

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	MODELLING THE COSTS AND CONSEQUENCES OF REDUCING HEALTHCARE ASSOCIATED INFECTIONS BY IMPROVING HAND HYGIENE IN AN AVERAGE HOSPITAL IN ENGLAND
AUTHORS	Guest, Julian F.; Keating, Tomas; Gould, Dinah; Wigglesworth, Neil

VERSION 1 - REVIEW

REVIEWER	Nicholas Graves QUT Australia I have recently been paid consulting fees by Essity Hygiene for work that relates to the contents of this paper.
REVIEW RETURNED	15-Mar-2019

GENERAL COMMENTS	<p>The authors have prepared a decision model to show the economic benefits of improving hand hygiene with an automated monitoring technology as compared to existing monitoring practices in a typical NHS hospital. The study was funded by Essity HBMJ. 2012 May 3;344:e3005. doi: 10.1136/bmj.e3005). There are many contemporary sources of data from routine surveillance of HAI done in the NHS that the authors appear to have overlooked.</p> <p>“Healthcare workers are a key risk group because of the nature of their work. We do not have accurate data on infections and ill health in this group”</p> <p>“Healthcare-associated infection (HAI) is an important cause of morbidity and mortality amongst hospital patients, especially with the increasing resistance of many human pathogens to antibiotics (e.g. methicillin-resistant Staphylococcus aureus: MRSA). However, the Health Safety Executive do not generally deal with clinical matters as these are more appropriately dealt with elsewhere.”</p> <p>The assumption that 3.5% of patients die from HAI is also poorly supported. There are many high quality reviews that address this parameter and the authors have not mentioned them in this manuscript.</p> <p>Perhaps the most important assumption is that the introduction of the electronic audit and feedback system leads to an additional</p>
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	<p>reduction in the incidence rate of HAI of 25%. This is a large effect size and the findings of the model are caused by this estimate. Yet the estimate is not based on any evidence. Rather it is a 'hypothetical' or a 'thought experiment'. This should be stated very clearly as it reduces the validity of the conclusions drawn by the authors.</p> <p>I have some other concerns about the use of NHS reference costs to value bed days released. The authors are implying that £586 would be saved per ward bed day freed up and £1621 would be saved for every ICU bed day. This is a naïve interpretation and does not directly address the economic opportunity costs of bed days. This works feels premature. I feel we do not have the evidence based – particularly for the effectiveness of automated hand hygiene monitoring to attempt this kind of decision model. If all the other parameters were carefully specified then there might be some value in modelling plausible effect sizes for automate hand hygiene monitoring. But in its current form I found this paper to be unconvincing</p> <p>The reviewer provided a marked copy with additional comments. Please contact the publisher for full details.</p>
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REVIEWER	Emily Sickbert-Bennett UNC Health Care, United States
REVIEW RETURNED	18-Mar-2019

GENERAL COMMENTS	<p>This is a very well written modeling paper with assumptions very clearly specified. There were a few assumptions that seemed unrealistic based on my US experience.</p> <p>Pg 9, line 16 - can you specify the types of HCAI that would be acquired by HCP. It seems like they would be most commonly respiratory viral infections spread by droplets. These droplet spread infections may be less impacted by a hand hygiene intervention.</p> <p>Pg 9, line 49 - the assumption of 90% of HCP with HCAI would stay home from work for a mean of 5 days seems very high (based on US experience). I notice there is a not a reference for those estimates - can you provide more rationale for those numbers?</p> <p>Pg 10, re: hand hygiene audit and feedback - other than accounting for the cost of this particular system isn't your model testing the ability to improve hand hygiene compliance with an intervention/technology? If so, I wonder if the authors would want to mention the value of improving hand hygiene overall and then weigh the cost ramifications of different solutions. Since electronic hand hygiene is not the standard at this point, that may give the assessment even more value.</p> <p>Pg 14, Line 53 - given that the impact of this system is very sensitive to the incidence of HCAI that can be reduced, I think the epidemiology of HCAI in England should be further described so the readers can assess the likelihood that a hand hygiene intervention will impact the incidence of HCAI (e.g., device related infections may be more likely acquired from the patients own flora).</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer(s)' Comments to Author:

Reviewer: 1

Reviewer Name: Nicholas Graves

Institution and Country: QUT Australia

Please state any competing interests or state 'None declared': I have recently been paid consulting fees by Essity Hygiene for work that relates to the contents of this paper.

The authors have prepared a decision model to show the economic benefits of improving hand hygiene with an automated monitoring technology as compared to existing monitoring practices in a typical NHS hospital. The methods are clear and the decision model is appropriate. Indeed, another analyst could use this papers to replicate the results, and in my opinion is the sign of a good model.

The model has been used to include healthcare workers suffering from an HAI, and this is a novel angle on the value of infection prevention. I know the literature on needle stick injuries arising among healthcare workers, but I have not seen much work on risks of HAI among health care professionals, The authors need to justify the inclusion of this group in the model. Can they set out the reasons why healthy people who work in hospital might acquire a HAI? Their immune systems should be normal, they are not exposed to surgery or insertion of devices and I am unsure the mechanisms by which they would acquire HAI. If we follow this logic then might all visitors or contractors who interest with the hospital also face some risk of HAI?

Guidance from the WHO highlights tuberculosis as an occupational risk factor for healthcare workers [https://www.who.int/occupational_health/topics/hcworkers/en/]. Healthcare workers are also at risk of acquiring bloodborne infections (e.g. HIV, hepatitis B and C). While healthcare workers may not be at high-risk of 'classic' healthcare-associated infections they are at risk of community-acquired infections brought into hospital by patients. These include gastrointestinal infections (e.g. norovirus) and respiratory infections (e.g. influenza, respiratory syncytial virus). Rarely, healthcare workers may also develop varicella, measles or mumps through patient contact. Risks of acquiring a HCAI are higher for healthcare workers than for members of the public visiting hospital because healthcare workers have more patient contacts than visitors and these are sustained over a longer period of time. Hands play an important role in the spread of gastrointestinal and intestinal infections [Fedeli U, Zanetti C, Saia B. Susceptibility of healthcare workers to measles, mumps, rubella and varicella. *J Hosp Infect* 2002 51 133-135; Hyams PS, Stuewe MCS, Heitzer V. Herpes zoster causing varicella [chickenpox] in hospital employees: cost of a casual attitude. *AJIC* 1984 12 2-5; Clark NM, Lynch JP. Influenza: epidemiology, clinical features, therapy and prevention. *Semin Crit Care Med* 2011 32 373-392]. The text has been amended accordingly.

The quality of this type of research study depends on the evidence used to update the model and I have some comments about this.

- The authors claim they have completed a systematic review for the data used, but there is not sufficient evidence of this, nor are the results presented in a way normally seen for a systematic review. I suggest the authors need to complete and report a systematic review using the PRISMA guidelines. At present, I would describe this as a narrative or discretionary review which is not sufficient to support the findings that arise from the modelling work they present. The Methods section

has been expanded to provide more details about the literature review. However, there was never any intention to publish the systematic literature review, but to use the findings to inform an economic study. Please note this article is not a health technology assessment and in line with numerous other published cost-effectiveness studies further information on the systematic literature review should not be a requirement. Nevertheless, many systematic reviews concerning the risks of healthcare-associated infections and their impact in both high and low income countries have been conducted - too many to quote. In particular, two systematic reviews explored the effectiveness of automated hand hygiene monitoring systems. Both reviews included electronic devices and both concluded that such systems may be of benefit but acknowledged that the primary studies were poorly controlled (pre/post test designs). Both systematic reviews recommended an economic analysis [Srigley JA, Gardam M, Fernie G, Lightfoot D, Lebovic G, Muller MP 2015. Hand hygiene monitoring: a systematic review of efficacy. *Journal of Hospital Infection* 89 51-60; Ward MA, Schweizer ML, Polgeen PM, Gupta K, Reisinger HS, Perencevich EN 2014. Automated and electronically assisted hand hygiene monitoring systems: a systematic review. *AJIC* 42 472-478].

- The assumption that 4.7% of patients will acquire an HAI needs justification. The authors treat this statistic like an incidence rate for the purposes of the modelling, yet it arises from a point prevalence survey of European hospitals for 2011-2012. Incidence rates and point prevalences measure quite different outcomes. The data are quite old and large improvements in hand hygiene have happened in the NHS since they were published. See BMJ 2012 May 3:344:e3005.doi 10.1136/BMJ.e3005). The article to which the reviewer refers evaluates very specific pathogens, namely MRSA bacteraemia in 170 hospitals and MSSA bacteraemia and C difficile infection in 165 hospitals. The authors used the report "Point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals" to inform the model since it is more comprehensive and covers all pathogens. The point prevalence of HAIs in England reported in the point prevalence survey is 6.0%. However, this survey reported the incidence as being between 4.6% and 4.8%, so the Authors used the average of 4.7%.

- There are many contemporary sources of data from routine surveillance of HAI done in the NHS that the authors appear to have overlooked. The assumption that 1.72% of staff will acquire an HAI needs to be justified. The evidence cited to support this statistic reads... "Healthcare workers are a key risk group because of the nature of their work. We do not have accurate data on infections and ill health in this group" "Healthcare-associated infection is an important cause of morbidity and mortality amongst hospital patients, especially with the increasing resistance of many human pathogens to antibiotics (e.g. methicillin-resistant *Staphylococcus aureus*: MRSA). However, the Health Safety Executive do not generally deal with clinical matters as these are more appropriately dealt with elsewhere." The cited evidence also states that healthcare workers are a key risk group because of the nature of their work. We do not have accurate data on infections and ill health in this group - but data from physician reporting schemes indicates infection rates of about 30 per 100,000 workers per year amongst nurses" (i.e. 0.03%). The authors also estimated from statistics provided in the other cited reference (i.e. Health & Safety Executive 2017) that 3.4% of healthcare workers would be absent from work due to work-related reasons other than musculoskeletal disorders, stress, depression or anxiety. The mean of these two independent sources of evidence is 1.72%. Sensitivity analyses showed that changing this value has negligible impact on the study's findings.

- The assumption that 3.5% of patients die from HAI is also poorly supported. There are many high quality reviews that address this parameter and the authors have not mentioned them in this manuscript. The source for this estimate was incorrect and should be the 2016 publication, Burden of Six Healthcare-Associated Infections on European Population Health. This has now been corrected. Sensitivity analyses show that changing this value has negligible impact on our results.

- Perhaps the most important assumption is that the introduction of the electronic audit and feedback system leads to an additional reduction in the incidence rate of HAI of 25%. This is a large

effect size and the findings of the model are caused by this estimate. Yet the estimate is not based on any evidence. Rather it is a 'hypothetical' or a 'thought experiment'. This should be stated very clearly as it reduces the validity of the conclusions drawn by the authors. This is not an accurate depiction of our model. The Authors are unaware of the effect size of the electronic audit and feedback system and therefore presented results for an effect size ranging from 5% to 25%. The Authors also estimated that if the introduction of the electronic audit and feedback system into current practice in a hypothetical general hospital in England can improve hand hygiene compliance among front-line HCPs leading to a reduction in the incidence of HCAs by $\geq 15\%$, it would potentially afford the NHS a cost-effective intervention.

- I have some other concerns about the use of NHS reference costs to value bed days released. The authors are implying that £586 would be saved per ward bed day freed up and £1621 would be saved for every ICU bed day. This is a naïve interpretation and does not directly address the economic opportunity costs of bed days. This is the Reviewer's opinion, but it does not appear to be substantiated. The Authors have calculated costs in accordance with the guidance provided by the National Institute for Health and Care Excellence (NICE), which recommends the use of the National Schedule of Reference Costs. We would therefore prefer to leave our costs unchanged. Notwithstanding this, the Authors have discussed the opportunity costs in the Discussion.
- This work feels premature. I feel we do not have the evidence based - particularly for the effectiveness of automated hand hygiene monitoring to attempt this kind of decision model. If all the other parameters were carefully specified then there might be some value in modelling plausible effect sizes for automated hand hygiene monitoring. But in its current form I found this paper to be unconvincing. This opinion is not shared by Reviewer 2

Reviewer: 2

Reviewer Name: Emily Sickbert-Bennett

Institution and Country: UNC Health Care, United States Please state any competing interests or state 'None declared': None declared.

This is a very well written modeling paper with assumptions very clearly specified. There were a few assumptions that seemed unrealistic based on my US experience.

- Pg 9, line 16 - can you specify the types of HCAI that would be acquired by HCP. It seems like they would be most commonly respiratory viral infections spread by droplets. These droplet spread infections may be less impacted by a hand hygiene intervention. Infections that healthcare workers might acquire include norovirus, flu and respiratory viruses like rotavirus, syncytial respiratory virus and possibly varicella. There is good evidence that some of these are spread by hands as well as by droplets and aerosols and for others it is likely that hands play a role. Hand hygiene would be more likely to be effective against respiratory viruses like norovirus and influenza etc than with 'conventional' nosocomial pathogens. The former are not adapted to survival on skin and are more easily dislodged by the mechanical effects of hand hygiene than for example, Staph aureus which does attach to skin. The text has been amended accordingly.
- Pg 9, line 49 - the assumption of 90% of HCP with HCAI would stay home from work for a mean of 5 days seems very high (based on US experience). I notice there is not a reference for those estimates - can you provide more rationale for those numbers? One of the clinical authors is a Director of Infection Prevention and Control at a large London-based hospital. It is NHS policy that any member of staff with an infection should remain absent from work until they are no longer

infectious. However, in practice this author estimated that 10% of staff members with an infection would attend work.

- Pg 10, re: hand hygiene audit and feedback - other than accounting for the cost of this particular system isn't your model testing the ability to improve hand hygiene compliance with an intervention/technology? If so, I wonder if the authors would want to mention the value of improving hand hygiene overall and then weigh the cost ramifications of different solutions. Since electronic hand hygiene is not the standard at this point, that may give the assessment even more value. Estimating the value of improving hand hygiene overall is beyond the remit of this study. The study limitations section has been expanded to include this point. Notwithstanding this, the Authors chose to focus on electronic monitoring systems because of their higher degree of accuracy and the amount of interest currently being shown in them. It is known that manual audit leads to a marked Hawthorne effect and other sources of bias e.g. postponing complicated clinical procedures until the auditor has gone [Srigley JA, Furness CD, Baker GR, Gardam M. Quantification of the Hawthorne effect in compliance monitoring: a retrospective cohort study. *BMJ Qual Saf* 2014; 23: 974-80]. The other method of measuring adherence is product consumption which is not very accurate and provides little information [Gould DJ, Creedon S, Jeanes A, Drey NS, Chudleigh J, Moralejo D. The Hawthorne and avoidance effects in hand hygiene practice and research: methodological reconsideration. *J Hosp Infect* 2017; 95: 169-174]. Inaccuracies associated with manual hand hygiene audit are such that it is no longer considered the best approach and there is increasing interest in combining periodic manual audit with continuing electronic monitoring to give an overall picture of behaviour [Marra AR, Edmond MB. Hand hygiene: state-of-the-art review with emphasis on new technologies and mechanisms of surveillance. *Curr Infect Dis Rep* 2012; 14: 585-591; Masroor N, Doll M, Stevens M, Bearman G. Approaches to hand hygiene monitoring: from low to high technology. *Internat J Infect Dis* 2017; 65: 101-4].

- Pg 14, Line 53 - given that the impact of this system is very sensitive to the incidence of HCAI that can be reduced, I think the epidemiology of HCAI in England should be further described so the readers can assess the likelihood that a hand hygiene intervention will impact the incidence of HCAI (e.g., device related infections may be more likely acquired from the patient's own flora). The epidemiology has been outlined in the Introduction. However a more detailed discussion is beyond the remit of this article. Nevertheless, the Reviewer seems to be suggesting that patients are more likely to acquire a HCAI from their own flora rather than by cross-infection via the hands of a health worker. However, a urinary tract infection in an inpatient is very likely to be of a hospital strain because the patient's gut flora has been replaced by hospital flora - which indicates that at some point, cross-infection must have occurred from the hospital environment to the patient and the main route of spread in any cross-infection is via health workers' hands. Moreover, observational studies of hand hygiene behaviour indicate that there is an abundant risk of exogenous [cross] infection as healthcare workers move rapidly between patients, often without undertaking adequate hand hygiene [Weber DJ, Rutala WA, Miller M, Huslage K, Sickert-Bennett MS. Role of hospital surfaces in the transmission of emerging health care-associated pathogens: Norovirus, *Clostridium difficile* and *Acinetobacter* species. *AJIC* 2010 38 S25-33; Derde LP, Cooper BS, Goossens H, Malhotra-Kumar S, Willems R, Gniadkowski M, Hryniewicz W, Empel J, et al. Interventions to reduce colonisation and transmission of antimicrobial-resistant bacteria in intensive care units: an interrupted time series study and cluster randomised trial. *Lancet* 2014; 14: 31-9]. Additionally, the intensive care environment is heavily contaminated with hospital strains of pathogenic organisms and these have been shown to cause infection [Wille I, Mayr A, Kreidl P, Bruhwasser C et al. Cross-sectional point prevalence survey to study the environmental contamination of nosocomial pathogens in intensive care units under real-life conditions. *J. Hosp Infect.* 2018; 98: 90-95]. However, increased hand hygiene performance has been shown to reduce endogenous infection [Rosenthal, V et al 2004. Effects of education and performance feedback on rates of catheter-associated urinary tract infection in intensive care units in Argentina. *Infect Control Hosp Epidemiol* 25 47-50; Gastmeier, P, Geffers, C

(2007). Prevention of ventilator-associated pneumonia: analysis of studies published since 2004. Journal of Hospital Infection 67 1-8]. The text has been amended to include this.

VERSION 2 – REVIEW

REVIEWER	Nicholas Graves QUT, Australia I have done work for essity on the economics of automated hand hygiene monitoring. They funded this study
REVIEW RETURNED	20-May-2019

GENERAL COMMENTS	The authors have rebutted all of my comments, and the changes made to the paper are cosmetic. I worry the conclusions readers draw from this manuscript might be quite wrong. Uncertain and low grade data are still used to make strong statements. There is no evidence at all for the effectiveness of automated HH monitoring and that the authors have made a guess at the values for this parameter. I accept they found a threshold at which the CE criterion is met. Had the authors made the changes requested then I would support publication, but they did not and so I can't, sorry.
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REVIEWER	Emily Sickbert-Bennett UNC Hospitals, NC, USA
REVIEW RETURNED	30-May-2019

GENERAL COMMENTS	I am satisfied with the revisions the authors have completed based on my previous review. Thank you.
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VERSION 2 – AUTHOR RESPONSE

We note that Reviewer 2 had no further comments, but are puzzled by Reviewer 1 since he stated we (the Authors) had rebutted all his comments, and the changes made were purely cosmetic. This is not accurate nor constructive. The Authors addressed all of Reviewer 1's comments and made substantial changes to the article in accordance with those comments (as shown in the tracked changes version of the manuscript).

The author provided a marked copy with additional comments. Please contact the publisher for full details.