Agent-based Modeling to Evaluate Nosocomial COVID-19 Infections and Related Policies

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ABSTRACT

To assess nosocomial spread of COVID-19 and policies to mitigate it, we develop an agent-based model (ABM) that simulates patient admissions to a mid-size hospital during the early phase of the COVID-19 pandemic in the United States. In this work, we demonstrate the viability and utility of ABMs to study COVID-19 transmission dynamics inside hospitals and care facilities. We also use an iterative stochastic sampling method to calibrate a Discrete-Time Markov Chain to model infection progression in patients and hospital staff, and evaluate the efficacy of various policies of personal protective equipment (PPE) use and COVID-19 testing in the hospital. The results highlight the importance of PPE in preventing nosocomial COVID-19.

KEYWORDS

Agent-based simulation, Discrete-Time Markov Chain, COVID-19, nosocomial infection

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1 INTRODUCTION

Healthcare-associated infections, or nosocomial infections, are those that are acquired in a hospital or other healthcare settings. Such infections are spread by various means, including between a healthcare worker and patients and between patients [1]. Nosocomial infections in the hospital are associated with increased length of stay, high health morbidity and mortality and significant economic burden globally [2]. To mitigate these types of infections, healthcare systems institute various policies, such as hand washing and equipment sterilization, with varying levels of compliance and success [3, 4].

The nature of the COVID-19 pandemic has created many challenges to containing its nosocomial spread within the hospital setting [5, 6]. Although the vast majority of COVID-19 infections may be asymptomatic or require home-based care, a significant portion of affected individuals require hospitalization. The SARS-Cov-2 virus, the cause of COVID-19 illnesses, is particularly transmittable in closed indoor settings, such as a hospital ward [7]. In addition, since the start of the pandemic, resources needed to prevent the spread, such as personal protective equipment (PPE) and testing, have been in limited supply and required management strategies [8, 9]. As a result, many health systems face difficult decisions on determining which policies would be most effective for controlling nosocomial COVID-19 spread among healthcare workers and patients. In this paper, we address this challenge through computer simulations projecting the impact of policies related to the frequency of testing and the use of PPE.

Computer simulations are commonly used for analyzing the performance of complex systems under various scenarios. In healthcare and medical decision-making, simulations such as compartmental epidemiological models have been employed for decades to study transmission dynamics and guide policy. Simulations combine domain knowledge, in the form of construction and logic, and data, in the form of parameter estimates, to create a virtual framework for experimentation. These models can empower decision-makers to explore scenarios that are too costly or impractical for real-world experimentation.

Agent-based models (ABMs) in particular are employed to study complex systems where the interactions between entities of interest (i.e. agents) play an important role in affecting system dynamics and outcomes. Over the past decade, there has been significant interest in the application of ABMs to problems in healthcare [10–12]. These span a range of topics from emergency room resource planning [13], epilepsy treatment [14] to infectious disease control, [15–17] During the COVID-19 pandemic, researchers have demonstrated the utility of agent-based models in analyzing community spread and efficacy of interventions [18–20]. However, to the best of our knowledge, there are no studies involving ABMs to evaluate nosocomial COVID-19 infections in the setting of a hospital or care-facility. Hence, the aim of this work is to demonstrate the

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feasibility and utility of ABMs to study COVID-19 transmission and control in hospitals.

2 METHODS

Settings

Our model hospital emulates a hypothetical mid-sized hospital in the state of New York and contains 98 beds. We simulated the first three months of the COVID-19 pandemic, from March to May 2020, when infection rate was high and hospitals were observing an increasing number of admitted patients with COVID-19. Impacts of personal protective equipment (PPE) use, COVID-19 testing, or quarantine were not clearly identified.

Model

We develop an ABM to simulate hospital activities and spread of COVID-19 infection in hospital, in order to evaluate the effects of different strategies on nosocomial infections and patient outcomes. Our ABM is a discrete-time simulation model that runs in a time unit of 5 simulated minutes. In the simulated hospital environment, we generate 2 types of agents: patients and staff. Both patients and staff are assigned to specific wards, rooms, and beds and probabilistically interact with each other. COVID-19 exposure occurs through the agent interactions, and infection state is modeled by a Markov transition matrix. We assume that other than staff and patients, visitors are not susceptible to COVID-19 infection and thus not considered a part of this model. Our methodology borrows significantly from Codella et al. [16] in both using an agent-based simulation to study nosocomial infection and a Markov Chain to model infection progression. However, we extend this work in several ways, namely by using COVID-19 as the target infectious disease, modeling infection progression in both patients and hospital staff, and allowing for uncertainty in symptomatic and severe COVID-19 infections through use of testing. Our model was written in Python 3.7 using the ABM package Mesa (0.8.7), which can be found here: https://github.com/projectmesa/mesa.

Agents, Environment, and Logic. We consider two different types of agents: patients and staff. Both agent types have common attributes that track COVID-19 status, COVID-19 test result, and usage of PPE. Agents can interact with each other in patient rooms and in ward stations. During each interaction, there is a probability of COVID-19 exposure, modeled by a Bernoulli distribution, if one of the interacting agents is infected.

Patient Agent For simulating patient agents, we use the Statewide Planning and Research Cooperative System (SPARCS) Inpatient De-identified File that contains discharge-level detail on patient characteristics, diagnoses, treatments, services, and charges [21]. This SPARCS data contains more than 2.3 million records from the patients admitted in 2016. We exclude records with missing facility IDs, records from the facilities that have fewer than 100 admission records in 2016, or records without gender information. In total, we exclude 0.2% of the original data.

At model initialization, agents that represent patients already admitted to the hospital are generated according to distributions of patient characteristics from the SPARCS data. Arrivals of new patients follows a Poisson process with a rate function that can be configured to be stationary or non-stationary.

We sample patient characteristics from SPARCS data to generate patient agents. Each agent has a set of unique attributes including patient ID, age, gender, race, ethnicity, admitting facility, type of admission (e.g. urgent, elective, etc), Major Diagnostic Categories (MDC), and length of stay (LOS) value. Patient agents are created based on the arrival rate of patients to the hospital and are admitted if there is sufficient bed capacity. Upon admission, a patient's COVID-19 status is sampled from a discrete-distribution over the possible COVID-19 states determined. Depending on the scenario, a COVID-19 test is conducted to determine whether or not to send a patient to the COVID-19 ward. Otherwise, initial ward assignment is determined by MDC and APR. Ventilator is assigned based on ICU admission or COVID-19 status (severe state). Each patient is assigned to a room, a bed, and a set of staff - each working in alternating shifts. Over the course of a patient's stay, the agent will be receive service from its assigned staff agents according to a staffing schedule, or via random chance of the patient requesting service, thus simulating both staff-driven and patient-driven interactions.

Although a patient's baseline length of stay is predetermined, if a patient is COVID-19 positive at the time of discharge, the length of stay is extended by one day until the patient recovers. Otherwise, based on a sampled probability of death, the patient is discharged alive or dead.

Staff Agent Staff agents are created at the initialization and placed in a specific ward, where they are assigned a set of rooms and beds. The number of bed and patient assignments vary according to staff availability. Staff work for 12 hour shifts. During a shift, each staff agent will visit its assigned patients or remain in its respective ward's station where it can interact with other staff. Staff also respond to patients' calls. While we do not add more staff during the run, there are a number of 'reserve' staff that do not get assigned to specific wards at the beginning. When there is a shortage of staff in any ward due to increasing patient admission or staff infection, reserve staff will take over the work. Infected staff, if test positive, will be immediately put into a quarantine mode and cannot interact with other agents.

Environment Our hospital model is composed of 6 wards, each containing a station and a number of staff, rooms and beds. In addition to general, pediatrics, psychiatric, obstetric (OB) wards and intensive care unit (ICU), we created a COVID-specific ward for placing identified infected patients. Some rules are applied to ward placement, such as maximum age limit for pediatric ward and gender limit for OB ward. Upon arrival, patients are assigned a ward based on MDC code, level of severity, and COVID-19 status. In the event the initially assigned ward is full, the patient is placed in an available ward after taking into consideration gender and age. If a patient tests positive at time of admission and the COVID ward is at capacity, an attempt is made to place the patient in an empty room in another ward, with priority going to the ward where the patient would have been initially placed using MDC code and severity. If there are no other available wards, the patient is diverted from the hospital.

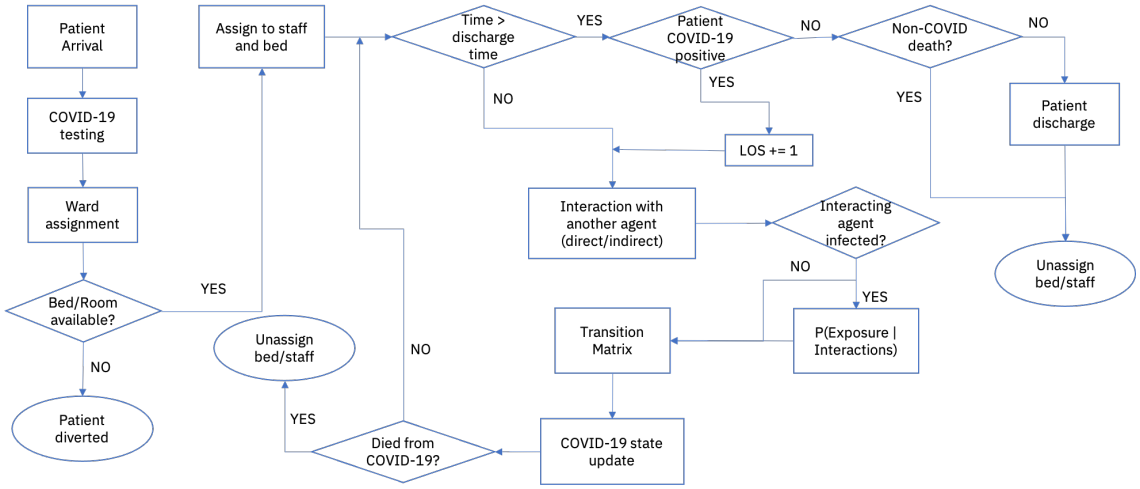

Figure 1: A flowchart depicting logic for each Patient agent type at each time step.

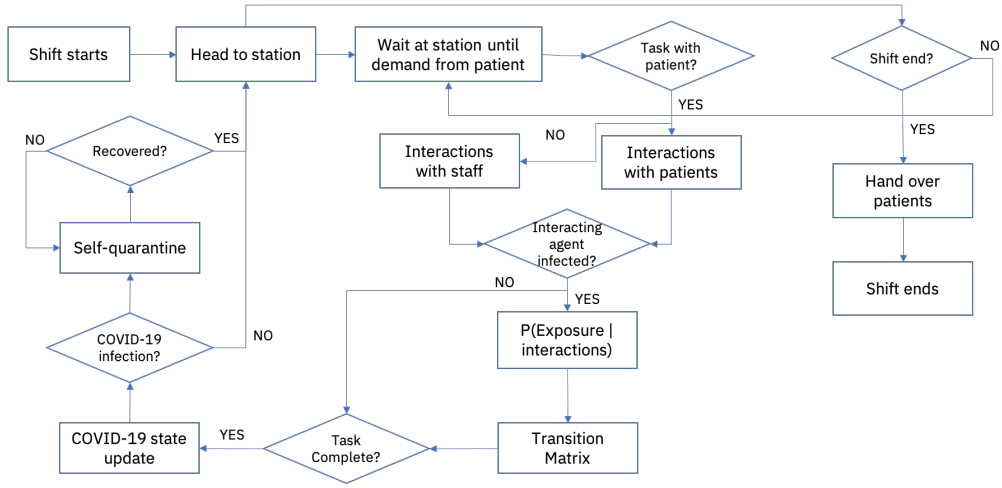

Figure 2: A flowchart depicting logic for each Staff agent type at each time step.

Interactions We implement two different types of interactions, direct and indirect, that occur depending on the involved agents. Interactions can happen in a patient room or in a staff station. In a patient room, a direct interaction occurs when a staff agent is treating its assigned patient. If there is another agent in the room (staff or patient), there is a possibility for an indirect interaction to occur between the staff and this other agent. An indirect interaction can also occur between patients sharing the same room. In the staff station, a direct interaction occurs between two staff agents. We generate unique two-pair combinations of the staff present in a ward's station room to simulate interactions. Each interaction type (direct, indirect) has an accompanying value by which the default probability of exposure is multiplied to simulate the effects of an interaction. During an indirect interaction where one agent is COVID-19 positive and the other agent is susceptible, the baseline probability of exposure to COVID-19 is decreased; during a direct interaction, under the same situation, this probability is increased.

Markov model for COVID-19 progression. Exposure, infection, and progression of COVID-19 is modeled using a Discrete-Time Markov Chain (DTMC) model (Figure 3) that updates every 12 simulation hours. Seven different states characterize the person's status: Susceptible (S), Exposed (E), Asymptomatic (A), Infected (I), Severe Infection (I+), Dead (D), and Recovered (R). When a Susceptible (S) agent interacts with someone in any of the three infected states (A, I, or I+), the agent can become Exposed (E). If exposed, infection probabilities (p_{EA} and p_{EI}) determine whether the exposed agent becomes truly infected (A or I), or moves back to the Susceptible (S) state. As the arrows indicate, we assume that an infected agent can remain in its state or progress to the next state but do not go back to the previous state (for example, an agent cannot go back from Severe Infection (I+) to Infected (I)). We also assume that COVID-19 mortality can only result from first progressing to a severe state (I+), and once recovered, agents do not get reinfected, but they can get re-exposed. Currently exposed (E) or Re-exposed (RE) agents

can expose other Susceptible (S) agents with a lower probability than can those who are infected.

Parameters

We obtained estimates for model input parameters from both SPARCS data and published literature. When a reliable estimate was not available from either source, we used our best knowledge to assign a parameter or evaluated different values in the sensitivity analysis as described below. Table 1 shows input parameters used in our model.

Calibration and Validation

Validation of the model, including the model calibration phase, comprises three stages.

Markov model calibration. COVID-19 state transition model parameters, i.e. Markov chain transition probabilities, were not readily available and were estimated via calibration method (Table 2). For each transition probability p_{ij}, we converted a continuous range of plausible values into discretized steps. Using these p_{ij}s, we created a large set of transition matrices P_x with entries p_{ij} representing transition probabilities. We imposed a set of constraints on n-step transition matrix P_x^n based on common sense logic and literature findings. For example, recovery probability from the Asymptomatic (A) state must be larger than that from Infected (I), which in turn must be larger than the recovery probability from Severe Infection (I+) state.

ABM validation. The next steps for Markov model calibration follows a heuristic similar to one found in literature [16]. From a large number of P_x, we randomly sampled 100 P_x for further calibration. For each P_x of the sampled 100, simulation was repeated 10 times to obtain pre-selected outcome values. These values were then compared to the benchmark values found from literature or data. The benchmarks include nosocomial infection rate (i.e. number of in-hospital acquired COVID-19 patients out of number all COVID-19 patients over time), COVID-19 death rate (i.e. number of patients who died due to COVID-19 out of number of all COVID-19 patients), and length of stay. Nosocomial infection rate benchmark was set at 13.5% [29] COVID-19 death rate at 20% [30], and length of stay at 5.4 days, which was the average length of stay in the SPARCS data set we used to sample patients from. For each iteration, we calculated mean percentage error (MPE) for each benchmark, and averaged the absolute value of the MPE to obtain the absolute mean percentage error (AMPE) values. The instance of P_x with the smallest AMPE value over 10 iterations was chosen as the final set of probabilities for the transition matrix.

Sensitivity Analysis. We performed one-way sensitivity analysis for a number of parameters, holding other parameters constant and varying one parameter at a time. In sensitivity analysis, we assume a policy including COVID-19 testing and PPE distribution, and vary patient arrival rate and how many patients arrive as COVID-infected (Asymptomatic (A), Infected (I), and Severe Infection (I+) states).

- **Increased arrivals.** Double the patient arrival rate (COVID-19 infection among arriving patients remains the same)
- **Increased COVID-19.** Increase the proportion of patients arriving with COVID-19 infected state from 25% to 35%
- **Increased arrivals and COVID-19.** Varying both the arrival rate and the proportion of patients arriving with COVID-19 infected state

Policy Evaluation

The goal of this work is to show how the ABM can be used to evaluate different hospital policies regarding COVID-19 while considering the risk of hospital acquired infections. After calibrating and validating the model, we tested several different policy scenarios to see which policy component has the most significant effect on the benchmark outcomes. Our focus was on COVID-19 testing and distribution of PPE, the two factors of great importance and limited availability at the early stages of the pandemic, and are still constrained in developing countries. Each scenario was run for 100 independent simulation replications. The scenarios tested include:

- Test patients at admission and test staff at every 12 hours, and provide PPE for everyone (staff, patient) every 4 hours. This represent the most rigorous infection control strategy.
- Test patients at admission, test staff at every 12 hours, but do not provide PPE for anyone. This represents a scenario at the beginning of the pandemic when significant PPE shortage was present.
- Test patients at admission, test staff at every 12 hours, and provide PPE with a limited supply. In this case, agents use PPE for longer time (6 hours rather than the default 4 hours).
- Do not perform any testing, but provide PPE for everyone. Without test, infected patients do not go to a separate ward or room and infected staff will keep working, both of which can lead to increased infection at hospital.
- Do not perform any testing, and do not provide PPE for any agents.

3 RESULTS

Calibration and Validation. Calibrating the Markov chain model, we obtained 23,040 initial P_x matrices from discretized probabilities. After imposing the constraints, this narrowed to 2,592 candidate P_x. Of the 100 randomly sampled P_x, we chose the best performance P_x in terms of MPE. The resulting MPE was 2.13% for nosocomial infection, 2.00% for COVID-19 death rate, and 12.12% for length of stay (AMPE=5.42%). This P_x was then used for subsequent analysis as the transition probability matrix. The values for non-zero elements of P_x are given in Table 2.

Policy Evaluation. We evaluated several hospital policies regarding COVID-19 and examined their impact on nosocomial infection rate, COVID-19 death rate and length of stay. Table 3 shows the result from evaluation experiments. We observed that the availability of PPE significantly affects the rate of nosocomial infection. When PPE was available to every agent without shortage, we saw very few nosocomial patient infections, ranging between 0 and 2 per replication, similar to what was reported in a recent work [6]. For staff members who have more frequent direct interactions than patients, infection rate was higher even with PPE. On the other hand, availability of COVID-19 testing did not result in significant changes in the infection rate. COVID-19 death rate was relatively

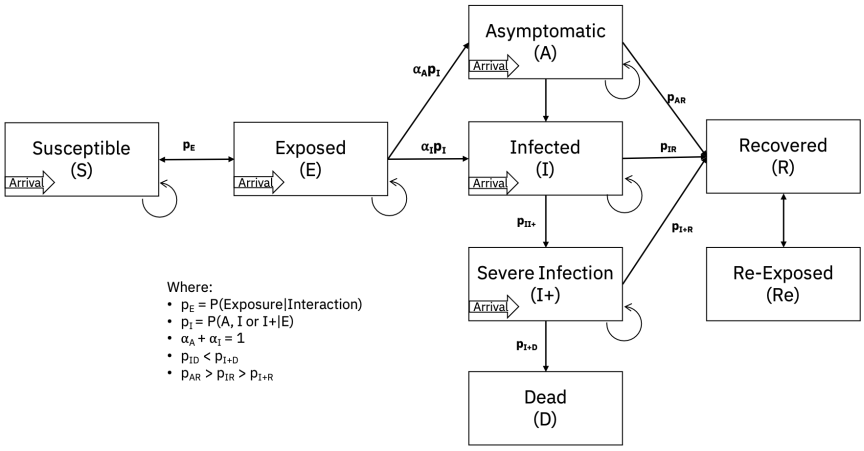

Figure 3: A state transition diagram for Markov model of COVID-19 exposure and progression.

Table 1: Default Input Parameters for the Agent Based Model

Parameter Category	Description	Default Value
Patient and Staff	Length of stay	Sampled from data
	Patient arrival rate	25
	Staff service time with patients (vary by patient severity)	5 to 20 minutes
Health Status	Proportion of patients arriving in Susceptible state	0.5
	Proportion of patients arriving in Exposed state	0.25
	Proportion of patients arriving in Asymptotic state	0.1
	Proportion of patients arriving in Infected state	0.05
	Proportion of patients arriving in Severe state	0.1
Hospital Structure	Number of total rooms (in 6 wards)	52
	Number of total beds	98
	Number of total staff stations	6
	Number of initial staff	67
	Number of reserve staffs	20
	PPE protection effect on probability of exposure	1.5
	Ventilator effect on probability of death	0.8
	COVID-19 test sensitivity	0.9
	COVID-19 test specificity	0.9
Resources	Number of ventilators	15
	PPE availability	Limitless
	PPE distribution	Yes
	PPE lifespan (Simulation time steps)	48
	PPE replenish (Simulation time steps)	4032
	PPE stock amount (Simulation time steps)	5000
Variable parameters	Initial hospital utilization rate	0.5
	COVID-19 prevalence in arriving population	0.25

stable across the experiments, ranging between 22% and 28% for patients and constantly being 18% for staff.

Sensitivity analysis. Sensitivity analysis results showed that the proportion of nosocomial infections and COVID-19 death rate remains relatively stable across different parameter configurations, indicating a level of robustness of the Policy Evaluation results against uncertainty of the patient arrival rate and COVID-19 admissions. The overall mean nosocomial infection rate (standard deviation) for increased patient arrival rate, increased proportion of COVID-19 admission, and combination of both was 0.11 (0.01), 0.12 (0.01), and 0.09 (0.01), respectively, compared to the overall mean of 0.14 (0.01) in the base case. The overall COVID-19 death rate was 0.17 (0.02), 0.19 (0.02), and 0.16 (0.02), respectively, compared to the 0.20 (0.02) in the base case.

Table 2: Calibration Parameters

Parameter	Description	Value	Min	Max	Source
Probability	Susceptible (S) to Exposed (E)	0.4	0.4	0.6	Hypothesized
	Exposed (E) to Infected (A or I)	0.186	0.186	0.349	[22, 23]
	Exposed (E) to asymptomatic (A)	0.669	-	-	[22, 24]
	Exposed (E) to symptomatic (I)	0.331	-	-	[22]
	Asymptomatic (A) to Recovered (R)	0.17	0.13	0.17	[25, 26]
	Asymptomatic (A) to Infected (I)	0.04	0.04	0.10	[25, 26]
	Infected (I) to Recovered (R)	0.1	0.10	0.15	[25]
	Infected (I) to Severe (S)	0.25	0.05	0.30	[25, 27]
	Severe (S) to Recovered (R)	0.09	0.05	0.10	[25]
	Severe (S) to Dead (D)	0.1	0.08	0.15	[25]
Constraints	Severe to Recovered in 7 days	-	-	0.6	[25]
	Severe to Dead in 8 days	-	-	0.636	[25]
	Severe to Dead in 16 days	-	-	0.78	[25]
	Asymptotic to Recovered > Infected to Recovered	-	-	-	-
	Infected to Recovered > Severe to Recovered	-	-	-	-
Interactions	Relative effect of indirect interaction on exposure probability (compared to direct interaction exposure probability)	1.5 (0.6)	1 (0.4)	2 (0.8)	[28]
	Staff interactions in station interval	30min	5min	30min	Hypothesized
	Patient-staff or patient-patient interaction in room interval	30min	5min	30min	Hypothesized

Table 3: Policy Evaluation Results. Proportion of infected agents, proportion of agent who died due to COVID-19, and length of hospital stay for patients (days)

	Nosocomial infection		COVID-19 death rate		Length of Stay (Days)
Mean (Std)	Patient	Staff	Patient	Staff	Patient
Policy Evaluation					
Test, PPE	< 0.001 (0.001)	0.50 (0.06)	0.25 (0.02)	0.18(0.07)	4.75 (0.16)
Test, no PPE	0.38 (0.04)	0.77 (0.05)	0.23 (0.02)	0.18 (0.05)	4.75 (0.17)
Test, PPE depletion	0.21 (0.04)	0.74 (0.04)	0.23 (0.02)	0.18 (0.05)	4.72 (0.16)
No Test, PPE	0.01 (0.005)	0.50 (0.04)	0.28 (0.02)	0.18 (0.06)	4.70 (0.15)
No Test, no PPE	0.44 (0.02)	0.56 (0.04)	0.22 (0.01)	0.18 (0.05)	4.65 (0.17)

4 DISCUSSION AND CONCLUSION

We develop an ABM to model COVID-19 transmission dynamics in a mid-sized hospital, calibrate a Discrete-Event Markov Chain model of COVID-19 exposure and progression in the patient and staff agents, and evaluate varying policies of PPE usage and COVID-19 testing. We demonstrate the viability and utility of using ABM to study viral spread and control in a care setting. The results show the effectiveness of PPE to prevent nosocomial COVID-19 infections for both patients and healthcare workers. This is particularly important in developing countries and countries experiencing disruptions in the supply-chain for PPE, which is still occurring as the pandemic evolves.

Our model is flexible and captures various scenarios, but also has a number of limitations. In the model logic, we assume that visitors are not susceptible agents who can transmit COVID-19. This is not true in the real world, and hospital visitor policy is a very important policy that needs evaluation. Another implicit assumption is made by not considering environmental contamination of high-touch surfaces and how it might impact transfer of COVID-19. However, according to CDC[31], infection risk through contaminated surface is generally low. Furthermore, we consider only two policies to control COVID-19 transmission, PPE use and testing, which identifies patients with COVID-19 and routes them to an isolated COVID-19 ward in the hospital. Future work of this model can be expanded to include additional polices, such as PPE reuse, pharmaceutical interventions (e.g. monoclonal antibody treatment or remdesivir), and ventilator usage (and supply). Lack of ground-truth data limits applicability of our study to real-world scenarios. We estimated input parameters and calibration parameters as best as we can, but they are obtained from limited prior evidence published to date or our best guess work. Additional studies will provide better parameter estimates the future. For example, we calibrate the model using the infection proportion rather than actual number of cases because there was no good benchmark value (definitive number of nosocomial cases) available considering the difference in study settings. Due to computational cost and time constrains, we sampled parameters from a larger pool of candidates. Latin Hypercubic sampling, along with other advanced sampled techniques (E.g. orthogonal sampling) are worth considering, and comparing against in future experiments.

In summary, our work demonstrates the feasibility and utility of developing ABMs to study COVID-19 dynamics in a hospital or care facility and highlights the importance of PPE in preventing nososcomial COVID-19 in both patients and hospital staff.

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