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Research paper

Quantifying the relative effect of environmental contamination on surgical ward MRSA incidence: An exploratory analysis

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Abstract *Background:* To investigate and quantify the contribution of environmental contamination towards methicillin-resistant *Staphylococcus aureus* (MRSA) incidence observed in a hospital ward using stochastic modelling.
Methods: A non-homogeneous Poisson process model was developed to investigate the relationship between environmental contamination and MRSA incidence in a UK surgical ward during a cleaning intervention study. The model quantified the fractional risks (FRs) from colonised patients, environmental contamination and a generic background source as a measure of their relative importance in describing the observed MRSA incidence.
Results: While the background source remained the most likely MRSA acquisition source for this ward (as measured by the FRs), environmental contamination was the second most likely source, ahead of colonised patients in the ward. The relative importance of environmental contamination was smaller in the enhanced cleaning period compared with the normal cleaning period, albeit with notable variability in the estimates.

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Conclusions: Accounting for environmental contamination in stochastic modelling of MRSA transmission within a hospital ward provides a richer interpretation of the FRs, and is particularly pertinent in quantitative investigations of hospital cleaning interventions to reduce MRSA acquisition.

Highlights

- Non-homogeneous Poisson process is used to quantify contributions of different MRSA transmission routes.
- Relative contribution of environmental contamination to MRSA acquisition risk was quantified.
- A large portion of MRSA cases observed was attributed to a generic background source.
- Relative contribution of environmental contamination would have otherwise been amalgamated into generic background source.

Introduction

Antimicrobial resistance is a serious global health issue that is becoming increasingly difficult to manage. This issue is particularly pertinent in the healthcare setting where vulnerable patients are more likely to develop infections, which in turn have limited treatment options. One way to mitigate this is to reduce or prevent such healthcare associated infections from occurring in the first place. For hospital multidrug-resistant organisms (MROs) such as methicillin-resistant *Staphylococcus aureus* (MRSA), where colonisation typically precedes infection, this involves preventing MRSA colonisation of susceptible patients from sources such as previously colonised patients [1], MRSA-positive healthcare workers [2] and contaminated environmental sources [3,4].

While previous research has associated environmental reservoirs with MRO incidence in hospital wards [5], only a small proportion of the mathematical modelling literature has explicitly included environmental contamination as a transmission source [6—10]. None of these papers used environmental surveillance data to estimate the parameters associated with transmission via environmental contamination. Rather, environmental contamination transmission parameter estimates were obtained by fitting simulations from models to observed MRSA patient data.

A non-homogeneous Poisson process (NHPP) is presented to model MRSA incidence in a UK surgical ward over one year. Patient and environmental data were collected for an earlier prospective cross-over cleaning study where a dedicated cleaner was introduced into the ward [11]. Hand-touch sites were screened for coagulase-positive staphylococci and aerobic colony counts (ACC) during both routine and enhanced cleaning periods. The incorporation of an explicit environmental contamination term in the model is a novel extension of previous NHPP applications for hospital MRO [12—16].

Materials and methods

NHPPs are stochastic models used to describe the number of events occurring over time. They are characterized by the instantaneous rate of event occurrences known as the intensity function $(\lambda(t))$, which varies with time (t).

For modelling MRSA incidence, the basic form of the model assumes that at any time t, the ward comprises $S(t)$ susceptible patients and $C(t)$ patients colonised with MRSA. Susceptible patients are at risk of instantaneous colonisation at a rate $\lambda(t)$ which is typically a function of $C(t)$ and a background term β_0 to represent other sources of colonisations not explicitly modelled. This means, over a small time period from t to $t + \Delta$, the probability of a susceptible patient being colonised is $\lambda(t)\Delta$.

Denoting the transmission coefficient of a colonised patient by β_1, this basic intensity function is $\lambda(t) = \beta_0 + \beta_1 C(t)$ which can be modified to represent features of the ward under study, provided that the intensity function remains positive. Examples of such modifications are the addition of a term to represent patients in isolation rooms [12] and step functions to represent different study phases [13]. Similar work analysing more than one ward [14—16] pooled estimates across wards using random-effects meta-analysis to summarise the overall efficacy of patient isolation.

A common finding of previous work is that the estimated generic background parameter β_0 forms a substantial proportion of the colonisation rate $\lambda(t)$. However, this finding does not lead to clear, practical recommendations as this term encompasses all other transmission sources not explicitly accounted for in the intensity function, e.g. contributions from environmental contamination, undetected patient carriers including prior room occupants, and mobile contaminated healthcare workers [12,14,16—18].

An issue common to the applications of such models to hospital infection data (or any epidemic surveillance data in general) is that the transmission process is imperfectly

observed, i.e. it is not possible to pinpoint the exact time a susceptible patient becomes colonised. To address this issue, the estimation procedure involves the imputation of these unobserved colonisation times along with parameter estimation. This is typically done using a data-augmented Markov chain Monte Carlo (MCMC) algorithm [19]. In particular, the imputed colonisation time for a patient is estimated from the intensity function values over the possible range of colonisation times for the patient. This range is determined by study features, such as how often patients are screened in the wards, previous (negative) screening dates of the patients and isolation of pathogen of interest (MRSA).

Details about the data set used in this paper, including its limitations, are discussed in the following subsection before describing the specific NHPP developed for this application. Additional details about the model are provided in the supplementary materials.

Data

The data were collected as part of a prospective cross-over study evaluating the impacts of an additional dedicated cleaner on ward cleanliness and MRSA incidence across two 21-bed surgical wards in a UK hospital [11]. Each ward was assigned the same cleaner for two separate six month periods and the number of new patient MRSA acquisitions with and without the extra cleaner were compared. Colonised patients were initiated on a topical clearance regimen (antiseptic nasal cream and body wash) on the date of first laboratory confirmation of MRSA positivity at any site, and remained so until discharge, or after three negative screens had been obtained one week apart. The data were collected over 59 weeks.

The NHPP model presented below used the dates of the first and last positive screening of all patients detected with MRSA within the data collection period, and the weekly aggregate environmental contamination data in the form of aerobic colony counts (ACC). The ACC data were measured in colony forming units (cfu) per cm^2 and aggregated from 10 sampling sites per ward each week.

All patients with a positive MRSA screen were included as colonised cases and cases were not distinguished between new acquisitions or otherwise as the model formulation was unable provide this distinction.

There were 28 patients detected with MRSA in Ward A during the first six months of the study when the ward received enhanced cleaning and a subsequent 15 colonised patients detected in the remainder of the study period when the ward received normal cleaning. In comparison, there were 8 colonised patients detected in the enhanced cleaning period for Ward B and 7 during the normal cleaning period.

This study therefore focused on one of the wards (Ward A) for the analysis presented, as the second ward (Ward B) had substantially fewer MRSA acquisitions, further complicating the estimation and potential inference in the presence of limited data. Results for Ward B are described in the supplementary material (Web Supplementary E).

The difference in MRSA colonisation pressure between Ward A and Ward B could be suggestive of unmeasured effects that differentiate the MRSA acquisition process in the two wards despite the wards having been matched for ward, staff and patient cohort characteristics [11]. Examples of such unmeasured effects include specific patient risk factors, potential staff MRSA carriers and staff compliance levels on routine infection control practices (such as hand hygiene).

Additionally, the counter-intuitive observations of increased MRSA cases in the enhanced cleaning period compared with the normal cleaning period (where the reverse might be expected) in both wards highlight the strong stochastic nature of hospital ward population dynamics and the need for models such as NHPPs to represent such data.

Non-homogeneous Poisson process formulation

The intensity function used here accounts for four different potential MRSA acquisition pathways: the generic background source (*bg*), undetected colonised patients (*cxt*), detected colonised patients (*ct*) and environmental contamination (*env*). A distinction is made between undetected colonised patients and detected colonised patients with the assumption that the contribution of an undetected colonised patient is greater than a detected colonised patient (β_1) by an amount of α_1. This is because all known colonised patients were given decolonisation treatment to minimise transmission. As such, the mathematical expression for the intensity function can be written as

$$\begin{aligned}\lambda(t) &= \lambda_{bg}(t) + \lambda_{cxt}(t) + \lambda_{ct}(t) + \lambda_{env}(t) \\ &= \beta_0 + (\beta_1 + \alpha_1)C_{xt}(t) + \beta_1 C_t(t) + \beta_2 E(t)\end{aligned} \quad (1)$$

where $C_{xt}(t)$ and $C_t(t)$ are the number of undetected and detected colonised patients in the ward at time t (in days), respectively. The environmental contamination measurement (ACC) in the ward at time t is represented by $E(t)$ with the corresponding transmission coefficient β_2. The background source is denoted by β_0 and accounts for transmissions not directly related to observed patient and environmental sources in the ward. Additionally, $\lambda_{bg}(t) = \beta_0$, $\lambda_{cxt}(t) = (\beta_1 + \alpha_1)C_{xt}(t)$, $\lambda_{ct}(t) = \beta_1 C_t(t)$ and $\lambda_{env}(t) = \beta_2 E(t)$. Mathematical details of the model are provided in Web Supplementary A.

The fractional risk (FR) measure (originally termed relative risk [20]) was used to quantify the relative importance of the different components in the intensity function for the observed patient MRSA acquisitions. Use of the FR was motivated by the fact that the covariates in the intensity function here $(C_{xt}(t), C_t(t)\ and\ E(t))$ are of different units, specifically it includes contributions from MRSA-positive patients and environmental contamination (measured in cfu per cm^2 as shown in Fig. 1). Direct comparison of the magnitudes of different model parameters $(\beta_0, \beta_1, \beta_2, \alpha_1)$, aside from the patient-related parameters β_1 and α_1, would not be meaningful.

The FRs estimate the average relative magnitudes of the components in the intensity function immediately prior to a patient being colonised and are defined mathematically as

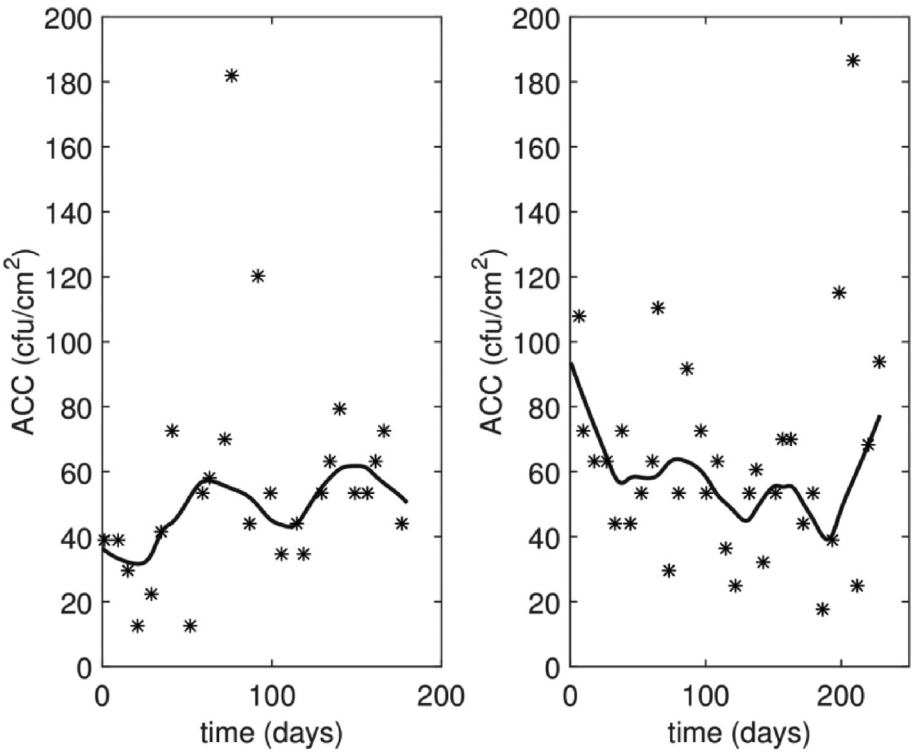

Figure 1 Smoothed time series of the environmental contamination measure (ACC) for the enhanced cleaning period (left) and normal cleaning period (right). Black asterisks denote the raw weekly data. Aerobic colony count (ACC) is measured in colony forming units per cm^2 (cfu/cm^2).

$$FR_j = \frac{1}{N_C}\sum_{i=1}^{N_C}\frac{\lambda_j\left(t_{C_i}^-\right)}{\lambda\left(t_{C_i}^-\right)}, j \in \{bg, cxt, ct, env\}$$

where N_C is the total number of colonised patients recorded in the ward for the particular time period, and $t_{C_i}^-$ is the time point immediately preceding the colonisation time of patient i. As such, FRs quantify the average MRSA acquisition risk from each pathway (or source) considered relative to the other MRSA acquisition pathways considered in the model for that time period.

Smoothing of environmental contamination data

In order to obtain daily estimates of environmental contamination, the weekly environmental contamination data were smoothed using a robust lowess smoother with a span of 0.3 [21] for each time period. These smoothed daily estimates $E(t)$ are used as inputs to the intensity function.

These daily estimates exhibited only small variations over time within each period compared with the weekly measurements (Fig. 1). The small variations are consistent with findings from a study which used an identical measurement protocol for environmental contamination but with repeat measurements taken from between 0 and 48 h of the cleaning procedure at the same site [22,23]. These studies found a substantial drop in ACC levels immediately following cleaning, though the change observed 24 h after cleaning was less dramatic. It would then be expected that a daily time series would not vary very much. If a finer time scale was used in the model instead, then it would be more appropriate to use a smoother which allows for greater variations in the smoothed values. This is subject to the availability of appropriately informative data on both patients and environment.

The choice of the span parameter of 0.3 was within the recommended range [21] and corresponds to 8 weeks for the enhanced cleaning period and 10 weeks for the normal cleaning period. These durations were within the time range (7 days—7 months) for MRSA persistence on dry inanimate surfaces [24]. Other spans and simple smoothers (loess smoothers and linear interpolation) were also investigated, though the differences estimated between the enhanced and normal cleaning periods were less evident due to the substantial increase in variability of the estimates.

The particular smoother used reflected the uncertainty surrounding two factors in the use of ACC for this application. The first was actually using ACC as a reflection of environmental contamination attributable to specific transmission events (MRSA acquisitions) in a hospital ward. The second was the measurement accuracy from aggregating a continuous measurement into categorical classifications (no growth, scanty growth, light growth and moderate growth categories, which were converted to numerical values per category) due to the resource burden needed to count colonies on dipslides [11].

Estimation procedure

The model parameters were estimated using a data-augmented MCMC algorithm [12,18] where the MRSA

patient unobserved colonisation times and discharge dates were imputed at each MCMC iteration, as detailed in Web Supplementary A. Uniform priors $(U(0,1))$ were assigned to the model parameters.

At each MCMC iteration, each parameter in the intensity function is independently updated using a Metropolis–Hastings step with an independent multiplicative random walk proposal [25] tuned to achieve acceptance rates between 0.1 and 0.6 [26].

Web Supplementary A expands on the data-augmented MCMC algorithm used. The estimation procedure was shown to be able to recover parameter values well from a simulation study (detailed in Web Supplementary B) and the posterior predictive test [27] indicated that fitted NHPP provides an adequate representation of patient MRSA acquisition in the ward (Web Supplementary C). Supplementary results for ward A are included in Web Supplementary C.

As the model parameters for the enhanced cleaning and normal cleaning periods were estimated independently, we can directly compare the difference of each estimate in the two periods. This provides a 'Bayesian hypothesis test' with the particular null hypothesis of interest here being if the parameter values in the two periods are equal.

Additionally, the full model was compared to a simplified model without environmental contamination (similar to previous modelling studies [12,14,16]). From the MCMC outputs, it is possible to evaluate and compare a measure of statistical fit of the fitted models. Due to the fact the models involve missing data (in the form of unobserved colonisation times), the DIC_6 model comparison measure [28] was used. The comparison assesses if there is a statistical preference for one of the models with a stronger preference for smaller DIC_6 values.

Results

For convenience and to assist readability, a summary table defining the model components discussed in this section is provided in Table 1.

The estimated posterior distributions for the four parameters in the intensity function (1) are summarised in Table 2 with the histograms of parameter differences between periods plotted in Fig. 2. The FRs estimated from the enhanced and normal cleaning periods are summarised in Table 3 and Fig. 3.

Individual patient and per unit environmental contamination transmission potential unaffected by enhanced cleaning

The transmission potential of an undetected MRSA patient, a detected MRSA patient and one unit of environmental contamination were statistically similar in both time periods (with posterior probabilities of the parameter values being larger in the enhanced cleaning period of 0.654, 0.674 and 0.429 for β_1, β_2 and α_1 respectively). These similarities were also evident from the histograms of the respective parameter differences across periods which were centred on 0 (Fig. 2). These are not surprising findings given that the introduction of an extra dedicated ward cleaner was unlikely to have impacted these transmission potentials.

The background source (amalgamating non-patient and non-environmental sources) transmission potential (β_0) was also statistically larger in the enhanced cleaning period compared to the normal cleaning period (with a posterior probability of 0.904 that β_0 in the enhanced cleaning period was larger than in the normal cleaning period). The larger

Table 1 Definitions of the model components discussed in the Results section.

Model component	Definition
β_0	Transmission potential of generic background source
β_1	Transmission potential of a single detected colonised patient
α_1	Additional transmission potential of a single colonised patient due to not having been detected
β_2	Transmission potential of a single unit of environmental contamination
FR_{bg}	Fractional risk measure of the relative importance of the background source in describing the observed MRSA acquisitions
FR_{cxt}	Fractional risk measure of the relative importance of the undetected colonised patients source in describing the observed MRSA acquisitions
FR_{ct}	Fractional risk measure of the relative importance of the detected colonised patients in describing the observed MRSA acquisitions
FR_{env}	Fractional risk measure of the relative importance of the ward environmental contamination in describing the observed MRSA acquisitions

Table 2 Summary of parameter estimates (multiplied by 10^5) from the combined sample of 2,400,000 iterations from three converged and well-mixed MCMC chains. MCSE denotes the Monte Carlo standard error and SD the posterior standard deviation. β_0, β_1, β_2 and α_1 are the coefficients in the intensity function associated with the background source, colonised patients, environmental contamination and additional contribution from being undetected while colonised, respectively.

Parameter ($\times 10^5$)	Enhanced cleaning				Normal cleaning			
	β_0	β_1	β_2	α_1	β_0	β_1	β_2	α_1
Mean	539	84.2	5.07	494	192	48.3	2.69	614
MCSE	0.5	0.1	0.009	0.6	0.2	0.07	0.004	0.7
SD	241	72.6	4.05	367	121	44.1	1.97	462
2.5% quantile	118	2.55	0.171	22.3	10.6	1.39	0.103	29.9
Median	526	65	4.12	423	179	35.7	2.33	520
97.5% quantile	1043	269	15	1381	457	164	7.27	1747

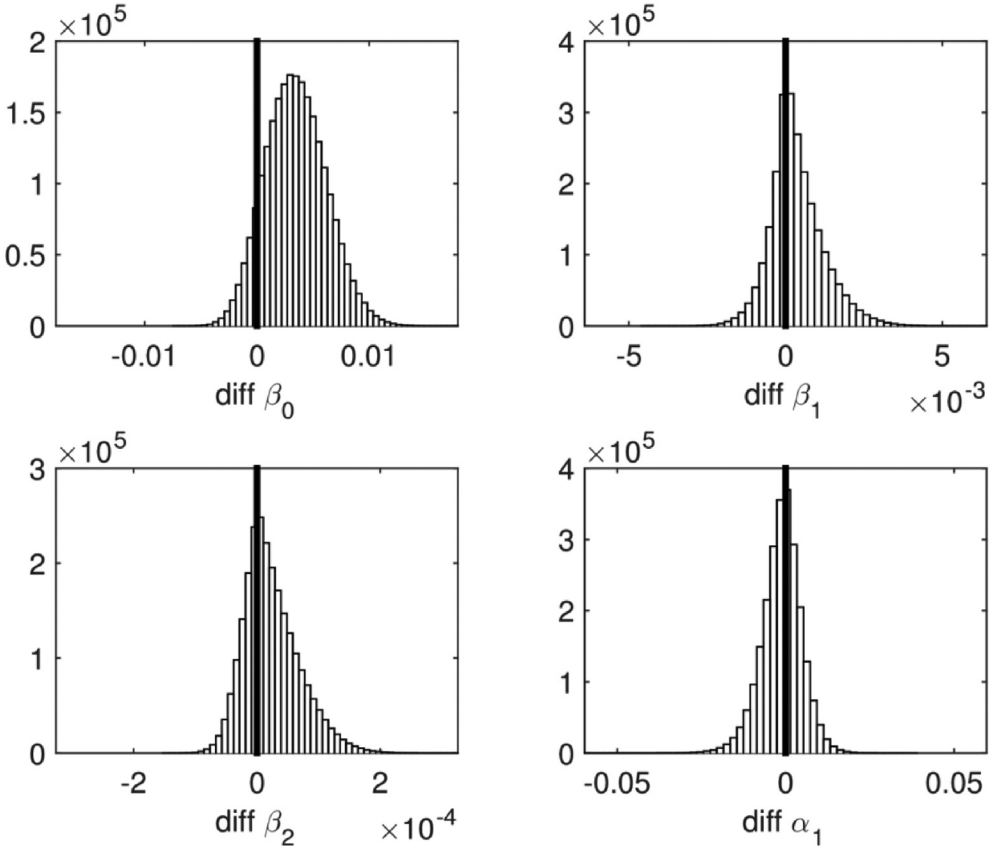

Figure 2 Histogram of the differences (diff) in parameter values between the enhanced cleaning period and normal cleaning period from the combined sample of 2,400,000 iterations from three converged and well-mixed MCMC chains. The parameters β_0, β_1, β_2 and α_1 are the coefficients in the intensity function associated with the background source, colonised patients, environmental contamination and additional contribution from being undetected while colonised, respectively.

Table 3 Summary of mean fractional risks (FRs) for the four different components of the intensity function for the enhanced and normal cleaning period. SD refers to the standard deviation. The background source is denoted by bg, undetected colonised patient by cxt, detected colonised patient by ct and environmental contamination by env.

	Enhanced cleaning				Normal cleaning			
	bg	*cxt*	*ct*	*env*	*bg*	*cxt*	*ct*	*env*
Mean	0.5	0.16	0.12	0.22	0.41	0.18	0.085	0.32
SD	0.19	0.079	0.097	0.17	0.22	0.088	0.072	0.22
2.5% quantile	0.12	0.03	0.0038	0.008	0.026	0.025	0.0026	0.013
Median	0.51	0.16	0.094	0.19	0.42	0.18	0.066	0.3
97.5% quantile	0.83	0.33	0.36	0.62	0.81	0.35	0.27	0.76

estimated background transmission potential was due to the larger number of colonised patients detected in the enhanced cleaning period, having accounted for the influences of the other colonised patients in the ward and the environmental contamination, noting that environmental contamination measurements were lower in the enhanced cleaning period (with an average of 49.2 cfu/cm^2 compared with 57.9 cfu/cm^2 in the normal cleaning period and as shown in Fig. 1).

Undetected colonised patient had a larger transmission potential compared with detected patient

In both time periods, an undetected colonised patient has a substantially larger additional contribution (α_1) to subsequent MRSA acquisitions in the ward compared with a detected colonised patient (β_1). The estimated posterior

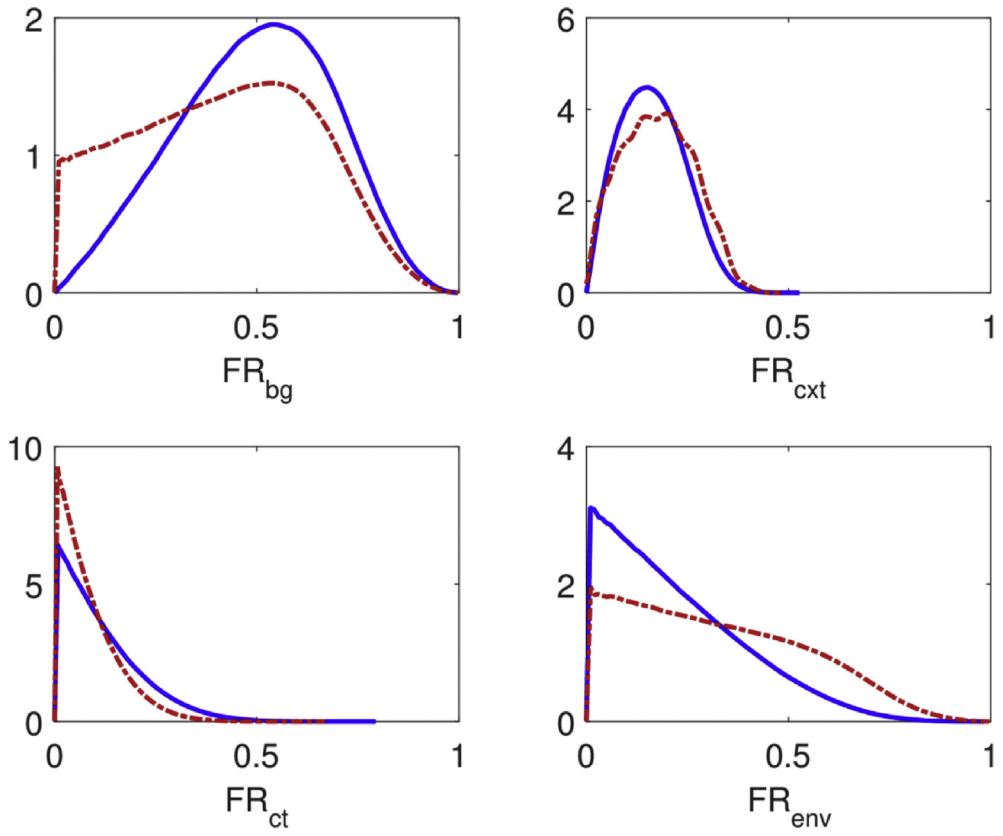

Figure 3 Kernel density estimates of mean fractional risks (FR). The solid blue and dashed red outlines correspond to the enhanced cleaning period and normal cleaning period, respectively. The background source is denoted by bg, undetected colonised patient by cxt, detected colonised patient by ct, and environmental contamination by env. (For interpretation of the references to color/colour in this figure legend, the reader is referred to the Web version of this article.)

probability of α_1 being greater than β_1 was 0.888 in the enhanced cleaning period and 0.951 in the normal cleaning period. This finding highlights the importance of ensuring hospital wards have adequate screening to minimise the number of undetected MRSA patients present in the ward, and shows the efficacy of the decolonisation treatment provided to detected patients in controlling MRSA transmission.

MRSA acquisition risk highest from background source unrelated to colonised patient and environmental contamination

The background source was the most likely MRSA acquisition pathway out of the four pathways considered. In both periods, the background source had the largest mean FR compared with environmental contamination, undetected MRSA patients and detected MRSA patients (Table 3).

Environment contamination was more likely to be a source of acquisition than detected or undetected colonised patients

Environmental contamination was the second most likely MRSA acquisition pathway, followed by undetected colonised patients and detected colonised patients, in both periods (as indicated by their mean FR estimates shown in Table 3). Both detected and undetected colonised patients were associated with small relative importance in explaining the observed MRSA acquisitions in the ward (as measured by their FR estimates), and their relative importance were similar between enhanced and normal cleaning periods (Fig. 3).

Enhanced cleaning lowered the MRSA acquisition risk from environment contamination

A smaller relative importance was assigned to the environmental contamination in the enhanced cleaning period compared with the normal cleaning period (with a mean FR estimate of 0.22 in the enhanced cleaning period and 0.32 in the normal cleaning period). This was also reflected in the notable shift when comparing the environmental contamination FR distributions in the both periods despite the large variability associated with the estimates (Fig. 3). In contrast, the relative importance of the background source was more pronounced in the enhanced cleaning period (with a mean of 0.50 and 0.41 in the enhanced and normal cleaning periods, respectively) as the fractional risk components sum to 1 and the patient contributions remained relatively similar across periods.

Environmental contamination accounts for a portion of background source in previous models

The results obtained from the full model described in the Methods section were compared with a simplified model without the environmental contamination component in order to investigate how the estimates differ for the various components (see Web Supplementary D for corresponding results and graphical outputs). Very similar results were obtained for the patient-related parameters β_1 and α_1, as well as their FR distributions, indicating that the environmental contamination component actually explains a portion of the general 'background' term in other similar models.

The full model had similar statistical model fits compared with the simplified model in both periods, indicating that needing an additional parameter in the full model did not disadvantage the model's performance (in terms of DIC_6) compared with the model without environmental contamination. The DIC_6 values for the full and simplified models were 317.75 (standard error (SE): 0.01) and 317.10 (SE: 0.009) respectively in the enhanced cleaning period, and 198.40 (SE: 0.01) and 198.13 (SE: 0.01) in the normal cleaning period. The full model is thus a viable alternative to the model without environmental contamination when environmental contamination data are available. Similar inferences were obtained with the other environmental data smoothers.

Discussion

For the chosen study ward, the environmental contamination was shown to have the second largest FR contribution (behind the generic background source) in the MRSA acquisition process in both normal and enhanced cleaning periods, with a slightly increased contribution in the normal cleaning period (Fig. 3 and Table 3). The environmental contamination contribution is greater than those from undetected and detected colonised patients, suggesting that it might be more beneficial to target improvements in cleaning practices rather than interventions solely targeting MRSA patients for this ward. The MRSA patient management practices currently in place appear efficacious noting the relatively smaller contributions from known and unknown colonised patients (*cxt* and *ct*).

The NHPP model presented is the first to incorporate environmental contamination into the intensity function and use environmental contamination data to estimate model parameters. The model was able to obtain good parameter estimates with limited data as well as highlighted clinically sensible differences, or lack thereof, between enhanced and normal cleaning periods. There was a larger background source parameter in the enhanced cleaning period accounting for the fact that there were more MRSA colonisations reported during enhanced cleaning. The model also showed very similar results for patient-related parameters and inferences across the periods, reflecting the fact that the cleaning intervention was unlikely to have affected the transmission intensity from direct contact with colonised patients.

Environmental contamination has been frequently speculated to contribute to the background source in similar modelling studies which did not explicitly model its contribution [12,14,16]. Our work provided quantitative evidence to support this claim, particularly when comparing the parameter estimates of the full model with the simplified model. However, the relative importance of the background source was still substantial, albeit smaller in the full model due to the inclusion of the environmental contamination term. The background source here relates to any potential transmission source that is not directly related to the colonised patients or the ward's environmental contamination. Examples of potential contributors to the background source here include contaminated equipment that is shared between wards, contaminated or colonised healthcare workers, and colonised visitors. The difficulty in attributing a specific cause to this background source remains a limitation of this work, and other similar modelling studies. Resolving the specific contributors to the background source would require continual comprehensive surveillance of patients, the ward environment, shared hospital equipment, visitors and healthcare workers, which is not generally feasible due to staffing, laboratory and cost constraints.

While the model estimated a larger relative colonisation risk from environmental contamination during normal cleaning compared with enhanced cleaning, this effect is dependent on the choice of smoother used for $E(t)$ where the more variable smoother might not provide as clear a separation between the results obtained for the different periods. Despite this, the model with the environmental contamination component provided similar DIC_6 estimates compared with the model without environmental contamination for both periods. Furthermore, a larger weight, as measured by the FRs, was merely assigned to the generic background source in the absence of an environmental contamination term in the intensity function. This particular inference does not provide a readily targeted transmission source and is of limited value to clinical decision makers.

The use of ACC as an indicator of environmental contamination contributing to MRSA transmission in a hospital ward is a proxy measure; there is a statistically significant positive association between ACC levels and detection of *S. aureus* in environmental samples [29]. While a more direct measure would be ideal, it is difficult to detect MRSA from a randomly sampled environmental site, and more sophisticated data collection methods are generally too costly.

The environmental contamination data smoother used here provided a conservative assumption on how closely ACC reflected the actual MRSA pressure from environmental contamination. The smoother could be extended to further scrutinize the role of environmental contamination in the MRSA colonisation process. Two noteworthy extensions are the use of more sophisticated smoothers such as generalized additive models [30] or Gaussian processes [31,32], and the addition of colonised patient covariates into the smoothing procedure to more realistically capture the interlinkage of MRSA-positive patients, environmental contamination and patient colonisation. The main challenge here would be to formulate a smoother that could handle the relative sparsity of the environmental contamination data in obtaining daily estimates (or finer) from weekly data as required by the NHPP model.

The NHPP patient model could also be extended subject to the availability of additional data. Extensions such as the inclusion of screening test sensitivity, and probabilistic colonisation upon admission have been proposed and implemented [12], but rely on data structures not available with this data set. Patient heterogeneity could be incorporated by including patient-specific covariates (for example, antibiotic use) into the intensity function, or extending the NHPP model to have a non-exponential tolerance level before developing an MRSA colonisation [33]. Such extensions however would result in the intensity function no longer being piecewise constant, complicating the inference procedure for this particular data set with limited information.

Recent research using whole genome sequencing inferred that colonised patients may not make as strong a contribution to the risk of colonisation in non-outbreak scenarios [34,35]. This is supported by the NHPP model in this study. Therefore, increasing model complexity in terms of patient heterogeneity might not yield substantially different findings at the cost of complicating the inference procedure further, particularly for limited-information data sets. Use of high resolution genetic data, such as whole genome sequencing data, of the pathogen to infer a detailed transmission network [36] also has its own set of difficulties [37] and could further complicate the modelling process. A more fruitful avenue of investigation might be to quantify the influx of community-associated MRSA [38] instead, as it may form a more substantial part of the background source term. The FR measure used here is readily adapted to handle this inclusion of another source term with a different unit.

Conclusions

The NHPP model presented here was able to infer that environmental contamination does play a contributory role toward MRSA incidence observed in the study ward despite limitations in the data set. It also showed that the environmental contamination component accounts for what would have been included in the background source in the absence of the component. A larger relative contribution from the environmental contamination was also inferred by the model during the normal cleaning period compared with the enhanced cleaning period.

Ethics

The manuscript uses previously published de-identified patient data from a study evaluating a hospital cleaning intervention. The patient data were collected as part of routine clinical practices. There was no direct patient interaction in the study. No individual patient data were reported in the manuscript.

Authorship statement

XJL and ANP conceived and developed the methods used in this study. SJD provided the data used this study, clinical knowledge of the application and key clinical input into the model development. ANP provided critical input into the model development and analysis. XJL conducted the analysis, wrote the manuscript and revised the manuscript following co-authors' feedback. ANP and SJD critically reviewed the manuscript. All authors approved the submitted version of the manuscript.

Conflicts of interest

Two authors declare that they have no conflicts of interest. One author has an editorial affiliation with the journal and is not involved with the review or decision process for this manuscript.

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Provenance and peer review

Not commissioned; externally peer reviewed.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.idh.2018.02.005.

References

[1] Tong SYC, Holden MTG, Nickerson EK, Cooper BS, Köser CU, Cori A, et al. Genome sequencing defines phylogeny and spread of methicillin-resistant *Staphylococcus aureus* in a high transmission setting. Genome Res 2015;25(1):111—8.

[2] Albrich WC, Harbarth S. Health-care workers: source, vector, or victim of MRSA? Lancet Infect Dis 2008;8(5):289—301.

[3] Dancer SJ. Controlling hospital-acquired infection: focus on the role of the environment and new technologies for decontamination. Clin Microbiol Rev 2014;27(4):665—90.

[4] Boyce JM, Potter-Bynoe G, Chenevert C, King T. Environmental contamination due to methicillin-resistant *Staphylococcus aureus*: possible infection control implications. Infect Control Hosp Epidemiol 1997;18(9):622—7.

[5] Weber DJ, Rutala WA. Introduction: understanding and preventing transmission of healthcare-associated pathogens due to the contaminated hospital environment. Infect Control Hosp Epidemiol 2013;34(5):449—52.

[6] McBryde ES, McElwain DLS. A mathematical model investigating the impact of an environmental reservoir on the prevalence and control of vancomycin-resistant enterococci. J Infect Dis 2006;193(10):1473—4.

[7] Wolkewitz M, Dettenkofer M, Bertz H, Schumacher M, Huebner J. Environmental contamination as an important route for the transmission of the hospital pathogen VRE: modeling and prediction of classical interventions. Infect Dis Res Treat 2008;1:3—11.

[8] Hall IM, Barrass I, Leach S, Pittet D, Hugonnet S. Transmission dynamics of methicillin-resistant *Staphylococcus aureus* in a medical intensive care unit. J R Soc Interface 2012;9(75): 2639—52.
[9] Wang X, Xiao Y, Wang J, Lu X. A mathematical model of effects of environmental contamination and presence of volunteers on hospital infections in China. J Theor Biol 2012;293: 161—73.
[10] Wang X, Xiao Y, Wang J, Lu X. Stochastic disease dynamics of a hospital infection model. Math Biosci 2013;241(1):115—24.
[11] Dancer S, White L, Lamb J, Girvan EK, Robertson C. Measuring the effect of enhanced cleaning in a UK hospital: a prospective cross-over study. BMC Med 2009;7:28.
[12] Forrester ML, Pettitt AN, Gibson GJ. Bayesian inference of hospital-acquired infectious diseases and control measures given imperfect surveillance data. Biostatistics 2007;8(2): 383—401.
[13] Cooper BS, Medley GF, Bradley SJ, Scott GM. An augmented data method for the analysis of nosocomial infection data. Am J Epidemiol 2008;168(5):548—57.
[14] Kypraios T, O'Neill PD, Huang SS, Rifas-Shiman SL, Cooper BS. Assessing the role of undetected colonization and isolation precautions in reducing methicilin-resistant *Staphylococcus aureus* transmission in intensive care units. BMC Infect Dis 2010;10(29).
[15] Worby CJ, Jeyaratnam D, Robotham JV, Kypraios T, O'Neill PD, De Angelis D, et al. Estimating the effectiveness of isolation and decolonization measures in reducing transmission of methicillin-resistant *Staphylococcus aureus* in hospital general wards. Am J Epidemiol 2013;177(11): 1306—13.
[16] Wei Y, Kypraios T, O'Neill PD, Huang SS, Rifas-Shiman SL, Cooper BS. Evaluating hospital infection control measures for antimicrobial-resistant pathogens using stochastic transmission models: application to vancomycin-resistant enterococci in intensive care units. Stat Methods Med Res 2018; 27(1):269—85. 0962280215627299.
[17] Forrester M, Pettitt AN. Use of stochastic epidemic modeling to quantify transmission rates of colonization with methicillin-resistant Staphylococcus aureus in an intensive care unit. Infect Control Hosp Epidemiol 2005;26(7):598—606.
[18] McBryde ES, Pettitt AN, Cooper BS, McElwain DLS. Characterizing an outbreak of vancomycin-resistant *Enterococci* using hidden Markov models. J R Soc Interface 2007;4(15): 745—54.
[19] Gibson GJ, Renshaw E. Estimating parameters in stochastic compartmental models using Markov chain methods. Math Med Biol 1998;15(1):19—40.
[20] Forrester ML. Epidemic models and inference for the transmission of hospital pathogens: school of mathematical sciences, faculty of science, Queensland University of Technology. 2006.
[21] Gijbels I, Prosdocimi I. Loess. Wiley Interdiscip Rev Comput stat 2010;2(5):590—9.
[22] Stewart M, Bogusz A, Hunter J, Devanny I, Yip B, Reid D, et al. Evaluating use of neutral electrolyzed water for cleaning near-patient surfaces. Infect Control Hosp Epidemiol 2014;35: 1505—10.
[23] Bogusz A, Stewart M, Hunter J, Yip B, Reid D, Robertson C, et al. How quickly do hospital surfaces become contaminated after detergent cleaning? Healthc Infect 2013;18:3—9.
[24] Kramer A, Schwebke I, Kampf G. How long do nosocomial pathogens persist on inanimate surfaces? A systematic review. BMC Infect Dis 2006;6:130.
[25] Sherlock C, Fearnhead P, Roberts GO. The random walk Metropolis: linking theory and practice through a case study. Stat Sci 2010;25(2):172—90.
[26] Brooks S, Gelman A, Jones G, Meng X-L. Handbook of Markov chain Monte Carlo. CRC press; 2011.
[27] Gelman A, Carlin JB, Stern HS, Rubin DB. Bayesian data analysis. Taylor & Francis; 2013.
[28] Celeux G, Forbes F, Robert CP, Titterington DM. others. Deviance information criteria for missing data models. Bayesian Anal 2006;1(4):651—73.
[29] Dancer SJ, White L, Robertson C. Monitoring environmental cleanliness on two surgical wards. Int J Environ Res Publ Health 2008;18(5):357—64.
[30] Wood S. Generalized additive models: an introduction with R. CRC press; 2006.
[31] Rasmussen CE, Williams CKI. Gaussian processes for machine learning. The MIT Press; 2006.
[32] Lloyd C, Gunter T, Osborne M, Roberts S, editors. Variational inference for Gaussian process modulated Poisson processes. International Conference on Machine Learning; 2015.
[33] Streftaris G, Gibson GJ. Non-exponential tolerance to infection in epidemic systems — modeling, inference, and assessment. Biostatistics 2012;13(4):580—93.
[34] Price JR, Golubchik T, Cole K, Wilson DJ, Crook DW, Thwaites GE, et al. Whole-genome sequencing shows that patient-to-patient transmission rarely accounts for acquisition of *Staphylococcus aureus* in an intensive care unit. Clin Infect Dis 2014;58(5):609—18.
[35] Long SW, Beres SB, Olsen RJ, Musser JM. Absence of patient-to-patient intrahospital transmission of *Staphylococcus aureus* as determined by whole-genome sequencing. mBio 2014;5(5).
[36] Worby CJ, O'Neill PD, Kypraios T, Robotham JV, De Angelis D, Cartwright EJP, et al. Reconstructing transmission networks for communicable diseases using densely sampled genomic data. Ann Appl Stat 2016;10(1):395—417.
[37] Worby CJ, Lipsitch M, Hanage WP. Within-host bacterial diversity hinders accurate reconstruction of transmission networks from genomic distance data. PLoS Comput Biol 2014; 10(3):e1003549.
[38] DeLeo FR, Otto M, Kreiswirth BN, Chambers HF. Community-associated meticillin-resistant *Staphylococcus aureus*. Lancet 2010;375:1557—68.