contact from REACH study team.	4

Primary outcome	To what extent is the trial's primary outcome directly relevant to participants?	Highly important, obvious and valued outcome to the hospital and to cleaning staff participants: Includes the incidence of a variety of healthcare associated infections and the cost effectiveness of the intervention (not evaluated in this paper but is part of the trial). Includes changes in knowledge, attitudes and practice (DAZO fluorescent marking gel and ultraviolet light assessment) of environmental cleaning staff.	5
Primary analysis	To what extent are all data included in the analysis of the primary outcome?	All available data included regardless of adherence or issues. No special allowance in the analysis for non-adherence, practice variability.	5

1. Loudon K, Treweek S, Sullivan F, Donnan P, Thorpe KE, Zwarenstein M. The PRECIS-2 tool: designing trials that are fit for purpose. BMJ : British Medical Journal. 2015;350.

2. Hall L, Farrington A, Mitchell BG, Barnett AG, Halton K, Allen M, et al. Researching effective approaches to cleaning in hospitals: protocol of the REACH study, a multi-site stepped-wedge randomised trial. Implementation Science. 2016;11(1):44.

3. Mitchell BG, Farrington A, Allen M, Gardner A, Hall L, Barnett AG, et al. Variation in hospital cleaning practice and process in Australian hospitals: A structured mapping exercise. Infection, Disease & Health. 2017;22(4):195-202.

Statistical methods supplement

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Purpose

In this supplement, we provide details of the statistical methods for the analysis of infection rates and fluorescent gel audits. Additional model assessment results are also reported. Unless otherwise stated, analysis were conducted using the lme4 package in R.

Primary outcome: Healthcare-associated infection (HAI) rates

Descriptive statistics

For each infection, reported cases and occupied bed days from all trial hospitals were combined for the calculation of unadjusted infection rates per 10,000 occupied bed days. Unadjusted rates were calculated separately for the pre-intervention and intervention periods, with definitions of each period as per the protocol analysis of HAI rates.

Model description

Each infection type was modeled separately using a Poisson generalized mixed model, to quantify the effect of the intervention on changes in HAI rates. Models were fitted using the glmer function available in lme4.

For infection type k, observed data were available as weekly numbers of reported infections, with y_{ijk} equal to the number of infections reported by hospital i in week j. These data were assumed to follow a Poisson distribution with rate parameter λ_{ijk}, which was defined per 10,000 occupied bed days (OBD).

A canonical log link function was assumed to relate the dependent variable to the linear predictor. The linear predictor consisted of an offset, a random intercept and fixed effects, adapted from Barnett et al. (2014):

$$\log(\lambda_{ijk}) = \log\left(\frac{OBD_{ij}}{10000}\right) + \beta_{0k} + u_{ik} + \beta_{1k}t_j + \delta_k x_{ij}$$

The random intercept $u_{ik} \sim \mathcal{N}(0, {\omega_k}^2)$ was included to account for between-hospital variation in infection rates. The linear term $\beta_{1k}t_j$ quantified the effect of calendar time, to account for any underlying temporal trends in infection rates not associated with the intervention. To ensure model convergence, t_j was scaled between 0 and 1, as a function of the number of weeks since the start of data collection; i.e. $t_j = \{week\}_j/116$, where $week = 0, 1, \ldots, 116$. Given this definition, the percentage change in relative risk for time, $100(e^{\beta_{1k}} - 1)$, represented the percentage change in infection rates over the study period.

The fixed effect δ_k characterized the effect of the intervention after adjusting for between-hospital differences in baseline rates and time. This effect therefore reflected the expected within-hospital change attributable to the intervention, and was assumed constant across all hospitals. The transition of each hospital from the pre-intervention to the intervention period was described by the binary independent variable x_{ij} that was equal to 0 for the pre-intervention period and equal to 1 once hospital i switched to the intervention period. The intervention commencement time for hospital i was denoted by T_i.

The timing of the binary switch to the intervention period was evaluated using two models, as per the methodology in the published protocol (Hall et al. (2015)). The first model (Model 1) assumed that the intervention effect came into effect after the first full month (4 weeks) of the intervention:

$$x_{ij} = \begin{cases} 1 & \text{if } t_j \geq (T_i + 4), \\ 0 & \text{otherwise} \end{cases}$$

The second model (Model 2) assumed a further four week delay in the intervention, corresponding to 8 weeks since each hospital's intervention start date.

$$x_{ij} = \begin{cases} 1 & \text{if } t_j \geq (T_i + 8), \\ 0 & \text{otherwise} \end{cases}$$

Model assessment

For each of the three infections, Models 1 and 2 were compared for relative goodness of fit using Akaike's Information Criterion (AIC). Smaller values of AIC were indicative of an improvement in model goodness of fit. To maintain consistency in the definition of the intervention effect, we chose the model with the best goodness of fit for at least 2 out of 3 infections.

To determine if the fitted models represented an adequate fit to the data, the autocorrelation function was applied to the deviance residuals, to check for any unmodelled temporal correlation. Posterior predictive simulation (Bates et. al, 2014) was also used to compare the total observed number of infections with model-based predictions, for both the pre-intervention and intervention periods. Functions to complete these assessments were available in the stats package in R (acf for autocorrelation function; simulate for predictive simulation).

Meta-analysis

Estimated intervention effects were combined using fixed-effects meta-analysis, as an overall measure of intervention effectiveness. Given an estimate of δ_k for each infection type, this combined estimate took the form:

$$\hat{\delta}_0 = \frac{\sum_{k=1}^{3} w_k \hat{\delta}_k}{\sum_{k=1}^{3} w_k}$$

where each fixed effect was weighted by its standard error by $w_k = 1/(SE(\delta_k))^2$. The corresponding 95% confidence interval (CI) was equal to $\hat{\delta}_0 \pm 1 \cdot 96\sqrt{(1/\sum_{k=1}^{3} w_k)}$, which was deemed to be statistically significant if it did not include zero.

Prediction of population level trends in infection rates

Parametric bootstrapping was used to compute predicted trends in infection rates over a two-year period. Using the bootMer function available in lme4, 1000 bootstrap replicates were generated using

residual resampling. Resulting predictions across bootstrap replicates were summarized in terms of a mean estimate and 95% prediction interval. The ability to calculate prediction intervals under bootstrapping provided a measure of uncertainty around the predicted trend for each infection type.

Sensitivity analysis

A number of sensitivity analyses were conducted to assess the robustness of parameter estimates to changes in the data and model assumptions. The results of this analysis are presented in the Supplementary Table S6.

The influence of each hospital on parameter estimation was examined using the `influence.me' package in R, which allowed the calculation of leave-one-out parameter estimates and Cook's distance at the hospital level (Nieuwenhuis et. al, 2012). The calculation of Cook's distance was for all parameter estimates combined.

Secondary outcome: Fluorescent Gel Audits

Monthly audit results were analyzed using a Binomial GLMM, where the response variable was the number of dots successfully removed, out of the total number of gel dot locations. The location of each frequent touch point was categorized by room (Bedroom Bathroom), which was as an independent variable. Similar to the analysis of infection rates, a random intercept was included for each hospital to account for baseline differences in cleaning performance.

A logit link related the success probability for hospital i at audit time j, for room type k. The linear predictor took the general form (excluding interaction terms):

$$log\left(\frac{p_{ijk}}{1-p_{ijk}}\right) = v_i + \beta_0 + \beta_1 x_{ijk} + \{\text{Intervention effect}\}_{ij}$$

The independent variable x_{ijk} was equal for 0 or 1 for Bathroom and Bedroom FTPs, respectively. The random intercept for each hospital (v_i) was assumed to be Normally distributed with unknown variance σ_v^2.

Three models were tested that varied in terms of specification of the intervention effect. A null model that assumed no intervention effect was also tested. For each model, we define t_{ij} as the time of audit j, measured in weeks since the commencement of the control period at hospital i. In contrast to the analysis of infection rates, an additional subscript (i) was included to index intervention time, as the time of completion of each audit varied slightly between hospitals.

The first intervention model assumed a step change at the commencement of the intervention. This model therefore assumed an immediate improvement in FTP cleaning:

$$\{\text{Intervention effect}\}_{ij} = \begin{cases} 0 & \text{if } t_{ij} < T_i, \\ \gamma & \text{if } t_{ij} \geq T_i \end{cases}$$

The second intervention model assumed a constant linear change over course of intervention:

$$\{\text{Intervention effect}\}_{ij} = \begin{cases} 0 & \text{if } t_{ij} < T_i, \\ \delta(t_{ij} - T_i) & \text{if } t_{ij} \geq T_i \end{cases}$$

The third intervention model combined a step change at the start of the intervention with a linear trend over intervention time. This model therefore assumed an immediate change at the start of the intervention, with further change over the course of each hospital's intervention period:

$$\{\text{Intervention effect}\}_{ij} = \begin{cases} 0 & \text{if } t_{ij} < T_i, \\ \gamma + \delta(t_{ij} - T_i) & \text{if } t_{ij} \geq T_i \end{cases}$$

All three intervention models assumed a constant success probability for the control period. This was due to data only being collected at two time points for each hospital, meaning there was insufficient data to model a separate temporal trend for the control period. Trend schematics for each model tested are illustrated in Figure S4.

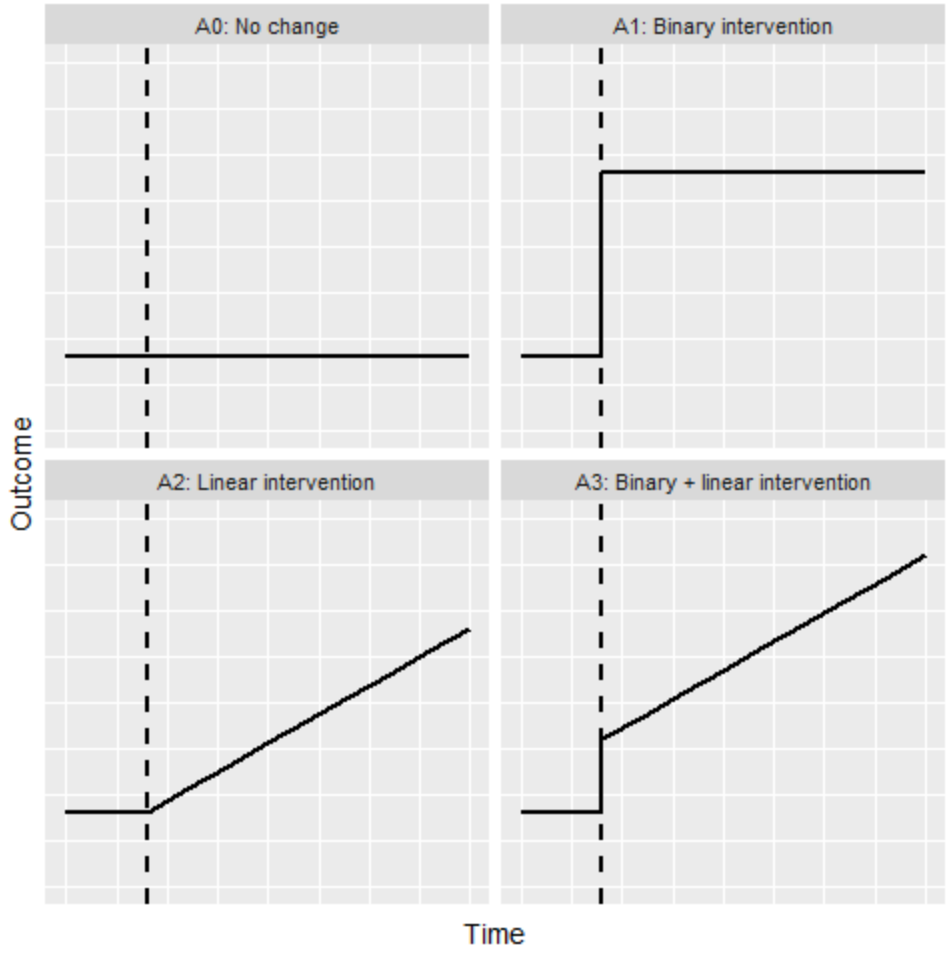

Figure S4: Summary of models tested in the analysis on monthly audit data, focusing on the trend in cleaning performance over time. Models A1, A2 and A3 correspond to the first, second and third intervention model described in text. Model A0 corresponds to the null model (no intervention effect). The lines show hypothetical effects.

Interaction terms between intervention effect(s) and room were also tested, corresponding to the null hypothesis that the intervention effect was consistent for both bathroom and bedroom FTPs.

Each model included data from two control audits and up to ten intervention audits, the latter depending on each hospital's randomization to the intervention.

Model assessment

Models were compared using AIC, with the selected model corresponding to the lowest AIC.

For the selected model, a similar leave-one-hospital-out analysis was conducted to assess the robustness of parameter estimates. This process involved re-fitting the model multiple times, leaving one hospital out each time. Parameter estimates and corresponding standard errors from each iteration were stored and Cook's distances calculated, in order to identify potential influential hospitals with respect to changes in overall audit results.

Prediction of overall trends in FTP cleaning

Parametric bootstrapping was used to summarize the predicted trend in outcomes over time. For both bathroom and bedroom, we calculated the mean % FTPs cleaned during the control period, at the start of the intervention period, and for every 10 weeks of intervention. Estimates were based on 1,000 bootstrap replicates, with uncertainty quantified using 95% prediction intervals.

Extension of linear intervention to first-order fractional polynomial

Improvements in model fit considered transformations of intervention time using first-order fractional polynomials (Royston and Altman, 1994). Each fractional polynomial tested a different transformation of intervention time $(t_{ij} - T_i)^p$, where p was chosen from the list: $\{-2, -1, -0 \cdot 5, 0, 0 \cdot 5, 1, 2, 3\}$. This set of powers included the original linear transformation $(p = 1)$ and $p = 0$, which corresponded to a log transformation: $(t_{ij} - T_i)^0 = log(t_{ij} - T_i)$. Model A3 was extended to accommodate this analysis, with evidence of improved model fit determined by changes in AIC and differences in model predictions over the course of the intervention.

Primary outcome: Additional model results

Additional model results for infection rates are based on Model 1, which was selected as the best fit for two out of three infection types (SAB, VRE).

Estimates of the random effects variance indicated that between-hospital differences in baseline rates were not consistent for the three infections and was largest for VRE (CDI = 0·44, SAB = 0·05, VRE = 1·97).

The autocorrelation function on the deviance residuals indicated an adequate fit to cases of CDI and SAB, across all hospitals. For VRE, evidence of unmodeled temporal correlation was detected for two of the eleven hospitals. Subsequent review of unadjusted infection rates revealed that neither hospital reported a VRE clinical isolate for the duration of the study period. The exclusion of these two hospitals from the model reduced the estimate of between-hospital variation, but had minimal impact on parameter estimates (Table S13).

The comparison of observed versus predicted infections provided further evidence of adequate model fit, with observed cases for both pre-intervention and intervention periods within close proximity of the predicted mode (Figure S5)

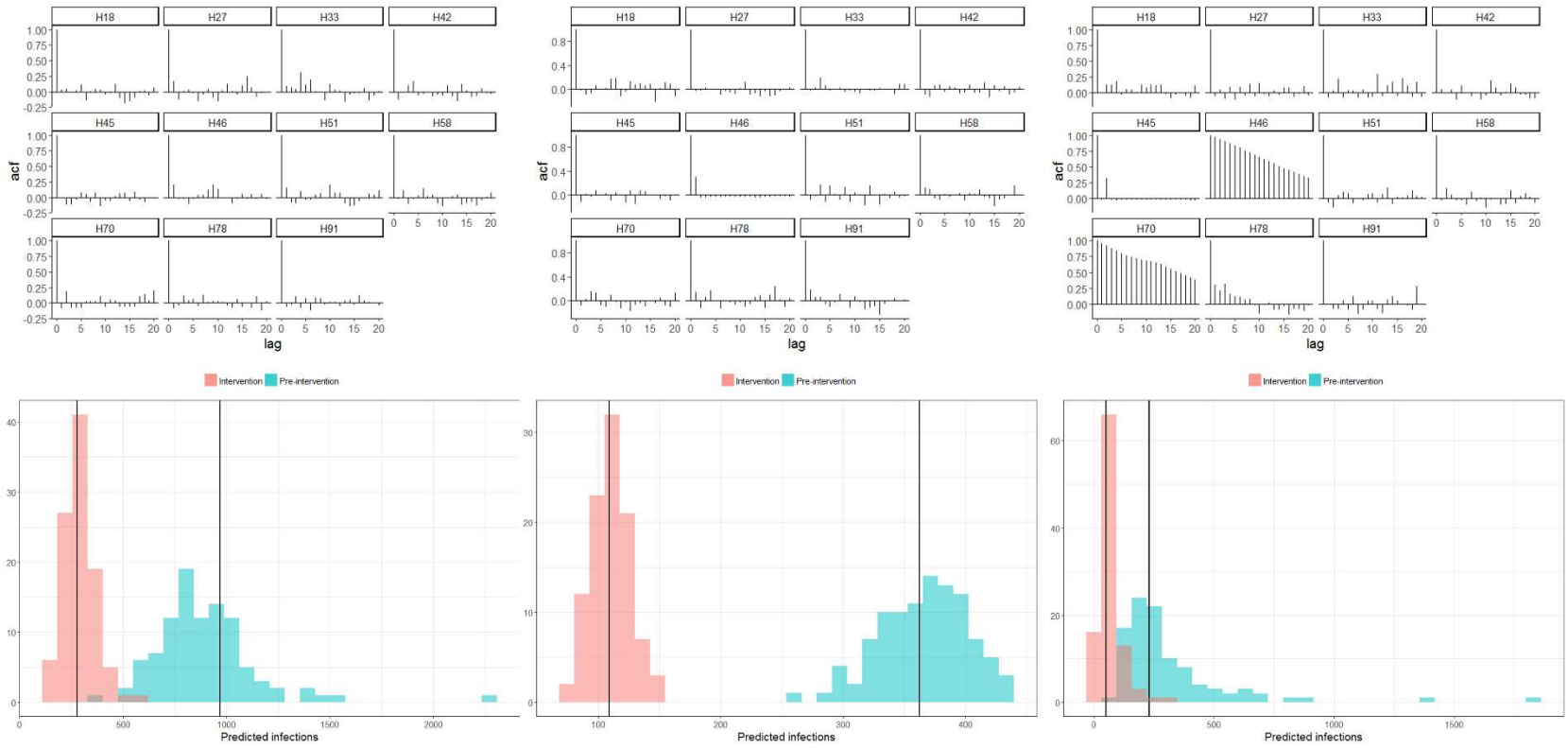

Figure S5: Top row: Autocorrelation function of deviance residuals from Model 1 by infection. (L-R): CDI, SAB, VRE. Bottom row: Histograms of predicted number of infections under Model 1, for the Pre-intervention (red) and Intervention (blue) periods. The solid vertical lines in each subfigure denoted the total observed number of infections in each period. (L-R): CDI, SAB, VRE.

	All Eleven hospitals	Nine hospitals with reported VRE clinical isolates
Percentage change in infection rates over course of study: No intervention		
Estimate (95% CI)	-15·6 (-53·1, 51·9)	-16·9(-53·6, 48·9)
p-value	0·57	0·53
Percentage change in infection rates over course of study: With intervention		
Estimate (95% CI)	-36·9 (-5·90, -2·8)	-36·1(-58·3, -2·2)
p-value	0·034	0.039
Random effects variance, ω_k^2	1·40	1·02

Table S13: Comparison of fixed effects estimates for VRE, with and without hospitals with no reported VRE clinical isolates in both pre-intervention and intervention periods. Results are summarized in terms of an estimate of percentage changes, 95% CI and p-value. The estimate of between-hospital variance (random effect) is also provided.

Secondary outcome: Additional model results

For Models A0-A3, estimates of the random effects variance (σ_v^2) were similar (Model A0: 0·44, Model A1: 0·47, Model A2: 0·52, Model A3: 0·51).

Further model assessment was based on Model A3 (binary + linear intervention), as the selected model with the smallest AIC.

The leave-one-hospital-out analysis indicated a greater hospital-level influence on the prediction of % FTPs cleaning, with Cooks' distances varying from 0·09 to 3·87 (Table S14). The omission of different hospitals from model fitting had the greatest impact on the estimation of the overall intercept (Figure S6), however conclusions regarding the statistical significance of each main effect was not affected.

					Intervention				Interaction				
	Intercept		Room = Bedroom		Step change		Time		Step change:Room		Intervention time:Room		
Hospital	**Est.**	**SE**	**Est.**	**SE**	**Est.**	**SE**	**Est.**	**SE**	**Est.**	**SE**	**Est.**	**SE**	**Cook's D**
H18	-0·19	0·14	-0·24	0·06	0·71	0·07	0·36	0·03	-0·06	0·09	-0·12	0·03	0·95
H27	-0·28	0·17	-0·25	0·06	0·74	0·06	0·34	0·02	-0·04	0·09	-0·09	0·03	0·27
H33	-0·43	0·18	-0·28	0·06	0·85	0·07	0·36	0·02	-0·14	0·09	-0·05	0·03	3·87
H42	-0·29	0·17	-0·25	0·06	0·8	0·07	0·31	0·02	-0·16	0·09	-0·04	0·03	0·32
H45	-0·38	0·17	-0·21	0·06	0·69	0·07	0·38	0·02	-0·08	0·09	-0·1	0·03	0·82
H46	-0·38	0·16	-0·25	0·06	0·74	0·06	0·34	0·02	-0·12	0·09	-0·06	0·03	0·09
H51	-0·24	0·17	-0·21	0·06	0·69	0·06	0·32	0·02	-0·07	0·09	-0·08	0·03	1·13
H59	-0·26	0·17	-0·24	0·06	0·68	0·07	0·34	0·02	-0·13	0·09	-0·05	0·03	0·37
H70	-0·24	0·17	-0·22	0·06	0·64	0·06	0·34	0·02	-0·08	0·09	-0·07	0·03	0·97
H78	-0·27	0·16	-0·21	0·06	0·81	0·07	0·29	0·02	-0·16	0·09	-0·01	0·03	1·16
H91	-0·28	0·16	-0·31	0·07	0·67	0·07	0·32	0·02	-0·06	0·09	-0·06	0·03	0·86

Table S14: Summary of leave-one-hospital-out analysis for monthly audit data under Model A3. Results are summarized in terms of revised parameter estimates and standard errors, for each fixed effect (including interaction terms). The overall Cook's distance is also calculated at the hospital level.

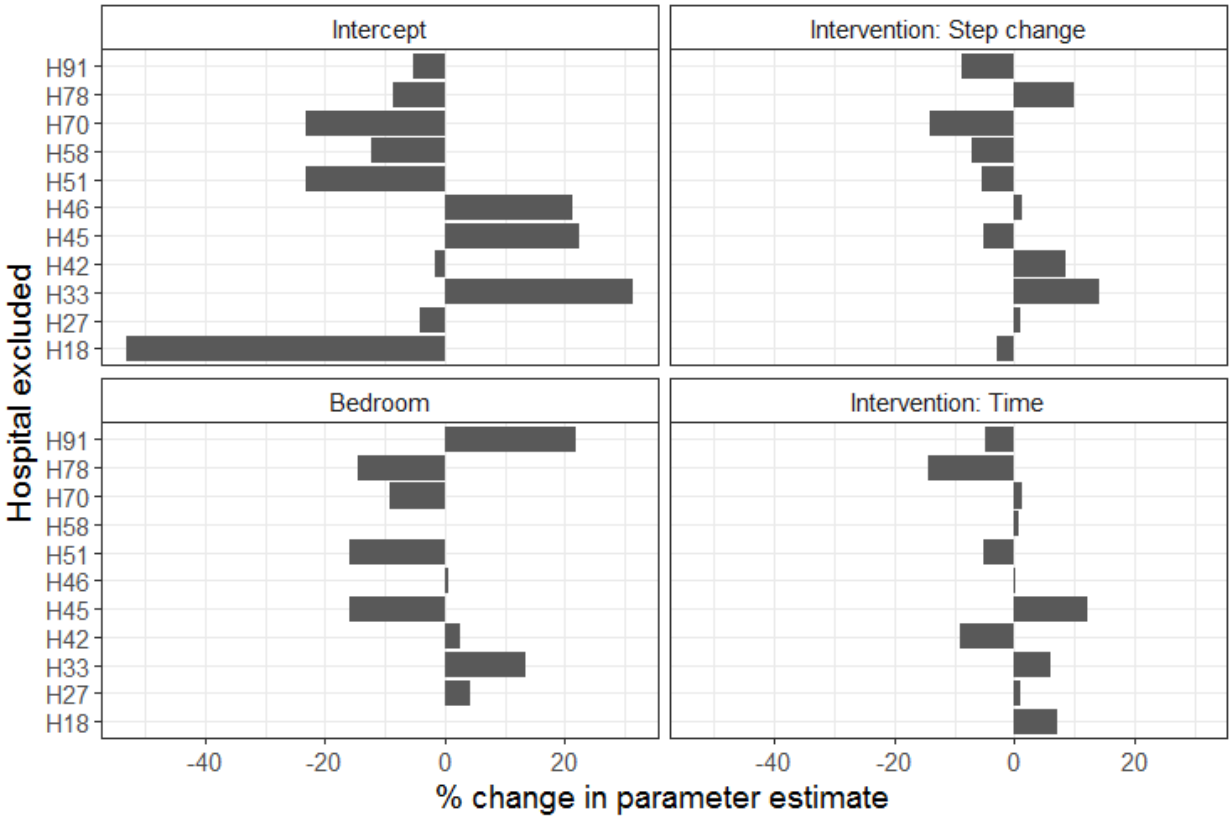

Figure S6: Percentage changes in each main effect from the leave-one-hospital-out analysis of monthly audit data. Each percentage change is relative to the model fitted to all 11 hospitals, such that a negative percentage change indicates a decrease in effect size.

The extension of Model A3 to include fractional polynomial effects on intervention time further improved model fit under AIC, with $p = -0 \cdot 5$ chosen as the best fitting model (AIC = 3497). Using parametric bootstrapping, predictions under the chosen fractional polynomial model were computed for the control period, at the commencement of the intervention period, and at 10 weekly intervals over the course of the intervention (Table S15, Figure S7). The comparison of these results with Table S9 indicated a smaller step change for both Bathroom and Bedroom, with similar predictions of cleaning performance thereafter.

	% Frequent touch points cleaned					
Room	Control Mean (95% PI)	Weeks since intervention start Mean (95% PI)				
		0	10	20	30	40
Bathroom	42·8 (40·6, 44·9)	50·4 (47·0, 53·9)	69·7 (68·6, 70·8)	76·7 (75·8, 77·6)	80·3 (79·3, 81·4)	82·5 (81·3, 83·8)
Bedroom	36·9 (35·1, 38·6)	43·2 (40·1, 46·3)	59·9 (58·8, 61·1)	66·9 (65·9, 67·8)	70·7 (69·5, 71·9)	73·1 (71·7, 74·6)

Table S15: Model based predictions of % FTPs cleaned under parametric bootstrapping: first-order fractional polynomial on intervention time, $p = -0 \cdot 5$. Predictions are summarized for both Bathroom and Bedroom FTPs in terms of a mean estimate and 95% prediction interval. PI = Prediction interval.

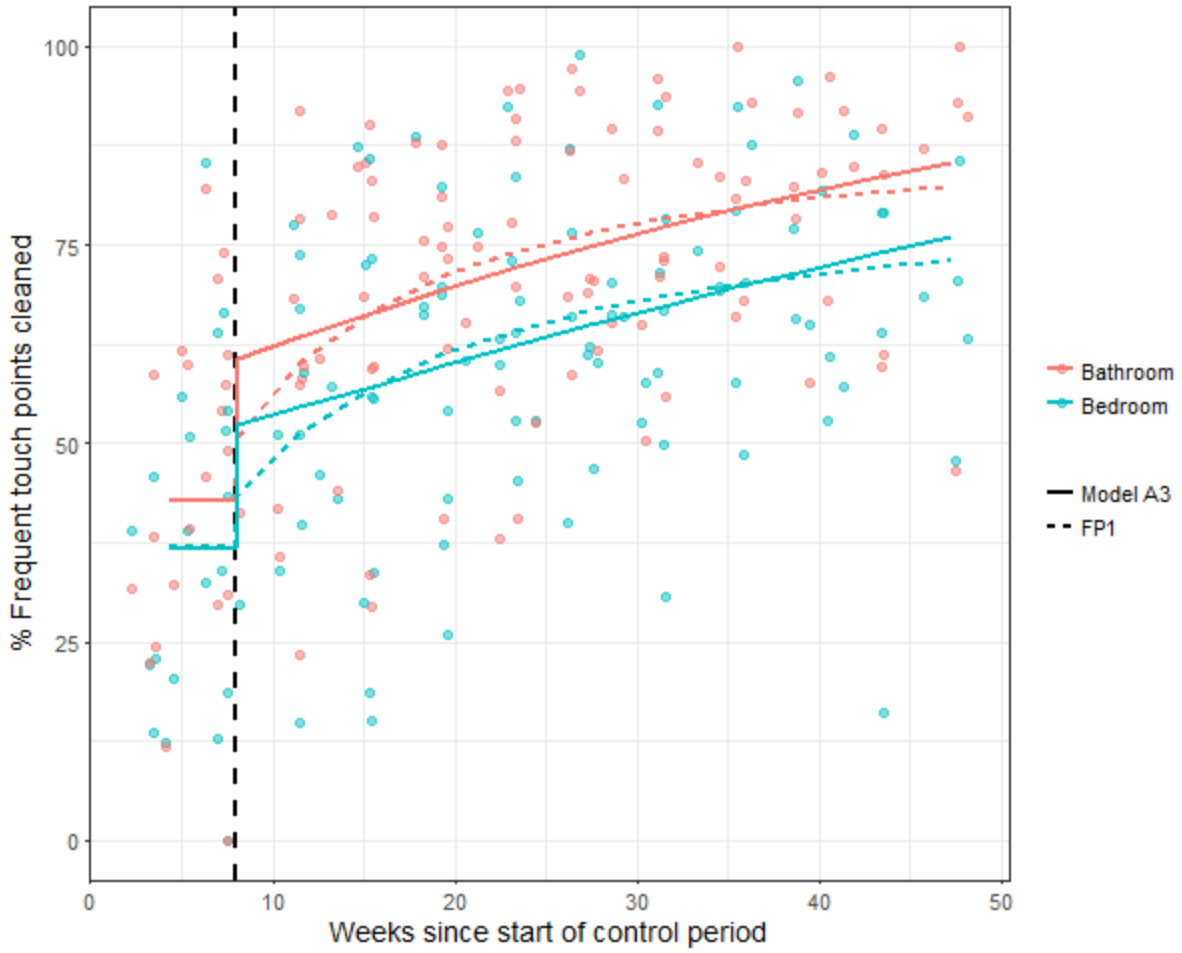

Figure S7: Predicted trend plot comparing the fit of Model A3 and the best fitting first-order fractional polynomial. Note that the fractional polynomial was an extension of Model A3, where the linear term for intervention time was raised to power = -0·5.

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