**Main Manuscript for**

Hospital environmental reservoirs could shape nosocomial transmission and implications for bacterial communities coexistance

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Main Text

Figures 1 to 6

Tables 1 to 2

**Abstract (244/250 words)**

**Significance Statement (118/120 words)**

**Main Text**

**Introduction**

Pathogenic bacteria asymptomatically colonize humans as they inhabit the human body across different body sites, i.e. are commensals with specialized niches. This has been referred to as the biogeography of bacterial communities in the human body. Researchers widely recognized this and focused research efforts on elucidating the diversity and distribution of the human microbiota. In hospital settings, once bacteria colonize typically sterile body sites, the human host cascades a series of immune responses toward treating the infection. This increases the length of stay and significantly contributes to mortality. Despite this fact understanding and quantifying in-hospital (nosocomial) transmission is tremendously challenging due to the different modes of transmission contributing to the burden, heterogeneous control in the hospital systems, imperfect observation of carriage and infection resulting in sparse data. Despite these difficulties, recent work suggests patient traffic determines nosocomial transmission, suggesting that bacterial pathogens have similar levels of transmission as well as possible similar modes.

Nosocomial transmission is thought to be a contribution of patient-to-patient, environmental, and health-care-workers associated transmission. This study compares different approaches to model patient-to-patient and environmental transmission dynamics. We consider first a model which tracks the environmental force of infection, assuming carriers are shedding bacteria at a constant rate to the environment, increasing the numbers of bacteria on surfaces, and thus increasing the force of infection. This environmental force of infection is also cleared constantly, reflecting the cleaning of surfaces in the hospital setting. Second, a more specified model would require explicit modeling of the bacterial communities in the environment. We simulate bacterium populations using a logistic growth to model a community of a bacterium in hospital surfaces. Third, bacteria live in multispecies communities on hospital surfaces. Consequently, we design a dynamic model that explicitly includes these multispecies communities co-existence. At last, we compared the transmission dynamics, i.e., the hospital prevalence and trade-off between the patient-to-patient and environmental transmission rates in the different models.

**Models of nosocomial transmission** **duet o person-to-person contact and environmental reservoirs**

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**Results**

### *Empirical patterns and heterogeneity of microorganism burden*

### *Identifiability: synthetic simulations and inference*

### *Inference using real data*

**Discussion**

**Materials and Methods**

### *Overview*

To estimate key epidemiological characteristics of AMROs, we developed an ABM to simulate the dynamics of these organisms in hospital settings. The model was informed by patient hospitalization and culture data from electronic healthcare records collected between February 1 2020 and February 28 2021. We coupled the ABM with a Bayesian inference algorithm and, using simulated outbreaks, validated the ability of this ABM-inference system to identify importation and nosocomial transmission rates. We then assimilated the real-world lab-confirmed positive case data and estimated the importation and nosocomial transmission rates for eight co-circulating organisms. Using these estimated parameters and the ABM, we were able to reproduce the time series of positive cases for six clusters of wards in the hospital system. The estimated importation rates and nosocomial transmission rates were compared for the eight organisms.

### *Data*

### *The transmission models with environmental force of infection*

### *Hospital-level Observational model*

### *Inference*

### *Identifiability: Synthetic simulations and inference*

### *Inference using real-world data*

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**Figures and Tables**Calendar

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**Figure 1. Empirical colonization of microbial organisms, hospital admissions and testing.** **A)** Incident observations for microorganisms of interest, from left to right and top to bottom: *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *MSSA*, *S. epidermis*, *Candida albicans*, *MRSA*, *E. faecalis*. **B)** Numbers of in-hospital patients (red) and admitted patients (blue) during the study period at daily resolution (weekly variability is evident). **C)** Numbers of in-hospital patients normalized by ward size (average occupancy per day during the study period); blue lines show the 10 most populated wards, green lines the 10 least populated, and the remaining wards are shown in gray in the background **D)** Heatmap showing the number of weekly cultures in each ward during the study period. **E)** Heatmap plot showing the number of patients admitted weekly to each ward during the study period.

Graphical user interface

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**Figure 2. A)** Adjacency matrix of transfers between wards during the study period. **B)** Adjacency matrix of transfers between clusters (aggregation of wards) during the study period. Color bar is in Log10 scale; darker colors indicate greater movement of individuals between each pair of wards or ward clusters. **C)** Incident colonization for the 8 study species; line color designates the cluster. **D)** Heatmap plot showing the number of weekly cultures identified in each ward cluster during the study period. **E)** Heatmap showing the number of patients admitted weekly to each ward cluster during the study period.

Text

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**Figure 3. Posterior parameter estimates.** Estimates for the **A)** importation rate and **B)** nosocomial transmission rate. Violin plots show the posterior distribution an estimates for the last iteration of the IF-EAKF (see Methods section) for 3 different runs of the model-inference system. Red dots show the value used in the synthetic simulation (i.e. the truth).Hospital-level simulations ofthe number of **C)** imported, **D)** nosocomial, and **E)** detected colonizations. Each column represents one scenario used for studying the identifiability of the system. Light and dark ribbons show the 95% and 50% uncertainty, respectively, constructed from 300 simulations of the posterior, and dots show the hospital-level observation of the synthetic simulation. Note, hospital level data were not used to optimize the model.

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**Figure 4. Posterior parameter estimates (A-B):** Violin plots show the posterior distribution and point estimates from the last iteration of the IF-EAKF (Methods section) for each of the microbial species (Data section). **C)** Hospital level fit: Light and dark ribbons show the 95% and 50% quantiles, respectively, constructed from 300 simulations with the posterior estimates of parameters. Observed carriage is plotted with dots at weekly time scale. D) Calibration plot. Hospital-level fit with 4 different confidence intervals (25%, 50, 75%, 95%). The black dotted line is the reference perfect calibration.

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**Figure 5. Importation and nosocomial contribution.** Weekly incident colonization of microbial species. Light and dark ribbons show the 95% and 50% quantiles, respectively, constructed from 300 simulations with the posterior estimates of parameters. Salmon/red color shows importation; light blue shows nosocomial transmission (left and right axis, respectively).

Diagram

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**Figure 6. A)** Schematic of agent states, S: susceptible to colonization and C: colonized. **B)** Model diagram showing the colonization process for a single ward facility; is the force of Infection for ward i, . **C)** Schematic of a hospital with 2 wards of different size; arrows show the movement process within the hospital at the ward level: admission to the hospital network, transfer between wards, and discharge from the hospital network.

**Table 1.** Parameters used for synthetic scenarios and investigation of ABM identifiability.

|  |  |  |
| --- | --- | --- |
|  | **Importation probability** | **Nosocomial contact transmission rate** |
| Scenario 1 | 0.10 | 0.04 |
| Scenario 2 | 0.05 | 0.04 |
| Scenario 3 | 0.07 | 0.04 |
| Scenario 4 | 0.10 | 0.01 |
| Scenario 5 | 0.03 | 0.02 |
| Scenario 6 | 0.03 | 0.025 |
| Scenario 7 | 0.015 | 0.02 |
| Scenario 8 | 0.15 | 0.04 |
| Scenario 9 | 0.20 | 0.03 |
| Scenario 10 | 0.30 | 0.035 |

**Table 2.** **Posterior estimates**. Mean posterior estimates for the eight species studied; both

importation and nosocomial transmission rates, γ and β, are presented as rates per day.

|  |  |  |
| --- | --- | --- |
| **Organism** | **Importation probability** | **Nosocomial transmission rate** |
| *E. coli* | 0.64 | 0.0022 |
| *K. pneumoniae* | 0.26 | 0.00875 |
| *MSSA* | 0.145 | 0.020 |
| *MRSA* | 0.11 | 0.0148 |
| *C. albicans* | 0.11 | 0.0244 |
| *S. epidermis* | 0.10 | 0.011 |
| *P. aeruginosa* | 0.09 | 0.055 |
| *E.faecalis* | 0.09 | 0.0052 |