Nosolink: An Agent-based Approach to Link Patient Flows and Staff Organization with the Circulation of Nosocomial Pathogens in an Intensive Care Unit

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Nosolink: An agent-based approach to link patient flows and staff organization with the circulation of nosocomial pathogens in an intensive care unit

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Abstract

Computational models and simulations are commonly employed to aid decision making in two areas of health care management: optimization of the use of hospital resources and control of the spread of hospital-acquired infections caused by antibiotic-resistant pathogens. We propose a model that combines the operational and the epidemiologic perspectives to size up the effect of understaffing and overcrowding on nosocomial contagion in a intensive-care unit. Specifically, we develop an agent-based model simulating contact-mediated pathogen transmission which allows establishing quantitative relations between patient flow, nurse staffing conditions and pathogen colonization in patients. The results of the model, once calibrated with data from the literature, should indicate under which conditions the variation in pathogen transmission resulting from management decisions can lead to significant increases in the incidence of health care-associated infections in the intensive care unit.

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Keywords: Intensive Care Unit; hospital acquired infection; staffing; nurse; agent-based modeling.

1. Introduction

Intensive-care units (ICUs) are essential departments in hospitals, but they are also very costly in terms of both equipment and staff. Efficient management of their resources is an imperative in the current context of increasing population demands and diminishing budgets [1-2]. Hospital-Acquired Infections (HAIs) are frequent adverse events in ICUs, where patients are vulnerable and require frequent interventions [3]. Besides threatening their safety, HAIs also increase the need for care and the length of stay of patients, they hinder the

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efficient management of the ICU and raise its overall costs [4]. The resulting disturbance deteriorates hygienic conditions and it favors the spreading of pathogens, leading to a vicious cycle of disorganization and infection [5].

Computational models have been widely used in the health care sector for decision making and for better understanding HAIs [6]. From the perspective of ICU management, operational models typically optimize the number of beds or the allocation of staff, while minimizing outcomes such as the queuing time of patients, or the number of cancelled surgeries or external referrals [7-8]. From the perspective of HAI control, epidemic models relate structural parameters (hospital facilities or staffing resources) and control strategies (*e.g.* patient isolation), with patient outcomes, such as the prevalence of colonization among patients, the incidence of infections or the emergence of antibiotic resistance [9-10]. Agent-based models (AbMs) are computational models that simulate the actions and interactions of multiple autonomous decision-making entities.

The objective of this communication is to demonstrate the potential of AbMs to tackle the relationship between patient flows, staffing levels and prevalence of pathogen colonization in the ICU. The remaining of the article is organized as follows: Section 2 describes related work regarding this topic, Section 3 describes the specifications of the model, Section 4 presents and discusses its results and Section 5 draws some conclusions and proposes further work.

2. Related works

Agent-based technology (*i.e.* multi-agent systems) is widely used in the management of the ICU to optimize bed occupancy of patients and to manage staffing resources [11-13]. It is also used to handle and process information in the monitoring of patients and in the surveillance of HAIs [14-15]. However, in multi-agent systems, agents do not necessarily represent real entities, but they refer to autonomous programs that interact with each other in order to improve an algorithmic search or a processing approach.

From now on, we restrict the definition of AbM to models whose agents explicitly represent an entity in the real world: either a patient, a Health Care Worker (HCW), a device or a hospital unit. Such models have been used in the management of health care services to optimize queuing problems [12-16], to compare cost-effectiveness of staffing policies [17] and to coordinate the strategy of multiple institutions for better controlling the spreading of HAIs [18]. AbMs describing a single ICU have been successfully employed to study particular aspects of the circulation of nosocomial pathogens in detail, for instance: the comparison of specific control strategies [19], the influence of the level of cohorting of patients [20-21], or the impact of heterogeneity in the compliance with hygienic measures [22], among others.

The AbM approach is particularly appropriate to model the spread of HAIs in the ICU under different organization regimes because it provides a natural description (it allows taking into account discrete events, the small size of the system and the stochastic nature of local interactions), it is flexible (it allows the incremental inclusion of complexity and the separate evaluation of factors that appear combined in reality), and it captures emergent phenomena. The vicious cycle of disorganization and infection presented in the first paragraph of the introduction is a typical example of emergence: the macro level behavior (*i.e.*: an increase in the incidence of infections) results from the micro level interactions (*i.e.*: the feedback between individual contagion and its promoting conditions).

This article presents an AbM for hand transmission of unspecified pathogens in a hospital ward, based on the model NOSOSIM [23] and focused on the characterization of patient fluxes and staff management. It is a first prototype for a decision support tool to guide ICU management heeding the control of HAIs.

3. Methods

3.1. The agent-based model Nosolink:

From the computational point of view, Nosolink is a finite-state automaton that can be described as a Moore machine: upon each time step (*ts*), the machine moves to the next state depending solely on its current state and according to predefined rules, which can be outlined in a state transition table or state diagram. However, such a description is cumbersome in this case due to the complexity of the model. For this reason, we present the model following a compact version of the standard ODD protocol [24].

The purpose of Nosolink is to relate patient flows, staffing levels and the circulation of pathogens in the ICU. It comprises three low-level entities: *patients*, and health care workers (HCWs) which are split into *nurses* or *physicians*. They may be either in a *healthy* or a *colonized* state. Additional characteristic variables of low-level entities are: *identifier*, location (*bed* and *sector*), *arrival* and *departure times* and daily *list of visits*. HCWs' are also characterized by their *work schedule, sick leaves*, *workload*, *fatigue,* and *occupation state*, which may be either *at work* or *at home*. The model iterates events in the ICU with a temporal resolution of one *ts* = 5 minutes and covering periods of 10^5 *ts* (approximately 250 days, or 8 months). The granularity of the model is the individual and its extent is the ICU, which is always divided into sectors of 6 beds each and which may comprise 6, 12, 18 or 24 beds, in total.

During the setup process, the model imports the work schedules of HCWs and it generates the individual variables for every agent. During the main loop of the simulator, actions are scheduled hierarchically and run sequentially. Each time step, the computes the moment of the day (*day*, *hour*, *time step*). Global events, such as shift of duties of HCWs or patient admission/discharge are carried out first, then, agents act one after each other without concurrency. The order of action of agents is set at random every time step and individual variables (*e.g.* colonization state) are updated after every agent's set of actions. Global variables (*e.g.* percentage of contagions from nurses to patients) are updated after all individuals have acted.

At the beginning of each day, the flow of patients is computed. First, discharge of patients in the ward is assessed: it occurs if patients stay in the ward exceeds a prefixed duration, the Length of Stay (LoS), which has been drawn from a long-tailed gamma distribution function at patient admission. Then, for every unoccupied bed, a new admission may occur with a pre-determined probability. As a result of this process, the daily bed occupation ratio (BO) varies between 65% and 100%. The workload and duties of HCWs are assessed next. Work organization of the staff follows labor standards in France (*i.e.:* working time set to 35 work hours per nurse per week, appropriate spacing of work/rest days and fair distribution of work schedules). Physicians work on two 12-hour duties, while nurses either work on two 12-hour duties or on three 8-hour duties. Nosolink allows the daily entry of a pathogen in the ward via a fixed probability of colonization at patient admission and through HCWs that remain colonized for successive work duties after contagion due to long-term carriage of the pathogen.

At the beginning of every hour, the workload and the fatigue modifier of working HCWs are updated and the working staff is relieved in correspondence with work schedules. At the beginning of each work duty, a set of assigned patients is defined for every working HCW and a list of daily visits is built for every agent. Patients are randomly assigned to nurses according to the nurse-to-patient ratio defined at setup (either 1:3 or 1:2), and subject to constraints imposed by understaffing. Physicians are assigned to each sector during the day shift and to the service as a whole during the night shift. One-to-one contacts are distributed throughout the duty and the order of visits to every patient is set at random.

At every time step, the colonization state of each agent is updated as a result of eventual contagion and natural recovery. Colonization of patients lasts through their stay. Duration of colonization of HCWs is set with an exponential distribution with mean: μ=10 hours. This implicitly accounts for any means of pathogen removal and it also allows for HCWs entering the ICU colonized as a result of long-term carriage. Pathogen transmission may occur in each one-to-one contact between a healthy HCW and a colonized patient, or *vice versa*. Transmission routes other than patient–HCW–patient are not accounted for. To create a realistic model of pathogen spread, we use published estimates of the per-contact transmission probability for methicillin-resistant *Staphylococcus aureus* (MRSA). Table 1 outlines the input values for the parameters of the model together with their sources.

Table 1. Model inputs: estimates of the performance of a prototype ICU and of the spreading of a prototype pathogen (MRSA).

Input parameter	Value	Reference
Patient-related		
- Bed Occupancy (daily patients per bed)	0.83	[27]*
- Length of Stay (characteristic parameters of the long-tailed distribution function; [LoS]=days)	Mean=4.2; Median=2.1 P(LoS<5)=80%; P(LoS>30)=1%	[28]
- Probability of colonization at admission	10% - 20 %	[29]
- Duration of colonization; [t_c(P)] = days	90	[30]
- Care requisites (number of daily visits)	6 nurse visits 1 physician visit day / night	[31]
HCW-related		
- Nurse-to-patient ratio	0.3 - 0.5	[27]
- Probability of pathogen transmission during a 30 - min patient-nurse visit	25 %	[21] †
- Probability of pathogen transmission during a 15 - min patient-physician visit	3 %	[21] †
- Duration of colonization; [t_c(HCW)] = days	0.43	[21] ‡
- Fatigue risk index of nurses (r_f)	0.5-2	[26]
- Hazard index for substitute nurses (s_f)	0.5-2	-

* Strictly speaking, bed occupancy is not an input parameter, but it is used to set the value of the probability of patient admission per empty bed (P_A). A bed occupancy of 83% is attained with P_A=60%.
† These values are computed from the minimal values given for 20-minutes visits using the formulae of the appendices.
‡ This value stands for the mean of an exponential distribution that implicitly accounts for the removal of pathogen carriage due to hand washing of HCWs. It is computed assuming an average50 % compliance and 90% effectiveness of hand-washing after each patient-HCW contact.

Nurses level of fatigue modifies the per-contact probability of pathogen transmission. Its value is calculated based on the current workload and previous roster history of the nurse (see Section 3.2). Nurses may also be absent from work during a predefined shortage period. The effect of absenteeism on the performance of the ICU is evaluated assuming different management strategies (see Section 3.3). Nosolink was implemented using Netlogo.4.1 [31], a free multi-agent modeling environment. The statistical analysis of the simulation outcomes was carried out using R [32], a free software environment for statistical computing.

3.2. Rosters and fatigue

Staff rosters list work duties of nurses during cycles of fixed duration. They are created using the software Shift Plan Assistant©, developed by Ximes (SPA) [25], which provides schedules compatible with a given set of constraints (maximum weekly workload, equitable shares, start and end times of duties, among others). The impact of the fatigue of nurses is described using the Fatigue and Risk Index© estimator developed by QinetiQ (FRI) [30], an empiric estimate deduced from statistical reports on fatigue-related workplace incidents.

FRI represents the relative risk of making a mistake while carrying out a routine procedure at any time, as compared to the average weekly risk of errors. Its value is computed at the beginning of every work duty based on the starting time and duration of the duty, the time span since the last break, and the general layout of the roster (*e.g.* number of successive work duties). Within Nosolink, FRI is used as a multiplicative factor of the per-contact pathogen transmission probability (r_f). Under the explored working conditions of nurses, $r_f \in [0.5,2]$. For physicians, fatigue is not explicitly described and the risk index is always set to r_f=1.

3.3. Sick leaves and absenteeism

Absenteeism is not explicitly described for physicians. Sick leaves of nurses are modeled by defining a shortage period (*e.g.* from day 100 to day 150) during which nurses may become sick with a given daily probability (p_n). Depending on the work schedule of sick nurses, sickness may lead to work absence. Approximately 40% of daily sick leaves throughout the shortage period result in work absence.

Whenever a nurse is absent, the model allows exploring three prototype management strategies to attend those patients assigned to the absent nurse: (i) *substitution*: the network of contacts is not altered but the individual per-contact probability of pathogen transmission is modified to represent the replacement with an external nurse; (ii) *over-task*: patients are assigned to other working nurses from the same sector; and (iii) *close bed*: patients are immediately removed from the model. In the current article, only substitution is explored.

4. Results and discussion

4.1. Analysis of uncertainty /robustness

Single simulation runs show random fluctuations that alternate between outbreaks of patient colonization and pathogen extinctions. Batch simulations comprising at least N=250 runs ensure that the mean prevalence of pathogen colonization in patients is predicted with 95% confidence and 5% resolution. The response time of the batch-averaged outcome to sudden changes in the model parameters lags up to 40 days. In order to ensure that our results capture stable simulation results rather than transient artifacts depending on the initial conditions, we assume a burnout period for the batch runs of 50 days.

4.2. Effect of the transmissibility of the pathogen

Here, we study variations in the predicted prevalence of pathogen colonization of patients that result from changes in pathogen transmissibility. Figure 1 depicts model predictions in an ICU with nurses working in 2x12 work duties and with a nurse-to-patient ratio of 1:2. Figure 1A shows the effect of varying the per-contact transmissibility of the pathogen between 0 and 1%. No significant differences are found in the model average outcomes when varying the size of the ward but a greater variance is observed for smaller wards.

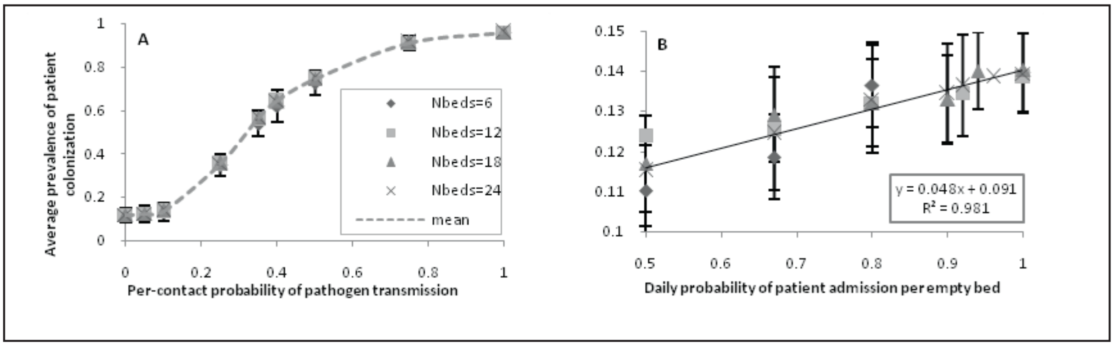

Fig. 1. Batch simulation of an ICU with nurses working with 2x12 duties. A) Prevalence of colonized patients averaged over 250 runs as a function of the probability of pathogen transmission per patient-nurse contact. B) Average prevalence of colonized patients as a function of bed occupancy when the probability of pathogen transmission per patient-nurse contact is set to 15%.

Figure 1A shows a sigmoidal response of the prevalence of colonization: for low values of the transmission probability, inter-individual transmission is less relevant than colonization at admission. Then, beyond a threshold value around 0.15 a sudden increase in prevalence of colonization is observed. Finally, for transmission probabilities over 0.5, an apparent saturation of spreading occurs. This behavior suggests the existence of a minimum effective transmissibility and a maximum carrying capacity of the system.

4.3. Effect of bed occupancy

Figure 1B shows a linear increase in the prevalence of colonized patients with bed occupancy when the probability of pathogen transmission per patient-nurse contact is set to 0.15. The daily probability of patient admission per empty bed varies from 0.5 to 1. As a consequence, the average bed occupation ratio varies from 65% to full capacity.

Two remarks should be made here. First: even if the model outcome fits well with a linear increase, the resulting slope is small compared to the variance of the mean predicted prevalence, therefore no statistical significance to grant the proportionality between pathogen spread and bed occupancy. And second, the reduction in colonization observed in the model for lower bed occupancy arises from an effective increase of the patient-to-nurse ratio. This would not occur in real-world ICUs, where staff would be relocated to other services. Finally, in real life, reductions of bed occupancy are usually occasional, while it was persistent in these simulations.

4.4. Effect of the nurse-to-patient ratio (NPR)

Figure 2 compares scenarios where nurses have either two (NPR=0.5) or three (NPR=0.33) assigned patients during their work duty. It shows model predictions in an ICU with nurses working in 2x12 work duties and using different values of pathogen transmissibility and sizes of the ward. Figure 2 suggests that decreasing the nurse-to-patient ratio increases the spread of the pathogen. This effect becomes more apparent for higher values of the per -contact probability of pathogen transmission. Again, no significant differences are found when the size of the ICU is varied, and greater variance is observed for smaller ICUs. The results presented up to now demonstrate the consistency of the model outcomes.

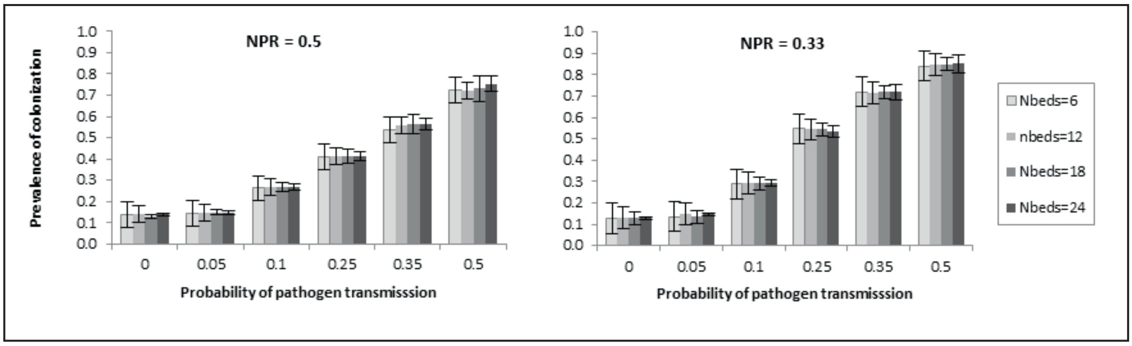

Fig. 2. Simulation results comparing an ICU with either two or three patients assigned to each nurse (NPR: nurse-to-patient ratio) for different values of pathogen transmissibility. Darker colors represent larger sizes of the ICU (N_{beds}=6, 12, 18 and 24).

4.5. Effect of nurse rosters and of fatigue-induced errors

The next example shows the effect of varying the rosters of nurses while maintaining all other working conditions constant. It considers a 12-bed ICU where nurses are working 35 hours per week in 3x8 shifts. Specifically, it compares two prototypical 15-day work cycles. During both work cycles, each team of nurses works three morning duties (D), three afternoon duties (A) and three night duties (N), and has six rest days (0). The work duties are scattered differently throughout each work cycle (Table 2), which leads to different values of the daily risk index averaged over the nurses on duty (Figure 3).

Table 2. Two nurse rosters (R_I and R_{II}) for nurses working 35 hours per week in 3x8 shifts and covering a 15-day work cycle, generated with the software SPA. D: morning duties, A: afternoon duties, N: night duties and 0: resting days.

day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
R_I	A	A	A	0	N	N	0	0	D	N	0	0	D	D	0
R_{II}	D	D	D	A	A	A	0	N	N	N	0	0	0	0	0

These rosters have distinct structures and they lead to different values of the risk index when fed into the FRI estimator: duties in roster R_I are evenly distributed, so that fatigue gradually increases during the cycle, while in roster R_{II} duties are stacked together, so that fatigue is accumulated over longer time and relieved during longer resting periods. Figure 3 shows the daily risk index computed for both rosters and averaged over all working nurses ($<r_f>$) over three work cycles: it shows that R_{II} registers higher values after stacked working periods ($<r_f>(R_I)$=1.05 against $<r_f>(R_{II})$=1.3) and slightly lower values after resting periods ($<r_f>(R_I)$=0.63 against $<r_f>(R_{II})$=0.66). In this case, the risk is not accumulated over successive cycles, thus meaning that a rest period of one day is enough to completely recover from fatigue after a row of two morning duties.

Rosters affect the predicted colonization prevalence in Nosolink in two ways: first, the per-contact probability of pathogen transmission is modified by the alteration of r_f. Second, the chance of HCWs re-entering the ICU while still colonized varies with the distribution and duration of the rest periods. When both effects are taken into account, we find that a mean predicted prevalence of 31% (95% prediction interval: [20%-41%]) for roster R_I and 41% (95% prediction interval: [28%-53%]) for roster R_{II}. These results suggest a mechanism by which nurse staffing may significantly affect the spreading of nosocomial pathogens.

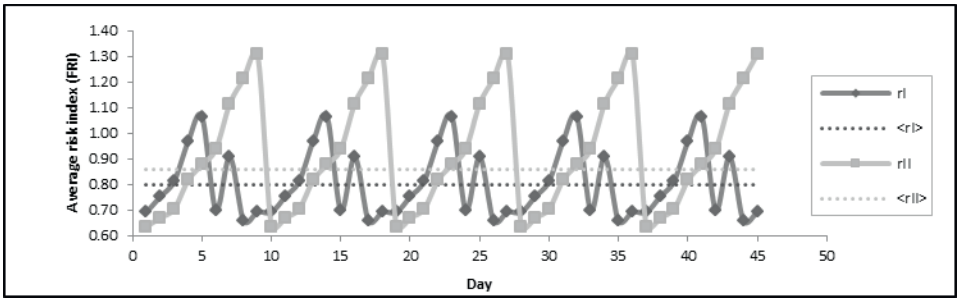

Fig. 3. Value of the fatigue risk index averaged overworking nurses for two rosters (R_I and R_{II}) and their temporal means ($\langle R_I \rangle$and $\langle R_{II} \rangle$).

4.6. Effect of nurse absenteeism and substitution

The last example uses Nosolink to evaluate the effect of replacing absent nurses with substitute nurses whose per-contact transmission probability is modified by a multiplying factor (s_f). Values of s_f lower than 1 indicate a lower risk of pathogen transmission with substitute nurses, while values larger than 1 indicate an increased risk. A measure of this effect is the hazard ratio, which is defined as the average prevalence of colonization among patients through the shortage period divided by the prevalence of colonization averaged outside this period.

Figure 4 presents the hazard ratios predicted for different values of the daily probability of a nurse being sick during the shortage period (p_n, ranging from 5 to 50%) and of the multiplying factor of the per-contact transmission probability for substitute nurses (s_f,= {0.8, 1.5 and 2}). It shows how the predicted hazard ratio depends both on the level of substitution and on the skills of substitute nurses. For instance, according to Nosolink, if we consider a daily probability of a nurse being sick around 25% (which renders to an average rate of nurse absenteeism around 10%) and we assume that the per-contact transmission probability of substitute nurses is twice that of the original nurses (s_f=2), substitution becomes significantly hazardous, and the risk of epidemic outbreaks relative to the risk without absenteeism increases by a factor 1.5.

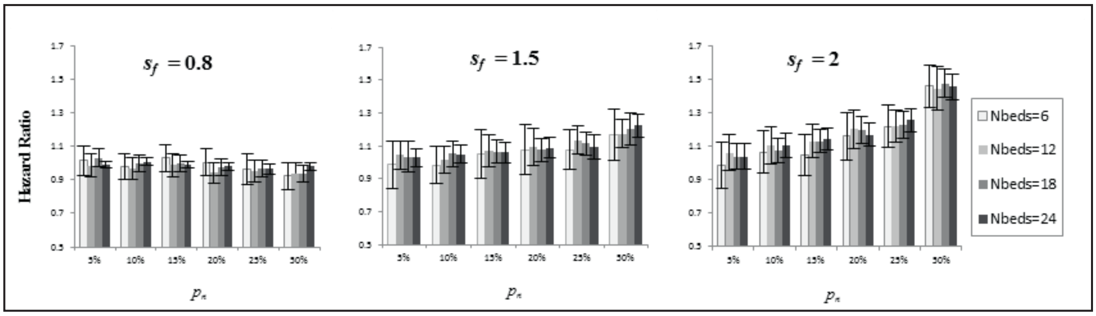

Fig. 4.Simulation results comparing substitution strategies for different percentages of sick nurses (p_n) and per-contact transmission probabilities for substitute nurses (multiplying factor s_f). The hazard ratio is the average prevalence of colonization among patients during shortage period, divided by the average prevalence outside this period. Darker colors represent larger sizes of the ICU.

5. Conclusions

We have presented Nosolink, an AbM designed to evaluate the relation between staff organization and pathogen spreading in the ICU. The model has been put to test on several prototype scenarios, in order to verify its validity. Nosolink is a potential tool for decision making in health care management because it allows: i) formalizing hypothesis on how staffing decisions affect pathogen transmission in the ward, ii) drawing quantitative predictions from them, and iii) establishing their degree of confidence. A more detailed description of the model, as well as an open-source sample version of the simulator are available from the authors on request.

Future research entails a systematic exploration of the scenarios presented here: more detailed studies will be carried out regarding patient flows, staff rosters, staff absenteeism and how it can be addressed. In a first step, model results should be compared to statistic epidemiological data from the literature in order to establish whether contact-mediated pathogen transmission suffices to explain the relations between organization of the ICU and incidence of HAIs observed in different settings. A second step would entail the calibration of the model to specific scenarios in order to take advantage of its predictions in the management of real ICUs.

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